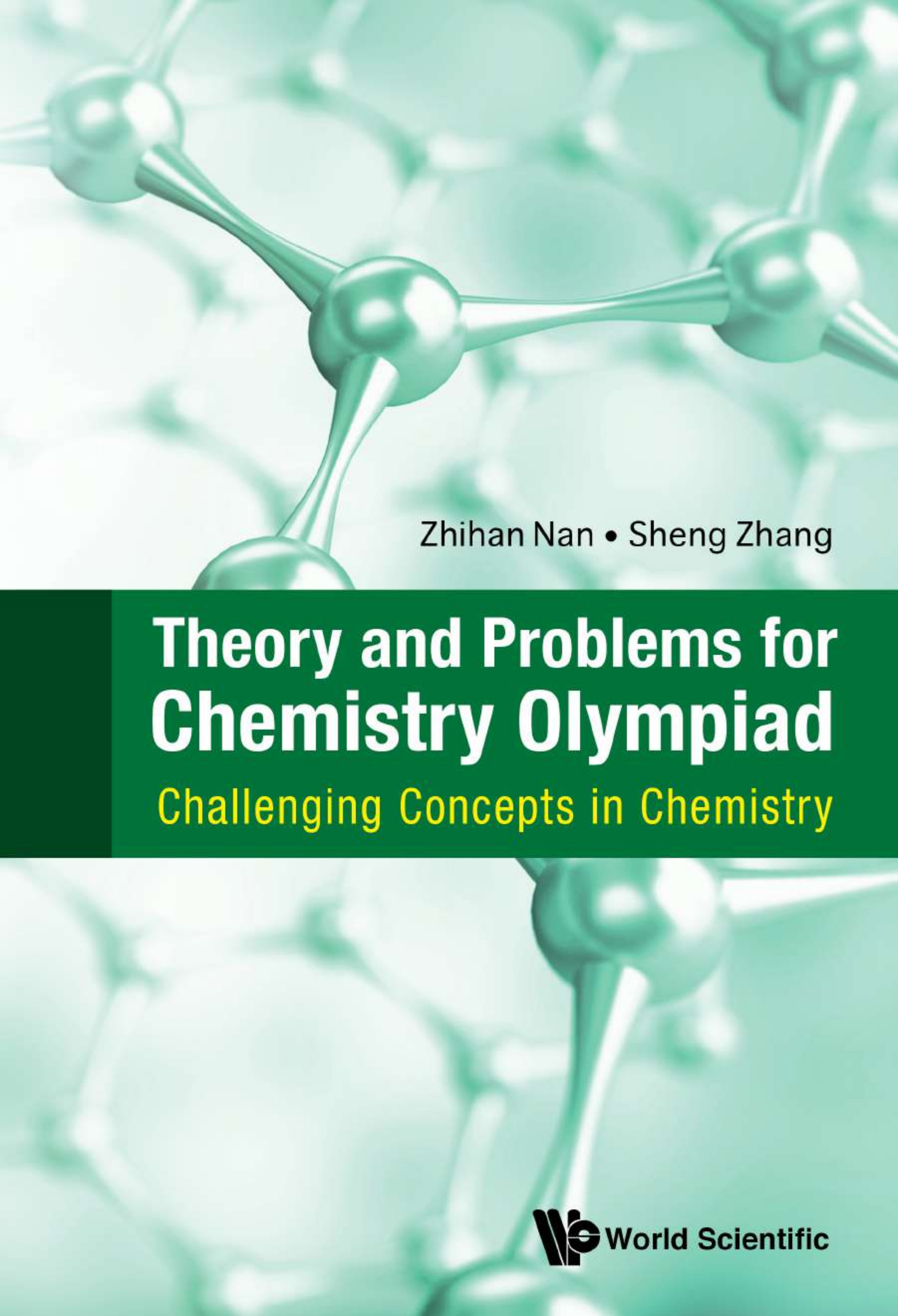

Zhihan Nan • Sheng Zhang

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Challenging Concepts in Chemistry

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Theory and Problems for Chemistry Olympiad

Challenging Concepts in Chemistry

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FOREWORD

The International Chemistry Olympiad (IChO) celebrated its 50th anniversary in 2018, growing from a small competition with only 3 participating countries and 18 competing students to what it is now — a worldwide event attracting 76 countries and 300 students. To select a team of students to represent Singapore at IChO, the Singapore Chemistry Olympiad (SChO) was launched in 1989 and it has become an annual event since then.

Chemistry Olympiad aims to motivate pre-tertiary students to study beyond the syllabus and stimulate their thinking through solving challenging chemistry problems. It is able to further develop the interest of pre-tertiary students in chemistry and improve chemistry education by providing interested students with more resources.

This book is the first textbook that caters specifically to students preparing for the Chemistry Olympiad competition. Previously, eager students had to browse through many university level textbooks to gain bits and pieces of information in the different fields of chemistry. The objective of this book is to bring down university level concepts to pre-tertiary students in a concise manner, combining important knowledge from all fields of chemistry into one book. The book presents chemical concepts in a succinct fashion, with key focus on the logical flow of concepts. Clear explanations are given such that students are able to fully understand the theories presented.

As I read through the draft of "Theories and Problems for Chemistry Olympiad", I was impressed by how the concepts taught in university are linked to the topics familiar to pre-tertiary students. The knowledge gap was bridged through detailed justification, with every physical chemistry equation derived and every organic reaction described by its mechanism. It was a joy to read through as there were many figures and diagrams used to illustrate the concepts. The writing is clear and easy to read, so it should help even a beginner get his/her bearing. In particular, the pedagogy is effective in keeping readers engaged as each chapter connects to the next. At the end of the book, students are also able to test their understanding by attempting sample IChO problems with detailed solutions.

Nan Zhihan has participated in IChO 2016, achieving a gold medal and the IUPAC prize for highest score in the experimental examination. After participating in the competition, he has devoted much of his efforts in mentoring and training the Singapore team for IChO 2017, 2018 and 2019. As a gold medallist, he understands the requirements and challenges in preparing for the competition and shares his personal experience in this book. Dr Zhang Sheng is a lecturer at the Department of Chemistry, NUS, and has been the mentor of the Singapore Chemistry Olympiad team for 9 years, training and leading the Singapore team for International Chemistry Olympiad competitions. Over the years of his mentorship, Singapore team has won a total of 16 Gold Medals and 19 Silver Medals in IChO. With vast experience in Chemistry Olympiad training, Nan Zhihan and Zhang Sheng form a formidable team to complete this valuable resource for perspective students.

I believe that this book is a valuable companion for students preparing for the Chemistry Olympiad competition. However, I would also recommend this book to any student curious to learn more about chemistry, including freshmen at university. With Chemistry Olympiad gaining prominence, I encourage interested students to take up the challenge and discover their passion in chemistry.

Professor Wong Ming Wah, Richard
Head, Department of Chemistry
National University of Singapore

ATTRIBUTIONS

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1. INTRODUCTION AND GENERAL TIPS TO PREPARE FOR CHEMISTRY OLYMPIAD

Welcome to Chemistry Olympiad! Chemistry Olympiad is a challenging competition that tests students on their higher-order thinking ability and encourages interested high school students to read up beyond the syllabus. This book was written to explain tough university chemistry concepts to high school students, by building up the student's knowledge slowly starting from the basics. When reading this book, please appreciate the logical flow of concepts and find the links between different topics. With time, I hope that you will see the beauty in chemistry, and have an enriching journey through Chemistry Olympiad.

As the flow of chapters and content in this book is meticulously designed, I would urge you to read the book following the order of the chapters and sub-chapters. This will ensure that you have the proper background knowledge required to understand every chapter fully. After completing the book once, it can be used as a reference book to refresh yourself on the relevant topics once in a while.

As a tip, it will be good to keep a notebook to write down important concepts and equations while reading the book. From the derivations of equations in physical chemistry to the mechanisms in organic chemistry, it is important to try these on your own to fully understand the concepts. While looking at complicated reactions or concepts, keep questioning in your head why each step proceeds the way it does. Note down any questions you have and ask your supervisor. While the learning curve is definitely steep, I am sure that the rewards are worth every bit of time and effort. The journey through Chemistry Olympiad is most rewarding when you are driven by your interest in chemistry and curiosity to learn more, instead of just going for a medal in the competition.

In Chemistry Olympiad, the competition is the final challenge to test your ability. In most countries, there are various national Olympiad competitions to select students for the International Chemistry Olympiad (IChO), the dream for most aspiring Chemistry Olympians. After all the hard work that is put into learning chemistry, it is critical to perform to the best of your ability at the competition. Here, the authors list some tips from experience to help students do their best at the competition.

For any competition, stress and mood through the examination play a significant role in how well we can think. When years of hard work culminate in a 5-hour long examination, it is difficult to not be overwhelmed by stress. Thus, you should face every competition with excitement, thinking of the competition as a new opportunity to learn more chemistry through problem-solving. Even if you are unsure of the solution to certain problems, do not let it discourage you, as the Olympiad competition is designed to be challenging. In the end, it is not the results that matter the most, but that you have given your best effort through the journey of learning chemistry.

Upon starting the paper, browse through all the questions first. Generally, Olympiad questions are not ranked by difficulty level. In particular, while one student may find an organic chemistry question more challenging, another student may have a difficult time solving a physical chemistry question. In the Olympiad competition, many students will find themselves having insufficient time to complete all the questions. Thus, find the questions that you are most confident in solving, and ensure that they are completed correctly and efficiently before attempting the more challenging problems.

For some common constants, you should use the value that is given in the "Constants and Formulae" table in front of the paper, regardless whether the value is the same or different compared to the value you have memorised. For example, the speed of light is given as $c = 3.000 \times 10^8\ \mathrm{m \cdot s^{-1}}$ (IChO 2011) and $c = 2.998 \times 10^8\ \mathrm{m \cdot s^{-1}}$ (IChO 2018). You should also use the atomic mass from the Periodic Table given in the question paper. For example, the mass of a hydrogen atom was given as 1.01 (IChO 2010), 1.008 (IChO 2011) and 1.00794 (IChO 2015).

For physical chemistry questions, it is important to show full workings on how the answer was obtained. Sometimes, there might be small errors during the calculation that lead to a different answer. If the final answer is incorrect, points may be awarded for correct equations in the working. To avoid losing all the points due to a small careless error, please show all key steps leading to the final answer. This also helps when checking the answer again for any errors. While working through physical chemistry problems, it is recommended to leave your answers in symbolic form while working through the problem. This makes it easier to spot any algebraic errors, and minimise the time spent on pressing the calculator. If any intermediate value is obtained, try to leave it to 1 or 2 more significant figures than the final required answer. You do not need to copy down all the decimal places from your calculator, because that's just a waste of your time and it will not affect your final results.

As per all scientific calculations, standard rules for decimal places and significant figures apply in Chemistry Olympiad calculation. If a question requires students to report the results to a certain number of significant figures, such requirement should be stated clearly in the question. If a question has not stated such a requirement, then you just need to report your value with a reasonable number of significant figures. For example, a concentration of $0.1028\ \mathrm{mol \cdot dm^{-3}}$ or $0.103\ \mathrm{mol \cdot dm^{-3}}$ is reasonable, but $0.102774125\ \mathrm{mol \cdot dm^{-3}}$ is obviously not reasonable although that's the value shown on the calculator.

For inorganic chemistry, it is important to be familiar with the properties of different elements and ions, such as the colour of transition metal cations in their various oxidation states, the flame test results of cations, common oxidation states of elements, solubility of common inorganic salts and colour of common precipitates. This information will often give intuition into the identity of unknown compounds in inorganic elucidation questions. While a summary is provided in the qualitative analysis Table 5.1, I would still encourage students to test out reactions and make the observations themselves.

You should also memorise the atomic mass of common elements, as this will allow you to easily access molecular masses of common compounds. This may be useful to deduce the identity of inorganic compounds in calculation-type questions. For example, a molecular mass of 18 suggests $\mathrm{H_2O}$, 28 suggests CO, and 44 suggests $\mathrm{CO_2}$. Now, try the following for yourself: 98, 100, 160. Of course, there are still many others. You should try to summarise your own table of common molecules and their molecular masses.

Other than deducing compound identity through calculations, it is also possible to make good judgements based on periodicity and the trends within each group.

Thus, it is good to have a brief understanding of the elemental trends in each group, as outlined in chapter 3.5.

For organic chemistry, it is useful to work on structural elucidation both forwards and backwards. The process of visualising a synthesis backwards is known as retrosynthesis, and is briefly discussed in chapter 4.16. You can compare the reactant and product to determine the parts of the molecule with no change. After identifying the parts that do not change in the reaction, it is possible to focus on the reactive site(s). This allows us to deduce the reaction mechanism, which may be single or multi-step.

From time to time, you will encounter some organic reagents that you have not met before. Based on structural features, it is possible to compare such reagents with familiar reagents to deduce its role, as solvent, catalyst, acid, base, oxidant, reductant, nucleophile or electrophile. Once its role is confirmed, it is possible to determine the reaction mechanism and predict the product.

When analysing reactions, pay special attention to selectivity, including chemoselectivity, regioselectivity and stereoselectivity. In particular, stereoselectivity is often encountered in Chemistry Olympiad. Sometimes, stereochemistry can be deduced either from the reactant one or several steps before, or from the product one or several steps after. Also, you should decide whether there is a retention or inversion of stereochemistry based on the reaction mechanism. In general, stereochemistry should be shown clearly with wedged or dotted lines.

The tips provided here in this chapter are general and more specific tips regarding each topic will be given as you move on into the book. I wish all students an enriching and rewarding Chemistry Olympiad journey!

2. PHYSICAL CHEMISTRY

Physical chemistry is the study of chemical matter and reactions by applying the principles of physics. Thus, we start with physical chemistry to build a solid foundation for us to better understand chemical systems and reactions. Using mathematical calculations, we are able to determine the theoretical feasibility of reactions and their rates. This chapter aims to provide students with all the required knowledge in physical chemistry topics through a logical and step-by-step approach, linking related topics to each other. It is important for students to realise the connections between the various topics and understand the physical basis of chemical reactions as a whole.

2.1 Thermodynamics

Thermodynamics is the study of energy changes during processes. Processes may include changes in temperature, pressure, volume and chemical reactions, where many changes may occur simultaneously. In this section we will explore the methods to determine energy changes from both chemical and physical processes. We will begin exploring thermodynamics through learning about gases, which is a form of matter that completely fills the volume it occupies.

2.1.1 *Physical and thermodynamic states*

The **physical state** of a substance is defined by its physical properties. **Physical property** is one that is displayed without any change in composition, also known as observables. Common physical properties include colour, density, ductility, conductivity, mass, volume and many others. In Table 2.1, we will focus on 4 main physical properties that are important in describing gases: Volume (V), Pressure (p), Temperature (T) and Amount of Substance (n).

Table 2.1. Physical properties and their units.

	Measure of...	S.I. unit
Volume	Amount of space occupied by the gas	$\mathrm{m^3}$
Pressure	Force exerted by the gas molecules on its container per unit area due to molecules colliding with the walls	Pa $(\mathrm{N \cdot m^{-2}})$
Temperature	Hotness of the gas	K
Amount of Substance	The number of atoms or molecules of gas in the container	mol

Background 2a. Units of measurement

In science, units of measurement are important as a standard reference for all scientific communications. Thus, it is important for such units to be accurately defined. The current system of units that is accepted and used is the International System of Units, known as S.I. units. These units are generally defined based on physical constants, as these constants are universally accepted and will not change. The only exception is the kilogram (kg) previously, which is defined by the International Prototype Kilogram "Le Grand K", an exactly one-kilogram alloy of Platinum and Iridium kept preserved under vacuum in the International Bureau of Weight and Measures. However, it is inevitable for physical objects to change over time, and the prototype kilogram is found to be gradually losing mass, albeit at a slow pace. As we push the frontiers of science, the requirements on the accuracy of measurements is higher, and small changes in the standard mass may lead to large deviations. Thus, metrologists have been working hard in finding a different way to redefine kilogram based

(*Continued*)

Background 2a. (*Continued*)

on physical constants. Recently in 2019, the definition of kilogram has been revised to be based on the Planck's constant. After the redefinition, all 7 S.I. base units are defined by fundamental constants. The base units are Metre (m) for length, Kilogram (kg) for mass, Second (s) for time, Ampere (A) for electric current, Kelvin (K) for temperature, Mole (mol) for amount of substance and Candela (cd) for luminous intensity. All other S.I. units can be derived from the 7 base units.

Background 2b. Conversion of units

It is important to note the conversion of units from commonly used units to S.I. units, as most equations have constants in S.I. units. Here we will discuss the conversion of units for the 4 main physical properties of gases.

For **Volume**, the units of millilitre (mL) and litre (L) are most commonly used in small scale laboratories. They correspond to cubic centimetre (cm^3) and cubic decimetre (dm^3) respectively. These units are used because the volumes used in the lab are much smaller than the S.I. unit of cubic metre (m^3). The common units used to measure volume are described in Table 2.2.

Table 2.2. Units of measurement for volume and their interconversion.

Units of Volume	Symbol	Value in terms of S.I. unit
Cubic Metre	m^3	—
Cubic Decimetre	dm^3	$1\ \mathrm{dm}^3 = 1 \times 10^{-3}\ \mathrm{m}^3$
Litre	L	$1\ \mathrm{L} = 1 \times 10^{-3}\ \mathrm{m}^3$
Cubic Centimetre	cm^3	$1\ \mathrm{cm}^3 = 1 \times 10^{-6}\ \mathrm{m}^3$
Millilitre	mL	$1\ \mathrm{mL} = 1 \times 10^{-6}\ \mathrm{m}^3$

For **Pressure**, there are many different units of measurement. Atmospheric pressure is conveniently represented as 1 atmosphere (atm), which is the pressure generated by a $760\ \mathrm{mm}$ tall column of Mercury under gravity. However, depending on the exact gravitational conditions, $1\ \mathrm{mmHg}$ may differ slightly. Thus, it is redefined using the standard density of mercury and gravity, giving a result that is marginally different from 1/760 of an atmosphere. Instead, Torr is defined exactly as 1/760 of an atmosphere. However, in common

Table 2.3. Units of measurement for pressure and their interconversion.

Units of Pressure	Symbol	Value in terms of S.I. unit
Pascal	Pa	—
Bar	bar	$1\ \mathrm{bar} = 1 \times 10^5\ \mathrm{Pa}$
Atmosphere	atm	$1\ \mathrm{atm} = 1.01325 \times 10^5\ \mathrm{Pa}$
Torr	Torr	$1\ \mathrm{Torr} = \frac{1}{760}\ \mathrm{atm} = 133.322\ \mathrm{Pa}$
Millilitres of mercury	mmHg	$1\ \mathrm{mmHg} = 133.322\ \mathrm{Pa}$
Pounds per square inch	psi	$1\ \mathrm{psi} = 6894.76\ \mathrm{Pa}$

(*Continued*)

Background 2b. (*Continued*)

use, especially when not dealing with extremely small pressures, these units can be treated as equal. Bar is defined from the pascal and is the standard pressure for reporting data. The units used for pressure and their interconversion are given in Table 2.3.

Temperature is commonly measured in degrees Celsius ($°\mathrm{C}$), where water freezes at $0°\mathrm{C}$ and boils at $100°\mathrm{C}$. The Kelvin scale has the same unit increment as the Celsius scale, just that the absolute zero is set as the null point ($0\ \mathrm{K}$), such that temperatures cannot take on negative values. Degrees Fahrenheit ($°\mathrm{F}$) is being phased out in laboratories, but still used extensively in the United States. Table 2.4 shows common units of temperature and their interconversion.

Table 2.4. Units of measurement of temperature and their interconversion.

Units of Temperature	Symbol	Value in terms of S.I. unit
Kelvin	K	—
Degrees Celsius	$°\mathrm{C}$	$\mathrm{T(K) = T(°C) + 273.15}$
Degrees Fahrenheit	$°\mathrm{F}$	$\mathrm{T(K)} = \frac{5}{9}(\mathrm{T(°F)} + 459.67)$

Amount of Substance is measured by mol. 1 mol of any substance contains 6.022141×10^{23} particles.

Background 2c. Standard experimental conditions

Most thermodynamic data are reported under two sets of standard conditions:

Standard Temperature and Pressure (STP):
A temperature of $273.15\ \mathrm{K}$ and pressure of $1\ \mathrm{bar}$.

Room Temperature and Pressure (RTP):
A temperature of $298.15\ \mathrm{K}$ and pressure of $1\ \mathrm{bar}$.

Tip 2a. Dimensional analysis

For all equations, the units on the left and right side must be equivalent. By checking the equivalence of units, we can double-check our work to make sure that our equation is correct. When substituting values into an equation, it is also important to make sure that the values follow the same units as used in the equation.

Here is a simple example of dimensional analysis for the Perfect Gas Law, which we will learn soon. We will try to find the units of the gas constant R.

$$pV = nRT$$

Considering the units of the quantities, we have:

$$\mathrm{Pa \cdot m^3 = mol \cdot K \cdot (units\ of\ } R\mathrm{)}$$

Thus, R must have the units:

$$\mathrm{Pa \cdot m^3 \cdot mol^{-1} \cdot K^{-1}}$$

(*Continued*)

Tip 2a. (*Continued*)

In practice, the unit of R is usually given as $\mathrm{J \cdot mol^{-1} \cdot K^{-1}}$, which is equivalent to the above.

By applying dimensional analysis, we can confirm the correct unit for the values to be substituted into equations and avoid careless mistakes.

A **thermodynamic state** is characterised by a set of **well-defined** and **unchanging** physical properties. For a physical property to be well-defined, it must have a specific value.

For a system to be in a thermodynamic state, it must be in **equilibrium**, such that its physical properties are unchanging. The 2 conditions for equilibrium are as follows:

1. The system's physical properties remain constant with time.
2. Isolating the system from the surroundings causes no change to the properties of the system.

If the first condition is satisfied but not the second, the system is said to be in **steady state**, but not equilibrium.

Let's take a look at an example as shown in Figure 2.1.1. Consider a system consisting a long metal rod. If constant heat is applied to one end of the metal rod for a long time, a temperature gradient will be established across the metal rod, and the physical property (temperature) of the metal rod will be unchanging. This rod is now in steady state, but not in equilibrium. Once the rod is removed from the surroundings, containing the heat source, the rod starts cooling down. After a long time, the rod will be in equilibrium as the rod is at a constant temperature that remains constant when the rod is isolated.

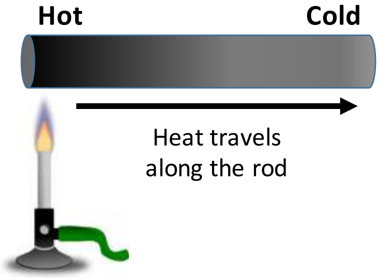


Figure 2.1.1. The heat distribution of a metal rod being heated at one end.

A thermodynamic state is defined by **thermodynamic state variables**, which are simply quantities that measure a physical property. In the case of a pure gas, we just need to consider the 4 thermodynamic state variables: Pressure (p), Volume (V), Temperature (T), Amount of substance (n).

However, it has been experimentally determined that these variables are **not independent**. It is sufficient to only specify three of these variables and the fourth variable will be fixed. Thus, each thermodynamic state can be described by an **equation of state**, where any one variable is a function of the other three variables:

$$p = f_p(n, V, T)$$
$$V = f_v(n, p, T)$$
$$n = f_n(p, V, T)$$
$$T = f_T(n, p, V)$$

2.1.2 *Gas laws*

To determine the equation of state, many scientists conducted experiments to obtain linear relations between thermodynamic state variables. These individual gas laws are determined by finding the relationship of one variable to another, keeping the other two variables constant.

Boyle's Law:
At constant n and T, $pV = \text{constant}$

Charles's Law:
At constant n and p, $V = \text{constant} \times T$

Gay-Lussac's Law:
At constant n and V, $p = \text{constant} \times T$

Avogadro's Principle:
At constant T and p, $V = \text{constant} \times n$

From the four individual gas laws, the equation of state of a perfect gas, also known as the **Perfect Gas Law**, is given as follows:

$$pV = nRT$$

Where:
p is Pressure, measured in Pascals (Pa)
V is Volume, measured in Cubic Metres (m^3)
n is Amount of Substance, measured in Moles (mol)
T is Temperature, measured in Kelvin (K)
R is the Gas Constant, which is empirically determined to be $8.314\ \mathrm{J \cdot mol^{-1} \cdot K^{-1}}$

2.1.3 *Perfect and real gases*

You may have been wondering, what is a perfect gas? Perfect gases are more commonly known as ideal gases, but the use of 'ideal' is confusing especially because 'ideal' used to describe mixtures differ from 'ideal' used when describing gases. An ideal mixture implies that all intermolecular interactions in the mixture are the same, while in the case of ideal gases, all intermolecular interactions are not only the same, but zero. Thus, the term perfect gas will be used in this text.

A perfect gas satisfies the following **three conditions**:

1. Molecular Motion: Gas molecules move in ceaseless random motion obeying the laws of classical mechanics.
2. Molecular Size: Volume of the gas molecules is zero.
3. Molecular Interactions: There are no intermolecular interactions other than elastic collisions between molecules.

It is clear that such a perfect gas would not exist, for the simple reason that molecules have finite size and there will always be London Dispersion Forces of attraction between molecules. So, how do real gases deviate from perfect gases?

Real gases deviate from perfect behaviour at **high pressure and low volume** situations. At high pressure and low volume, the gas molecules are squeezed tightly together and the assumption that molecular size is negligible no longer holds. As the molecules are closer together, the intermolecular dispersion forces between the molecules also become more significant. Larger gases deviate more significantly, as the assumptions of negligible volume and interactions become less valid.

To account for molecular size and interactions, the perfect gas law can be improved to the **Van der Waals equation of state**:

$$p = \frac{nRT}{V - nb} - a\left(\frac{n^2}{V^2}\right)$$

where a and b are constants to be determined and differ for each type of gas.

The physical meaning behind the constants:

a: a is the measure of the **strength of the attractive intermolecular forces** between the gas molecules. Notice that the term $-a\left(\frac{n^2}{V^2}\right)$ lowers the pressure that the gas exerts because the intermolecular forces between the molecules are attractive in nature and reduce the force and frequency of collisions between the gas molecules and the walls of the container. $\frac{n^2}{V^2}$ provide a measure of how close the gas molecules are to each other, and the closer the gas molecules are together, the more significant the intermolecular forces are. The greater the value of a, the stronger the intermolecular attractive interactions. Thus, a values are larger for larger molecules (stronger dispersion forces) and polar molecules (dipole-dipole interactions).

b: b is the measure of the **size of the gas molecules**. The term $V - nb$ measures the space available for the molecules to move around, as it takes the total volume subtracting the volume occupied by the gas molecules. Thus, the larger the value of b, the larger the size of the gas molecules.

The most general equation used to describe gases is the **Virial equation of state**:

$$p = \frac{nRT}{V}\left[1 + B\left(\frac{n}{V}\right) + C\left(\frac{n}{V}\right)^2 + \cdots\right]$$

The coefficients B, C, …, are **temperature dependent** and are known as the second, third, …, **virial coefficients**. The first virial coefficient is 1. This equation allows us to mathematically fit the properties of any gas by including more terms and coefficients, but it is beyond current IChO syllabus.

2.1.4 *The kinetic theory of gases and equipartition theorem*

Given the three conditions for a perfect gas, we can propose a model to calculate the kinetic energy of gas molecules. Consider a single gas molecule with mass m in a cubic container of side length a. The molecule will have velocity:

$$\boldsymbol{v} = v_x\hat{\boldsymbol{i}} + v_y\hat{\boldsymbol{j}} + v_z\hat{\boldsymbol{k}}$$

Consider only the molecular motion in the *x*-axis, in the $\hat{\boldsymbol{i}}$ direction. The time taken for the molecule to hit the wall of the box is the time it takes to travel a distance a at the speed v_x.

$$\Delta t = \frac{a}{v_x}$$

Each collision is treated as perfectly elastic. That is, the molecule collides with the wall at $v_x\hat{\boldsymbol{i}}$ and rebounds with velocity $-v_x\hat{\boldsymbol{i}}$. The change in momentum of the molecule is given as:

$$\Delta p_x = m\Delta v_x = m(2v_x) = 2mv_x$$

The force exerted by the molecule on the wall is:

$$F_x = \frac{\Delta p_x}{\Delta t} = \frac{2mv_x}{\frac{a}{v_x}} = \frac{2mv_x^2}{a}$$

By hitting the wall with the force above, the molecule exerts a pressure on the wall. The area of the square wall is a^2, but the molecule rebounds between two such square walls, so the total area that is being hit by the molecule is $2a^2$. The pressure exerted by the molecule can thus be given as:

$$P_x = \frac{F_x}{A} = \frac{\frac{2mv_x^2}{a}}{2a^2} = \frac{mv_x^2}{a^3} = \frac{mv_x^2}{V}$$

Since $V = a^3$ is the volume of the container. For this section, pressure is represented by P to avoid confusion with momentum p.

Given a total of N molecules, we need to define the average v_x^2 of all the molecules. This is denoted as $\langle v_x^2 \rangle$, where:

$$\langle v_x^2 \rangle = \frac{1}{N} \sum_{i=1}^{N} v_{x,i}^2$$

Then, the total pressure exerted by all the molecules in the $\hat{\boldsymbol{i}}$ direction is:

$$P_{x,\text{total}} = \frac{mN\langle v_x^2 \rangle}{V}$$

Since gases are isotropic, the pressures must be equal for all three directions. Thus:

$$P = \frac{mN\langle v_x^2 \rangle}{V} = \frac{mN\langle v_y^2 \rangle}{V} = \frac{mN\langle v_z^2 \rangle}{V}$$

and $\langle v_x^2 \rangle = \langle v_y^2 \rangle = \langle v_z^2 \rangle$, which comes from the first assumption that the gas molecules are in ceaseless random motion.

Next, we consider the kinetic energy of the gas molecules. The kinetic energy for all N gas molecules can be given as:

$$KE = \frac{1}{2} mN\langle v^2 \rangle$$

where $\langle v^2 \rangle$ is the average of the total velocity of the molecules:

$$\langle v^2 \rangle = \frac{1}{N} \sum_{i=1}^{N} |\boldsymbol{v}|^2$$

Thus,

$$\langle v^2 \rangle = \langle v_x^2 \rangle + \langle v_y^2 \rangle + \langle v_z^2 \rangle = 3\langle v_x^2 \rangle$$

Then, total kinetic energy is:

$$KE = \frac{3}{2} mN\langle v_x^2 \rangle$$

Since $PV = mN\langle v_x^2 \rangle$,

$$KE = \frac{3}{2} PV = \frac{3}{2} nRT$$

For a **single molecule**,

$$n = \frac{1}{N_A}$$

$$KE = \frac{3}{2} \frac{R}{N_A} T = \frac{3}{2} k_B T$$

where $k_B = \frac{R}{N_A}$ is the Boltzmann constant.

This is an important result that shows that **total kinetic energy is only dependent on temperature** when the composition is not changed, in equation:

$$KE \propto T$$

$$KE = aT$$

where a is a constant to be determined.

From the above example of considering a **molecule** of monoatomic perfect gas, we see that:

$$a = \frac{3}{2}k_B$$

To find the constants for other molecules, we can consider the **equipartition theorem**:

> In a sample at temperature T, all quadratic contributions to the total energy have the same mean value, namely $\frac{1}{2}k_BT$.

A **quadratic contribution** is one that depends on the **square of the velocity**. In the case of translational kinetic energy such as described above,

$$KE = \frac{1}{2}mv_x^2 + \frac{1}{2}mv_y^2 + \frac{1}{2}mv_z^2$$

Each term contributes $\frac{1}{2}k_BT$ to the energy such that $KE = \frac{3}{2}k_BT$ as shown above. The **total energy is equally partitioned over all available modes of motion**, also known as **degrees of freedom**.

Molecular modes of motion have different components. Every atom in a molecule can move independently in the *x*, *y* or *z* directions. Given a molecule with n atoms, the molecule has $3n$ total possible motions. These motions are divided into three types: **Translational**, **Rotational** and **Vibrational** modes of motion.

Translation occurs when all atoms of the molecule move together in the same direction. **Every molecule has 3 translational modes of motion** for movement in the *x*, *y* or *z* directions.

Rotation occurs when molecules rotate as a whole along an axis. **Non-linear molecules can rotate about 3 different axes**, while **linear molecules can only rotate about 2 axes**, since rotation about the bonding axis does not change the molecule.

Vibration accounts for the rest of the modes of motion, mostly involving the stretching and bending of bonds. **Linear molecules have 3N-5 vibrational modes of motion** while **non-linear molecules have 3N-6 vibrational modes of motion**. Note that vibrational degrees of freedom are electronic in nature and require high amounts of energy to excite. They are **only significant at high temperature**.

Table 2.5 summarises the degrees of freedom for different types of molecules.

Table 2.5. Different types of molecules and their degrees of freedom.

Type of molecule	Examples	Translation	Rotation	Vibration	Constant *a* in *KE* = *aT*
Monoatomic	Ar, Ne	3	0	0	$\frac{3}{2}k_B$
Polyatomic Linear	N_2, CO_2	3	2	$3N$-5	$\frac{5}{2}k_B$
Polyatomic Non-Linear	H_2O	3	3	$3N$-6	$3k_B$

2.1.5 *Thermodynamic systems, internal energy and thermodynamic state functions*

In every thermodynamics discussion, we always consider the **system, surroundings and universe**. The **system** is a part of the universe that we picked to study, for example a gas or a chemical reaction. The **surroundings** is everything else in the universe other than the system. The system and surroundings together make up the **universe**, which encompasses everything.

There are three types of thermodynamic systems:

1. **Open System**: A system where there is **both mass transfer and energy transfer**.
2. **Closed System**: A system where there is **energy transfer but no mass transfer**.
3. **Isolated System**: A system where there is **neither mass transfer nor energy transfer**.

Consider heating a pot of water without a lid on. Taking the water as the system, it is an open system because water is escaping as vapour (mass transfer) and heat energy is being added into the system (energy transfer). Now if we put an airtight lid on the pot, the water becomes a closed system because no vapour can escape (no mass transfer) but heat is still being added to the system (energy transfer). However, removing the heat source does not render the water an isolated system, as energy can still flow between the surroundings and the system. An example of an isolated system is a closed Thermos flask, if we assume that the Thermos flask is able to completely prevent any heat transfer to the water. However, there is no perfect isolated system, other than the universe itself.

In the context of gases, the gas (system) must be in a container. There are 3 different properties of system walls:

1. **Rigid/Non-Rigid**: A rigid wall cannot move while a non-rigid wall can move. Only gas systems in non-rigid walls can do pressure-volume work (we will cover this next).
2. **Permeable/Impermeable**: Permeable walls allow matter to pass through while impermeable walls trap all matter inside. It determines whether there is mass transfer in a system.
3. **Diathermic/Adiabatic**: Diathermic walls allow heat to pass through while adiabatic walls prevent heat flow. It determines whether there is energy transfer in a system.

A system containing matter has energy, known as its **Internal Energy** (U). Internal energy is a thermodynamic state variable, which means that it is a property of the system. Internal energy is the **total sum of potential energy and kinetic energy of the atoms or molecules** in the system.

$$U = PE + KE$$

The potential energy comes from the electronic, vibrational and intermolecular interactions. At $T = 0$, $KE = 0$, thus the molar potential energy (for one mole of substance) can be represented by $U_m(0)$, where the subscript m stands for "molar". Thus, combining this concept with the concept of kinetic energy from the previous part gives U_m for a monoatomic gas:

$$U_m = U_m(0) + \frac{3}{2}RT$$

since $n = 1$ in the molar context. As potential energy $U_m(0)$ is a constant, total potential energy U_m is a linear function with respect to **temperature** (that is only dependent on temperature).

Internal energy is a **thermodynamic state function**, which means that the value of the thermodynamic state variable **depends only on the thermodynamic state of the system**. Such variables are **path-independent**, meaning that the value is independent of the way the state was achieved.

2.1.6 *Work, heat and the first law of thermodynamics*

Work and **Heat** are **modes of energy transfer**. They are not energy possessed by a system, but instead only comes into existence during a **change in the system**. Nevertheless, as measures of energy flow, work and heat are measured with the unit of energy, Joules (J).

Work, represented by w, is done through a **force exerted over a distance**. It is used to achieve motion against an opposing force. Work is done when there is an **imbalance of forces** present, which gives rise to a change in the system. There are many types of work, including electrical work (work done by an electric current through resistance), spring work (by elastic energy of springs) and most importantly **Pressure-Volume work**, which we will refer to as PV-work from now on and will describe in more detail in the next section.

Heat, represented by q, is **energy transfer between two systems**. Energy transfer as heat usually results from a **temperature difference** between the system and the surroundings, or **phase transition of substances** (which will be discussed in chapter 2.3). Energy transfer through heat is only possible with diathermic boundaries, and adiabatic boundaries prevent all heat transfer.

Experimentally, it is found that if a system is isolated from its surroundings, then there is no change in internal energy. This leads to the **First Law of Thermodynamics**.

The internal energy of an isolated system is constant.

The internal energy of a system can be changed by both work and heat, in equivalent ways. Thus, in the case of a system that is not isolated, we write the mathematical statement for the first law as:

$$\Delta U = q_{\text{gained}} + w_{\text{on}}$$

Where:
ΔU is the change in internal energy of the system.
q_{gained} is the amount of **heat energy gained** by the system.
w_{on} is the amount of **work done on** the system.

This is essentially a statement of the **conservation of energy**, where the change in internal energy must equal the total energy flow into the system.

Tip 2b. Sign convention for heat and work

Heat and work are always represented by the symbols q and w, but the subscripts are rarely indicated. This has led to problems with sign convention, where the first law has been presented as both $\Delta U = q + w$ and $\Delta U = q - w$. In both cases, there are no mistakes, just that the first equation uses w as the work done on the system, and the second equation uses w as the work done by the system. This is because:

$$w_{\text{on}} = -w_{\text{by}}$$

$$q_{\text{gained}} = -q_{\text{lost}}$$

Work done on the system and heat added to the system increase the internal energy, thus bearing positive sign. On the other hand, work done by the system takes a negative sign as it reduces the internal energy. I recommend that when tackling thermodynamic problems, always include the subscripts below q and w. This will be used throughout this book to make it clearer when energy is being calculated.

2.1.7 *Expansion work and reversible processes*

While internal energy is a thermodynamic state function, heat and work are not properties of a system and are **path variables**. Path variables are dependent on how the process is conducted, as opposed to state variables, which only depend on the initial and final states of the system. Using the example of expansion work, we will show that different processes leading from the same initial states to final states have different values of heat and work.

Background 2d. Terms used to specify types of processes

Most thermodynamic processes have at least one constant state variable, and by categorising processes based on that, we can summarise properties of each type of process.

- An **isochoric** process is a process that occurs at constant V
- An **isobaric** process is a process that occurs at constant p
- An **isothermal** process is a process that occurs at constant T

In the case of gases, we also specify the reactions as a **compression** or **expansion**, or whether they are **adiabatic**. As we will see later, another important property of a reaction is whether it is **reversible**. By classifying reactions into these categories, we can analyse the reactions using the important features of each of these reactions.

We will now examine how to evaluate PV-work. Work is defined in physics as the amount of energy required to move an object a distance $\mathrm{d}x$ against an opposing force, F.

$$\mathrm{d}w_{\mathrm{on}} = -F\mathrm{d}x$$

It is important to note that the system is doing work by moving the object, so the internal energy of the system decreases, thus work done on the system is negative. Since PV-work is done by gases, we will consider a piston of area A pushing on the system with external pressure of p_{ex}. The force is then given as:

$$F = p_{\mathrm{ex}}A$$

Substituting this into the work equation:

$$\mathrm{d}w_{\mathrm{on}} = -p_{\mathrm{ex}}A\mathrm{d}x = -p_{\mathrm{ex}}\mathrm{d}V$$

since the volume element $\mathrm{d}V = A\mathrm{d}x$.

We can thus express PV-work as:

$$w_{\mathrm{on}} = -\int_{V_i}^{V_f} p_{\mathrm{ex}}\mathrm{d}V$$

To maximise the PV-work done by a system, we have to consider the process, as work is path dependent. There are two distinct types of thermodynamic processes, **reversible**

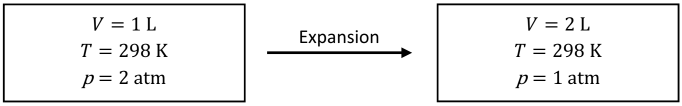


Figure 2.1.2. Depiction of the isothermal expansion process.

and **irreversible** processes. **Reversible processes maximise the work done by a system**. For a process to be reversible, the process must be **quasi-static**. This means that the system is **always in thermodynamic equilibrium** during the process, never more than infinitesimally far from a thermodynamic state. Thus, there is no perfect reversible process. Instead, by carrying out the process **very slowly**, we are giving the system time to attain thermodynamic equilibrium, and such a process can be approximated as reversible. One simple way to check if a process is reversible is to imagine the process as a movie. If the process can be played backwards and still seem possible, the process is reversible.

With this in mind, let us consider 3 different types of **isothermal expansion** processes with the same initial and final states, given in Figure 2.1.2.

1. Isolated **free expansion**: Free expansion into vacuum.
   This is an irreversible process because the system is not near a thermodynamic state during the rapid expansion of gas into the vacuum. In this case, there is no opposing force for the system to do work on, thus $w_{\text{on}} = 0$. From a mathematical perspective, since $p_{\text{ex}} = 0$, work must be zero. The walls of the container are adiabatic, allowing no energy transfer, such that $q_{\text{gained}} = 0$.
   From the first law of thermodynamics,

   $$\Delta U = q_{\text{gained}} + w_{\text{on}} = 0 + 0 = 0$$

   In this case, the expansion into vacuum does not vary the temperature, only the pressure and volume.
2. **Isothermal expansion against a constant external pressure** of 1 atm.
   This is also an irreversible process as the external pressure is constant and significantly different from the pressure of the system. Thus the expansion of gas would also be rapid and the system will not be near thermodynamic equilibrium. When external pressure is constant, the integral to find work simplifies to:

   $$w_{\text{on}} = -p_{\text{ex}} \int_{V_i}^{V_f} \mathrm{d}V = -p_{\text{ex}} \Delta V$$

   In this case,

   $$w_{\text{on}} = -(1.01325 \times 10^5)\left(\frac{2-1}{1000}\right) = -101\ \mathrm{J}$$

   Note that the units for pressure and volume must be changed to S.I. units for any computation. The gas is doing work by expanding, so the work done by the gas is positive and the work done on the gas is negative. Note that internal energy is dependent only on temperature, and since $\Delta T = 0$, $\Delta U = 0$. By the first law,

$$q_{\text{gained}} = \Delta U - w_{\text{on}} = 0 - (-101) = 101\ \text{J}$$

3. **Reversible isothermal expansion**

How can we carry out the expansion in a reversible fashion? The external pressure has to be kept at the pressure of the system and reduced **extremely slowly** from 2 atm to 1 atm such that the system is always infinitesimally close to a thermodynamic state (i.e. the external pressure is equivalent to the pressure in the system). As such,

$$p_{\text{ex}} = p_{\text{gas}} - \mathrm{d}p \approx p_{\text{gas}}$$

Combining this result with the perfect gas law that we have discussed previously,

$$\begin{aligned} w_{\text{on}} &= -\int_{V_i}^{V_f} p_{\text{ex}}\mathrm{d}V \approx -\int_{V_i}^{V_f} p_{\text{gas}}\mathrm{d}V \\ &= -\int_{V_i}^{V_f} \frac{nRT}{V}\mathrm{d}V = -nRT\ln\left(\frac{V_f}{V_i}\right) = nRT\ln\left(\frac{V_i}{V_f}\right) \end{aligned}$$

This is an important result that holds true for all reversible isothermal expansions.

In this process, the composition of the gas and temperature remain constant such that:

$$p_i V_i = p_f V_f = nRT$$

$$\begin{aligned} w_{\text{on}} &= nRT\ln\left(\frac{V_i}{V_f}\right) = p_i V_i \ln\left(\frac{V_i}{V_f}\right) \\ &= (2\times 1.01325\times 10^5)\times(1\times 10^{-3})\times\ln\left(\frac{1}{2}\right) = -140\ \text{J} \end{aligned}$$

Similarly, since $\Delta U = 0$,

$$q_{\text{gained}} = \Delta U - w_{\text{on}} = 0 - (-140) = 140\ \text{J}$$

Table 2.6 compares the 3 different processes.

Table 2.6. Different isothermal processes and their change in internal energy, heat and work.

Processes	ΔU	q_{gained}	w_{on}
Free expansion	0	0	0
Isothermal expansion against constant external pressure	0	101 J	–101 J
Reversible isothermal expansion	0	140 J	–140 J

Since ΔU is a state function, it is the same regardless of the process and $\Delta U = 0$ because temperature is not changed in any process. However, the work done is clearly different in the three cases. While it is clear that in the case of reversible isothermal expansion the system does the most work ($w_{\mathrm{by}} = -w_{\mathrm{on}} = 140\ \mathrm{J}$), we have yet to justify it. Remember that work is defined as energy used to push against an external force. In the case of reversible expansion, the external pressure is always kept only infinitesimally lower than the gas pressure, which is the **maximum pressure** possible for the gas to still expand. Since the gas is pushing against the maximum pressure, the work done by the gas is the greatest in reversible processes. In conclusion, a reversible process **maximises the work done by a system** and **minimises the work done on a system** during a change in thermodynamic state.

2.1.8 *Heat capacity and calorimetry in isochoric processes*

Given the first law:

$$\Delta U = q_{\mathrm{gained}} + w_{\mathrm{on}}$$

When the volume of the system is kept constant, and considering a simple gaseous system that can only do PV-work, we note that:

$$w_{\mathrm{on}} = -\int_{V_i}^{V_f} p_{\mathrm{ex}} \mathrm{d}V = 0$$

In that case,

$$\Delta U = q_V$$

Where q_V is the heat gained by the system at constant volume. Note that ΔU is dependent only on temperature, thus q_V must cause a change in temperature to change ΔU. To measure the change in temperature from a heat gain or loss, we define the **heat capacity at constant volume**:

$$C_V \equiv \left(\frac{\partial U}{\partial T}\right)_V$$

Which is the **change in internal energy with respect to change in temperature** at constant volume. Since heat capacity is defined by energy over temperature, the **units of heat capacity is $\mathbf{J \cdot K^{-1}}$**. Heat capacity is an **extensive property** that depends on the amount of substance, 100g of any substance will be require 100 times the energy compared to 1g of the same substance to change the temperature by the same amount. To make this an **intensive property** (independent on system size or amount of material), we define the **molar heat capacity** and **specific heat capacity** as follows:

$$C_{V,m} = \frac{C_V}{n}$$

$$C_{V,s}(\text{or sometimes just } c) = \frac{C_V}{m}$$

Where $C_{V,m}$ is the heat capacity per mole in units of $\mathbf{J \cdot K^{-1} \cdot mol^{-1}}$ and $C_{V,s}$ is the heat capacity per kilogram in units of $\mathbf{J \cdot K^{-1} \cdot kg^{-1}}$.

By rearranging the equation defining heat capacity,

$$\mathrm{d}U = C_V \mathrm{d}T$$

$$U = \int_{T_i}^{T_f} C_V \mathrm{d}T$$

Heat capacity C_V is a **function of temperature** but over small ranges of temperature above room temperature, it is possible to **approximate C_V as a constant**.

Then the equation can be simplified to:

$$\Delta U = q_V = C_V \Delta T$$

This result is useful as we move on to discuss **calorimetry**, which is the study of energy transfer in the form of heat. A **calorimeter** is a device used to measure energy transferred as heat, and we will focus on the **adiabatic bomb calorimeter**. Adiabatic bomb calorimeters operate under **constant volume**, and have adiabatic walls that **do not allow energy transfer between the system and the surroundings**. The 'bomb' is the system inside the calorimeter, and it is usually a combustion reaction. The steps to use a calorimeter is as follows:

1. Calibrate the calorimeter: We need to find calorimeter constant C which is the amount of heat required to increase the calorimeter temperature by 1°C. This is done by heating the calorimeter with a known amount of electrical energy and measuring the temperature change. Then:

$$C = \frac{q_{\text{electric}}}{\Delta T_{\text{electric}}}$$

2. Load sample and excess oxygen for combustion reaction and initiate the reaction.
3. Measure the change in temperature change caused by the reaction, and:

$$\Delta U = q_V = C \Delta T_{\text{rxn}}$$

This technique of calorimetry can be used to find the ΔU for reactions.

2.1.9 *Enthalpy and isobaric processes*

While we can carry out reactions in constant volume conditions, such as in sealed containers, it is rare and chemical reactions are more commonly carried out in open vessels on laboratory benches. In this case, the constant state variable is pressure, as the system is always under atmospheric pressure. For isochoric processes as seen earlier, we have:

$$\Delta U = q_V$$

For isobaric processes, we define **Enthalpy** (H):

$$H \equiv U + pV$$

Such that

$$\Delta H = q_p$$

This result can be shown as follows:

$$\mathrm{d}H = \mathrm{d}U + \mathrm{d}(pV) = \mathrm{d}U + p\mathrm{d}V + V\mathrm{d}p$$

From the first law of thermodynamics,

$$\mathrm{d}U = \mathrm{d}q + \mathrm{d}w$$

and

$$\mathrm{d}w = -p\mathrm{d}V$$

for PV-work.

This gives us:

$$\mathrm{d}H = \mathrm{d}q - p\mathrm{d}V + p\mathrm{d}V + V\mathrm{d}p = \mathrm{d}q_p$$

since $\mathrm{d}p = 0$ at constant pressure.

Enthalpy is a **thermodynamic state function**, since internal energy, pressure and volume are all state functions. Similarly, we define **heat capacity at constant pressure**:

$$C_p \equiv \left(\frac{\partial H}{\partial T}\right)_p$$

Which is the **change in enthalpy with respect to change in temperature** at constant pressure. The **molar heat capacity at constant pressure** is also defined as an intensive property of a substance and can be defined as:

$$C_{p,m} = \frac{C_p}{n}$$

To measure enthalpy changes, we use **isobaric calorimeters**, such as the **adiabatic flame calorimeter**, or more sophisticated methods such as the **differential scanning calorimeter**. These calorimetric methods work similarly to isochoric calorimeters previously discussed, involving calibration followed by measurement.

2.1.10 *Adiabatic processes*

The key feature of adiabatic processes is $q = 0$. Thus the first law of thermodynamics is simplified to:

$$\Delta U = w_{\mathrm{on}}$$

By compressing the gas, $w_{\text{on}} > 0$, thus $\Delta U > 0$ and temperature increases since internal energy increase. Vice versa, the gas cools during adiabatic expansion. Opposed to isothermal processes where heat is transferred to maintain a constant temperature, adiabatic processes prevent heat transfer and the work done is directly translated to change in internal energy.

Applying the laws of thermodynamics that we have previously studied, we will derive properties of adiabatic processes. From $\Delta U = w_{\text{on}}$, we have:

$$\mathrm{d}U = \mathrm{d}w_{\text{on}}$$

From the definition of heat capacity at constant volume, we have:

$$C_V \equiv \left(\frac{\partial U}{\partial T}\right)_V$$

$$\mathrm{d}U = C_V \mathrm{d}T$$

We will now assume that the gas is a **perfect gas** and the process is **reversible**.

Tip 2c. Molar heat capacity of perfect gases

Remember that we have found the expression for internal energy of gases previously as a sum of potential and kinetic energy. Only kinetic energy is a function of temperature, and we can thus find the **molar heat capacity at constant volume for monoatomic gas**:

$$U_m = U_m(0) + \frac{3}{2}RT$$

$$C_{V,m} = \frac{\partial U_m}{\partial T} = \frac{3}{2}R$$

To find the molar heat capacity at constant pressure, we go back to the definition of enthalpy:

$$H = U + pV$$

From the perfect gas law,

$$pV = nRT$$

Such that:

$$H = U + nRT$$

$$\frac{\partial}{\partial T}(H) = \frac{\partial}{\partial T}(U + nRT)$$

$$\frac{\partial H}{\partial T} = \frac{\partial U}{\partial T} + nR$$

$$C_p = C_V + nR$$

When $n = 1$,

$$C_{p,m} = C_{V,m} + R$$

(*Continued*)

Tip 2c. (*Continued*)

This is an important result that always holds true for perfect gases.

We summarise the molar heat capacities for different perfect gases in Table 2.7:

Table 2.7. Molar heat capacities of different types of perfect gases.

Type of molecule	**Examples**	$C_{V,m}$	$C_{p,m}$
Monoatomic	Ar, Ne	$\frac{3}{2}R$	$\frac{5}{2}R$
Polyatomic Linear	N_2, CO_2	$\frac{5}{2}R$	$\frac{7}{2}R$
Polyatomic Non-Linear	H_2O	$3R$	$4R$

$$\mathrm{d}W_{\mathrm{on}} = -p\mathrm{d}V$$

Substituting back into the equation for the first law:

$$C_V \mathrm{d}T = -p\mathrm{d}V$$

By the perfect gas equation $pV = nRT$ and integrating both sides,

$$C_V \int_{T_i}^{T_f} \frac{1}{T}\mathrm{d}T = -nR\int_{V_i}^{V_f} \frac{1}{V}\mathrm{d}V$$

Thus, **for small changes in temperature**, we can assume that C_V does not vary significantly with temperature.

$$C_V \ln\left(\frac{T_f}{T_i}\right) = -nR\ln\left(\frac{V_f}{V_i}\right)$$

Using the properties of logarithmic functions,

$$\ln\left(\frac{T_f}{T_i}\right)^c = \ln\left(\frac{V_i}{V_f}\right)$$

Where $c = \frac{C_V}{nR} = \frac{C_{V,m}}{R}$

Or more simply:

$$VT^c = \text{constant}$$

This can be expressed as:

$$c\ln\left(\frac{T_f}{T_i}\right) = \ln\left(\frac{V_i}{V_f}\right)$$

From perfect gas equation $pV = nRT$ we can substitute T in the previous equation,

$$c\ln\left(\frac{\frac{p_f V_f}{nR}}{\frac{p_i V_i}{nR}}\right) = \ln\left(\frac{V_i}{V_f}\right)$$

$$c\ln\left(\frac{p_f}{p_i}\right)=(1+\mathrm{c})\ln\left(\frac{V_i}{V_f}\right)$$

Since:

$$\frac{1+c}{c}=\frac{1+\frac{C_{V,m}}{R}}{\frac{C_{V,m}}{R}}=\frac{R+C_{V,m}}{C_{V,m}}=\frac{C_{p,m}}{C_{V,m}}$$

We can simplify the expression to:

$$\ln\left(\frac{p_f}{p_i}\right)=\frac{C_{p,m}}{C_{V,m}}\ln\left(\frac{V_i}{V_f}\right)=\gamma\ln\left(\frac{V_i}{V_f}\right)$$

Where we define $\gamma=\frac{c_{p,m}}{c_{V,m}}$.

Thus we arrive at the result:

$$p_iV_i^{\gamma}=p_fV_f^{\gamma}$$

Or more simply,

$$pV^{\gamma}=\text{constant}$$

From here, we have results relating:

Temperature with Volume: $\ln\left(\frac{T_f}{T_i}\right)^c=\ln\left(\frac{V_i}{V_f}\right)$

Pressure with Volume: $pV^{\gamma}=\text{constant}$

It is important to be familiar with these results and understand the assumptions used in deriving these results, which are:

1. The gas is a perfect gas.
2. The process is reversible.
3. The process is adiabatic.
4. The temperature change is small.

2.1.11 *Joule-Thomson effect*

Joule-Thomson effect is the **temperature change of a gas that is forced through a valve rapidly**, known as a **throttling process**. This is done under adiabatic conditions to prevent heat transfer with the surroundings. This is a classical adiabatic process, and it is **irreversible** due to the rapid nature of the process. It is also an **isenthalpic process** where the enthalpy is unchanged. We will proceed to prove it by considering the gas movement.

Volume of gas inside the container moved out: $\Delta V_{\text{inside}}=-V_i$, where V_i is the original volume of the gas while inside the container. Once outside the container, the gas rapidly expands:

$$\Delta V_{\text{outside}} = V_f$$

Since this is an adiabatic process:

$$\Delta U = w_{\text{on}}$$

Again, since we are only considering PV-work,

$$\Delta U = U_f - U_i = -p_f V_f + p_i V_i$$

$$U_f + p_f V_f = U_i + p_i V_i$$

Since $H = U + pV$,

$$H_f = H_i$$

Since the Joule-Thomson effect causes a change in temperature due to a pressure difference, we define the Joule-Thomson coefficient, μ, as follows:

$$\mu \equiv \left(\frac{\partial T}{\partial p}\right)_H$$

Which is a measure of how much the temperature of a gas changes with respect to the pressure change, due to the Joule-Thomson effect.

To qualitatively understand the Joule-Thomson effect, we refer back to the kinetic model of gases. Since gas molecules possess attractive intermolecular forces (London dispersion forces), the expansion of gas causes the molecules to move apart and there to be less attraction, increasing the potential energy. This potential energy needed to separate the molecules must come from the kinetic energy, thus by the conservation of energy, the kinetic energy of the molecules decreases and the temperature decreases. From this understanding, we see that:

$\mu = 0$ for perfect gases with no intermolecular forces.
$\mu > 0$ for most gases, in conditions where the attractive forces are dominant. This causes the cooling effect, as $\Delta p < 0$, so $\Delta T < 0$ for $\mu > 0$.
$\mu < 0$ in rare cases of smaller-size gases at low temperatures, where the repulsive forces are dominant. This causes a heating effect, as $\Delta p < 0$, so $\Delta T > 0$ for $\mu < 0$.

2.1.12 *Energy in chemical reactions and enthalpies of change*

From an energy perspective, a chemical reaction is just a series of bond breaking and bond formation processes. Since chemical bonds store potential energy, more commonly known as bond energy, it requires energy to break bonds by separating the bonded atoms, and energy is released when a bond is formed. This allows us to define the **enthalpy change of a reaction**, ΔH_r.

To define other enthalpies of transitions, we need to define **standard and reference states**.

Standard State:
The standard state of a **substance** at a **specified temperature** is its **pure form** at **1 bar**.

Reference State:
The reference state of an **element** is its **most stable state** at the **specified temperature** at **1 bar**.

Note that standard state can refer to any substance, including mixtures, but reference state is only defined for elements. In the definition of the states, the standard pressure of 1 bar is used, but no temperature is specified. Thus the states can vary depending on the temperature.

The different enthalpies of chemical processes are defined in Table 2.8:

Table 2.8. Definitions of different enthalpies of change.

Symbol	Process	Description
ΔH_r^0	Reactants to Products	$\Delta H_r^0 = \sum \text{Bond Energy (broken)} - \sum \text{Bond Energy (formed)}$
ΔH_f^0	Elements to Compound	Enthalpy change from **elements in reference state** to form 1 mole of the **compound in standard state**
ΔH_c^0	Substance combustion	Enthalpy change for the full combustion of 1 mole of a **substance at standard state** in **excess oxygen**
ΔH_{at}^0	Substance to atoms	Enthalpy change from a **substance at standard state** to separate **gaseous atoms at standard state**
ΔH_{IE}^0	Atom to Cation	**Ionisation Energy**: Enthalpy change to **remove an electron** from a gaseous atom
ΔH_{EA}^0	Atom to Anion	**Electron Affinity**: Enthalpy change to **add an electron** to a gaseous atom
ΔH_{hyd}^0	Ion to Aqueous Ion	Enthalpy change when **gaseous ions dissolve in water**: $A^{\pm}_{(g)} \rightarrow A^{\pm}_{(aq)}$
ΔH_{LE}^0	Ions to Crystal Lattice	**Lattice Energy**: Enthalpy change when **gaseous cation and anion** come together to form a **crystal lattice**
ΔH_{sol}^0	Solute to Solution	Enthalpy change for any solute to dissolve into a solution, involving **overcoming solute-solute and solvent-solvent interactions** and **forming solute-solvent interactions**
ΔH_{mix}^0	Pure compounds to mixture	Enthalpy change when mixing different substances A and B together, involving **overcoming A-A, B-B interactions** and **forming A-B interactions**
ΔH_{fus}^0	Solid to Liquid	**Latent Heat of Fusion**: Enthalpy change for the phase transition of a substance from **solid to liquid**, with no temperature change.

(*Continued*)

Table 2.8. (*Continued*)

Symbol	Process	Description
$\Delta H^{0}_{\mathrm{vap}}$	Liquid to Gas	**Latent Heat of Vaporisation**: Enthalpy change for the phase transition of a substance from **liquid to gas,** with no temperature change.
$\Delta H^{0}_{\mathrm{sub}}$	Solid to Gas	**Latent Heat of Sublimation**: Enthalpy change for the phase transition of a substance from **solid to gas**, with no temperature change.

Tip 2d. Symbol for enthalpies of change

$$\Delta H^{0}_{change}$$

The subscript describes the change, while the superscript (0) means that the process has occurred under standard conditions. The subscript can be placed behind Δ as well to describe the change and the superscript is sometimes written with a strikethrough $(\ominus)$. Thus a perfectly acceptable way to write it would be:

$$\Delta_{change}H^{\ominus}$$

This would be an alternative representation that means the same thing.

Enthalpy of change can be calculated by constructing cycles, as **enthalpy is a state function**. One common diagram that is used to determine Lattice Energy is the **Born-Haber Cycle**, and an example is shown in Figure 2.1.3.

Here we can see that the unknown lattice energy of CsCl can be determined using the cycle given the other standard enthalpies. This is making use of the fact

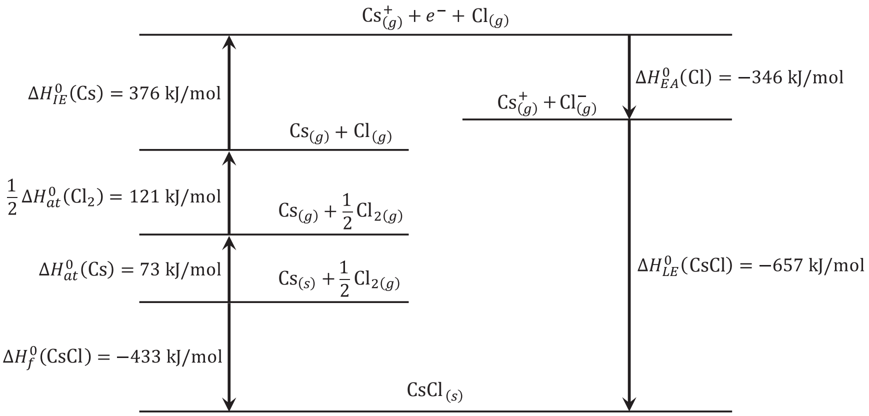


Figure 2.1.3. Born-Haber cycle for caesium chloride.

that the standard enthalpy of formation of CsCl is the enthalpy change from the elements to the ionic solid. By forming the ionic solid step by step, we can find the lattice energy of CsCl.

This method of finding enthalpy through taking alternate pathways is generalised in **Hess's Law**:

> The standard enthalpy of an overall reaction is the sum of the standard enthalpies of the individual reactions into which a reaction may be divided.

Simply put, this law is just a statement of conservation of energy and that enthalpy is a state function. This law gives us an important equation:

$$\Delta H_{\mathrm{r}}^{0} = \sum_{\mathrm{J}} v_{\mathrm{J}} \Delta H_{\mathrm{f}}^{0}(\mathrm{J})$$

Where v_{J} is the **stoichiometric number** for compound J in the reaction, positive for products (being formed) and negative for reactants (being consumed). It is not to be confused with **stoichiometric coefficients**, v, that are always positive regardless.

This equation can be used to calculate the **enthalpy change of any reaction**, as the sum of enthalpies of formation of products subtract the sum of enthalpies of formation of reactants, multiplied by the stoichiometric coefficients:

$$\Delta H_{\mathrm{r}}^{0} = \sum_{\text{Products}} v \Delta H_{\mathrm{f}}^{0} - \sum_{\text{Reactants}} v \Delta H_{\mathrm{f}}^{0}$$

How does this follow from Hess's Law?

Following Hess's Law, every reaction is **divided** into the **reactants being broken down into their elements in reference state** and these **elements combining again to form the products**. Chemically and mechanistically, this does not actually happen. However, since enthalpy is a state function, any path that goes from the same initial state to final state will give the same enthalpy change.

2.1.13 *Entropy, thermodynamic cycles and the second law of thermodynamics*

Entropy is a measure of **disorder**, or statistically speaking, the **number of possibilities** accessible to the particles that make up the system. This is known as the **microscopic definition of entropy**, where:

$$S = k_B \ln W$$

where k_B is the Boltzmann constant and W is the number of **microstates**, which is the number of ways the molecules can be arranged while keeping the total energy constant. We can thus conclude that a sample with more possibilities available to it will have a greater entropy.

The microscopic definition of entropy is not very useful in thermodynamics because it is difficult to find the number of microstates in a large and complex system. W is usually a very large number that is difficult to determine. This definition gives the **absolute entropy**, but we are usually more concerned with the **entropy change** of common processes. We thus look towards the macroscopic definition of entropy, also known as the **thermodynamic definition of entropy**:

$$\mathrm{d}S = \frac{\mathrm{d}q_{\mathrm{rev}}}{T}$$

Thus, change in entropy is given by:

$$\Delta S = \int \frac{\mathrm{d}q_{\mathrm{rev}}}{T}$$

Note that to calculate entropy between two states, we must find q_{rev}, the heat transfer through **reversible processes**, as heat is a path variable but **entropy is a state function**. We can prove that entropy is a state function by showing:

$$\oint \mathrm{d}S = \oint \frac{\mathrm{d}q_{\mathrm{rev}}}{T} = 0$$

The contour integral denotes **integration around a closed path**, where the processes start and end at the same thermodynamic state. All state functions are unchanged as long as the thermodynamic state is unchanged, no matter the process taken.

We will consider an important thermodynamic cycle, the **Carnot cycle**, using a PV diagram.

Background 2e. Using a PV diagram to represent thermodynamic processes

PV diagrams are extremely useful in representing complex thermodynamic processes that we have discussed. Figure 2.1.4 shows how the basic processes look on the PV diagram.

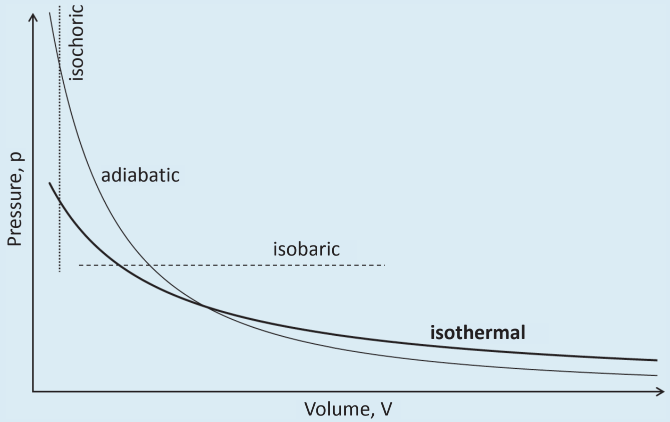


Figure 2.1.4. Lines representing different processes on a PV diagram.

(*Continued*)

Background 2e. (*Continued*)

Isochoric and isobaric processes appear as straight lines because volume and pressure respectively are kept constant. Isothermal processes follow:

$$pV = k$$

for some arbitrary constant $k = nRT$ such that

$$p = \frac{k}{V}$$

Giving the curve of a reciprocal function.

Similarly, adiabatic functions follow the relation:

$$pV^{\gamma} = k$$

where $\gamma = \frac{C_{p,m}}{C_{V,m}} > 1$ since $C_{p,m} = C_{V,m} + R$

$$p = \frac{k}{V^{\gamma}}$$

Thus adiabatic processes follow a curve that is **steeper** than isothermal processes.

The usefulness of PV diagrams come from the ability to directly calculate work from the diagram. Since the work that gases do is PV-work, the **work done by the gas is given by the area under the graph**, for a process that moves from lower to higher V, since gaseous **expansion** does positive work. Vice versa, in the case of a **compression**, the **work done on the gas is given by the area under the graph**, since compressions perform work on the gas. As previously mentioned, the magnitude is the same but the sign convention is important when dealing with work done.

The Carnot cycle can be represented on a PV diagram as shown in Figure 2.1.5.

The Carnot heat engine is designed to convert heat energy to work through the Carnot cycle, and consists of four reversible stages:

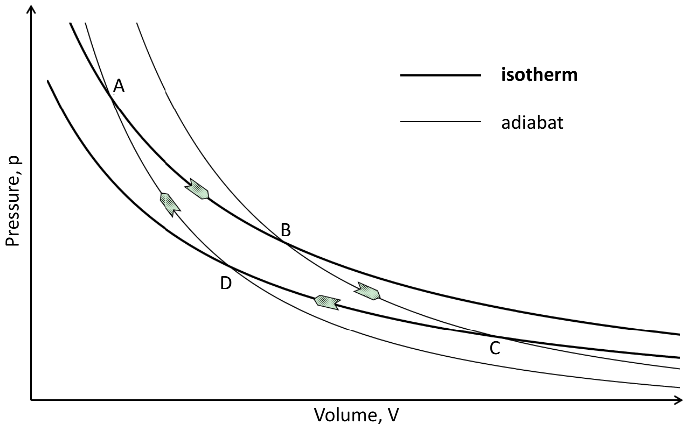


Figure 2.1.5. Carnot cycle represented on a PV diagram.

1. **Reversible Isothermal Expansion** from A to B

   For an isothermal process,

   $$\Delta U = q_{\text{gained}} + w_{\text{on}} = 0$$

   Since it is a reversible process, given the starting volume V_{A} and final volume V_{B},

   $$w_{\text{on}} = -nRT_h \ln\left(\frac{V_B}{V_A}\right)$$

   The temperature of this isothermal process is denoted as T_h, which refers to the hotter temperature.

   $$q_{\text{gained}} = -w_{\text{on}} = nRT_h \ln\left(\frac{V_B}{V_A}\right)$$

2. **Reversible Adiabatic Expansion** from B to C

   For an adiabatic process,

   $$q = 0$$

   We can express ΔU in terms of heat capacity:

   $$\Delta U = nC_{V,m}\Delta T = w_{\text{on}}$$

   $$w_{\text{on}} = nC_{V,m}(T_c - T_h)$$

   Where T_c is the cooler temperature which the gas cools to during this process.

3. **Reversible Isothermal Compression** from C to D

   For an isothermal process,

   $$\Delta U = q_{\text{gained}} + w_{\text{on}} = 0$$

   Since it is a reversible process, given the starting volume V_{C} and final volume V_{D},

   $$w_{\text{on}} = -nRT_c \ln\left(\frac{V_D}{V_C}\right)$$

   The temperature of this isothermal process is denoted as T_c, which refers to the cooler temperature.

   $$q_{\text{gained}} = -w_{\text{on}} = nRT_c \ln\left(\frac{V_D}{V_C}\right)$$

4. **Reversible Adiabatic Compression** from D to A

   For an adiabatic process,

   $$q = 0$$

   We can express ΔU in terms of heat capacity:

   $$\Delta U = nC_{V,m}\Delta T = w_{\text{on}}$$

$$w_{\text{on}} = nC_{V,m}(T_h - T_c)$$

Where T_h is the hotter temperature which the gas heats up to during this process.

The Carnot heat engine is the **most efficient heat engine** possible, where efficiency, η, is defined as:

$$\eta = \frac{w_{\text{by}}}{q_h}$$

In other words, how much work can the system do given q_h amount of heat?

The Carnot heat engine is the most efficient heat engine because all four stages are **reversible**, and as we have shown previously, reversible processes **do the maximum work** and **require the minimum work**. The rationale of the Carnot heat engine is to let the gas **do more expansion work at a higher temperature** and then cool it down so we require **less work to compress it at a lower temperature**. The net difference is the work done by the heat engine. The adiabatic processes only serve to change the temperature and the net work from them is 0. We will now proceed to calculate the efficiency of the Carnot engine. From the equations governing reversible adiabatic processes,

$$VT^c = \text{constant}$$

For process 2 from B to C,

$$V_B T_h^c = V_C T_c^c$$

For process 4 from D to A,

$$V_A T_h^c = V_D T_c^c$$

Combining the above equations, we have:

$$\frac{V_B}{V_A} = \frac{V_C}{V_D}$$

Thus total work done by the gas through the whole cycle is:

$$w_{\text{by}} = -w_{\text{on}} = nRT_h \ln\left(\frac{V_B}{V_A}\right) + nRT_c \ln\left(\frac{V_D}{V_C}\right) = nR(T_h - T_c)\ln\left(\frac{V_B}{V_A}\right)$$

The supply of heat from the hot reservoir is:

$$q_h = nRT_h \ln\left(\frac{V_B}{V_A}\right)$$

Thus the efficiency of the Carnot heat engine is:

$$\eta = \frac{w_{\text{by}}}{q_h} = \frac{nR(T_h - T_c)\ln\left(\frac{V_B}{V_A}\right)}{nRT_h \ln\left(\frac{V_B}{V_A}\right)} = 1 - \frac{T_c}{T_h}$$

This is an important result and gives the **maximum efficiency** of a heat engine operating between temperatures T_h to T_c.

Now that we understand the Carnot cycle, we want to show that the change in entropy around the cycle is 0. We first find the total change in entropy as:

$$\oint \mathrm{d}S = \frac{q_h}{T_h} + \frac{q_c}{T_c}$$

From the thermodynamic definition of entropy.

$$\oint \mathrm{d}S = \frac{nRT_h \ln\left(\frac{V_B}{V_A}\right)}{T_h} + \frac{nRT_c \ln\left(\frac{V_D}{V_C}\right)}{T_c} = nR\left[\ln\left(\frac{V_B}{V_A}\right) + \ln\left(\frac{V_D}{V_C}\right)\right]$$

Since $\frac{V_B}{V_A} = \frac{V_C}{V_D}$,

$$\oint \mathrm{d}S = nR\left[\ln\left(\frac{V_B}{V_A}\right) - \ln\left(\frac{V_B}{V_A}\right)\right] = 0$$

This shows that the net entropy change in a Carnot cycle is 0, and we move on to generalise this conclusion to any cycle. Any general thermodynamic cycle can be divided into many Carnot cycles, and in the limit of infinitesimally small Carnot cycles, we will be able to exactly fit any thermodynamic cycle using Carnot cycles such that $\oint \mathrm{d}S = 0$. Thus we conclude that **entropy is a state function**.

With our understanding of entropy, we can move on to study the **Second Law of Thermodynamics**:

> The entropy of an isolated system can only increase over time.

This law was discovered through empirical results, though it can be shown through statistical methods to hold true. In our context, the isolated system considered is usually **the universe**, such that:

$$\Delta S_{\text{uni}} = \Delta S + \Delta S_{\text{sur}} \geq 0$$

For any process. Note that ΔS_{uni}, the change in entropy of the universe, is the sum of ΔS, the change in entropy of the system and ΔS_{sur}, the change in entropy of the surroundings. From the second law, we can provide a more rigorous classification for **reversible and irreversible processes**. **Reversible processes have $\Delta S_{\text{uni}} = 0$**, such that the reverse process also has $\Delta S_{\text{uni}} = 0$. **Irreversible processes have $\Delta S_{\text{uni}} > 0$**, such that the reverse process has $\Delta S_{\text{uni}} < 0$, which is impossible by the second law.

To calculate ΔS for a system, we look back to the definition:

$$\mathrm{d}S = \frac{\mathrm{d}q_{\text{rev}}}{T}$$

q_{rev} must come from a reversible process that goes from initial to final state. If the process we are analysing is irreversible, we must use a **hypothetical reversible path** that goes from the same initial state to final state. For all such reversible paths, $\Delta S_{\text{uni}} = 0$ such that $\Delta S = -\Delta S_{\text{sur}}$. Here we will show how to calculate ΔS for different reversible processes:

1. **Reversible Adiabatic process**:
   Since $q_{\text{rev}} = 0$,
$$\Delta S = 0$$
2. **Reversible Isobaric process**:
$$\mathrm{d}q_{\text{rev}} = nC_{p,m}\mathrm{d}T$$
$$\mathrm{d}S = \frac{\mathrm{d}q_{\text{rev}}}{T} = \frac{nC_{p,m}\mathrm{d}T}{T}$$
$$\Delta S = nC_{p,m}\int_{T_i}^{T_f}\frac{\mathrm{d}T}{T} = nC_{p,m}\ln\left(\frac{T_f}{T_i}\right)$$
3. **Reversible Isochoric process**:
$$\mathrm{d}q_{\text{rev}} = nC_{V,m}\mathrm{d}T$$
$$\mathrm{d}S = \frac{\mathrm{d}q_{\text{rev}}}{T} = \frac{nC_{V,m}\mathrm{d}T}{T}$$
$$\Delta S = nC_{V,m}\int_{T_i}^{T_f}\frac{\mathrm{d}T}{T} = nC_{V,m}\ln\left(\frac{T_f}{T_i}\right)$$
   We can observe that it is similar to the isobaric process, just that we use heat capacity at constant volume instead of constant pressure.
4. **Reversible Isothermal process**:
$$\mathrm{d}U = \mathrm{d}q_{\text{rev}} + \mathrm{d}w_{\text{on}} = 0$$
$$\mathrm{d}q_{\text{rev}} = -w_{\text{on}} = p\mathrm{d}V$$
$$\mathrm{d}q_{\text{rev}} = \frac{nRT}{V}\mathrm{d}V$$
$$\mathrm{d}S = \frac{\mathrm{d}q_{\text{rev}}}{T} = \frac{nR}{V}\mathrm{d}V$$
$$\Delta S = \int_{V_i}^{V_f}\frac{nR}{V}\mathrm{d}V = nR\ln\left(\frac{V_f}{V_i}\right)$$

Other than gaseous processes, phase transitions also cause changes in entropy. Phase transitions at constant pressure allow us to equate the heat gained with the enthalpy of the process:
$$q_{\text{rev}} = \Delta H_{\text{trn}}$$

This gives the general expression for the entropy change of a phase transition:

$$\Delta S_{\text{trn}} = \frac{\Delta H_{\text{trn}}}{T}$$

Trouton's Rule is an empirical rule that states:

$$\Delta S^0_{\text{vap}} \approx 85\,\text{kJ/mol}$$

This holds true for most substances with weak intermolecular interactions. For substances with strong intermolecular interactions, such as water with hydrogen bonding, the liquid state has a lower entropy due to ordering and the entropy change going from liquid to gas will be greater.

2.1.14 *The third law of thermodynamics*

From the thermodynamic definition of entropy, we can find change in entropy easily. However, it is difficult to find the standard molar entropy of a substance. We can do so by considering all the entropy changes from $0\ \text{K}$:

$$\begin{aligned} S^0_m(T) = S^0_m(0) + \int_0^{T_f} \frac{C_{p,m,s}(T)}{T}\mathrm{d}T + \frac{\Delta H_{\text{fus},m}}{T_f} \\ + \int_{T_f}^{T_b} \frac{C_{p,m,l}(T)}{T}\mathrm{d}T + \frac{\Delta H_{\text{vap},m}}{T_b} + \int_{T_b}^{T} \frac{C_{p,m,g}(T)}{T}\mathrm{d}t \end{aligned}$$

This is the process of heating the solid to melting point, T_f, melting it, then heating the liquid to boiling point, T_b, vaporising it and heating the vapour to the final temperature T. In this equation, the only value that we cannot find is $S^0_m(0)$, the standard molar entropy at $0\ \text{K}$. The **Third Law of Thermodynamics** defines this as follows:

> The entropy of all perfect crystalline substances is zero at $T = 0\ \text{K}$.

Thus, the entropies derived based on the third law through the method shown above are known as **third law entropies**. Similar to enthalpy and Hess's law, the standard reaction entropy can be defined as the difference between the molar entropies of the pure, separated products and the pure, separated reactants, all substances being in their standard states at the specified temperature.

$$\Delta S^0_r = \sum_{\text{J}} \nu_{\text{J}} S^0_m(\text{J})$$

Or more simply,

$$\Delta S^0_r = \sum_{\text{Products}} \nu \Delta S^0_m - \sum_{\text{Reactants}} \nu \Delta S^0_m$$

The **entropies of ions in solution** is defined differently, and we define the entropy of one ion in solution so that the entropies of the rest of the ions will be relative to it. This ion is the proton, H^+, ion, and we have:

$$S_m^0(\mathrm{H}^+,\mathrm{aq}) = 0$$

And this definition holds true **at all temperatures**. Thus, entropies of ions in solution may be **positive or negative**, relative to H^+. Small, highly charged ions will have negative entropy as they induce local structure in water, while large, singly charged ions have positive entropy as they do not induce as much order in water as H^+.

2.1.15 *Free energies*

Free energy of a system is the **amount of energy left for a system to do work**. From the second law of thermodynamics, we have:

$$\Delta S_{\mathrm{uni}} = \Delta S + \Delta S_{\mathrm{sur}} \geq 0$$

This is the criteria for any process to occur.

For a **constant volume** process,

$$\Delta S_{\mathrm{sur}} = -\frac{q_V}{T} = -\frac{\Delta U}{T}$$

$$\Delta S_{\mathrm{uni}} = \Delta S - \frac{\Delta U}{T} \geq 0$$

$$\Delta U - T\Delta S \leq 0$$

Here, we define **Helmholtz free energy**, A, as follows:

$$A \equiv U - TS$$

Similarly, for a **constant pressure** process,

$$\Delta S_{\mathrm{sur}} = -\frac{q_p}{T} = -\frac{\Delta H}{T}$$

$$\Delta S_{\mathrm{uni}} = \Delta S - \frac{\Delta H}{T} \geq 0$$

$$\Delta H - T\Delta S \leq 0$$

Here, we define **Gibbs free energy**, G, as follows:

$$G \equiv H - TS$$

This is such that we can obtain the **criteria of spontaneous change** as:

$$\Delta A_{T,V} < 0 \text{ and } \Delta G_{T,p} < 0$$

A spontaneous process is an **irreversible process** that **releases free energy** for the system to move to a **lower energy state**, which is more thermodynamically stable. In most chemical processes, we consider constant pressure reactions, thus the Gibbs free energy is more relevant. In this case, we define the **standard Gibbs energy of reaction** at **constant temperature** and **pressure**:

$$\Delta G_r^0 \equiv \Delta H_r^0 - T\Delta S_r^0$$

Where it can be calculated from the reaction enthalpy and entropy. Similarly, we can define the **molar standard Gibbs energy of formation** for the reaction to form a compound from its elements in their reference states as $\Delta G_{f,m}^0$. This will allow us to calculate the standard Gibbs energy of reaction:

$$\Delta G_r^0 = \sum_{\mathrm{J}} v_{\mathrm{J}} G_m^0(\mathrm{J})$$

Or more simply,

$$\Delta G_r^0 = \sum_{\text{Products}} v\Delta G_m^0 - \sum_{\text{Reactants}} v\Delta G_m^0$$

2.2 Chemical Equilibria

At the end of chemical thermodynamics, we discussed how free energies contribute to the spontaneity of the reactions. As reactions proceed, they slowly reach a point where they proceed with equal forward and backward rates with no net change in the amount of reactants and products, which is the point of **dynamic equilibria**. In this chapter, we will first use the concepts from the previous chapter to develop an understanding of chemical equilibria, before learning to solve complex chemical equilibria systems.

2.2.1 *Chemical potential, Gibbs energy and chemical equilibria*

Chemical potential, μ_{J}, is defined as the **partial molar Gibbs energy** for any substance in a multicomponent system with **constant pressure and temperature**:

$$\mu_{\mathrm{J}} \equiv \left(\frac{\partial G}{\partial n_{\mathrm{J}}}\right)_{p,T,n'}$$

In the special case of a **pure substance**, the chemical potential is equivalent to its molar Gibbs energy:

$$\mu_{\mathrm{J}} = G_{\mathrm{J},m}$$

In systems with no change in composition, we can simply write their Gibbs energy expression as:

$$G = H - TS$$

$$\mathrm{d}G = \mathrm{d}H - T\mathrm{d}S - S\mathrm{d}T$$

From the definition of enthalpy H:

$$H = U + pV$$

$$\mathrm{d}H = \mathrm{d}U + p\mathrm{d}V + V\mathrm{d}p$$

From the first law of thermodynamics:

$$\mathrm{d}U = \mathrm{d}q + \mathrm{d}w$$

Considering only PV-work, and the macroscopic definition of entropy:

$$\mathrm{d}w = -p\mathrm{d}V$$

$$\mathrm{d}S = \frac{\mathrm{d}q}{T}$$

$$\mathrm{d}q - T\mathrm{d}S$$

Combining into the expression for Gibbs energy,

$$\mathrm{d}G = \mathrm{d}U + p\mathrm{d}V + V\mathrm{d}p = T\mathrm{d}S - S\mathrm{d}T$$

$$\mathrm{d}G = T\mathrm{d}S - p\mathrm{d}V + p\mathrm{d}V + V\mathrm{d}p - T\mathrm{d}S - S\mathrm{d}T$$

$$\boldsymbol{\mathrm{d}G = V\mathrm{d}p - S\mathrm{d}T}$$

When composition is varying, we extend the equation to include chemical potential:

$$\mathrm{d}G = V\mathrm{d}p - S\mathrm{d}T + \mu_\mathrm{A}\mathrm{d}n_\mathrm{A} + \mu_\mathrm{B}\mathrm{d}n_\mathrm{B} + \cdots$$

For a system with components $\mathrm{A}, \mathrm{B}, \ldots$, this equation is known as the **fundamental equation of chemical thermodynamics**.

Similarly, when other physical properties are constant, chemical potential describes how other extensive thermodynamic properties vary with chemical composition. We can write chemical potential as the derivatives of the different energies we have learnt in thermodynamics:

$$\mu_\mathrm{J} = \left(\frac{\partial G}{\partial n_\mathrm{J}}\right)_{p,T,n'} = \left(\frac{\partial A}{\partial n_\mathrm{J}}\right)_{V,T,n'} = \left(\frac{\partial U}{\partial n_\mathrm{J}}\right)_{S,V,n'} = \left(\frac{\partial H}{\partial n_\mathrm{J}}\right)_{S,p,n'}$$

This is why chemical potential is a central concept in thermodynamics.

Now, we will look at the fundamental equation of chemical thermodynamics considering chemical equilibria. In a reaction system reaching equilibrium, the pressure and temperature are usually constant. In this case we simplify the equation and obtain:

$$\mathrm{d}G = \mu_\mathrm{A}\mathrm{d}n_A + \mu_\mathrm{B}\mathrm{d}n_\mathrm{B} + \cdots$$

Such that total G can be given as:

$$G = \sum_\mathrm{J} \mu_\mathrm{J} n_\mathrm{J}$$

At chemical equilibria, from the second law of thermodynamics, the entropy of the universe is maximised. We have previously concluded that at constant pressure and temperature, this can be represented by a minimum Gibbs energy. To find this minimum point, we use the property of stationary points to write:

$$\mathrm{d}G = 0$$

Thus we need to find the point where:

$$\mathrm{d}G = \sum_{\mathrm{J}} \mu_{\mathrm{J}} \mathrm{d}n_{\mathrm{J}} = 0$$

To solve this equation, we note that n_{J} cannot vary arbitrarily: For any given reaction, n_{J} must vary according to stoichiometric numbers ν_{J}. To mathematically express this concept, we define the **extent of reaction**, ξ, such that ξ is the number of moles of reaction that proceeded:

$$\mathrm{d}n_{\mathrm{J}} = \nu_{\mathrm{J}} \mathrm{d}\xi$$

Thus we can write:

$$\mathrm{d}G = \sum_{\mathrm{J}} \mu_{\mathrm{J}} \nu_{\mathrm{J}} \mathrm{d}\xi = 0$$

For any small change in ξ, $\mathrm{d}G = 0$. This means that the condition for equilibrium is:

$$\sum_{\mathrm{J}} \mu_{\mathrm{J}} \nu_{\mathrm{J}} = 0$$

Thus, we define the **reaction Gibbs energy** as follows:

$$\Delta G_r \equiv \left(\frac{\partial G}{\partial \xi} \right)_{p,T} = \sum_{\mathrm{J}} \mu_{\mathrm{J}} \nu_{\mathrm{J}}$$

Now, let's consider the chemical potential of a pure perfect gas. In the case of an isothermal reaction, the partial pressure of the gas will change with the composition of the gas. From this change in pressure, we can find the change in chemical potential. Since it is a pure perfect gas, we simplify the fundamental equation of chemical thermodynamics:

$$\mathrm{d}G = V\mathrm{d}p - S\,\mathrm{d}T$$

In the case of constant temperature, $\mathrm{d}T = 0$. Then,

$$\mathrm{d}G = V\mathrm{d}p$$

Note that for pure substances,

$$\mathrm{d}\mu = \mathrm{d}G_m = V_m\,\mathrm{d}p = \frac{RT}{p}\mathrm{d}p$$

$$\Delta\mu = \int_{p_i}^{p_f} \frac{RT}{p}\mathrm{d}p = RT\ln\left(\frac{p_f}{p_i}\right)$$

If we set $p_i = p^0 = 1\ \text{bar}$,

$$\mu = \mu^0 + RT\ln\left(\frac{p}{p^0}\right)$$

Although this equation is derived from a system of pure perfect gas, it can be generalised to any gas in a perfect gas mixture, since there are no significant interactions between components of a perfect gas mixture:

$$\mu_\mathrm{J} = \mu_\mathrm{J}^0 + RT\ln\left(\frac{p_\mathrm{J}}{p^0}\right)$$

where p_J is the **partial pressure** of component J.

Background 2f. Partial pressure

When dealing with mixtures of perfect gas, we assume that the gases do not interact significantly with each other, and thus the property of each specific gas can be neglected. All the gases are treated as equivalent and that means each gas contributes equally to the pressure, depending on how much of it there is. We define the **mole fraction**, χ:

$$\chi_\mathrm{J} = \frac{n_\mathrm{J}}{n_T}$$

Where n_T is the total number of moles of gas in the system. Using the mole fraction, we define partial pressure as:

$$p_\mathrm{J} = \chi_\mathrm{J} p_T$$

Using reaction Gibbs energy,

$$\Delta G_r = \sum_\mathrm{J} \mu_\mathrm{J} v_\mathrm{J} = \sum_\mathrm{J} \mu_\mathrm{J}^0 v_\mathrm{J} + RT\sum_\mathrm{J} v_\mathrm{J} \ln\left(\frac{p_\mathrm{J}}{p_0}\right)$$

Note that the standard reaction Gibbs energy can be expressed as:

$$\Delta G_r^0 = \sum_\mathrm{J} \mu_\mathrm{J}^0 v_\mathrm{J}$$

Such that:

$$\Delta G_r = \Delta G_r^0 + RT\sum_\mathrm{J} v_\mathrm{J} \ln\left(\frac{p_\mathrm{J}}{p_0}\right)$$

Using the property of natural logarithm that $a\ln b = \ln b^a$ and $\ln a + \ln b = \ln(ab)$,

$$\Delta G_r = \Delta G_r^0 + RT\ln\prod_\mathrm{J}\left(\frac{p_\mathrm{J}}{p_0}\right)^{v_\mathrm{J}}$$

For simplicity, we define the **reaction quotient**, Q, as:

$$Q = \prod_\mathrm{J} a_\mathrm{J}^{v_\mathrm{J}}$$

where a_J is the **activity** of component J. The reaction quotient is defined as the ratio of the activities of products to activities of reactants raised to the power given by the stoichiometric coefficient. Note that since activities are dimensionless, the reaction quotient is also dimensionless. This allows us to write the important thermodynamic equation that gives us **the reaction Gibbs energy at an arbitrary stage** as:

$$\Delta G_r = \Delta G_r^0 + RT \ln Q$$

Background 2g. Thermodynamic activity

Activity is a measure of "effective concentration" of a species in a mixture. Thus, for **pure liquids and solids the activity is taken to be 1**, assuming that the volume remains constant.

For **gases**,

$$a_J = \frac{f_J}{p^0}$$

Where f is the fugacity of the gas.

Fugacity accounts for the deviation of real gases from perfect gas behavior. We define the fugacity coefficient, ϕ, as follows:

$$\phi = \frac{f}{p}$$

Such that

$$\ln \phi = \frac{1}{RT} \int_0^p (V_m - V_{m,\,\text{perfect}}) \mathrm{d}p$$

This accounts for the deviation from perfect gas pressures. These deviations are present because of intermolecular forces between gas molecules and the non-negligible size of gas molecules. If we assume that it is a perfect gas,

$$\phi = 1$$

$$a_J = \frac{p_J}{p^0}$$

This is the most common way we express reaction quotients, using the partial pressures.

For **electrolyte solutes in solution**,

$$a_J = \frac{\gamma_J [J]}{c^0}$$

Where γ_J is the activity coefficient of the solute.

This coefficient accounts for all deviations from ideality. Ideal solutions are solutions where the solvent-solute interactions are the same as solvent-solvent and solute-solute interactions. This is usually not true, however, we can usually approximate $\gamma_J = 1$ for very dilute solutions.

(Continued)

Background 2g. (*Continued*)

However, a big problem is that cations and anions in the same solution will have strong electrostatic interactions between them. This will cause significant deviation from ideality. Near any given ion, it is more likely to find counter-ions. This is known as the ionic atmosphere around the central ion. The energy, and therefore the chemical potential, of any given central ion is lowered by its electrostatic interaction with its ionic atmosphere. In this case, the activity coefficient must be calculated using Debye-Hückel Theory. Debye-Hückel limiting law is stated below (this law can be extended by adding more constants):

$$\lg\gamma_{\pm} = -A|z_+z_-|I^{\frac{1}{2}}$$

Where I is the ionic strength of the solution. Ionic strength is a measure of the concentration of the ions in the solution and clearly emphasises the charge of the ions.

The reaction Gibbs energy change through a reaction is shown in Figure 2.2.1. When $\Delta G_r < 0$, the forward reaction is spontaneous. When $\Delta G_r > 0$, the reverse reaction is spontaneous. When $\Delta G_r = 0$, the reaction is in equilibrium.

At chemical equilibrium,

$$\Delta G_r = \Delta G_r^0 + RT\ln Q = 0$$

Thus,

$$\Delta G_r^0 = -RT\ln Q_{\text{eq}}$$

We define the **equilibrium constant**, K, to be:

$$K \equiv Q_{\text{eq}}$$

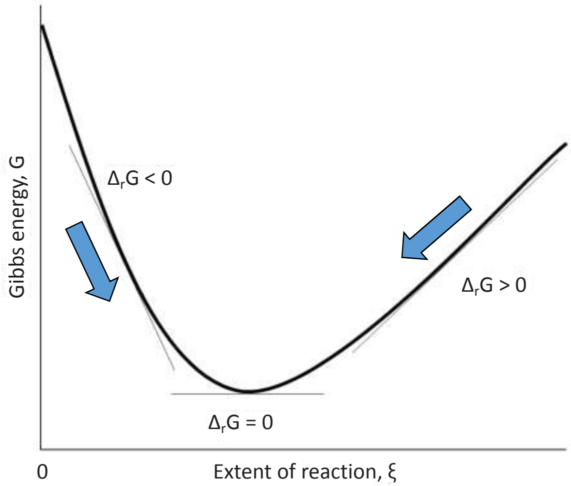


Figure 2.2.1. Graph of Gibbs energy against extent of reaction for a spontaneous reaction.

The equilibrium constant is just the reaction quotient when the reaction is at equilibrium, evaluated using equilibrium activities. This gives us the important property,

$$\Delta G_r^0 = -RT\ln K$$

2.2.2 *Van't Hoff equation*

Recall that when deriving the equilibrium constant, we have used an isothermal assumption. Thus, the **equilibrium constant varies with temperature**. We will find the relationship between equilibrium constant and temperature.

From $\Delta G_r^0 = -RT\ln K$,

$$\ln K = -\frac{\Delta G_r^0}{RT}$$

Taking a derivative with respect to temperature,

$$\frac{\mathrm{d}\ln K}{\mathrm{d}T} = -\frac{1}{R}\frac{\mathrm{d}}{\mathrm{d}T}\left(\frac{\Delta G_r^0}{T}\right)$$

Now we have to evaluate $\frac{\mathrm{d}}{\mathrm{d}T}\left(\frac{\Delta G_r^0}{T}\right)$ by considering the fundamental equation of thermodynamics:

$$\mathrm{d}G = V\mathrm{d}p - S\mathrm{d}T$$

Using the quotient rule of differentiation,

$$\mathrm{d}\left(\frac{G}{T}\right) = \frac{T\mathrm{d}G - G\mathrm{d}T}{T^2}$$

$$\mathrm{d}\left(\frac{G}{T}\right) = \frac{TV\mathrm{d}p - TS\mathrm{d}T - G\mathrm{d}T}{T^2}$$

Note that $H = G + TS$, such that:

$$\mathrm{d}\left(\frac{G}{T}\right) = \frac{TV\mathrm{d}p - TS\mathrm{d}T - G\mathrm{d}T}{T^2} = \frac{TV\mathrm{d}p - (G+TS)\mathrm{d}T}{T^2} = \frac{TV\mathrm{d}p - H\mathrm{d}T}{T^2}$$

$$\mathrm{d}\left(\frac{G}{T}\right) = \frac{V}{T}\mathrm{d}p - \frac{H}{T^2}\mathrm{d}T$$

In the constant pressure case, $\mathrm{d}p = 0$. We write

$$\left(\frac{\mathrm{d}\left(\frac{G}{T}\right)}{\mathrm{d}T}\right)_p = -\frac{H}{T^2}$$

In the case of ΔG_r^0,

$$\left(\frac{\mathrm{d}\left(\frac{\Delta G_r^0}{T}\right)}{\mathrm{d}T}\right)_p = -\frac{\Delta H_r^0}{T^2}$$

From here we obtain the **van't Hoff equation**:

$$\frac{\mathrm{d}\ln K}{\mathrm{d}T} = \frac{\Delta H_r^0}{RT^2}$$

We can solve this equation through integration,

$$\int_{T_1}^{T_2} \mathrm{d}\ln K = \int_{T_1}^{T_2} \frac{\Delta H_r^0}{RT^2}\mathrm{d}T$$

If we **assume that ΔH_r^0 is constant over a small range of temperatures**, we obtain the most commonly used formed of van't Hoff equation:

$$\ln\left(\frac{K_2}{K_1}\right) = -\frac{\Delta H_r^0}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right)$$

This equation gives us the **temperature dependence of *K***.

2.2.3 *Le Chatelier's principle*

The value of the equilibrium constant only changes during a temperature change. All other changes in thermodynamic properties (pressure/volume/composition) do not affect the equilibrium constant. However, any change in the system will cause a shift in equilibrium. This can be predicted by **Le Chatelier's principle**, which states that:

> A system at equilibrium, when subjected to a disturbance, responds in a way that tends to counteract the disturbance to establish a new equilibrium.

Here, we will explore the different possible changes to a chemical system, and how we can predict the equilibrium shift by Le Chatelier's principle. For every change, we can rationalise the shift logically by Le Chatelier's principle and mathematically by considering the equilibrium constant. For the purpose of explanation, we will consider the sample reaction:

$$\mathrm{N}_{2(\mathrm{g})} + 3\mathrm{H}_{2(\mathrm{g})} \rightleftharpoons 2\mathrm{NH}_{3(\mathrm{g})} \qquad \Delta H_r^0 < 0, K = \frac{p_{\mathrm{NH}_3}^2}{(p_{\mathrm{N}_2})(p_{\mathrm{H}_2}^3)}$$

For a change in **pressure caused by a change in volume**:

By Le Chatelier's principle, the system will counteract the disturbance, such that if the pressure is increased, the system will try to reduce it and vice versa. This is done by shifting the equilibrium according to the number of moles of gas on each side of the reaction. In the case of the sample reaction, we see that the reaction proceeds with 4 moles of gas in the reactant to form 2 moles of gas in the product:

$$\text{4 moles of gas} \rightleftharpoons \text{2 moles of gas}$$

Logically, when pressure increases, to counteract this change and reduce the pressure, the equilibrium shifts to the right such that the number of moles of gas is reduced. Mathematically, we can consider the equilibrium constant. We may express it as:

$$K = \frac{p_{\mathrm{NH_3}}^2}{(p_{\mathrm{N_2}})(p_{\mathrm{H_2}}^3)} = \frac{\chi_{\mathrm{NH_3}}^2}{(\chi_{\mathrm{N_2}})(\chi_{\mathrm{H_2}}^3)} \times \frac{1}{p_T^2}$$

Since the equilibrium constant K does not change with pressure, when total pressure p_T increases, the equilibrium must shift to the right such that $\chi_{\mathrm{NH_3}}$ increases while $\chi_{\mathrm{N_2}}$ and $\chi_{\mathrm{H_2}}$ decreases and K will remain the same.

For a change in **pressure caused by addition of inert gas at constant volume**:

There is no way to rationalise this change by Le Chatelier's principle, since there is no way for the system to counteract this disturbance by removing the inert gas. Instead, some may consider the addition of inert gas as a method to increase pressure, and apply the Le Chatelier's principle as outlined above. However, the mathematical argument above does not hold when the partial pressures are changed because the addition of perfect gas changes the total number of moles of gas in the system. We revise our mathematical statement taking into consideration that $\chi_{\mathrm{J}} = \frac{n_{\mathrm{J}}}{n_{\mathrm{T}}}$ and $p_{\mathrm{J}} = \frac{n_{\mathrm{J}}}{n_{\mathrm{T}}} p_{\mathrm{T}}$:

$$K = \frac{p_{\mathrm{NH_3}}^2}{(p_{\mathrm{N_2}})(p_{\mathrm{H_2}}^3)} = \frac{\chi_{\mathrm{NH_3}}^2}{(\chi_{\mathrm{N_2}})(\chi_{\mathrm{H_2}}^3)} \times \frac{1}{p_T^2} = \frac{n_{\mathrm{NH_3}}^2}{(n_{\mathrm{N_2}})(n_{\mathrm{H_2}}^3)} \times \left(\frac{n_T}{p_T}\right)^2$$

By perfect gas law $pV = nRT$, at constant $V, T, n \propto p$. Thus, $\frac{n_T}{p_T}$ is constant. There will be no change in the amount of reactant and product to keep equilibrium constant K constant. The equilibrium does not shift with the addition of the inert gas.

For a change in amount of **reactant or product**:

By Le Chatelier's principle, it is straightforward that the addition of reactant will shift equilibrium to the right while the addition of product will shift equilibrium to the left. This can also be mathematically justified:

$$K = \frac{p_{\mathrm{NH_3}}^2}{(p_{\mathrm{N_2}})(p_{\mathrm{H_2}}^3)}$$

With an addition in either product or reactant, the partial pressure of the species will increase accordingly. This will cause a change of equilibrium to ensure that K remains constant. This method is commonly used by chemists to maximise reaction yield, usually by removing the product during the reaction to push the reaction to completion.

For a change in **temperature**:

By Le Chatelier's principle, the system will counteract the change by reducing the temperature when temperature is increased and increasing the temperature when temperature is decreased. Since the reaction is a process of bond breaking and forming, the difference in energy can be expressed by the change in enthalpy of the reaction, ΔH_r^0, which at constant pressure $\Delta H_r^0 = q_p$. This is the heat absorbed or released in the reaction, depending on the sign of ΔH_r^0. In this case $\Delta H_r^0 < 0$ and the reaction is exothermic, releasing heat. With an increase in temperature, the equilibrium shifts left as the reverse reaction is endothermic and absorbs heat, lowering the temperature. Mathematically, we can justify this using the van't Hoff equation that we have derived previously:

$$\ln\left(\frac{K_2}{K_1}\right) = -\frac{\Delta H_r^0}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right)$$

When $\Delta H_r^0 < 0,\ T_2 > T_1$, then $\ln\left(\frac{K_2}{K_1}\right) < 0$ and $K_2 < K_1$. With a smaller equilibrium constant, the equilibrium shifts left just as predicted by the Le Chatelier's principle.

For an addition of **catalyst**:

By Le Chatelier's principle, this addition does not cause any disturbance to the thermodynamic properties of the system, and thus there should be no shift in equilibrium. A catalyst increases both the forward and reverse rates of the reaction equally by providing an alternate reaction pathway with lower activation energy. This will allow the reaction to attain equilibrium faster, but does not affect the equilibrium position.

2.2.4 *Problem solving with the ICE (Initial/Change/Equilibrium) table*

With the previous sections, we have covered the gist of the theory behind chemical equilibria. While chemical equilibrium is a short topic which builds up on the concepts covered in thermodynamics, it is an important topic that can be explored in many ways. In the next sections, we will look into different types of reactions through examples. First, we will explore the method to solve simple chemical equilibria problems, through the ICE table.

Given any simple equilibrium and the initial conditions, we are able to find the final conditions through this method. Let us consider a general equilibrium:

$$\mathrm{A_{(g)}} + \mathrm{B_{(g)}} \rightleftharpoons \mathrm{C_{(g)}} + \mathrm{D_{(g)}} \qquad K = \frac{(p_\mathrm{C})(p_\mathrm{D})}{(p_\mathrm{A})(p_\mathrm{B})} = 10$$

Given the initial conditions that $p_A = 0.400\ \text{bar}$, $p_B = 0.300\ \text{bar}$, $p_C = 0.200\ \text{bar}$ and $p_D = 0.100\ \text{bar}$, we will use the ICE table to solve for the final concentrations of the 4 species in this reaction.

Table 2.9 is the general ICE table for this reaction:

Table 2.9. General ICE table for a reaction with no values entered.

Reaction	$\mathbf{A}_{(\mathbf{g})}$	$+$	$\mathbf{B}_{(\mathbf{g})}$	$\rightleftharpoons$	$\mathbf{C}_{(\mathbf{g})}$	$+$	$\mathbf{D}_{(\mathbf{g})}$
Initial							
Change							
Equilibrium							

In the row "Initial", we fill in the initial conditions, that the question has provided us, as shown in Table 2.10:

Table 2.10. ICE table with the initial conditions inputted.

Reaction	$\mathbf{A}_{(\mathbf{g})}$	$+$	$\mathbf{B}_{(\mathbf{g})}$	$\rightleftharpoons$	$\mathbf{C}_{(\mathbf{g})}$	$+$	$\mathbf{D}_{(\mathbf{g})}$
Initial	0.400		0.300		0.200		0.100
Change							
Equilibrium							

In the row "change", we predict the change in the number of moles of each component based on their **stoichiometry**. We present this row usually as a function of x, since we would not know the value yet, as shown in Table 2.11.

Table 2.11. ICE table with initial conditions and change inputted.

Reaction	$\mathbf{A}_{(\mathbf{g})}$	$+$	$\mathbf{B}_{(\mathbf{g})}$	$\rightleftharpoons$	$\mathbf{C}_{(\mathbf{g})}$	$+$	$\mathbf{D}_{(\mathbf{g})}$
Initial	0.400		0.300		0.200		0.100
Change	$-x$		$-x$		$+x$		$+x$
Equilibrium							

In this case, it is quite obvious that we have more reactant than product, and since the equilibrium constant $K > 1$, the equilibrium must favour the products. Thus, we can be confident that the equilibrium shifts to the right such that A and B are consumed while C and D are produced. In some other cases, it might not be so straightforward whether the reaction proceeds forwards or backwords. There is no need to worry, as solving for x will result in a negative value if the reaction is meant to proceed backwards. However, in complicated equations (to higher powers), there will always be both positive and negative solutions, and it is important to reject all the impossible answers to obtain the correct answer. Finally, the row for equilibrium is calculated by taking the sum of the initial and change in amount of each species. This completes the ICE table, which is given in Table 2.12.

Table 2.12. Completed ICE table that can be used to solve the equilibria.

Reaction	$\mathbf{A}_{(\mathbf{g})}$	$+$	$\mathbf{B}_{(\mathbf{g})}$	$\rightleftharpoons$	$\mathbf{C}_{(\mathbf{g})}$	$+$	$\mathbf{D}_{(\mathbf{g})}$
Initial	0.400		0.300		0.200		0.100
Change	$-x$		$-x$		$+x$		$+x$
Equilibrium	$0.400 - x$		$0.300 - x$		$0.200 + x$		$0.100 + x$

The system will have to satisfy the equilibrium condition at equilibrium:

$$K = \frac{(p_\mathrm{C})(p_\mathrm{D})}{(p_\mathrm{A})(p_\mathrm{B})} = \frac{(0.200 + x)(0.100 + x)}{(0.400 - x)(0.300 - x)} = 10$$

This equation simplifies to a quadratic equation:

$$9x^2 - 7.3x + 1.18 = 0$$

Applying the quadratic formula $x = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a}$,

$$x = 0.588,\ 0.223$$

Note that the partial pressure of any gas can never be negative, thus we reject the answer $x = 0.588$ (which leads to negative partial pressures for A and B) and arrive at the accepted answer of $x = 0.223$. This leads us to the equilibrium partial pressures of the 4 species to be $p_A = 0.177$ bar, $p_B = 0.0771$ bar, $p_C = 0.423$ bar and $p_D = 0.323$ bar.

The ICE table can be used in any simple equilibria questions and the question need not necessarily provide you with all the initial conditions. Sometimes, certain initial and final conditions may be provided and the ICE table can be used similarly, just by filling in the table accordingly. The table is just a way to systematically consider the stoichiometry of the reaction.

2.2.5 *Acid-base equilibria and the Henderson-Hasselbalch equation*

In the examples above, we have mainly been dealing with gaseous equilibria. However, there are many other common forms of equilibria that will be introduced here. Firstly, we will examine acid-base equilibria, which is important for weak acids and bases that do not fully dissociate, and certain multiprotic acids.

Before we discuss acids and bases, we must first understand the properties of water, which acts as the solvent for acid-base equilibria. Water may be **autoionised**, which means that it reacts with itself to generate ions. The reaction may be given as:

$$\mathrm{H_2O + H_2O \rightleftharpoons H_3O^+ + OH^-}$$

The equilibrium constant of this reaction, K_w, may be written as:

$$K_w = \frac{a(\mathrm{H_3O^+}) \cdot a(\mathrm{OH^-})}{a(\mathrm{H_2O})^2}$$

As mentioned in background *2g*, the activity of a species in a solution may be taken to be its concentration. As only a very small fraction of water molecules are ionised, the concentration of water, $[\mathrm{H_2O}]$, remains virtually unchanged. Thus we may use $\mathrm{H^+}$ and $\mathrm{H_3O^+}$ interchangeably, and consider the reaction to be essentially:

$$\mathrm{H_2O} \rightleftharpoons \mathrm{H^+} + \mathrm{OH^-}$$

However, we must still keep in mind that protons will associate with water to form hydronium ions in an acidic solution. It is only that we may use the concentration of proton to refer to the concentration of hydronium ion as the concentration of water remains largely constant. In this book, from this point onwards, we will use proton concentration for calculation as it simplifies the equation and eliminates the need to consider the unnecessary proton association with water:

$$\mathrm{H^+} + \mathrm{H_2O} \rightarrow \mathrm{H_3O^+}$$

With all the simplifications, we write the **ionic product of water**, K_w, as:

$$K_w = [\mathrm{H^+}][\mathrm{OH^-}] = 1.0 \times 10^{-14}$$

The value of the ionic product is determined empirically at 25°C and varies slightly with temperature. The ionic product must hold true in any aqueous acid-base solution.

We measure the strength of acids and bases through the amount of protons and hydroxide ions they produce in solution. We define the **potential of hydrogen** (pH) and the **potential of hydroxide** (pOH) based on the activity of proton and hydroxide in the solution. The small letter **p indicates the base-10 cologarithm** of the value, and it is used to give a value that isn't too large or too small.

$$pH = -\lg(a(\mathrm{H^+}))$$

$$pOH = -\lg(a(\mathrm{OH^-}))$$

Since activity of a solute in an ideal dilute solution is equal to its concentration, we may rewrite the equations as follows:

$$pH = -\lg[\mathrm{H^+}]$$

$$pOH = -\lg[\mathrm{OH^-}]$$

In doing so, we must keep in mind that we are only concerned with the numerical value of the concentration and that we cannot take the logarithm of values with units. We may derive a relationship between pH and pOH using K_w:

$$-\lg([\mathrm{H^+}][\mathrm{OH^-}]) = -\lg(1.0 \times 10^{-14})$$

$$pH + pOH = 14$$

Using K_w, we may find the concentration of hydroxide from the proton concentration, and vice versa.

For weak acids that do not dissociate fully, the acid dissociation constant, K_a, measures the extent to which they dissociate. For the general dissociation of a monoprotic weak acid:

$$\mathrm{HA} \rightleftharpoons \mathrm{H^+} + \mathrm{A^-}$$

We may write the expression for K_a:

$$K_a = \frac{[\mathrm{H^+}][\mathrm{A^-}]}{[\mathrm{HA}]}$$

Similarly, for weak bases, we define a base dissociation constant, K_b, for a general reaction of a weak base:

$$\mathrm{A^-} + \mathrm{H_2O} \rightleftharpoons \mathrm{HA} + \mathrm{OH^-}$$

Since the concentration of water remains virtually constant, we have:

$$K_b = \frac{[\mathrm{HA}][\mathrm{OH^-}]}{[\mathrm{A^-}]}$$

In the case of an **acid with its conjugate base**, we can find the special property:

$$K_a \cdot K_b = \frac{[\mathrm{H^+}][\mathrm{A^-}]}{[\mathrm{HA}]} \cdot \frac{[\mathrm{HA}][\mathrm{OH^-}]}{[\mathrm{A^-}]} = [\mathrm{H^+}][\mathrm{OH^-}] = K_w$$

This relation shows that a strong acid will have a weak conjugate base while a weak acid has a strong conjugate base.

A **buffer solution** is a solution prepared by mixing a weak acid with its conjugate base or a weak base with its conjugate acid. It is capable of **resisting** pH **changes** and **maintaining the** pH **of a solution**. That is because all buffers contain a weak acid mixed with a weak base that is able to soak up excess protons and fill up proton deficiencies. If we consider a solution of a weak acid with its conjugate base, HA and $\mathrm{A^-}$:

When base $(\mathrm{B^-})$ is added, $\mathrm{HA} + \mathrm{B^-} \rightarrow \mathrm{HB} + \mathrm{A^-}$

When acid (HB) is added, $\mathrm{A^-} + \mathrm{HB} \rightarrow \mathrm{HA} + \mathrm{B^-}$

This allows the buffer to counteract any changes in pH. We may calculate the pH of a buffer solution by considering the K_a of the weak acid.

$$K_a = \frac{[\mathrm{H^+}][\mathrm{A^-}]}{[\mathrm{HA}]}$$

$$[\mathrm{H}^+] = \frac{K_a[\mathrm{HA}]}{[\mathrm{A}^-]}$$

$$-\lg[\mathrm{H}^+] = -\lg K_a - \lg\frac{[\mathrm{HA}]}{[\mathrm{A}^-]}$$

Simplifying the terms, we arrive at the **Henderson-Hasselbalch equation**:

$$pH = pK_a + \lg\frac{[\mathrm{A}^-]}{[\mathrm{HA}]}$$

This equation provides us with a convenient method to calculate the pH of a buffer solution. In a buffer solution, there are 2 species that are able to neutralise acid and base respectively, maintaining the pH. The **maximum buffering capacity** occurs when the 2 species are equal in concentration, since the buffer can neutralise acid and base equally effectively. Applying the Henderson-Hasselbalch equation, we substitute the condition of maximum buffering capacity:

$$[\mathrm{HA}] = [\mathrm{A}^-]$$

$$pH = pK_a$$

Thus, the maximum buffering capacity occurs when the pH of the buffer is the pKa of the weak acid. While it is possible to make buffers of different pH using the same conjugate acid-base pair, we should choose the conjugate acid-base pair with the closest pK_a to the pH value for maximal buffering capacity. Thus, an acetic acid-acetate buffer will have maximal buffering capacity at $pH = 4.8$ while an ammonia-ammonium buffer will have maximal buffering capacity at $pH = 9.2$.

2.2.6 *Solubility equilibria*

Solubility equilibria deals with the dissolution of solids in water. From the thermodynamics perspective, this mainly depends on 2 factors: Lattice energy and Hydration energy. Lattice energy refers to the energy required to break the crystal lattice of the salt into ions and hydration energy is the energy gained from the interactions of water with the ions to stabilise them. The solubility of a substance depends on its relative stability in aqueous phase compared to solid phase. Let us use the example of the silver halides to demonstrate the solubility product and what it represents.

$$\mathrm{AgCl}_{(s)} \rightleftharpoons \mathrm{Ag}^+_{(aq)} + \mathrm{Cl}^-_{(aq)}$$

We may write the expression for equilibrium constant of this equation to be:

$$K = \frac{a\left(\mathrm{Ag}^+_{(aq)}\right)\cdot a\left(\mathrm{Cl}^-_{(aq)}\right)}{a\left(\mathrm{AgCl}_{(s)}\right)} = [\mathrm{Ag}^+][\mathrm{Cl}^-]$$

The activity of solids are taken to be 1 as their concentration does not change. This shows that the equilibrium depends entirely on the concentration of ions in solution and not the amount of solid. Addition of solid will not shift the equilibrium and allow more solid to dissolve. For dissolution reactions, **K_{sp} is known as the solubility product**.

To decide the state of the equilibrium system, we may use the **ion product Q**, which has the same expression as K, except that the concentrations may not be at equilibrium. The system may be in any of the 3 states:

1. When $Q > K$, the solution is **supersaturated**. The solid will start precipitating out of the solution until $Q = K$.
2. When $Q = K$, the solution is **saturated**. The solution is holding the maximum amount of ions it can.
3. When $Q < K$, the solution is **unsaturated**. The solution is holding less than the maximum amount of ions it can and more solid will still dissolve until the solution is saturated.

Solubility equilibria is important because it is possible to separate ions by **fractional precipitation**. This method allows us to separate ions by their differences in solubility. For example, we may use $\mathrm{Ag^+}$ ions to separate a solution of $\mathrm{Br^-}$ and $\mathrm{Cl^-}$ ions. We have the solubility products of sodium chloride and sodium bromide as follows:

$$K_{sp}(\mathrm{AgCl}) = [\mathrm{Ag^+}][\mathrm{Cl^-}] = 1.6 \times 10^{-10}$$

$$K_{sp}(\mathrm{AgBr}) = [\mathrm{Ag^+}][\mathrm{Br^-}] = 7.7 \times 10^{-13}$$

If the original concentration of $[\mathrm{Br^-}] = [\mathrm{Cl^-}] = 0.010\ \mathrm{mol \cdot dm^{-3}}$, AgBr will start precipitating when the concentration of silver ions is:

$$[\mathrm{Ag^+}] = \frac{K_{sp}(\mathrm{AgBr})}{[\mathrm{Br^-}]} = 7.7 \times 10^{-11}\ \mathrm{mol \cdot dm^{-3}}$$

AgCl will start precipitating when the concentration of silver ions is:

$$[\mathrm{Ag^+}] = \frac{K_{sp}(\mathrm{AgCl})}{[\mathrm{Cl^-}]} = 1.6 \times 10^{-8}\ \mathrm{mol \cdot dm^{-3}}$$

Since AgBr is less soluble than AgCl, AgBr will precipitate out of the solution first when the silver ion concentration is lower. The question now is that what concentration of $\mathrm{Br^-}$ remains when AgCl starts to precipitate. When AgCl starts to precipitate,

$$[\mathrm{Ag^+}] = 1.6 \times 10^{-8}\ \mathrm{mol \cdot dm^{-3}}$$

$$[\mathrm{Br^-}] = \frac{K_{sp}(\mathrm{AgBr})}{[\mathrm{Ag^+}]} = 4.81 \times 10^{-5}\ \mathrm{mol \cdot dm^{-3}}$$

We may find the percentage of $\mathrm{Br^-}$ remaining in the solution:

$$\%\,\mathrm{Br^-} = \frac{4.81\times10^{-5}}{0.010}\times100\% = 0.481\%$$

This shows that most $\mathrm{Br^-}$ ions have been selectively precipitated out by this technique. This offers a very good separation of the $\mathrm{Br^-}$ and $\mathrm{Cl^-}$ ions in solution.

2.2.7 *Complex-ion equilibria*

A **metal complex** consists of a **central metal cation** bonded to **one or many molecules or ions**, known as **ligands**. The chemistry of such complexes is interesting and will be discussed in chapter 3.7 of this book. The binding of ligands to the central metal cation follows a series of equilibria, which is shown in Table 2.13 for a sample complex $\mathrm{[Cu(NH_3)_4]^{2+}}$.

Table 2.13. Equilibrium equations and constants for the formation of tetraammine copper(II) complex.

Series of equilibria to form $\mathrm{[Cu(NH_3)_4]^{2+}}$	**Stepwise equilibrium constants (β)**
$\mathrm{Cu^{2+} + NH_3 \rightleftharpoons [Cu(NH_3)]^{2+}}$	$\beta_1 = 2.2\times10^4$
$\mathrm{[Cu(NH_3)]^{2+} + NH_3 \rightleftharpoons [Cu(NH_3)_2]^{2+}}$	$\beta_2 = 3.2\times10^3$
$\mathrm{[Cu(NH_3)_2]^{2+} + NH_3 \rightleftharpoons [Cu(NH_3)_3]^{2+}}$	$\beta_3 = 1.2\times10^3$
$\mathrm{[Cu(NH_3)_3]^{2+} + NH_3 \rightleftharpoons [Cu(NH_3)_4]^{2+}}$	$\beta_4 = 76$

To find the overall equilibrium constant for the formation of the tetraammine copper(II) complex, we may **multiply the stepwise equilibrium constants**:

$$K_f = \beta_1\beta_2\beta_3\beta_4 = 6.4\times10^{12}$$

Formation of complexes is a common way to increase the solubility of insoluble salts, such as silver chloride as silver forms complexes with ammonia in a 1:2 ratio. The equilibrium is given as follows:

$$\mathrm{Ag^+ + 2\ NH_3 \rightleftharpoons [Ag(NH_3)_2]^+} \qquad K_f = 1.5\times10^7$$

Removal of silver cations from the solution through the complex formation with ammonia will allow more silver chloride salt to dissolve. We may attempt to find the molar solubility of silver chloride in a solution of $1.0\ \mathrm{mol\cdot dm^{-3}}$:

$$\mathrm{AgCl}_{(s)} \rightleftharpoons \mathrm{Ag}^+_{(aq)} + \mathrm{Cl}^-_{(aq)} \qquad K_{sp} = 1.6\times10^{-10}$$

We may write the overall reaction from both reactions:

$$\mathrm{AgCl}_{(s)} + 2\ \mathrm{NH}_{3(aq)} \rightleftharpoons \mathrm{[Ag(NH_3)_2]}^+_{(aq)} + \mathrm{Cl}^-_{(aq)}$$

The equilibrium constant for the overall reaction may be computed by multiplying the stepwise equilibrium constants:

$$K = K_f \cdot K_{sp} = 2.4 \times 10^{-3}$$

This problem deals with 2 simultaneous equilibria and may be considered a multiple equilibria problem that requires the use of the techniques from the next section. However, by making reasonable assumptions, we may solve the equilibria through the ICE table. The assumption that we will make here is that all the silver in the solution is complexed in the form of $[Ag(NH_3)_2]^+$. This is because the silver concentration is very low, ammonia is in large excess and the formation constant $K_f = 1.5 \times 10^7$ is very large. Thus we may just solve the overall equation using the ICE table (Table 2.14), noting that we do not consider the activity of solids as they are treated as 1:

Table 2.14. ICE table for the overall equation after making reasonable assumptions.

Reaction	$\mathbf{AgCl_{(s)}}$	+	$\mathbf{2\ NH_{3(aq)}}$	$\rightleftharpoons$	$\mathbf{[Ag(NH_3)_2]^+_{(aq)}}$	+	$\mathbf{Cl^-_{(aq)}}$
Initial	—		1.0		0		0
Change	—		$-2x$		$+x$		$+x$
Equilibrium	—		$1.0 - 2x$		x		x

$$K_f = \frac{[Ag(NH_3)_2^+][Cl^-]}{[NH_3]^2} = \frac{x^2}{(1.0-2x)^2} = 2.4 \times 10^{-3}$$

We may find the molar solubility, x, as:

$$x = 0.045\ \mathrm{mol \cdot dm^{-3}}$$

This is significantly larger than the original solubility of $1.3 \times 10^{-5}\ \mathrm{mol \cdot dm^{-3}}$. The solubility of silver chloride has been significantly increased by the addition of ammonia through the formation of the diammine silver(I) complex.

2.2.8 *Mass and charge balance in multiple equilibria*

When dealing with complex systems with multiple equilibria, it is more difficult to apply the ICE table that is mentioned above. Instead, we make use of the overall conditions of the system to help us establish more equations and solve the equilibria.

To demonstrate the concepts, we will be considering a multiprotic acid H_3PO_4, with $pK_{a1} = 2.16$, $pK_{a2} = 7.21$ and $pK_{a3} = 12.32$, and trying to find the pH of $1.0\ \mathrm{mol \cdot dm^{-3}}$ Na_3PO_4. We may first establish the basic equilibrium equations based on the acid dissociation constants and the ionic product for water, as shown in Table 2.15.

Table 2.15. Acid dissociation reactions and equilibrium constants for phosphoric acid.

Reaction	**Equation**
$H_3PO_4 \rightleftharpoons H^+ + H_2PO_4^-$	$K_{a1} = \frac{[H^+][H_2PO_4^-]}{[H_3PO_4]} = 10^{-2.16}$
$H_2PO_4^- \rightleftharpoons H^+ + HPO_4^{2-}$	$K_{a2} = \frac{[H^+][HPO_4^{2-}]}{[H_2PO_4^-]} = 10^{-7.21}$
$HPO_4^{2-} \rightleftharpoons H^+ + PO_4^{3-}$	$K_{a3} = \frac{[H^+][PO_4^{3-}]}{[HPO_4^{2-}]} = 10^{-12.32}$
$H_2O \rightleftharpoons H^+ + OH^-$	$K_w = [H^+][OH^-] = 10^{-14}$

Mass balance uses the condition that the total amount of substance in the reaction mixture must remain constant. This condition must be fulfilled for every species in the reaction, although it can only be used for certain species. In this case, we cannot mass balance the protons or hydroxide ions as they may be generated by the autoionisation of water. Species that do not get added or removed from the reaction mixture are phosphate ions, which may exist in the form of H_3PO_4, $H_2PO_4^-$, HPO_4^{2-} and PO_4^{3-}, and sodium ions. We may write the mass balance equations as follows:

$$[PO_4^{3-}]_0 = [H_3PO_4] + [H_2PO_4^-] + [HPO_4^{2-}] + [PO_4^{3-}] = 1.0\ \mathrm{mol \cdot dm^{-3}}$$

$$[Na^+] = 3 \times 1.0 = 3.0\ \mathrm{mol \cdot dm^{-3}}$$

$[PO_4^{3-}]_0$ is known as the **analytical concentration**, which may also be expressed as $c(PO_4^{3-})$. The analytical concentration is the concentration of the species at the start, before any equilibration occurs. The mass balance equation tells us that no matter how the equilibria establish, the total concentration of phosphate must remain the same at the end as there is no net inflow or outflow of phosphate. Since the sodium counterion does not participate in any reactions, its concentration will remain the same.

Charge balance uses the condition that all solutions must maintain charge neutrality, where the amounts of positive and negative charges are the same. Note that in solutions with a buffer, we cannot apply the charge balance condition since we are unsure of the contents of the buffer. Instead, the buffer maintains the solution at a certain pH, which gives us the proton concentration that we can use for calculation. In this case, we may write the charge balance equation as follows:

$$[Na^+] + [H^+] = [H_2PO_4^-] + 2\ [HPO_4^{2-}] + 3\ [PO_4^{3-}] + [OH^-]$$

Note that if a species has a charge of 2–, we must account for that by multiplying its concentration by 2.

Proton balance uses the condition that with reference to the original compounds, Na_3PO_4 and H_2O, the amount of protons gained and lost must be the same. Thus we are able to equate the excess protons and deficient protons to give a proton balance equation.

$$[H^+] + 3\,[H_3PO_4] + 2\,[H_2PO_4^-] + [HPO_4^{2-}] = [OH^-]$$

Note that the proton balance equation is not an independent equation and may be derived from the mass and charge balance equations. However, it may be used as an **alternative to charge balance** equation as it is usually more concise.

2.2.9 *Tips in multiple equilibria*

As we can see from above, multiple equilibria questions usually leave us with many equations with large exponentials. While writing down the equations require the use of chemistry knowledge, many believe that solving the equations just requires math skills. In fact, understanding the system allows us to **make assumptions** based on the properties of the system. These assumptions may help us significantly by simplifying the calculations.

We make assumptions by neglecting terms that are **much smaller than others in addition or subtraction equations**. When making assumptions, it is important to justify the assumption through **comparison**, not only because the term is small. That is because a small term may be significant when the other terms appearing in the equation are also small. After the equilibrium is solved through the assumptions, it is important to **check that the assumptions hold**. If they do not hold, the equilibrium must be solved again using different assumptions. Let us consider the example we have above and solve for the pH of $1.0\,\mathrm{mol \cdot dm^{-3}}\ Na_3PO_4$.

The first step is understanding the pH of the system. PO_4^{3-} that forms after dissociation is basic because it can gain protons to form HPO_4^{2-}, $H_2PO_4^-$ and H_3PO_4. Since K_{a3} of the acid is very small ($10^{-12.32}$), we will expect a lot of PO_4^{3-} to associate with H^+ and form HPO_4^{2-}, leaving the solution rather basic. In a basic solution, further association of HPO_4^{2-} is difficult since the concentration of proton is low and that K_{a2} and K_{a1} are significantly larger than K_{a3}. It is also important to consider that $[PO_4^{3-}]_0$ is $1.0\,\mathrm{mol \cdot dm^{-3}}$ and much larger than the autoionisation of water. Thus we will expect that HPO_4^{2-}, PO_4^{3-} and OH^- are the major species in the solution and the concentrations of other species are much lower. The assumptions are:

$$[H_3PO_4] \ll [HPO_4^{2-}]$$

$$[H_2PO_4^-] \ll [HPO_4^{2-}]$$

$$[H^+] \ll [OH^-]$$

Thus the mass balance and proton balance condition may be simplified to:

$$[\mathrm{HPO_4^{2-}}]+[\mathrm{PO_4^{3-}}]=1.0\ \mathrm{mol\cdot dm^{-3}}$$

$$[\mathrm{HPO_4^{2-}}]=[\mathrm{OH^-}]$$

We may proceed to solve the equations by using K_{a3} and K_w:

$$[\mathrm{PO_4^{3-}}]=\frac{K_{a3}[\mathrm{HPO_4^{2-}}]}{[\mathrm{H^+}]}$$

$$[\mathrm{OH^-}]=\frac{K_w}{[\mathrm{H^+}]}$$

Substituting the equations into the simplified mass and proton balance conditions:

$$[\mathrm{HPO_4^{2-}}]\left(1+\frac{K_{a3}}{[\mathrm{H^+}]}\right)=1.0\ \mathrm{mol\cdot dm^{-3}}$$

$$[\mathrm{HPO_4^{2-}}]=[\mathrm{OH^-}]=\frac{K_w}{[\mathrm{H^+}]}$$

Combining the 2 equations, we have:

$$\frac{K_w}{[\mathrm{H^+}]}\left(1+\frac{K_{a3}}{[\mathrm{H^+}]}\right)=1.0\ \mathrm{mol\cdot dm^{-3}}$$

$$[\mathrm{H^+}]^2-K_w[\mathrm{H^+}]-K_{a3}K_w=0$$

This is a quadratic equation that may be solved by the quadratic formula to give 2 solutions, and the negative solution must be rejected to give:

$$[\mathrm{H^+}]=7.436\times10^{-14}\ \mathrm{mol\cdot dm^{-3}}$$

$$pH=-\lg(7.436\times10^{-14})=13.1$$

The solution is highly basic as expected, which means that our basis for assumption is most likely correct, and that our assumption of $[\mathrm{H^+}]\ll[\mathrm{OH^-}]$ is certainly true. We may proceed to compute the concentration of the other species to justify the other assumptions:

$$[\mathrm{H_3PO_4}]=1.743\times10^{-18}\ \mathrm{mol\cdot dm^{-3}}$$

$$[\mathrm{H_2PO_4^-}]=1.622\times10^{-7}\ \mathrm{mol\cdot dm^{-3}}$$

$$[\mathrm{HPO_4^{2-}}]=0.1345\ \mathrm{mol\cdot dm^{-3}}$$

$$[\mathrm{PO_4^{3-}}]=0.8655\ \mathrm{mol\cdot dm^{-3}}$$

It is clear that the other two assumptions that $[\mathrm{H_3PO_4}]\ll[\mathrm{HPO_4^{2-}}]$ and $[\mathrm{H_2PO_4^-}]\ll[\mathrm{HPO_4^{2-}}]$ are valid as well.

Making assumptions should always be the preferred choice when solving multiple equilibria problems. However, for some tricky systems, it might be difficult to make the right assumptions and it is possible to solve the system of equations through the **iteration method**. We will demonstrate solving the above system through iteration, without making assumptions. We must substitute all our K_a and K_w equations into the mass and proton balance, and we have:

$$[\mathrm{H_3PO_4}]\left(1+\frac{K_{a1}}{[\mathrm{H^+}]}+\frac{K_{a1}K_{a2}}{[\mathrm{H^+}]^2}+\frac{K_{a1}K_{a2}K_{a3}}{[\mathrm{H^+}]^3}\right)=1.0\ \mathrm{mol\cdot dm^{-3}}$$

$$[\mathrm{H^+}]+[\mathrm{H_3PO_4}]\left(3+\frac{2\cdot K_{a1}}{[\mathrm{H^+}]}+\frac{K_{a1}K_{a2}}{[\mathrm{H^+}]^2}\right)=\frac{K_w}{[\mathrm{H^+}]}$$

We combine the equation, and for iteration, we must express the equation in the form of $x=f(x)$ where x is the variable which we are solving for in the equation, which is $[\mathrm{H^+}]$:

$$[\mathrm{H^+}]=\frac{K_w}{[\mathrm{H^+}]}-\frac{1.0}{\left(1+\frac{K_{a1}}{[\mathrm{H^+}]}+\frac{K_{a1}K_{a2}}{[\mathrm{H^+}]^2}+\frac{K_{a1}K_{a2}K_{a3}}{[\mathrm{H^+}]^3}\right)}\cdot\left(3+\frac{2\cdot K_{a1}}{[\mathrm{H^+}]}+\frac{K_{a1}K_{a2}}{[\mathrm{H^+}]^2}\right)$$

Firstly, we save the values of the equilibria constants in our calculator so that it will be easier to enter. Then, we have to make an initial guess for the value and key it into the calculator. In this case, we know that the solution is basic, so we guess that $[\mathrm{H^+}]=1.0\times10^{-10}\ \mathrm{mol\cdot dm^{-3}}$. The closer the initial guess to the answer, the faster the iteration will complete. If the guess is too far away from the desired answer, the iteration may not converge or converge into another answer that is undesired. Now, the calculator has saved the answer as 1.0×10^{-10}. We proceed to key in the above equation, replacing $[\mathrm{H^+}]$ with Ans, so we key:

$$\frac{K_w}{\mathrm{Ans}}-\frac{1.0}{\left(1+\frac{K_{a1}}{\mathrm{Ans}}+\frac{K_{a1}K_{a2}}{\mathrm{Ans}^2}+\frac{K_{a1}K_{a2}K_{a3}}{\mathrm{Ans}^3}\right)}\cdot\left(3+\frac{2\cdot K_{a1}}{\mathrm{Ans}}+\frac{K_{a1}K_{a2}}{\mathrm{Ans}^2}\right)$$

Every time we press enter, our value should get closer to the actual answer. When the value no longer changes, the equation is solved. In this case, our answer converges to –3.0023, which is not the root that we want as it is impossible for concentration to be negative.

A better mathematical method for approximation is the **Newton-Raphson method**. This requires us to write our equation as a standard polynomial function so that it is easily differentiable. The rearrangement of the equations is, however, rather tedious and the final equation is:

$$[\mathrm{H^+}]^5+(K_{a1}+3)[\mathrm{H^+}]^4+(2K_{a1}+K_{a1}K_{a2}-K_w)[\mathrm{H^+}]^3+(K_{a1}K_{a2}+K_{a1}K_{a2}K_{a3}-K_wK_{a1})[\mathrm{H^+}]^2$$
$$+(-K_wK_{a1}K_{a2})[\mathrm{H^+}]+(-K_wK_{a1}K_{a2}K_{a3})=0$$

This is a polynomial of the fifth power, and we generalise it to:

$$ax^5 + bx^4 + cx^3 + dx^2 + ex + f = 0$$

To iterate, we must again make an initial guess, for example, $[\mathrm{H}^+] = 1.0 \times 10^{-10}$ $\mathrm{mol \cdot dm^{-3}}$. Then, we apply the Newton's method by using the algorithm:

$$x_{n+1} = x_n - \frac{f(x_n)}{f'(x_n)}$$

We will key into the calculator:

$$\mathrm{Ans} - \frac{a \cdot \mathrm{Ans}^5 + b \cdot \mathrm{Ans}^4 + c \cdot \mathrm{Ans}^3 + d \cdot \mathrm{Ans}^2 + e \cdot \mathrm{Ans} + f}{5a \cdot \mathrm{Ans}^4 + 4b \cdot \mathrm{Ans}^3 + 3c \cdot \mathrm{Ans}^2 + 2d \cdot \mathrm{Ans} + e}$$

Where the coefficients a, b, c, d, e, f follow from the final equation and should be saved values in the calculator. This converges to the answer in 13 iterations and we have:

$$[\mathrm{H}^+] = 7.436 \times 10^{-14}\ \mathrm{mol \cdot dm^{-3}}$$

The solution is correct and same as what we obtained by making assumptions. We do see that making assumptions is still a much more reliable and efficient method to solve the multiple equilibria. We should always strive to make assumptions before solving the equations mathematically.

2.3 Thermodynamics of Phase Transitions

In this chapter, we explore the phases of pure substances and their transformations. This is a simple application of the concepts from thermodynamics into chemistry. We will discuss the different processes of phase transitions using the theories from thermodynamics, focusing on applying the Gibbs energy to explain the spontaneity of phase transitions. We shall learn to interpret phase diagrams that provide us with information about the thermodynamic conditions for phase equilibria and transitions of a pure substance.

2.3.1 *Phase transitions and equilibria of pure substances*

To discuss phase equilibria, we must first define a **phase**. A phase is any physically distinct, homogeneous part of a system. Rigorously, a phase can be defined as:

> A form of matter having **uniform chemical composition** and **uniform state of aggregation** on both microscopic and macroscopic length scales.

A phase must be uniform and homogenous throughout. Homogenous mixtures and solutions are considered as a single phase, such as salt water, as long as the salt is fully dissolved in the water. However, suspensions and emulsions (such as milk, an emulsion of fats and water) are heterogeneous and considered separate phases.

A pure substance may have different phases in the same state. As we will see later, ice has ten different solid states when at different temperatures and pressures. Another example would be carbon, which can exist as both graphite and diamond, two different solid phases.

A **phase transition** is the spontaneous conversion of one phase into another, that occurs at a specific temperature for a given pressure. Across phases, the mass of the substance is constant with a change in volume, leading to a **change in density**. Phase transition is driven by the **minimisation of Gibbs energy**, as we will justify later. At the phase transition temperature and pressure, the different phases will co-exist and be in the state of **phase equilibrium**, which means that the chemical potential of the substance is the same for all the phases in equilibria. This can be justified by assuming otherwise, when one phase has a higher chemical potential than the other phase $(\mu_1 > \mu_2)$. Then, a transfer of $\mathrm{d}n$ of the substance from phase 1 to 2 will be accompanied by a change in Gibbs energy $\mathrm{d}G = (\mu_2 - \mu_1)\mathrm{d}n < 0$, a spontaneous change, indicating that the system is yet to achieve equilibrium.

Next, we will continue to look at the different phase transitions and the properties of phase transitions. There are 6 types of phase transitions between the three states, and there may be more than one phase in a state. Firstly, let us consider the 6 types of phase transitions between states shown in Table 2.16.

Table 2.16. All 6 types of phases transitions and their properties.

Phase transitions	**Change in state**	**Heat**	**Sign of ΔH_{trn}**
Fusion	Solid to Liquid	Absorbed	+
Freezing	Liquid to Solid	Released	−
Vaporisation	Liquid to Gas	Absorbed	+
Condensation	Gas to Liquid	Released	−
Sublimation	Solid to Gas	Absorbed	+
Deposition	Gas to Solid	Released	−

Although there is heat absorbed and released during phase transitions, **the temperature does not change** during the phase transition. As we learnt in thermodynamics, the kinetic energy is dependent only on the temperature. Thus, the kinetic energy does not change during phase transitions. Instead, the **heat energy changes the potential energy** of the substance by changing the average intermolecular distances. During phase transitions with significant change in volume (usually between a condensed phase and a gaseous phase), gaseous PV-work is also done.

Next, we will take a look at a case study on **liquid-vapour phase equilibria**. In a closed container, the liquid will vaporise while the gas will condense. At dynamic equilibrium, the rate of condensation is the same as the rate of vaporisation. The **equilibrium vapour pressure** is defined as the pressure of the vapour in equilibrium with the liquid inside a closed vessel and it is a **function of temperature**. At the same temperature, if we reduce the pressure in the container by increasing the volume, the liquid will vaporise more to restore the vapour pressure to the equilibrium vapour pressure, unless there is insufficient number of moles of substance in the container. For water, we may calculate the **relative humidity** ($RH\%$) of air-water mixture at a given temperature as follows:

$$RH\%(T) = \frac{p_{\text{water vapour, actual}}}{p_{\text{water vapour, equilibrium}}(T)} \times 100\%$$

2.3.2 *Phase diagrams of pure substances*

The phase diagram is a **Pressure against Temperature graph** that describes the information about the phases of the substance, showing the regions of pressure and temperature where the various phases are thermodynamically stable. While a phase diagram may be plotted based on any two thermodynamic variables (such as volume against temperature), we will only study the most commonly plotted phase diagrams based on pressure and temperature.

As an example, we will start by studying the phase diagram of carbon dioxide shown in Figure 2.3.1, which is the most representative phase diagram.

Each phase is represented by an **area** in the phase diagram. The substance will be in the phase when its pressure and temperature marks a point that falls within the area of the phase. The **lines** on the phase diagram represent phase boundaries,

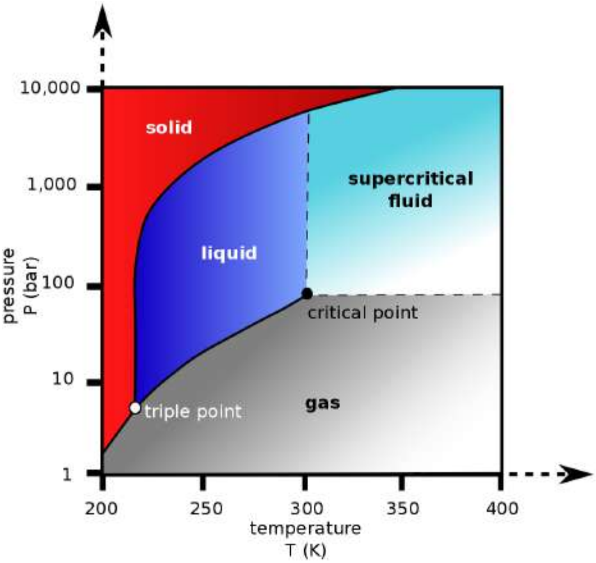


Figure 2.3.1. Phase diagram of carbon dioxide.

separating the phases. At the pressures and temperatures corresponding to points on the phase boundaries, the two phases are in phase equilibria, which means that the two phases have equal chemical potential. The **standard melting point** and **standard boiling point** of a substance is defined as the phase equilibria temperature between solid and liquid phase and liquid and gas phase respectively at **standard pressure** ($p^0 = 1 \text{ bar}$). At **atmospheric pressure**, the phase equilibria temperatures are known as the **normal melting point** and **normal boiling point**. The **triple point** is the temperature and pressure where three phases of the substance have the same chemical potential and thus coexist in equilibrium. Substances exist as **supercritical fluid** when it has a temperature higher than **critical point** temperature and a pressure higher than critical point pressure. It is when the liquid and vapour phases of the substance have the **same density** and thus become one single phase. While there are many processes that can be carried out to bring the pressure and temperature high enough for the substance to exist in supercritical fluid phase, we will describe a process where the substance is brought to the critical point following the liquid-vapour phase boundary.

We start from the substance being in liquid and vapour phase equilibrium in a **rigid closed vessel**. The volume of the vessel is fixed and chosen to maintain the two phases in equilibrium. As we heat the vessel slowly, the pressure and temperature will increase together, following the phase boundary exactly. The density of the liquid phase decreases slowly due to thermal expansion while the density of the vapour phase increases rapidly due to the increase of the equilibrium vapour pressure with temperature. At the critical point, the density of the two phases are equal and the phase boundaries disappear. The two phases become one phase, which is known as supercritical fluid.

The **phase rule** gives us the number of parameters that can be varied independently while the number of phases in equilibrium is preserved.

$$F = C - P + 2 - R$$

Where:

F is the number of parameters that can be varied independently, also known as the number of independent intensive variables needed to specify the intensive state of the system.

C is the number of components, which are chemically independent constituents of a system.

P is the number of phases in equilibrium.

R is the number of added constraints, which is usually zero.

Let us apply the phase rule to the phase diagram that we have just studied. As we only consider pure substances, $C = 1$. When the substance is in a single phase, $P = 1$. In this case, $F = 1 - 1 + 2 = 2$, and two intensive variables may be varied to preserve the number of phases in equilibrium. Both the temperature and pressure can be varied (as long as it is within the region of the phase), and the substance will still remain in the same phase. If the substance is at a phase boundary, two phases are in phase equilibria such that $P = 2$ and $F = 1 - 2 + 2 = 1$. Only one intensive variable may be changed and the other variable will change accordingly. For example, at any certain pressure, there is a corresponding temperature where the substance will be in phase equilibrium. Finally, at the triple point, three phases are in phase equilibria and $P = 3$. $F = 1 - 3 + 2 = 0$, which means that no intensive variable may be varied. As expected, the triple point of any substance occurs at a specific temperature and pressure. The critical point is where the liquid and vapour phases are in equilibrium, but there is an additional constraint that the densities of liquid and vapour are equal ($R = 1$), thus $F = 1 - 2 + 2 - 1 = 0$ and the critical point occurs only at a specific temperature and pressure.

Now that we understand how the phase rule works, we have to rationalise this general rule. In the case of one component systems with two phases α and β in phase equilibrium, we can write:

$$\mu_\alpha(p,T) = \mu_\beta(p,T)$$

This is one equation relating the two variables such that only one variable may be varied. If three phases α, β and γ are in equilibrium, we have:

$$\mu_\alpha(p,T) = \mu_\beta(p,T) = \mu_\gamma(p,T)$$

This gives us two equations $\mu_\alpha(p,T) = \mu_\beta(p,T)$ and $\mu_\beta(p,T) = \mu_\gamma(p,T)$ to solve for the two variables. Thus in this case the two variables have specific solutions. We have to move on to generalise this rule, beyond one component systems. We consider the intensive variables: Pressure, p, temperature, T and the mole fraction of each component in a multicomponent system χ_J. To specify the composition of the system, we must specify $C - 1$ mole fractions of the components, since we know the sum of mole fractions must be 1. As each component may exist in any of the P phases, the total number of such variables to specify composition is $P(C - 1)$. Thus we utilise $2 + P(C - 1)$ intensive variables to specify the intensive state of a general system. When P phases are in equilibrium, we have $\mu_\alpha(p,T) = \mu_\beta(p,T) = \mu_\gamma(p,T)\ldots$ for P phases with P terms, which gives us $P - 1$ independent equations for each component. With a total of C components, the total number of independent equations is $C(P - 1)$. Each equation reduces our freedom to vary one intensive variable, such that the total number of intensive variables we may vary is:

$$F = 2 + P(C - 1) - C(P - 1) = C - P + 2$$

This gives us the phase rule.

2.3.3 *Slopes of phase boundaries*

At any given temperature and pressure, the most stable phase is the phase with the minimum chemical potential, μ. From thermodynamics, we have learnt that:

$$\mathrm{d}\mu - \mathrm{d}G_m = V_m\mathrm{d}p - S_m\mathrm{d}T$$

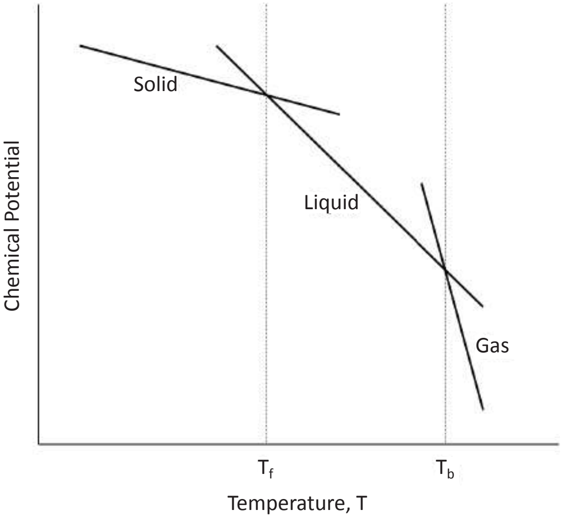


Figure 2.3.2. Graph of chemical potential against temperature for the three phases.

Now we will look at the cases where we vary temperature with constant pressure and where we vary pressure with constant temperature.

When **pressure is constant and temperature is varied**, we consider:

$$\left(\frac{\mathrm{d}\mu}{\mathrm{d}T}\right)_p = -S_m$$

From this equation, we are able to plot the graph of chemical potential against temperature at constant pressure, as shown in Figure 2.3.2.

Since the gas phase has the greatest entropy, followed by the liquid phase, and the solid phase with the least entropy, the gradient of the chemical potential against temperature line is steepest for gas, followed by liquid and then solid. This explains why gaseous state is the most stable at high temperatures. The intersections between the graph represent the temperatures in which the phases are in equilibrium at the pressure where this graph is plotted, and are labelled as the boiling point and melting point of the substance at that pressure.

When **temperature is constant and pressure is varied**, we consider:

$$\left(\frac{\mathrm{d}\mu}{\mathrm{d}p}\right)_T = V_m$$

From this equation, we are able to plot the graph of chemical potential against pressure at constant temperature, as shown in Figure 2.3.3.

Similarly, we observe that for most substances, the molar volume of the gas is the greatest, followed by liquid and finally solid, and the gradient of the lines follow this trend. However, some special substances have greater density in the liquid state

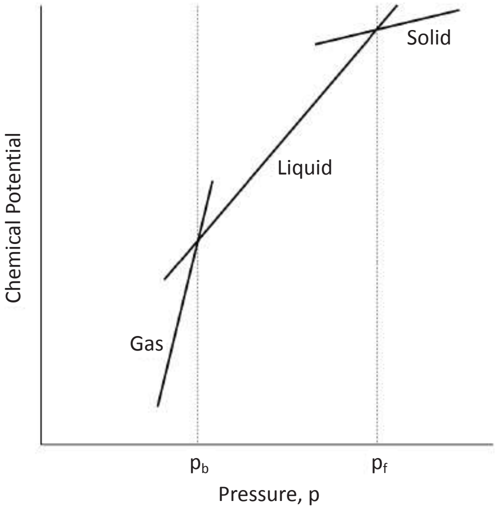


Figure 2.3.3. Graph of chemical potential against pressure for the three phases.

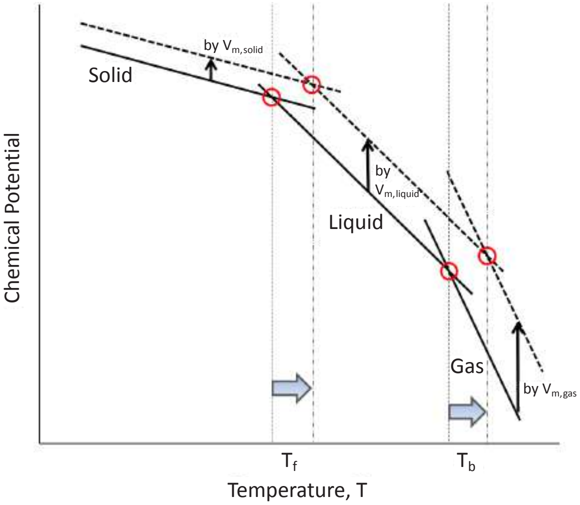


Figure 2.3.4. Graph of chemical potential against temperature reacting to a pressure change.

than solid state. As we combine our observations from the two graphs, we will try to derive the phase diagram.

The phase diagram is a pressure against temperature graph, and we can obtain it by considering the chemical potential against temperature graph at different pressures. When pressure is increased, the chemical potential of the different phases will increase to different extents, depending on V_m. For most substances, we will obtain the chemical potential against temperature graph shown in Figure 2.3.4.

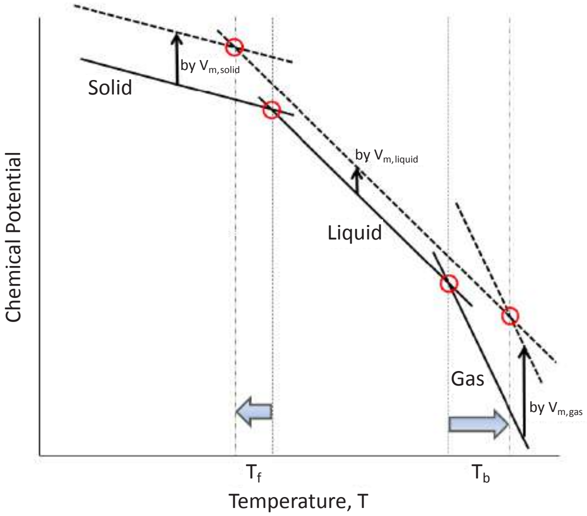


Figure 2.3.5. Graph of chemical potential against temperature reacting to a pressure change for the exceptional cases.

Note that the circled points represent points where the two phases are in equilibrium, and by joining them together, we may obtain the phase boundaries in the phase diagram. For some substances, namely **water**, **gallium** and **bismuth**, they have special packing in solid state such that the solid state is less dense than the liquid state. For water, we know that expansion starts occurring when water is cooled below 4°C. This means that $V_{m,(s)} > V_{m,(l)}$, and we obtain a different graph as shown in Figure 2.3.5.

Notice that the solid-liquid phase boundary now has a negative gradient. For these three special molecules, they have a **negative solid-liquid phase boundary** in their phase diagram. From our understanding of phase diagrams, we deduce that when pressure is increased, there is boiling point elevation and melting point elevation (melting point depression for water, gallium and bismuth).

2.3.4 *Clapeyron equation*

While the phase diagram provides us with an intuitive and clear representation of phase boundaries, we need to find the equations of the phase boundaries for accurate calculation, which is $\frac{dp}{dT}$. This can be done by first using the fact that the chemical potential of two phases at the phase boundary must be equal. Considering two general phases α and β, we have:

$$\mu_\alpha(p,T) = \mu_\beta(p,T)$$

Since $d\mu = dG_m = V_m dp - S_m dT$, at another point on the phase boundary with a small change in pressure dp and temperature dT, we have:

$$-S_{m,\alpha}dT + V_{m,\alpha}dp = -S_{m,\beta}dT + V_{m,\beta}dp$$

Grouping $\mathrm{d}p$ and $\mathrm{d}T$ to obtain $\frac{\mathrm{d}p}{\mathrm{d}T}$,

$$(V_{m,\beta} - V_{m,\alpha})\mathrm{d}p = (S_{m,\beta} - S_{m,\alpha})\mathrm{d}T$$

Finally, we arrive at the **Clapeyron equation**:

$$\frac{\mathrm{d}p}{\mathrm{d}T} = \frac{\Delta S_{m,\mathrm{trn}}}{\Delta V_{m,\mathrm{trn}}}$$

Where:

$$\Delta S_{m,\mathrm{trn}} = S_{m,\beta} - S_{m,\alpha}$$

$$\Delta V_{m,\mathrm{trn}} = V_{m,\beta} - V_{m,\alpha}$$

We will now solve the exact Clapeyron equation for the different phase boundaries by making approximations. We first use the macroscopic definition of entropy that $\Delta S_{m,\mathrm{trn}} = \frac{\Delta H_{m,\mathrm{trn}}}{T}$,

$$\frac{\mathrm{d}p}{\mathrm{d}T} = \frac{\Delta S_{m,\mathrm{trn}}}{\Delta V_{m,\mathrm{trn}}} = \frac{\Delta H_{m,\mathrm{trn}}}{T\Delta V_{m,\mathrm{trn}}}$$

This equation will allow us to determine the **relative densities of the various phases** based on the **gradient of the phase boundary**. Considering the sign of each variable in the equation for each phase boundary, we can find the sign of $\Delta V_{m,\mathrm{trn}}$ and since mass does not change during phase transition, a positive $\Delta V_{m,\mathrm{trn}}$ will indicate a decrease in density through the phase transition and a negative $\Delta V_{m,\mathrm{trn}}$ will indicate an increase in density through the phase transition. A more convenient method to rank the densities of the different phases is to make use of the fact that a **denser phase is more condensed and therefore more stable at a higher pressure**.

For the **solid-liquid phase boundary**, the phase transition is fusion, and we write:

$$\frac{\mathrm{d}p}{\mathrm{d}T} = \frac{\Delta H_{m,\mathrm{fus}}}{T\Delta V_{m,\mathrm{fus}}}$$

We may **assume that $\Delta H_{m,\mathrm{fus}}$ and $\Delta V_{m,\mathrm{fus}}$ are constant with temperature**. This is because enthalpy is relatively constant over a small range of temperatures and the volumes of condensed phases change very little with temperature. Using the assumptions, we may proceed to solve the differential equation:

$$\int_{p_1}^{p_2} \mathrm{d}p = \frac{\Delta H_{m,\mathrm{fus}}}{\Delta V_{m,\mathrm{fus}}} \int_{T_1}^{T_2} \frac{1}{T} \mathrm{d}T$$

$$p_2 - p_1 = \frac{\Delta H_{m,\mathrm{fus}}}{\Delta V_{m,\mathrm{fus}}} \ln\left(\frac{T_2}{T_1}\right) = \frac{\Delta H_{m,\mathrm{fus}}}{\Delta V_{m,\mathrm{fus}}} \ln\left(\frac{T_1 + \Delta T}{T_1}\right) = \frac{\Delta H_{m,\mathrm{fus}}}{\Delta V_{m,\mathrm{fus}}} \ln\left(1 + \frac{\Delta T}{T_1}\right)$$

We may use the Taylor series to expand $\ln\left(1 + \frac{\Delta \mathrm{T}}{T_1}\right) = \frac{\Delta \mathrm{T}}{T_1} - \frac{1}{2}\left(\frac{\Delta \mathrm{T}}{T_1}\right)^2 + \cdots$

Assuming that $\frac{\Delta \mathrm{T}}{T_1}$ is small, $\frac{\Delta \mathrm{T}}{T_1} \ll 1$, we may approximate $\ln\left(1+\frac{\Delta \mathrm{T}}{T_1}\right) \approx \frac{\Delta \mathrm{T}}{T_1}$ and:

$$p_2 - p_1 = \frac{\Delta H_{m,\mathrm{fus}}}{\Delta V_{m,\mathrm{fus}}} \frac{\Delta T}{T_1}$$

From this equation, we can see that the solid-liquid phase boundary is **linear**.

For the **liquid-vapour phase boundary**, the phase transition is vaporisation, and we write:

$$\frac{\mathrm{d}p}{\mathrm{d}T} = \frac{\Delta H_{m,\mathrm{vap}}}{T \Delta V_{m,\mathrm{vap}}}$$

Since the phase transition is from a condensed phase to vapour phase, we have:

$$\Delta V_{m,\mathrm{vap}} = V_{m,(g)} - V_{m,(l)} \approx V_{m,(g)}$$

We assume that the **volume of the liquid is much smaller than the volume of the vapour**. We also assume that $\boldsymbol{\Delta H_{m,\mathrm{vap}}}$ **is constant with temperature** and that the **vapour behaves as a perfect gas**, such that $V_{m,(g)} = \frac{RT}{p}$. This allows us to write:

$$\frac{\mathrm{d}p}{\mathrm{d}T} = \frac{\Delta H_{m,\mathrm{vap}}}{T \Delta V_{m,\mathrm{vap}}} = \Delta H_{m,\mathrm{vap}} \frac{p}{RT^2}$$

We may proceed to solve this differential equation by variable separation:

$$\int_{p_1}^{p_2} \frac{1}{p} \mathrm{d}p = \frac{\Delta H_{m,\mathrm{vap}}}{R} \int_{T_1}^{T_2} \frac{1}{T^2} \mathrm{d}T$$

Applying the laws of integration, we have:

$$\ln\left(\frac{p_2}{p_1}\right) = -\frac{\Delta H_{m,\mathrm{vap}}}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right)$$

Here, we see that the liquid-vapour phase boundary is no longer linear, and follows a **curve**.

We may apply the same considerations to the **solid-vapour phase boundary**, only that we use $\Delta H_{m,\mathrm{sub}}$ instead for the sublimation enthalpy. We have:

$$\ln\left(\frac{p_2}{p_1}\right) = -\frac{\Delta H_{m,\mathrm{sub}}}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right)$$

2.4 Thermodynamics of Mixtures

In the previous chapter, we have dealt exclusively with pure substances and their phase transitions. However, many chemical systems consist of multiple substances, and we will now move on to study the properties of such mixtures. During our discussion in chapter 2.2 (chemical equilibria), we have spent a lot of effort characterising mixtures with the concept of chemical potential. In this chapter, we will continue to explore the properties of mixtures using chemical potential and consider the colligative properties of mixtures. Finally, we will look at the phase diagrams for binary mixtures, which are mixtures of two substances.

2.4.1 *Ideal solutions and Raoult's law*

Background 2h. Mixtures and solutions

If we put any substances together, we can form a **mixture**. If we are able to mix these substances together homogenously to form a uniform mixture, it is known as a **solution**. A solution can be formed with mixtures of substances in any phase, but we will focus our discussion in this chapter on liquid mixtures.

In chapter 2.1, we have mentioned that we will refer to gases as perfect gases instead of ideal gases to avoid confusion with ideal solutions. For a perfect gas, we have assumed that the volume of the gas molecules is negligible and that the interactions among the gas molecules are negligible. In a condensed phase, it is not possible to ignore the size of the molecules and the interactions between the molecules. Without intermolecular interactions, condensed phases such as liquid and solid will not be possible. Thus we state the **assumptions for an ideal solution**:

The interactions between all the components of an ideal solution are equal. For a binary solution of A and B, we are assuming that the intermolecular interactions between A-A, A-B and B-B are all equal.

The rigorous definition of ideal solution stems from Raoult's law, which we will move on to explain. Raoult's law is used to find the partial vapour pressures of components in an ideal solution. We may start by defining new quantities for pure substances as opposed to substances in solutions. We will use the * to denote quantities for pure substances. For example, μ_{A}^* is the chemical potential of pure A and p_{A}^* as the vapour pressure of pure A. We understand that the rates of vaporisation (r_{vap}^*) and condensation (r_{cond}^*) on the surface of a pure liquid can be represented by the following equations:

$$r_{\mathrm{vap}}^* = k_{\mathrm{vap}} S$$

$$r_{\mathrm{cond}}^* = k_{\mathrm{cond}} S p^*$$

Where S is the surface area of the liquid. The equations are relating the rate of vaporisation of the liquid to the surface area (which is the amount of molecules exposed to the air and able to escape into vapour phase) and relating the rate of condensation to the surface area and the partial pressure of the vapour. At dynamic equilibrium, the rates of vaporisation and condensation are equal.

$$r^*_{\mathrm{vap}} = r^*_{\mathrm{cond}}$$

$$k_{\mathrm{vap}} S = k_{\mathrm{cond}} S p^*$$

Rearranging to find the expression for p^*, we have:

$$p^* = \frac{k_{\mathrm{vap}}}{k_{\mathrm{cond}}}$$

If we reconsider the vaporisation and condensation of this liquid in an ideal solution, we write:

$$r_{\mathrm{vap}} = k_{\mathrm{vap}} S x$$

$$r_{\mathrm{cond}} = k_{\mathrm{cond}} S p$$

Note that the mole fraction of liquid, x, is taken into consideration when considering the rate of vaporisation, because only this fraction of the surface is available for the liquid to escape. In an ideal solution, the surface area available for evaporation can be taken to be shared equally among the components and the strength of intermolecular interactions are taken to be equal. The rate of condensation will depend on the **partial vapour pressure** of the liquid in equilibrium with the solution, which will change due to the change in rate of vaporisation. We notice that $x < 1$ and that the rate of vaporisation is reduced, thus we expect the partial vapour pressure of the liquid in a solution to be reduced. Indeed, we may use the dynamic equilibrium condition to find that:

$$k_{\mathrm{vap}} S x = k_{\mathrm{cond}} S p$$

$$p = x\left(\frac{k_{\mathrm{vap}}}{k_{\mathrm{cond}}}\right) = x p^*$$

This gives us **Raoult's law**, which we may write generally for some liquid A as a component of an ideal solution:

$$p_{\mathrm{A}} = x_{\mathrm{A}} p^*_{\mathrm{A}}$$

Using Raoult's law, we may calculate the chemical potential of liquids in ideal solutions and use it as a more rigorous definition of ideal solution. We have learnt from chapter 2.2 that the chemical potential of vapour can be given by:

$$\mu_{\mathrm{J}} = \mu^0_{\mathrm{J}} + RT\ln\left(\frac{p_{\mathrm{J}}}{p^0}\right)$$

For pure liquid J in liquid-vapour equilibrium with vapour J we may write:

$$\mu^*_{\mathrm{J,\,liq}} = \mu^*_{\mathrm{J,\,vap}} = \mu^*_{\mathrm{J}} + RT\ln\left(\frac{p^*_{\mathrm{J}}}{p^0}\right)$$

When liquid J is in solution, at liquid-vapour equilibrium, the chemical potential of J in solution is equal to the chemical potential of its vapour. We may write:

$$\mu_{\mathrm{J,\,sol}} = \mu_{\mathrm{J,\,vap}} = \mu^0_{\mathrm{J}} + RT\ln\left(\frac{p_{\mathrm{J}}}{p^0}\right)$$

Using Raoult's law for ideal solutions $p_{\mathrm{J}} = x_{\mathrm{J}}p^*_{\mathrm{J}}$, we have:

$$\mu_{\mathrm{J,\,sol}} = \mu^0_{\mathrm{J}} + RT\ln\left(\frac{x_{\mathrm{J}}p^*_{\mathrm{J}}}{p^0}\right) = \mu^0_{\mathrm{J}} + RT\ln\left(\frac{p^*_{\mathrm{J}}}{p^0}\right) + RT\ln x_{\mathrm{J}}$$

Note that $\mu^*_{\mathrm{J}} = \mu^0_{\mathrm{J}} + RT\ln\left(\frac{p^*_{\mathrm{J}}}{p^0}\right)$, thus we may substitute it into the equation and obtain:

$$\mu_{\mathrm{J,\,sol}} = \mu^*_{\mathrm{J,\,liq}} + RT\ln x_{\mathrm{J}}$$

Since $x_{\mathrm{J}} < 1$, $\ln x_{\mathrm{J}} < 0$, thus we see that the **chemical potential of a component is lower in the solution than that in the pure liquid**. This important result brings us to the rigorous definition of an ideal solution, which is a solution where the chemical potential of its components may be expressed as $\mu_{\mathrm{J,\,sol}} = \mu^*_{\mathrm{J,\,liq}} + RT\ln x_{\mathrm{J}}$.

From Raoult's law, we can consider a theoretical binary solution of A and B such that:

$$p_{\mathrm{A}} = x_{\mathrm{A}}p^*_{\mathrm{A}}$$

$$p_{\mathrm{B}} = x_{\mathrm{B}}p^*_{\mathrm{B}}$$

We want to find the molar fractions of A and B in the vapour phase, which we will denote as y_{A} and y_{B}. This can be determined by:

$$y_{\mathrm{A}} = \frac{p_{\mathrm{A}}}{p_{\mathrm{A}} + p_{\mathrm{B}}}$$

$$y_{\mathrm{B}} = \frac{p_{\mathrm{B}}}{p_{\mathrm{A}} + p_{\mathrm{B}}}$$

For the purpose of understanding distillation and binary phase diagrams in the later parts of this chapter, we will move on to show that if $p^*_{\mathrm{A}} > p^*_{\mathrm{B}}$, then $y_{\mathrm{A}} > x_{\mathrm{A}}$.

$$y_{\mathrm{A}} = \frac{p_{\mathrm{A}}}{p_{\mathrm{A}} + p_{\mathrm{B}}} = \frac{x_{\mathrm{A}}p^*_{\mathrm{A}}}{x_{\mathrm{A}}p^*_{\mathrm{A}} + x_{\mathrm{B}}p^*_{\mathrm{B}}}$$

Since $x_A + x_B = 1$,

$$y_A = \frac{x_A p_A^*}{x_A p_A^* + (1 - x_A) p_B^*} = \frac{x_A p_A^*}{x_A (p_A^* - p_B^*) + p_B^*}$$

We want to show that:

$$y_A = \frac{x_A p_A^*}{x_A (p_A^* - p_B^*) + p_B^*} > x_A$$

$$\frac{p_A^*}{x_A (p_A^* - p_B^*) + p_B^*} > 1$$

$$p_A^* > x_A (p_A^* - p_B^*) + p_B^*$$

$$p_A^* - p_B^* > x_A (p_A^* - p_B^*)$$

Since $x_A < 1$ in a solution, this equation holds true. We have shown that the mole fraction of the more volatile component is higher in the vapour phase than the liquid phase, or more simply that the **more volatile component is enriched in the vapour phase**. It is incorrect to write that the vapour pressure in the vapour phase is higher for the more volatile component, as it depends on the relative amount of each component.

For ideal solutions, we may derive the change in thermodynamic variables for the process of mixing. We will start by considering the Gibbs energy change of mixing two liquids A and B. Before mixing, we may find the Gibbs energy of the pure liquids as follows:

$$G_{\text{pure}} = n_A \mu_A^* + n_B \mu_B^*$$

After mixing and assuming that the solution is ideal, we may find the new chemical potential of the liquid in solution using the equation derived above:

$$\mu_{J,\text{sol}} = \mu_{J,\text{liq}}^* + RT \ln x_J$$

This gives us the total Gibbs energy after mixing as:

$$G_{\text{sol}} = n_A \mu_{A,\text{sol}} + n_B \mu_{B,\text{sol}} = n_A (\mu_A^* + RT \ln x_A) + n_B (\mu_B^* + RT \ln x_B)$$

We may find the change in Gibbs energy:

$$\Delta G_{\text{mix}} = G_{\text{sol}} - G_{\text{pure}} = RT (n_A \ln x_A + n_B \ln x_B)$$

If we express $n_A = x_A n$ and $n_B = x_B n$ then we have:

$$\Delta G_{\text{mix}} = nRT (x_A \ln x_A + n_B \ln x_B)$$

The mixing of two liquids is a spontaneous process because $x_A, x_B < 1$ and $\ln x_A, \ln x_B < 0$ such that $\Delta G_{\text{mix}} < 0$.

From the previous chapter, we have seen that $\mathrm{d}G = V\mathrm{d}p - S\mathrm{d}T$, and we can write:

$$\left(\frac{\partial G_{\text{mix}}}{\partial T}\right)_p = -S$$

$$\Delta S_{\text{mix}} = -\left(\frac{\partial G_{\text{mix}}}{\partial T}\right)_p = -nR\,(x_{\text{A}} \ln x_{\text{A}} + n_{\text{B}} \ln x_{\text{B}}) > 0$$

This is consistent with the second law of thermodynamics, where entropy increases for mixing of liquids. We may derive the overall enthalpy change of the process to be zero:

$$\Delta H_{\text{mix}} = \Delta G_{\text{mix}} + T\Delta S_{\text{mix}} = 0$$

This can be rationalised as there is no heat released or added into the system during the mixing process since the interactions between the liquids are equal in an ideal solution. Similarly, due to the equal intermolecular interactions, the volume does not change during the mixing:

$$\Delta V_{\text{mix}} = \left(\frac{\partial G_{\text{mix}}}{\partial p}\right)_T = 0$$

2.4.2 *Real solutions and Henry's law*

Real solutions will deviate from Raoult's law because A-B intermolecular interactions are different from A-A and B-B intermolecular interactions. This gives us **positive** and **negative deviations** from ideal solutions.

The graph for the solution of carbon disulfide (CS_2) and acetone (C_3H_6O) is shown in Figure 2.4.1. We see that there is a **positive deviation** from Raoult's law. The straight lines on the graph represent the Raoult's law predicted trend while the actual measured vapour pressure is higher than the predicted vapour pressure. This means that the A-B interactions are **weaker** than the A-A and B-B interactions, thus the carbon disulfide and acetone molecules have **higher tendency to enter vapour phase**. This occurs because the large difference in polarity of carbon disulfide and acetone causes the intermolecular interactions between carbon disulfide and acetone to be weak.

On the other hand, there is a **negative deviation** from Raoult's law (for the solution of chloroform and acetone) (Figure 2.4.2). This means that the A-B interactions are **stronger** than the A-A and B-B interactions, thus the chloroform and acetone molecules have **lower tendency to enter vapour phase**. This occurs because of the strong hydrogen bonding between chloroform and acetone.

However, for a highly dilute solution, we may be able to treat the **solute** and **solvent** separately. The solute is the component in the solution with the lower mole fraction and the solvent is the component in the solution with the higher mole fraction. For a highly dilute solution, we may consider the **solvent using Raoult's**

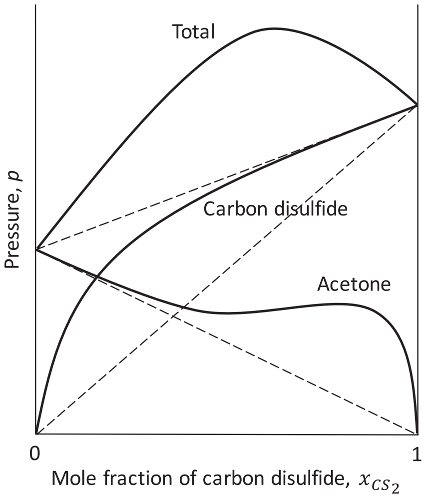


Figure 2.4.1. Graph of pressure against mole fraction for acetone and $\mathrm{CS_2}$ solution.

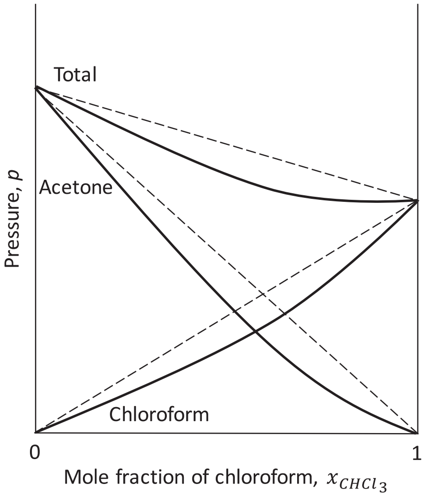


Figure 2.4.2. Graph of pressure against mole fraction for acetone and $\mathrm{CHCl_3}$ solution.

law since the solvent molecules are only in a slightly different environment from the pure liquid.

$$p_{\text{solvent}} = x_{\text{solvent}} p^*_{\text{solvent}}$$

However, the environment of the solute is largely different from an ideal solution as the solute molecules are almost entirely surrounded by solvent molecules. The solute will follow **Henry's law**:

$$p_{\text{solute}} = x_{\text{solute}} K_{\text{solute}}$$

where K_{solute} is the **Henry's constant**, which is an empirically determined constant that differs for every solute. It is determined experimentally that in highly dilute solutions, the solute vapour pressure is still proportional to its mole fraction, but with a different constant of proportionality.

Henry's Law can also be expressed using **molality** of the solute, just that the constant of proportionality is different.

$$p_{\text{solute}} = b_{\text{solute}} K_{\text{solute}}$$

Note that the two different constants of proportionality can be differentiated by their units. For the equation $p_{\text{solute}} = x_{\text{solute}} K_{\text{solute}}$, K_{solute} has the units of pressure (usually kPa) as mole fraction is dimensionless. On the other hand, for $p_{\text{solute}} = b_{\text{solute}} K_{\text{solute}}$, molality has the units $\text{mol} \cdot \text{kg}^{-1}$, thus K_{solute} has the units of $\text{kPa} \cdot \text{kg} \cdot \text{mol}^{-1}$.

In the case that the solute is a gas, the second expression of Henry's law may be used to calculate its **molar solubility**, especially because its solubility is usually low in liquids and thus the solution is highly dilute. We may calculate its solubility from molality as follows:

$$[\text{Solute}] = b_{\text{solute}} \times \rho_{\text{solvent}}$$

Note that this equation is **treating the solution as pure solvent**, which holds for highly dilute solutions. The molality of the solute can be given by Henry's Law:

$$b_{\text{solute}} = \frac{p_{\text{solute}}}{K_{\text{solute}}}$$

Thus the solubility of the gaseous solute can be written as:

$$[\text{Solute}] = \frac{p_{\text{solute}}}{K_{\text{solute}}} \times \rho_{\text{solvent}}$$

The solubility may be calculated based on the partial pressure of the gas using Henry's law.

We move on to explain the behaviour of such highly dilute solutions by using the graph in Figure 2.4.3.

We see that when $x_{\text{B}} \to 0$, the behaviour of the solution follows closely to Henry's law, as it is the solute. When $x_{\text{B}} \to 1$, the behaviour of the solution follows Raoult's law, as it is the solvent. We know such highly dilute solutions as **ideal dilute solutions**, where the **solute obeys Henry's law** and the **solvent obeys Raoult's law**.

2.4.3 *Colligative properties*

Colligative properties are properties **that depend only on the ratio of solute to solvent molecules, not the chemical nature of the solute or solvent**. We usually discuss colligative properties of a solution containing **non-volatile solutes**. Unlike the mixtures we discussed previously where both the solute and solvent are

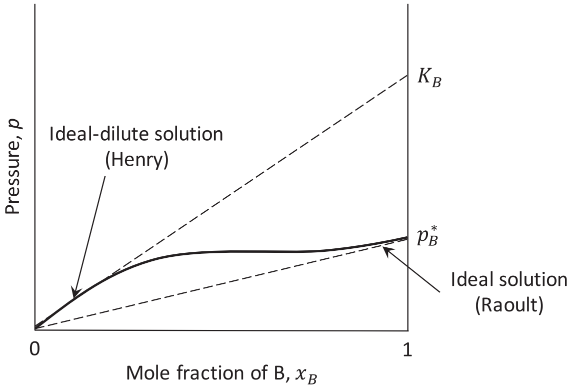


Figure 2.4.3. Graph of pressure against mole fraction for a real solution, showing the lines for Raoult's law and Henry's law.

volatile, colligative properties are properties of solutions with solutes that do not vaporise. From Raoult's law for ideal dilute solutions, we have:

$$\mu_{\text{solvent}} = \mu^*_{\text{solvent}} + RT \ln x_{\text{solvent}}$$

Since $x_{\text{solvent}} < 1$ for any solution containing solute, there is lowering of chemical potential with the addition of solute.

Since this property depends on the amount of solute present in the solution, it is important to consider the electrolytic properties of the solute if the solute is a strong electrolyte. Ideal solutes are highly soluble and do not dissociate or associate in solution, such as sucrose. Most salts are strong electrolytes that dissociate in water to generate ions and increase the amount of solute present in the solution, further lowering the vapour pressure. To account for the dissociation of electrolytes, we make use of the **van't Hoff factor** (denoted by i). The van't Hoff factor measures the amount of atoms or ions formed in solution per molecule of solute added into the solution. For non-electrolytes, the van't Hoff factor is 1. For strong electrolytes, such as soluble salts, we can estimate their van't Hoff factors through their formula unit, assuming a complete dissociation. For example, the van't Hoff factor in an ideal dilute solution of Magnesium Chloride ($MgCl_2$) will be 3, as 3 ions can be formed upon complete dissociation of $MgCl_2$ in solution. However, salts rarely fully dissociate and ion association can occur to lower the van't Hoff factor. The observed van't Hoff factor in a 0.05 mol/kg solution is 2.7 instead of 3 for $MgCl_2$.

The **3 main colligative properties** are:

1. Vapour pressure lowering

The vapour pressure will be lowered following Raoult's Law that:

$$p_{\text{solvent}} = x_{\text{solvent}} p^*_{\text{solvent}}$$

2. Boiling point elevation and freezing point depression

At a set pressure, the temperatures of phase transitions are the temperatures where the chemical potentials of the phases are equal. With the addition of solute, the chemical potential of liquid is lowered while the chemical potentials of the other phases are kept the same. This affects the temperatures of phase transitions according to the graph shown in Figure 2.4.4.

The graph shows that the addition of solute causes boiling point elevation and freezing point depression. The effect of freezing point depression is often greater than the effect of boiling point elevation due to the gradients of the chemical potentials of the phases.

We are able to derive the change in boiling point by considering the chemical potential of the new solution, if we let A be the solvent and B be the solute. We may apply Raoult's law for the solvent in an ideal dilute solution:

$$\mu_{\mathrm{A}(l)} = \mu^*_{\mathrm{A}(l)} + RT \ln x_{\mathrm{A}}$$

At the boiling point, the pure vapour and liquid in solution are in phase equilibrium with the same chemical potential:

$$\mu^*_{\mathrm{A}(g)} = \mu_{\mathrm{A}(l)}$$

Combining the 2 equations, we have:

$$\mu^*_{\mathrm{A}(g)} = \mu^*_{\mathrm{A}(l)} + RT \ln x_{\mathrm{A}}$$

$$\ln x_{\mathrm{A}} = \frac{\mu^*_{\mathrm{A}(g)} - \mu^*_{\mathrm{A}(l)}}{RT}$$

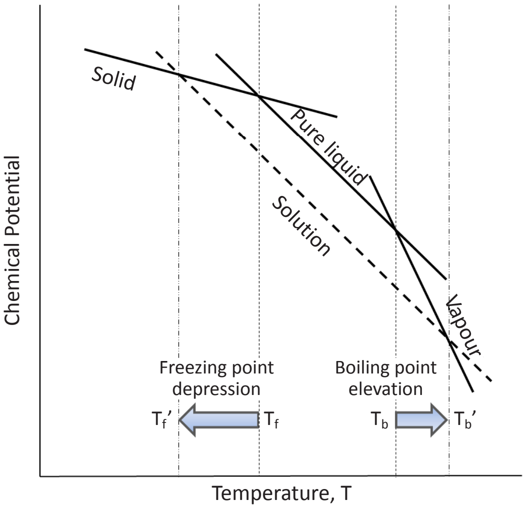


Figure 2.4.4. Graph showing change in chemical potential from liquid to solution and the resulting changes in phase equilibria temperatures.

Note that for pure substances, the chemical potential is equal to the molar Gibbs free energy:

$$\mu^*_{\mathrm{A}(g)} - \mu^*_{\mathrm{A}(l)} = G_{m(g)} - G_{m(l)} = -G_{\mathrm{vap},m}$$

$$\ln x_{\mathrm{A}} = \frac{-G_{\mathrm{vap},m}}{RT}$$

To express the change in boiling point temperature as a result of change in composition, we find:

$$\frac{\mathrm{d}\ln x_{\mathrm{A}}}{\mathrm{d}T} = \frac{1}{R}\frac{\mathrm{d}\left(\frac{-G_{\mathrm{vap},m}}{T}\right)}{\mathrm{d}T} = -\frac{-H_{\mathrm{vap},m}}{RT^2}$$

Since, referring to section 2.2.2, we have:

$$\frac{\mathrm{d}\left(\frac{G}{T}\right)}{\mathrm{d}T} = -\frac{H}{T^2}$$

Assuming that $\Delta H_{\mathrm{vap},m}$ is independent of temperature, we can solve the differential equation by variable separation:

$$\int_0^{\ln x_{\mathrm{A}}} \mathrm{d}\ln x_{\mathrm{A}} = -\frac{-H_{\mathrm{vap},m}}{R}\int_{T^*}^{T}\frac{1}{T^2}\mathrm{d}T$$

Where T^* is the boiling point of the pure liquid and T is the boiling point of the solution.

$$\ln x_{\mathrm{A}} = \frac{-H_{\mathrm{vap},m}}{R}\left(\frac{1}{T} - \frac{1}{T^*}\right)$$

Expressing in terms of the amount of solute B, we may use the relation $x_{\mathrm{B}} = 1 - x_{\mathrm{A}}$:

$$\ln(1 - x_{\mathrm{B}}) = \frac{-H_{\mathrm{vap},m}}{R}\left(\frac{1}{T} - \frac{1}{T^*}\right)$$

We may simplify the equation by making appropriate assumptions. Since the solution is an ideal dilute solution with $x_{\mathrm{B}} \ll 1$, we may use the Taylor series:

$$\ln(1 - x_{\mathrm{B}}) = -x_{\mathrm{B}} - \frac{1}{2}x_{\mathrm{B}}^2 - \frac{1}{3}x_{\mathrm{B}}^3 - \cdots \approx -x_{\mathrm{B}}$$

We may also assume that the change in boiling point is small such that $T \approx T^*$:

$$\frac{1}{T} - \frac{1}{T^*} = \frac{-\Delta T}{TT^*} \approx \frac{-\Delta T}{T^{*2}}$$

Thus we arrive at:

$$-\Delta T = \frac{RT^{*2}}{-H_{\mathrm{vap},m}}x_{\mathrm{B}}$$

Experimentally, we determine the empirical boiling point constant based on the molality of solute, b_{solute}, where:

$$b_{\text{solute}} = \frac{n_{\text{B}}}{m_{\text{A}}}$$

Since $n_{\text{A}} \gg n_{\text{B}}$, we may express:

$$x_{\text{B}} = \frac{n_{\text{B}}}{n_{\text{A}} + n_{\text{B}}} \approx \frac{n_{\text{B}}}{n_{\text{A}}}$$

Since $m_{\text{A}} = M_{\text{A}} n_{\text{A}}$,

$$x_{\text{B}} = M_{\text{A}} b_{\text{solute}}$$

$$-\Delta T = \frac{RM_{\text{solvent}} T^{*2}}{-H_{\text{vap},m}} b_{\text{solute}} = K_{\text{b}} b_{\text{solute}}$$

Where the boiling point elevation constant, K_{b}, is:

$$K_{\text{b}} = \frac{RM_{\text{solvent}} T^{*2}}{-H_{\text{vap},m}}$$

As can be seen from the equation, K_{b} depends only on the identity of the solvent and not the solute.

For general solutes, including strong electrolytes, we must consider their dissociation in solution and account for it by multiplying the van't Hoff factor, and the full equation for boiling point elevation is:

$$\Delta T_{\text{b}} = i \cdot K_{\text{b}} \cdot b_{\text{solute}}$$

For freezing point depression, we can similarly write:

$$-\Delta T_{\text{f}} = -i \cdot K_{\text{f}} \cdot b_{\text{solute}}$$

Noting that the change in freezing point is negative. The freezing point depression constant is also given as follows:

$$K_{\text{f}} = \frac{RM_{\text{solvent}} T^{*2}}{-H_{\text{fus},m}}$$

3. Osmotic pressure

Osmosis is the process of solvent molecules flowing across a semipermeable membrane from a region of lower solute concentration to higher solute concentration. This can be justified chemically as a region with higher solute concentration will have lower chemical potential, urging the solvent to flow over until the chemical potential is equal, which is when the solute concentration is the same. To prevent this influx of solvent, we may apply pressure to maintain the same chemical potential on both sides of the membrane. This pressure is known as **osmotic pressure**, Π, which may be evaluated by chemical potential:

$$\mu_A^*(p) = \mu_A(x_A, p+\Pi)$$

Using Raoult's law for ideal dilute solutions,

$$\mu_A(x_A, p+\Pi) = \mu_A^*(p+\Pi) + RT\ln x_A$$
$$-RT\ln x_A = \mu_A^*(p+\Pi) - \mu_A^*(p)$$

Recall from the fundamental equation of thermodynamics that:

$$dG = Vdp - SdT$$

Since temperature does not change, $dT = 0$ and we have:

$$dG = Vdp$$

For molar quantities,

$$dG_m = V_m dp$$

This allows us to find the change in Gibbs energy with pressure:

$$\int_p^{p+\Pi} dG_m = \int_p^{p+\Pi} V_m dp$$

Since the molar volume of a condensed state does not change with pressure,

$$G_m(p+\Pi) - G_m(p) = V_m\Pi$$

As the molar Gibbs energy is equal to chemical potential for a pure substance,

$$\mu_A^*(p+\Pi) - \mu_A^*(p) = G_m(p+\Pi) - G_m(p) = V_m\Pi$$
$$-RT\ln x_A = V_m\Pi$$

Since $x_A = 1 - x_B$ and $x_B \ll 1$, we have $\ln x_A = \ln(1-x_B) \approx -x_B$ such that:

$$RTx_B = V_m\Pi$$

We may approximate $x_B \approx \frac{n_B}{n_A}$ since $n_B \ll n_A$, noting that $n_A V_m = V$, we have:

$$\Pi = \frac{n_{\text{solute}}RT}{V}$$

2.4.4 *Phase diagrams of binary solutions*

With binary solutions of 2 volatile components, we need to consider the composition in addition to pressure and temperature. Thus, 2D graphs may be plotted with **total pressure against composition** or **temperature against composition**. Unlike pure substances, mixtures boil in a **boiling point range**, with the composition of the liquid and vapour phases constantly changing.

The pressure against composition graph may be constructed by finding the equations of the 2 lines: pressure against x_A and pressure against y_A, where x_A and y_A are the mole fractions of component A in liquid and vapour phase respectively. We may apply Raoult's law:

$$p_A = x_A p_A^*$$

$$p_B = x_B p_B^*$$

Since $x_B = 1 - x_A$,

$$p_{\text{total}} = p_A + p_B = p_B^* + (p_A^* - p_B^*)x_A$$

This is a linear graph with gradient $(p_A^* - p_B^*)$ and intercept p_B^*.

To find total pressure against y_A, we may write:

$$y_A = \frac{p_A}{p_{\text{total}}} = \frac{x_A p_A^*}{p_B^* + (p_A^* - p_B^*)x_A}$$

Combining this equation with the equation of total pressure with x_A, we derive:

$$p_{\text{total}} = \frac{p_A^* p_B^*}{p_A^* + (p_B^* - p_A^*)y_A}$$

This shows that the pressure against y_A graph is a curve.

To plot the pressure-composition phase diagram, we use z to express the overall composition of the system. z_A is the mole fraction of A in the whole system, which does not change in a closed system. The phase diagram may be plotted as a graph of total pressure against z_A, with the 2 lines indicating total pressure against x_A and y_A, as shown in Figure 2.4.5.

To interpret phase diagrams, we need to understand the properties of **vertical (isopleth)** and **horizontal (tie line)** lines. In a closed system where we vary pressure, the process may be represented by a vertical line, known as an isopleth. This is because no matter the phase transitions and the composition of the liquid and vapour phases, the overall composition in a closed system must remain the same. The tie line is a horizontal line that marks the state at which the liquid and vapour phases are in equilibrium and gives the composition of the liquid and vapour phases for any pressure or temperature.

We will consider a process following an isopleth from a to a_4, as described in Figure 2.4.6. At the start, the solution is in pure liquid phase at state a. As we reduce the pressure, the solution starts to boil at a_1. The composition of the liquid solution is denoted by the point a_1 which is the same as the overall composition of the solution since the solution has only just started to boil. We may draw a tie line to find out

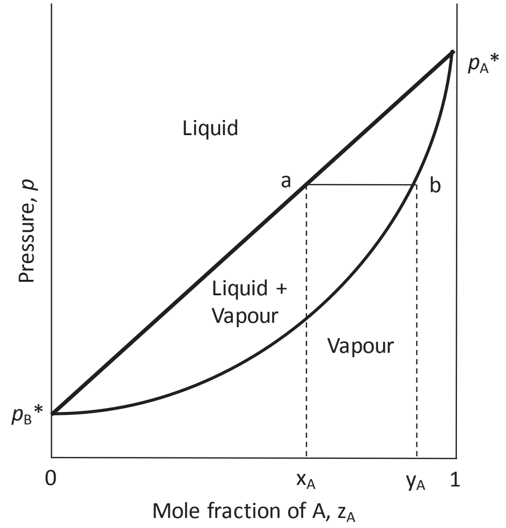


Figure 2.4.5. Pressure-composition binary phase diagram.

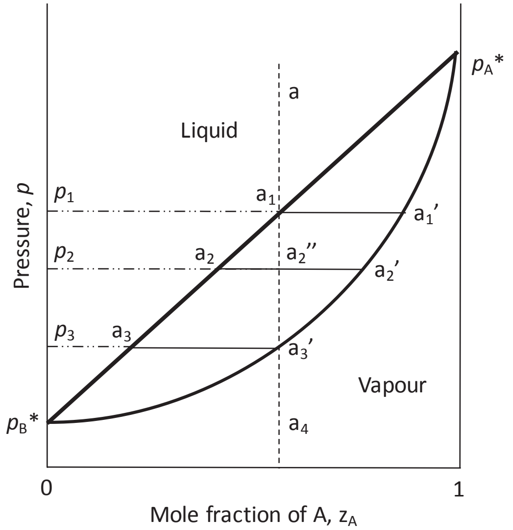


Figure 2.4.6. The pressure is reduced from point *a* to point a_4 and the solution changes from liquid to vapour phase.

the composition of the first trace of vapour formed, denoted by the point a_1'. As the solution continues to boil to reach point a_2'', we may draw a tie line to find the composition of the liquid a_2 and the composition of the vapour a_2'. At every pressure where the solution exists as a mixture of liquid and vapour, we may use a tie line to find out its composition in the liquid and vapour phase. Upon reaching a_3', the solution has just been completely changed into vapour phase and the last trace of liquid has the composition a_3. After all the solution is vaporised at a_4, the composition of the vapour is again the overall composition of the solution.

While the composition of the liquid and vapour phases can be determined by the tie lines, we are unable to determine the extent of vaporisation, or how much of the solution is in liquid and vapour phase. We may do that by using the **Lever Rule**:

$$n_\alpha l_\alpha = n_\beta l_\beta$$

where n_α and n_β are the amounts of substance in phase α and β respectively, and l_α and l_β are distances measured along the tie line, from the isopleth to phase α and β respectively. This is graphically shown in Figure 2.4.7.

The lever rule may be used to find the ratio of the amount of substance in each phase, and can be combined with the total amount of substance to solve for the exact amount of substance in each phase, which is simultaneously solving the following 2 equations:

$$n_\alpha l_\alpha = n_\beta l_\beta$$

$$n_\alpha + n_\beta = n_{\text{total}}$$

The lever rule may be derived by considering the total amount of one substance, A:

$$n_\mathrm{A} = n_\alpha x_{\mathrm{A},\alpha} + n_\beta y_{\mathrm{A},\beta}$$

We may also express n_A using z_A:

$$n_\mathrm{A} = n_{\text{total}} z_\mathrm{A} = n_\alpha z_\mathrm{A} + n_\beta z_\mathrm{A}$$

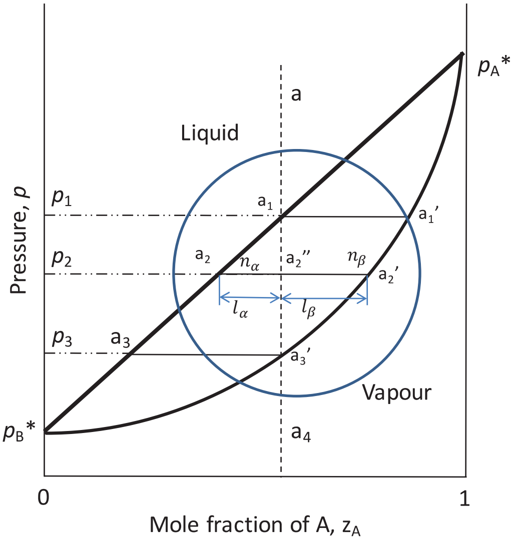


Figure 2.4.7. The application of the lever rule and how to obtain distances l_α and l_β.

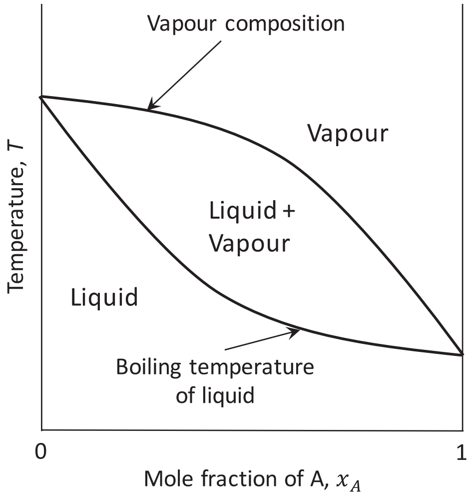


Figure 2.4.8. The temperature-composition phase diagram of a solution corresponding to the pressure-composition phase diagram in the previous part.

Solving the two equations simultaneously, we have:

$$n_{\alpha}(z_{\mathrm{A}} - x_{\mathrm{A},\alpha}) = n_{\beta}(y_{\mathrm{A},\beta} - z_{\mathrm{A}})$$

Which corresponds to the lever rule.

The temperature-composition phase diagram is shown in Figure 2.4.8. It may be plotted with 3 key differences from the pressure-composition phase diagram:

1. The liquid phase in the temperature-composition phase diagram is below while the liquid phase in the pressure-composition phase diagram is above, because the liquid phase is more stable than the vapour phase at lower temperature and higher pressure.
2. In the temperature-composition phase diagram, both lines for composition of the liquid and vapour phases are curves. The equations of the lines may be approximated using the Clapeyron equation but it is not the focus of our book.
3. In the temperature-composition phase diagram, the gradient of the two lines have opposite sign to the lines in the pressure-composition phase diagram. This is because the more volatile component will have a higher vapour pressure and lower boiling point.

We can use the temperature-composition phase diagram to explain the process of distillation. Distillation is a separation technique used to separate the components in a solution based on their different volatilities. There are 2 types of distillation, **simple distillation** and **fractional distillation**. Simple distillation is the process of boiling a solution and passing the vapour through a condenser to be collected as a liquid.

Fractional distillation adds a fractionating column to condense the vapour generated and the boiling and condensation cycle is repeated successively.

Simple distillation involves boiling the solution and collecting the vapour. Separation occurs because the more volatile component will be enriched in the vapour phase. Thus, the distillate should be enriched in the more volatile component while the less volatile component will remain in the flask.

The temperature-composition phase diagram shown in Figure 2.4.9 is for the case when component A is more volatile than B. The solution is heated to boil and the vapour produced is enriched in A. The solution remaining in the flask becomes more and more saturated in B. At the end, the distillate collected will be a mixture of A and B that is enriched in A, meaning that it has a higher mole fraction of A than the original solution, and pure B will remain in the flask.

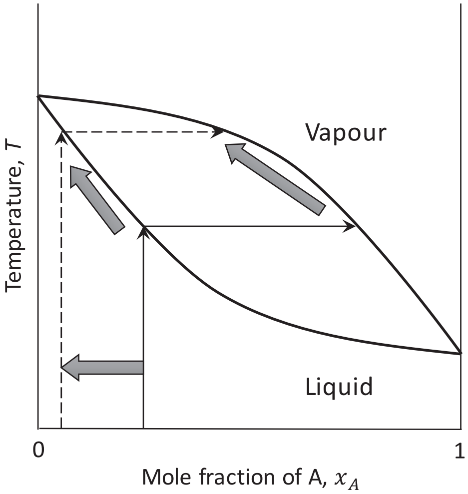


Figure 2.4.9. Simple distillation shown on a temperature-composition phase diagram.

In fractional distillation, the solution is heated to boil and the vapour produced is enriched in A. This vapour will condense in the fractionating column to give a liquid solution enriched in A. The solution will boil to give vapour that is even more enriched in A, and this vaporisation and condensation cycle repeats until the vapour travelling to the condenser is pure A. With A being removed from the solution and B being condensed and returned to the solution, the solution remaining in the flask becomes enriched in B. When all of A has been distilled, the remaining solution in the flask is pure B. We can tell that all of A has been distilled by monitoring the temperature of the vapour entering the condenser. The temperature of the vapour will be the boiling point of pure A until all of A has been distilled, then it will rise towards the boiling point of pure B. The heating should be stopped once the temperature starts to rise, as the distillation is complete and further heating will vaporise B that will

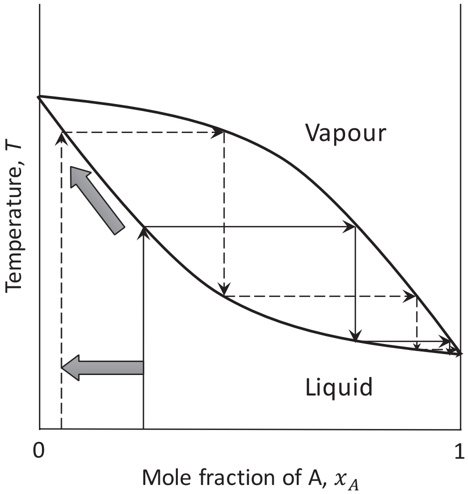


Figure 2.4.10. Fractional distillation shown on a temperature-composition phase diagram.

contaminate the pure A collected. Figure 2.4.10 describes fractional distillation on a temperature-composition phase diagram.

The binary phase diagrams that we have drawn earlier are for ideal solutions, as we applied Raoult's law to derive the equations of the lines. In reality, the graphs may appear different but the same analysis can be applied. However, for real solutions that deviate greatly from ideal solutions due to the exceptionally strong or weak intermolecular forces, they may form azeotropic mixtures that have significantly different properties from ideal solutions.

There are 2 types of azeotropes stemming from the positive and negative deviation from Raoult's law. **High-boiling azeotropes** stem from negative deviation from Raoult's law, where $\mathrm{A{-}B}$ intermolecular interactions are stronger than $\mathrm{A{-}A}$ and $\mathrm{B{-}B}$ interactions. High-boiling azeotropes show a maximum boiling point that is higher than the boiling points of pure A and B. Figure 2.4.11 shows the temperature-composition phase diagram for high-boiling azeotropes.

Fractional distillation is unable to fully separate azeotropic mixtures. For high-boiling azeotropes, during fractional distillation, the azeotropic composition will always remain in the flask while either pure A or B can be collected as the distillate depending on whether the original composition had more A or B than the azeotropic composition.

Low-boiling azeotropes stem from positive deviation from Raoult's law, where $\mathrm{A{-}B}$ intermolecular interactions are weaker than $\mathrm{A{-}A}$ and $\mathrm{B{-}B}$ interactions. Low-boiling azeotropes show a minimum boiling point that is lower than the boiling points of pure A and B. Figure 2.4.12 shows the the temperature-composition phase diagram for low-boiling azeotropes.

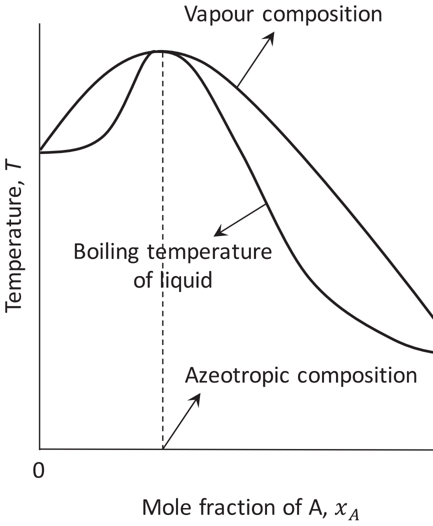


Figure 2.4.11. Temperature-composition phase diagram of a high-boiling azeotrope.

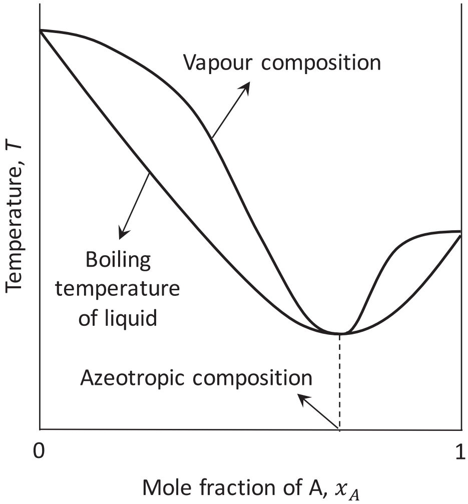


Figure 2.4.12. Temperature-composition phase diagram of a low-boiling azeotrope.

In the case of low-boiling azeotropes, the azeotropic composition will always be collected as the distillate. Either pure A or B will remain in the flask depending on whether the original composition had more A or B than the azeotropic composition.

Azeotropes pose a problem in separation of liquids as distillation is unable to completely separate azeotropes into the pure substances. The most common azeotrope is the ethanol-water azeotrope at 96% ethanol in water. Thus it was historically difficult to obtain ethanol above the concentration of 96%. In modern day chemistry, we may use molecular sieves to adsorb all the remaining water and obtain anhydrous ethanol. Azeotropes may also be used to our advantage, as adding toluene to water forms a low-boiling azeotrope that makes removal of water from a reaction mixture much easier.

2.5 Electrochemistry

Electrochemistry is the area of chemistry studying electron transfer reactions between chemical species, also known as redox reactions. Electrochemical reactions are common in all fields of chemistry, but we will be focusing on the physical aspects of electrochemistry. In this sense, electrochemistry uses many similar concepts from thermodynamics and equilibria, but we apply these concepts to electrochemical reactions.

2.5.1 *Oxidation and reduction*

Oxidation and reduction, commonly referred to as **redox**, is a common type of reaction that can be identified by considering a few factors as shown in Table 2.17.

The first 2 characteristics on electron transfer and change in oxidation state are more important as they occur for any redox reaction. The properties involving change in oxygen and hydrogen only occur for certain redox reactions, thus they may be used to analyse a redox reaction involving transfer of oxygen and hydrogen, but there are also redox reactions without transfer of oxygen and hydrogen.

The easiest way to identify and analyse redox reactions is through **oxidation states**. The oxidation state of an atom in a chemical compound is the theoretical charge of the atom if all heteronuclear bonds are treated as fully ionic, while homonuclear bonds are ignored. When treating heteronuclear bonds as ionic, all the electrons in the bond are assigned to the more electronegative element. Thus the oxidation state of any element is 0 and the total oxidation state of all atoms in a compound is equal to the charge of the compound. Oxidation states may be fractions, but IUPAC recommends against the use of it. Instead, the group of atoms should be considered as a whole with a whole number oxidation state. We will assign oxidation states to the atoms in $S_2O_8^{2-}$ as an example to show the formal process of assigning oxidation

Table 2.17. Characteristics of oxidation and reduction reactions.

Oxidation	Reduction
Losing electrons	Gaining electrons
Increase in oxidation state	Decrease in oxidation state
Gaining oxygen	Losing oxygen
Losing hydrogen	Gaining hydrogen

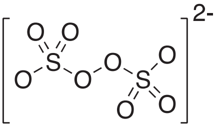


Figure 2.5.1. Lewis structure of $S_2O_8^{2-}$.

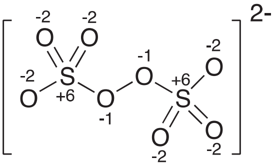


Figure 2.5.2. Lewis structure of $S_2O_8^{2-}$ with oxidation state of atoms assigned.

states. The first step is drawing the Lewis structure of $S_2O_8^{2-}$ as shown in Figure 2.5.1 (refer to chapter 3.3 for the details on how to draw Lewis structures).

Since oxygen is more electronegative than sulfur, we assign all the electrons in sulfur-oxygen bonds to oxygen, while for the homonuclear oxygen-oxygen bond, one electron may be assigned to each oxygen. Thus, the terminal oxygens have 8 electrons each, the peroxide oxygens have 7 electrons each and the sulfurs has no electrons. The original valence electrons of sulfur and oxygen are 6, so the oxidation states of the terminal oxygens, peroxide oxygens and sulfurs are –2, –1 and +6 respectively, as shown in Figure 2.5.2.

Note that the sum of the oxidation states is equal to the overall charge of the compound:

$$(-2)\times 6+(-1)\times 2+(+6)\times 2=-2$$

In simpler compounds, it is usually possible to assign oxidation states by considering that the oxidation state of hydrogen is +1 and the oxidation state of oxygen is –2. However, as per the example shown above, there is an exception when there is a peroxide $O{-}O$ bond, or in cases with more electronegative atoms, such as fluorine (e.g. +2 oxygen in OF_2). In the case of hydrogen, it usually has +1 oxidation state unless in metal hydrides, where it takes the oxidation state –1.

Redox reactions are reactions where one species is reduced and another species is oxidised. Since it is an electron-transfer reaction, there must be a pair of oxidant and reductant in a full redox reaction in a stoichiometric ratio such that there are no free electrons after the reaction. We will first analyse a simple redox reaction between peroxydisulfate and iodide:

$$S_2O_8^{2-}+2\ I^- \rightarrow 2\ SO_4^{2-}+I_2$$

This reaction has been extensively studied for its kinetics, and is often known as the iodine-clock reaction. First, we may assign oxidation states to the different atoms in the reactants. We have studied the oxidation state of the atoms in $S_2O_8^{2-}$

above, and the oxidation state is –1 for iodine in I^-. In the product, we see that the peroxide $O–O$ bond is broken, thus the oxidation state of all the oxygen atoms are –2 in SO_4^{2-}. The oxidation state of iodine in I_2 is 0. Thus the 2 peroxide oxygen atoms in $S_2O_8^{2-}$ are reduced as their oxidation states decreased from –1 to –2 while the 2 iodine atoms in I^- are oxidised as their oxidation states increased from –1 to 0. This means that each iodide ion transferred one electron to one peroxide oxygen in $S_2O_8^{2-}$. The species that is reduced, which is $S_2O_8^{2-}$ in this reaction, is known as the **oxidising agent** or **oxidant**. The species that is oxidised, which is I^- in this reaction, is known as the **reducing agent** or **reductant**.

Redox reactions are usually broken down into **half-equations**. Half-reactions describe either the oxidation or reduction half of the redox reaction, and any redox reaction may be constructed from a pair of reduction and oxidation half-equations. Half-equations express the change in oxidation state of a certain atom or group of atoms in a compound, and the change in oxidation state may be positive or negative for an oxidation or reduction half-equation respectively. This allows us to analyse many redox equations as combination of half-equations, and half-equations help us to balance complicated redox reactions.

As an example, Table 2.18 shows the redox equation above as a pair of half-equations:

Table 2.18. Oxidation and reduction half equations for iodine-clock reaction.

Oxidation:	$2\ I^- \rightarrow I_2 + 2\ e^-$
Reduction:	$S_2O_8^{2-} + 2\ e^- \rightarrow 2\ SO_4^{2-}$

The most significant difference between half-equations and full redox equations is the presence of electrons in the equation. We see that in the oxidation half-equation, electrons are lost, while in the reduction half-equation, electrons are gained. When we add the half equations together, the electrons on the reactant and product side must cancel out. Sometimes, the half-equations may need to be multiplied by stoichiometric coefficients such that the number of electrons is the same for the oxidation and reduction half-equations.

Balancing redox equations may be tricky at first, since both number of atoms and total charge must be balanced on both sides of the equation. In complicated cases, it is difficult to directly balance the redox equations. Instead, it may be easier to balance the half-equations before combining them to get the overall equation.

The overall steps to balancing redox equations are:

1. Identify the half-equations
2. Balance the half equations individually
   a. Elements (except H and O)
   b. O (using H_2O in acid, OH^- in base)

   c. H (using $\mathrm{H^+}$ in acid, $\mathrm{H_2O}$ in base)
   d. Charge (using $\mathrm{e^-}$)

3. Equal the number of electrons in both half-equations
4. Combine and cancel electrons and other species present on both sides of the equation

Let us consider an example: $\mathrm{MnO_4^- + Fe^{2+} \rightarrow Mn^{2+} + Fe^{3+}}$ in acidic solution.

1. We identify the half equations:
   Oxidation half-equation: $\mathrm{Fe^{2+} \rightarrow Fe^{3+}}$
   Reduction half-equation: $\mathrm{MnO_4^- \rightarrow Mn^{2+}}$
2. We balance the half equations individually. For the oxidation half-equation,
   a. The element Fe is already balanced.
   b. There is no O to balance.
   c. There is no H to balance.
   d. 1 electron must be added to the right side for the charge to be balanced.

   The balanced oxidation half-equation is: $\mathrm{Fe^{2+} \rightarrow Fe^{3+} + e^-}$
   For the reduction half-equation,

   a. The element Mn is already balanced.
   b. We add $\mathrm{4\ H_2O}$ to the product side to balance the 4 excess O in the reagent side, since it is in acidic solution. We arrive at the half-equation:

$$\mathrm{MnO_4^- \rightarrow Mn^{2+} + 4\ H_2O}$$

   c. Now that there are 8 extra H in the product side, we need to add $\mathrm{8\ H^+}$ to the reactant side to balance the H. We arrive at the half-equation:

$$\mathrm{MnO_4^- + 8\ H^+ \rightarrow Mn^{2+} + 4\ H_2O}$$

   d. We need to add 5 electrons to the left side for the charge to be balanced.

   The balanced reduction half-equation is: $\mathrm{MnO_4^- + 8\ H^+ + 5\ e^- \rightarrow Mn^{2+} + 4\ H_2O}$
3. We need to multiply the oxidation half-equation by 5 to get the same electrons in both half equations. We arrive at $\mathrm{5\ Fe^{2+} \rightarrow 5\ Fe^{3+} + 5\ e^-}$.
4. We combine the 2 half-equations together, cancelling out all the electrons. It is important to ensure that the overall redox equation does not have any free electrons. In this case, there are no other species present on both sides of the equation, thus the overall redox equation is:

$$\mathrm{5\ Fe^{2+} + MnO_4^- + 8\ H^+ \rightarrow 5\ Fe^{3+} + Mn^{2+} + 4\ H_2O}$$

We will look at a similar reaction $\mathrm{MnO_4^- + Fe^{2+} \rightarrow MnO_2 + Fe^{3+}}$ in basic solution. Note that redox reactions may have different products in different pH as stability of ions and oxidation states are pH-dependent.

1. We identify the half equations:
   Oxidation half-equation: $\mathrm{Fe^{2+} \rightarrow Fe^{3+}}$
   Reduction half-equation: $\mathrm{MnO_4^- \rightarrow MnO_2}$
2. We balance the half equations individually.

   From the previous example, the balanced oxidation half-equation is: $\mathrm{Fe^{2+} \rightarrow Fe^{3+} + e^-}$
   For the reduction half-equation,

   a. The element Mn is already balanced.
   b. It is more complicated to balance O in basic solution. We have to add $\mathrm{OH^-}$ to the product side, but we must consider that we have to add $\mathrm{H_2O}$ to the reagent side to balance the H in the next step. We have to add $\mathrm{H_2O}$ to the reagent side and 2 $\mathrm{OH^-}$ to the product side, keeping the H balanced while adding 1 O. Since we need to add 2 O, we need to add 2 $\mathrm{H_2O}$ to the reagent side and 4 $\mathrm{OH^-}$ to the product side. We arrive at:

   $$\mathrm{MnO_4^- + 2\ H_2O \rightarrow MnO_2 + 4\ OH^-}$$

   c. H is balanced simultaneously with O in the previous step.
   d. We need to add 3 electrons to the left side for the charge to be balanced.

   The balanced reduction half-equation is: $\mathrm{MnO_4^- + 2\ H_2O + 3e^- \rightarrow MnO_2 + 4\ OH^-}$

   Another method to balance the reduction half-equation in basic solution is to first balance it as though it is in an acidic solution, to get:

$$\mathrm{MnO_4^- + 4\ H^+ + 3\ e^- \rightarrow MnO_2 + 2\ H_2O}$$

As $\mathrm{H^+}$ does not exist in basic solution, we 'neutralise' the $\mathrm{H^+}$ by adding $\mathrm{OH^-}$ to both sides of the half-equation:

$$\mathrm{MnO_4^- + 4\ H_2O + 3\ e^- \rightarrow MnO_2 + 2\ H_2O + 4\ OH^-}$$

Since $\mathrm{H_2O}$ is on both sides of the equation, we can cancel them out and arrive at the same balanced half-equation $\mathrm{MnO_4^- + 2\ H_2O + 3\ e^- \rightarrow MnO_2 + 4\ OH^-}$.

3. We need to multiply the oxidation half-equation by 3 to get the same electrons in both half equations. We arrive at $\mathrm{3\ Fe^{2+} \rightarrow 3\ Fe^{3+} + 3\ e^-}$.
4. We combine the 2 half-equations together, cancelling out all the electrons. The overall redox equation is:

$$\mathrm{3\ Fe^{2+} + MnO_4^- + 2\ H_2O \rightarrow 3\ Fe^{3+} + MnO_2 + 4\ OH^-}$$

One tip to check that the half-equations are balanced correctly is to analyse the oxidation state of the element being oxidised or reduced in each species. In the oxidation half-equation, the Fe increases its oxidation state by 1, thus 1 electron is lost. In $\mathrm{MnO_4^-}$, the oxidation state of Mn is +7. It gains 5 electrons in acidic medium to form $\mathrm{Mn^{2+}}$ and gains 3 electrons in basic medium to form $\mathrm{MnO_2}$. The change in oxidation state must always correspond to the number of electrons transferred.

2.5.2 *Electrochemical cells and potentials*

We can break up redox reactions into their individual half-reactions and allow the electrons to transfer through a wire. This gives us the set-up for an electrochemical cell. When the overall redox reaction is spontaneous, we have a **galvanic cell**, which converts chemical energy into electrical energy. When the overall redox reaction is not spontaneous, we have an **electrolytic cell**, where electrical energy is supplied and converted into chemical energy.

In Figure 2.5.3, each beaker is a half-cell, where a half-reaction is occurring. The electron transfer is through the wire connecting the anode to cathode. In the galvanic cell, the copper is reduced while the zinc is oxidised. This reaction is spontaneous with a **standard cell potential, E^0**, of $+1.1\ \mathrm{V}$. The cell potential is the potential difference between the 2 electrodes. When both electrodes are in standard state ($c^0 = 1\ \mathrm{mol \cdot dm^{-3}}$, $p^0 = 1\ \mathrm{bar}$), we may measure the standard cell potential directly with a voltmeter.

In both cases, **oxidation occurs at the anode and reduction occurs at the cathode**. However, the direction of electron flow and the polarity of each electrode is different for galvanic and electrolytic cells. This is because we can think of electrolysis as using electrical energy to force the electrons to flow in the opposite direction such that the non-spontaneous reaction occurs.

The last important feature of a cell is the **salt bridge** connecting the 2 half-cells. The salt bridge is usually prepared with cotton wool saturated with $\mathrm{NaNo_3}$ or $\mathrm{KNO_3}$ solution. The salt bridge is present to maintain the charge neutrality of the 2 half-solutions, so it must be an ionic salt that does not react with the species in the solutions. The best candidate would be alkali metal nitrates, since both alkali

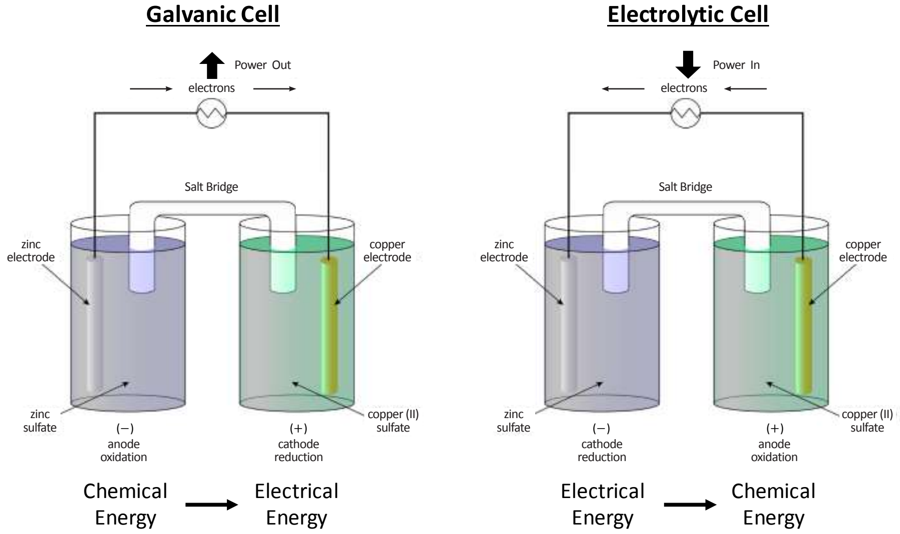


Figure 2.5.3. Diagram of sample galvanic and electrolytic cells.

metal cation and nitrate anion do not precipitate with most other ions. The charge imbalance builds up gradually with the reaction due to the anode producing Zn^{2+} cations and the cathode removing Cu^{2+} ions. Thus, NO_3^- can flow into the Zn^{2+} solution while Na^+/K^+ can flow into the Cu^{2+} solution to maintain the charge balance.

Electrochemical cells may be represented using **cell notation**. It is a concise way of representing an electrochemical cell such that all essential details are shown. Cell notation may be constructed with the following steps:

1. Use a double vertical line (||) to represent the salt bridge. The salt bridge is not specified because it is not important in the reaction.
2. On the left hand side of the salt bridge, write the species for the oxidation half-cell. Divide species in different phases with a single vertical line (|). Species in the same phase are separated with a comma (,). On the extreme left side, write the anode material (which may or may not be reacting).
3. On the right hand side of the salt bridge, write the species for the reduction half-cell. Divide species in different phases with a single vertical line (|). Species in the same phase are separated with a comma (,). On the extreme right side, write the cathode material (which may or may not be reacting).

As an example, we will express the galvanic cell above with cell notation (Figure 2.5.4). In this case, the overall reaction is:

$$\mathrm{Zn} + \mathrm{Cu}^{2+} \rightarrow \mathrm{Zn}^{2+} + \mathrm{Cu}$$

An important quantity in electrochemical reactions is the **number of electrons transferred in the reaction, *n***. In this case, 2 electrons are being transferred from Zn to Cu^{2+} in each reaction. We would express this as a molar quantity, so for every mole of reaction, there are 2 moles of electrons transferred and $n = 2\ \mathrm{mol}$.

As mentioned in the previous part, we can gain insights of many redox reactions by considering their half-reactions. An important property of half-reactions is the **standard reduction potential**, $\boldsymbol{E^0_{red}}$, which is the half-cell potential for the reduction reaction between 2 species under standard state. The potential for the reverse oxidation reaction is just $E^0_{ox} = -E^0_{red}$. The question now is: How are we able to measure the potential for a half-reaction when we can only measure the potential

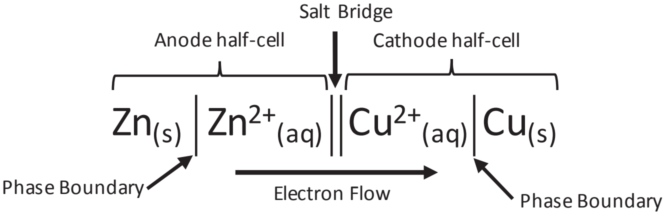


Figure 2.5.4. Sample cell notation for the zinc-copper galvanic cell.

of a full redox reaction? In this case, we must use the **standard hydrogen electrode (SHE)** as a reference electrode. The SHE makes use of the redox half-reaction of H^+ ions to H_2 gas: $2\ \mathrm{H^+}\ (\mathrm{aq},\ 1\ \mathrm{mol \cdot dm^{-3}}) + 2\ \mathrm{e^-} \rightarrow \mathrm{H_2}\ (\mathrm{g},\ 10^5\ \mathrm{Pa})$. The standard reduction potential of SHE is taken to be 0. All other half-cell potentials are taken with reference to SHE.

A negative E^0_{red} signifies that the reduced species is easily oxidised and a good reducing agent while a positive E^0_{red} signifies that the oxidised species is easily reduced and a good oxidising agent. The E^0_{red} values for common species may be easily found online and in textbooks, thus they are not tabulated here.

2.5.3 *Electrochemistry calculations*

Using the standard E^0_{red} values, we are able to calculate and derive thermodynamic properties for electrochemical cells. Firstly, we have to combine the E^0_{red} values of the 2 half-cells to get the overall E^0_{cell}. We may use the equation:

$$E^0_{cell} = E^0_{red}(\mathrm{reduction}) - E^0_{red}(\mathrm{oxidation})$$

The E^0_{red} of the oxidation reaction must be subtracted as E^0_{red} expresses the potential of the reduction half-equation, but the reverse oxidation reaction is occurring.

Cell potential is a form of potential difference, or voltage, and it is physically defined as:

$$E^0 = \frac{U}{Q}$$

Where U is the electrical potential energy and Q is the charge. The free energy for a reaction to do work is ΔG^0, and the electrical potential energy of the cell is $U = -\Delta G^0$. The charge comes from the electrons that flow in the wire, and the Faraday's constant (F) is defined as the charge carried by 1 mole of electrons. Thus we have:

$$Q = nF$$

Combining the above equations, we arrive at the relationship between Gibbs free energy and cell potential, allowing us to freely interconvert between thermodynamic variables and cell potential.

$$\Delta G^0 = -nFE^0$$

Since $\Delta G^0 = -RT\ln K$, we may derive:

$$E^0 = \frac{RT}{nF}\ln K$$

The 2 equations show that **ΔG^0, K and E^0 are inherently equivalent quantities that can be easily interchanged**. In complex systems, we may be given information about reactions through any of the 3 quantities. To combine them, we have to convert them all to the same quantity. Let's consider an example where we are given 4 reactions.

Reaction 1: $\mathrm{A + B \rightarrow C + 2\ D}$
Reaction 2: $\mathrm{B \rightarrow 2\ E}$
Reaction 3: $\mathrm{C \rightarrow A}$
Reaction 4: $\mathrm{A + B \rightarrow C + D + E}$

Given thermodynamic data for reaction 1, 2 and 3, we want to find the thermodynamic quantities for reaction 4. We can see that reaction 1 + reaction 2 – reaction 3 will give us:

$$\mathrm{2\ A + 2\ B \rightarrow 2\ C + 2\ D + 2\ E}$$

Which is twice of reaction 4.

If we convert all the data in reaction 1, 2 and 3 to $\boldsymbol{\Delta G^0}$ or $\boldsymbol{E^0}$, we may directly add, subtract and divide to get the corresponding thermodynamic quantity for reaction 4.

$$\Delta G_4^0 = \frac{\Delta G_1^0 + \Delta G_2^0 - \Delta G_3^0}{2} \quad \text{and} \quad E_4^0 = \frac{E_1^0 + E_2^0 - E_3^0}{2}$$

However, if we convert all the data in reaction 1, 2 and 3 to $\boldsymbol{K}$, we have to multiply, divide and square root to get the corresponding thermodynamic quantity for reaction 4.

$$K_4 = \sqrt{\frac{K_1 K_2}{K_3}}$$

This is because ΔG^0 and E^0 are related to K through a natural logarithm function, and the result follows from the laws of logarithm.

It is important to know a few physical formulae from electrical circuitry that may come in handy during calculations. Current, I, is the rate of flow of charge:

$$I = \frac{Q}{t} = \frac{nF}{t}$$

Power, P, is the rate of work done, or the rate of transfer of energy:

$$P = \frac{Energy}{t} = I \times E^0$$

These formulae should be used when current or power is given as information in the question.

Lastly, we will look at the **Nernst equation**, which is one of the most commonly used equations in electrochemistry. It allows us to calculate the **cell potential at non-standard states**. We have to make use of the equilibria equation that we have derived in chapter 2.2.

$$\Delta G = \Delta G^0 + RT \ln Q$$

Substituting $\Delta G = -nFE$, we have:

$$-nFE = -nFE^0 + RT \ln Q$$

From here, we arrive at the Nernst equation:

$$E = E^0 - \frac{RT}{nF}\ln Q$$

This allows us to derive the non-standard cell potential when the reaction cell is not held at standard state. Q is the reaction quotient which changes with partial pressure and concentration of reactants and products. Many times, Nernst equation may be applied to calculate the unknown concentration of a species given that we can measure the cell potential.

2.5.4 *Electrochemical diagrams*

Many redox and electrochemical concepts may be represented by diagrams that allow us to visualize the information more clearly. We will discuss **Latimer diagrams** and **Frost-Ebsworth diagrams**, the 2 most commonly seen diagrams.

The **Latimer diagram** is a linear diagram that summarises the standard reduction potentials of an element. From left to right, we write all the species of the element in the order of decreasing oxidation number. We will look at the Latimer diagram of manganese as shown in Figure 2.5.5.

Note that the oxidation states of Mn from left to right is +7, +6, +4, +3, +2 and 0. The value above each reaction arrow tells us the standard reduction potential for the specific reduction reaction. For example, the standard reduction potential of the $\mathrm{Mn}^{2+}/\mathrm{Mn}$ couple is $-1.19\mathrm{V}$. The Latimer diagram is a simple way of organising the reduction potentials such that we may calculate the combined reduction potential between 2 non-adjacent species. While we have mentioned that we may add and subtract for ΔG^0 and E^0 previously, that is only true when the number of electrons, n, stays the same. In general, we may only sum ΔG^0. Thus, to find the standard reduction potential from $[\mathrm{MnO_4}]^-$ to $\mathrm{MnO_2}$, we will have to convert all the E^0 to ΔG^0, summing the ΔG^0 together, and then converting the overall ΔG^0 back to E^0.

$$E^0_{[\mathrm{MnO_4}]^-/\mathrm{MnO_2}} = \frac{-(1)F(+0.90) + [-(2)F(+2.10)]}{-(3)F}$$

We see that the Faraday's constant cancels out and we may find the potential through a shortcut method. We may find the combined reduction potential by summing the number of electrons multiply reduction potential (nE^0) for each individual reduction reaction and dividing it by the total number of electrons. Thus, it is a good

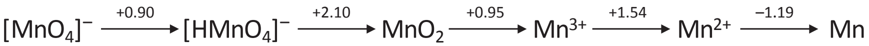


Figure 2.5.5. Latimer diagram of Mn at pH = 0.

$$[\mathrm{MnO_4}]^- \xrightarrow[+1\,e^-]{+0.90} [\mathrm{HMnO_4}]^- \xrightarrow[+2\,e^-]{+2.10} \mathrm{MnO_2} \xrightarrow[+1\,e^-]{+0.95} \mathrm{Mn^{3+}} \xrightarrow[+1\,e^-]{+1.54} \mathrm{Mn^{2+}} \xrightarrow[+2\,e^-]{-1.19} \mathrm{Mn}$$

Figure 2.5.6. Latimer diagram with the number of electrons annotated.

practice to annotate the Latimer diagram with the number of electrons transferred in each step, as shown in Figure 2.5.6.

Note that Latimer diagrams will change with pH, as the overall redox reaction changes. The Latimer diagram is the most common diagram that is usually used to provide standard reduction potential data.

Once we have the Latimer diagram, we may plot our data into a graph, known as the **Frost-Ebsworth diagram** (or Frost diagram, for short). This graph allows us to visualise the redox properties of the element. The Frost diagram is a plot of $-\frac{\Delta G^0}{F}$ against N, where N is the oxidation number. To plot the Frost diagram, we may construct a table (Table 2.19) from the data we obtain from the Latimer diagram.

Table 2.19. Table of points to plot for Frost diagram.

N	Species	$-\Delta G^0/F = nE^0$ (rel. Mn(0))
0	Mn	0
+2	$\mathrm{Mn^{2+}}$	$2(-1.19) = -2.38$
+3	$\mathrm{Mn^{3+}}$	$1(1.54) + (-2.38) = -0.84$
+4	$\mathrm{MnO_2}$	$1(0.95) + (-0.84) = +0.11$
+6	$[\mathrm{HMnO_4}]^-$	$2(2.10) + 0.11 = +4.31$
+7	$[\mathrm{MnO_4}]^-$	$1(0.90) + 4.31 = +5.21$

In the Frost diagram, every value of $-\frac{\Delta G^0}{F}$ plotted is **relative to the 0 oxidation state of the element**. Thus, we write the table starting from oxidation state 0, moving step by step towards the larger oxidation states. Note that in every step, we add the standard reduction potential multiply by electrons to the previous result, such that the final result is always relative to the 0 oxidation state. After constructing the table, we may plot the Frost diagram using the values on the table, connecting the points with straight lines, as shown in Figure 2.5.7.

The Frost-Ebsworth diagram contains the same information as the Latimer diagram. However, it presents the information in a way that allows us to predict the reactivity of the species better. We may interpret the Frost diagram in the following manner:

1. The lowest-lying species is the most stable species. Since all data points are plotted with respect to the 0 oxidation state, the lowest-lying species will be the most stable. In this case, we see that $\mathrm{Mn^{2+}}$ is most stable, and we can say that the most stable oxidation state of Mn is +2.

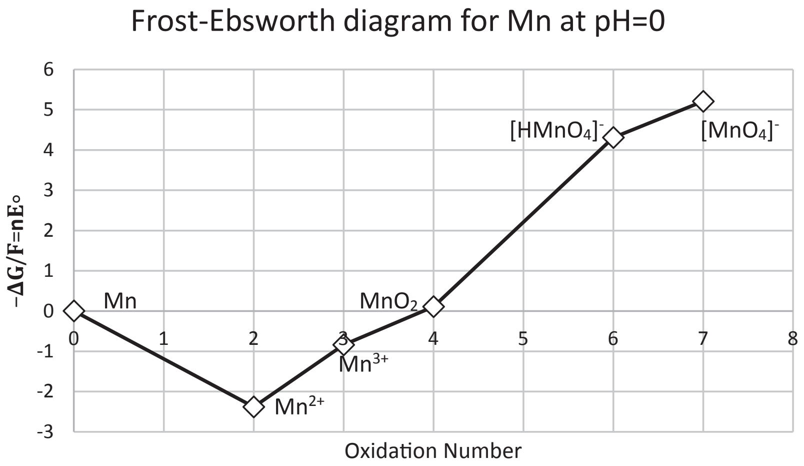


Figure 2.5.7. Frost-Ebsworth diagram for Mn at pH = 0.

2. For any slope, the higher-lying species has the tendency to go down the slope to form the lower-lying species, which is more stable. Thus, for a positive slope, the higher-lying species is a good oxidising agent, while for a negative slope, the higher-lying species is a good reducing agent.
3. Since we are plotting nE^0 against n, the slope of the graph is E^0.
4. A species at a convex point may undergo disproportionation while a species at a concave point may undergo comproportionation. We can tell if a species is at a convex or concave point by using a straight line to link up the 2 adjacent points to it. If the point lies above the line, it is at a convex point, while if it lies below the line, it is at a concave point. For example, $[\mathrm{HMnO_4}]^-$ readily undergoes disproportionation to $\mathrm{MnO_2}$ and $[\mathrm{MnO_4}]^-$ as it is at a convex point. Meanwhile Mn and Mn^{3+} may undergo comproportionation to Mn^{2+} as Mn^{2+} is at a concave point.

By making use of the ideas above, we are able to have a good understanding of the redox chemistry of an element from the Latimer and Frost diagrams.

2.6 Reaction Kinetics

In the previous chapters, we have been mainly concerned with the thermodynamics of reactions, evaluating the favourability of reactions through energetics. However, we have not considered how long it takes for a reaction to reach its final state, even if it is thermodynamically favoured. One famous example is the equilibrium between the 2 allotropes of carbon, diamond and graphite. Graphite is thermodynamically more stable under room temperature and pressure, but we never observe diamond becoming graphite. This is because the conversion is extremely slow. To wrap up physical chemistry, we will discuss the rates of reactions and factors that affect them. It is important to keep in mind that as we move on to inorganic and organic chemistry, reactions require to be both thermodynamically and kinetically favoured to proceed. Sometimes, when the 2 effects favour different products, we will get a mixture of products and must vary reaction conditions to selectively achieve a certain product.

2.6.1 *The definition of rate and monitoring rate*

We qualitatively understand rate as the speed of a reaction, but we must quantitatively define rate in order to measure it. As such, for a reaction:

$$a\,\mathrm{A} + b\,\mathrm{B} \rightarrow c\,\mathrm{C} + d\,\mathrm{D}$$

We may define the **rate** as the **change in concentration with respect to time**:

$$\text{Rate} = -\frac{1}{a}\frac{\mathrm{d}[\mathrm{A}]}{\mathrm{d}t} = -\frac{1}{b}\frac{\mathrm{d}[\mathrm{B}]}{\mathrm{d}t} = \frac{1}{c}\frac{\mathrm{d}[\mathrm{C}]}{\mathrm{d}t} = \frac{1}{d}\frac{\mathrm{d}[\mathrm{D}]}{\mathrm{d}t}$$

Note that for reactants, the rate is negative change in concentration with respect to time as the reactants are being consumed and a reaction is faster if the reactants are being consumed faster. Since rate is concentration divided by time, it has the unit $\mathrm{mol \cdot dm^{-3} \cdot s^{-1}}$. Rates are always defined for an instant, and we should never define rate as the average rate of reaction.

As rates are always varying with the concentration, it is a challenge to monitor rates experimentally when analysing the kinetics of a reaction. We may determine rate by monitoring:

1. Concentration over a period of time using techniques such as titration.
2. Light absorbance, if the reactant or product is coloured.
3. Conductivity for ionic reactants or products.
4. Pressure for gaseous reactants or products.

2.6.2 *Rate laws*

It was experimentally observed that the rate of a reaction usually depends on the concentrations of the reactants. For the sample reaction above,

$$a\,\mathrm{A} + b\,\mathrm{B} \rightarrow c\,\mathrm{C} + d\,\mathrm{D}$$

We may write the rate as:

$$\text{Rate} = k[\mathrm{A}]^m[\mathrm{B}]^n$$

Where k is the rate constant for the reaction while m and n are the orders of the reaction with respect to reactants A and B respectively. The overall order of the reaction is the sum of the individual orders, which is $m+n$ in this case.

We need to understand that most chemical reactions consist of multiple elementary reactions. **Elementary reactions** are reactions where the reagents collide to form a single transition state before forming the product. Thus, each reaction to form an intermediate may be considered an elementary reaction. For elementary reactions, the **order of reaction with respect to each reactant is the stoichiometric coefficient of the reactant**. If the above reaction is an elementary reaction, $m=a$ and $n=b$.

The reaction order describes the dependence of rate on the concentration of a reactant. Most commonly, there are 3 possible reaction orders: zeroth, first and second order. It is possible to have fractional reaction orders for an overall reaction as it may be a combination of multiple elementary reactions. It is extremely rare to encounter reaction orders above 2 because reactions generally occur as unimolecular or bimolecular. The probability for a termolecular reaction is very low as it requires 3 molecules colliding simultaneously. We will proceed to analyse the rate laws for each of the 3 common reaction orders and solve the differential equations to obtain the **integrated rate laws**.

A **zeroth order reaction** indicates that the rate is independent of the concentration of the reactant. The rate law is:

$$\text{Rate} = -\frac{\mathrm{d}[\mathrm{A}]}{\mathrm{d}t} = k[\mathrm{A}]^0 = k$$

We proceed to solve for the integrated rate law:

$$\int_{[\mathrm{A}]_0}^{[\mathrm{A}]_t} \mathrm{d}[\mathrm{A}] = -k\int_0^t \mathrm{d}t$$

$$[\mathrm{A}]_t - [\mathrm{A}]_0 = -kt$$

From the integrated rate law, we are able to determine the **half-life $t_{½}$**, which is the time taken for the concentration of the reactant to be reduced by half. To determine half-life, we substitute $[\mathrm{A}]_t = \frac{1}{2}[\mathrm{A}]_0$:

$$\frac{1}{2}[\mathrm{A}]_0 - [\mathrm{A}]_0 = -kt_{½}$$

$$t_{½} = \frac{[\mathrm{A}]_0}{2k}$$

A **first order reaction** indicates that the rate is linearly dependent on the concentration of the reactant. The rate law is:

$$\text{Rate} = -\frac{\mathrm{d}[\mathrm{A}]}{\mathrm{d}t} = k[\mathrm{A}]$$

We proceed to solve for the integrated rate law:

$$\int_{[\mathrm{A}]_0}^{[\mathrm{A}]_t} \frac{1}{[\mathrm{A}]} \mathrm{d}[\mathrm{A}] = -k \int_0^t \mathrm{d}t$$

$$\ln[\mathrm{A}]_t - \ln[\mathrm{A}]_0 = \ln\frac{[\mathrm{A}]_t}{[\mathrm{A}]_0} = -kt$$

We determine the half-life as follows:

$$\ln\frac{\frac{1}{2}[\mathrm{A}]_0}{[\mathrm{A}]_0} = -kt_{½}$$

$$t_{½} = \frac{\ln 2}{k}$$

It is worthy to note that the **half-life for first-order reactions is constant**.

A **second order reaction** indicates that the rate is dependent on the square of the concentration of the reactant. The rate law is:

$$\mathrm{Rate} = -\frac{\mathrm{d}[\mathrm{A}]}{\mathrm{d}t} = k[\mathrm{A}]^2$$

We proceed to solve for the integrated rate law:

$$\int_{[\mathrm{A}]_0}^{[\mathrm{A}]_t} \frac{1}{[\mathrm{A}]^2} \mathrm{d}[\mathrm{A}] = -k \int_0^t \mathrm{d}t$$

$$\frac{1}{[\mathrm{A}]_0} - \frac{1}{[\mathrm{A}]_t} = -kt$$

$$\frac{1}{[\mathrm{A}]_t} - \frac{1}{[\mathrm{A}]_0} = kt$$

We determine the half-life as follows:

$$\frac{1}{\frac{1}{2}[\mathrm{A}]_0} - \frac{1}{[\mathrm{A}]_0} = kt_{½}$$

$$t_{½} = \frac{1}{k[\mathrm{A}]_0}$$

It is important to remember these results to easily determine the order of the reaction from experimental data. For reactions with only one reactant, we may use 2 methods to determine the reaction order from experimental data of concentration against time:

1. **Integrated rate law method**:
   We may determine the reaction order by plotting the concentration against time graph from the experimental results. We must plot a linear graph for us to be sure of the reaction order.
   For zeroth order reactions, the graph of $[\mathrm{A}]$ against t is a straight line.
   For first order reactions, the graph of $\ln[\mathrm{A}]$ against t is a straight line.
   For second order reactions, the graph of $\frac{1}{[\mathrm{A}]}$ against t is a straight line.
   To use this method, we must first guess the reaction order before plotting the graph. If the graph is not linear, we have to guess a different reaction order and replot the graph, until we obtain a linear plot.
2. **Half-life method**:
   It is usually possible to find a few half-lives from the experimental data set. We may consider how the half-life varies with concentration to determine the reaction order.
   For zeroth order reactions, $t_{½}$ is proportional to $[\mathrm{A}]$.
   For first order reactions, $t_{½}$ is constant, independent of $[\mathrm{A}]$.
   For second order reactions, $t_{½}$ is proportional to $\frac{1}{[\mathrm{A}]}$.

The above 2 methods are easy and efficient methods to determine reaction order for reactions with only one reactant. For reactions with multiple reactants, it is trickier to determine the reaction order with respect to each reactant. To do so, we may use 2 other methods:

1. **Initial rate method**:

We can control the initial concentration of the reagents, and measure the initial rate of the reaction when we just start the reaction. Thus, for the sample reaction:

$$a\,\mathrm{A} + b\,\mathrm{B} \rightarrow c\,\mathrm{C} + d\,\mathrm{D}$$

We may write the initial rate, Rate_0, as:

$$\mathrm{Rate}_0 = k[\mathrm{A}]_0^m[\mathrm{B}]_0^n$$

Since we can control the values for $[\mathrm{A}]_0$ and $[\mathrm{B}]_0$, we may change the value of $[\mathrm{A}]_0$ to $[\mathrm{A}]'_0$ in a second experiment while keeping the value for $[\mathrm{B}]_0$ constant. We will get a new initial rate:

$$\mathrm{Rate}'_0 = k[\mathrm{A}]_0'^m[\mathrm{B}]_0^n$$

Since we do not know the rate constant, we can eliminate it through division:

$$\frac{\mathrm{Rate}_0}{\mathrm{Rate}'_0} = \frac{k[\mathrm{A}]_0^m[\mathrm{B}]_0^n}{k[\mathrm{A}]_0'^m[\mathrm{B}]_0^n} = \left(\frac{[\mathrm{A}]_0}{[\mathrm{A}]'_0}\right)^m$$

Through this calculation, we may find m, the reaction order with respect to A. We may repeat the process to find n, and so on for reactions with more reagents.

2. **Isolation method**:

We may choose the concentration for one reagent to be much lower than the other reagent(s). For the sample reaction above, we may choose the initial concentrations such that $[\mathrm{A}]_0 \ll [\mathrm{B}]_0$. As a result, $\frac{\mathrm{d}[\mathrm{B}]}{\mathrm{d}t} \approx 0$. Such a reaction is known as a **pseudo first order reaction.** The rate law may be approximated as follows:

$$\text{Rate} = k[\mathrm{A}]^m[\mathrm{B}]^n \approx k_{eff}[\mathrm{A}]^m$$

Where $k_{eff} = k[\mathrm{B}]^n$ since $[\mathrm{B}]^n$ is treated as constant. We may proceed to determine the reaction order with respect to A using either of the 2 methods described above for reactions with only one reactant. We may then determine the order with respect to other reagents by repeating the same method with the concentration of other reagents being very small.

2.6.3 *Kinetic theories and equilibria*

The rate laws and Arrhenius equation (which we will visit next) are all based on kinetic theories. The simplest theory proposed in 1917 is the **collision theory**. Collision theory states that reactions may be treated as the collision of hard spheres. The spheres must collide above a minimum energy, known as **activation energy**, for the reaction to occur. Using the Maxwell-Boltzmann energy distribution, we may write:

$$\text{Rate} \propto e^{-\frac{E_a}{RT}}[\mathrm{A}]^m[\mathrm{B}]^n$$

For a reaction with reactants A and B.

Since the spheres must also collide in the right orientation, we may add a steric factor such that only a certain proportion of colliding molecules complete the reaction:

$$\text{Rate} \propto Ae^{-\frac{E_a}{RT}}[\mathrm{A}]^m[\mathrm{B}]^n$$

This is the basis for **Arrhenius equation**, which states that:

$$k = Ae^{-\frac{E_a}{RT}}$$

Where A is the Arrhenius pre-exponential factor, an empirical constant characteristic for each reaction. This equation relates the rate of reaction with temperature. At higher temperatures, the chance of collision is higher and the average energy of the molecules is greater, allowing reactions to proceed faster.

Since the value of factor A is often difficult to determine, we may use a reference point to calculate the change in rate with temperature, using the equation:

$$\ln\left(\frac{k_2}{k_1}\right) = -\frac{E_a}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right)$$

We can see from the equation that for a reaction with low activation energy, the rate constant depends weakly on temperature, while for a reaction with high activation energy, the rate constant depends strongly on temperature.

From this understanding of kinetics, we may proceed to relate kinetics to equilibrium. When we discussed equilibria, we mentioned that equilibrium is a dynamic process where the forward and backward reactions proceed with the same rate. For reversible reactions, we are able to see that the equilibrium constant is the ratio of the 2 rate constants. Consider a reversible reaction:

$$\mathrm{A} \rightleftharpoons \mathrm{B}$$

Where the forward rate constant is k_1 and the backward rate constant is k_{-1} and the reaction starts with an initial concentration of A, $[\mathrm{A}]_0$, and no B.

$$\frac{\mathrm{d}[\mathrm{A}]}{\mathrm{d}t} = k_{-1}[\mathrm{B}] - k_1[\mathrm{A}] = k_{-1}([\mathrm{A}]_0 - [\mathrm{A}]) - k_1[\mathrm{A}]$$

We may solve this differential equation by separation:

$$\int_{[\mathrm{A}]_0}^{[\mathrm{A}]} \frac{1}{k_{-1}[\mathrm{A}]_0 - (k_1 + k_{-1})[\mathrm{A}]}\mathrm{d}[\mathrm{A}] = \int_0^t \mathrm{d}t$$

$$[\mathrm{A}] = \frac{\left(k_{-1} + k_1 e^{-(k_1 + k_{-1}t)}\right)}{k_1 + k_{-1}}[\mathrm{A}]_0$$

Since $[\mathrm{B}] = [\mathrm{A}]_0 - [\mathrm{A}]$,

$$[\mathrm{B}] = [\mathrm{A}]_0\left(1 - \frac{\left(k_{-1} + k_1 e^{-(k_1 + k_{-1}t)}\right)}{k_1 + k_{-1}}\right)$$

After a long time, the reaction reaches equilibrium, such that:

$$\lim_{t \to \infty} e^{-kt} = 0$$

$$[\mathrm{A}]_{eq} = \frac{k_{-1}}{k_1 + k_{-1}}[\mathrm{A}]_0$$

$$[\mathrm{B}]_{eq} = \frac{k_1}{k_1 + k_{-1}}[\mathrm{A}]_0$$

We can see that at equilibrium, the forward rate is equal to the backward rate:

$$k_1[\mathrm{A}]_{eq} = k_{-1}[\mathrm{B}]_{eq}$$

We may find the equilibrium constant to be:

$$K = \frac{[\mathrm{B}]_{eq}}{[\mathrm{A}]_{eq}} = \frac{k_1}{k_{-1}}$$

Using the Arrhenius equation, we may also qualitatively understand the effects of temperature on equilibria. For an exothermic reaction, the activation energy of the backward reaction is higher than the activation energy of the forward reaction. Thus the dependence of the backward rate on temperature is higher than forward rate. At equilibria, the forward and backward rates are equal. If we increase the temperature, the backward rate will increase more than the forward rate. Thus the equilibrium will be shifted to the left. Vice versa, for an endothermic reaction, the equilibrium will be shifted to the right with an increase in temperature.

For systems that form 2 different products from 2 different reactants in equilibrium, we may determine the final product equilibrium using the **Curtin-Hammett principle**. First, we consider the sample reaction:

$$\mathrm{C} \leftarrow \mathrm{A} \rightleftharpoons \mathrm{B} \rightarrow \mathrm{D}$$

Curtin-Hammett principle states that when the rate of interconversion between A and B is fast compared to the formation of products, the product ratio does not depend on the A:B ratio, but the difference in activation energy between the 2 reactions $\mathrm{A} \rightarrow \mathrm{C}$ and $\mathrm{B} \rightarrow \mathrm{D}$. This principle is widely applied in stereoselective synthesis, where we can form one product selectively by reducing the activation energy of the reaction to that product.

2.6.4 *Solving reaction rate*

Other than reversible reactions which we have discussed earlier, there are other reaction types, most commonly **sequential reactions** and **parallel reactions**.

Sequential reactions refer to reactions that occur one after another. The product of the first reaction reacts in the second reaction and so on. We consider a sample reaction going through an intermediate, I:

$$\mathrm{A} \rightarrow \mathrm{I} \rightarrow \mathrm{P}$$

The rate constant for the 2 reactions are k_1 and k_2 respectively. We may express the rate of change of the 3 species as follows:

$$\frac{\mathrm{d}[\mathrm{A}]}{\mathrm{d}t} = -k_1[\mathrm{A}]$$

$$\frac{\mathrm{d}[\mathrm{I}]}{\mathrm{d}t} = k_1[\mathrm{A}] - k_2[\mathrm{I}]$$

$$\frac{d[P]}{dt} = k_2[I]$$

Using the initial condition that the system contains only A at an initial concentration $[A]_0$, we may solve the set of differential equations by separation:

$$[A] = [A]_0 e^{-k_1 t}$$

$$[I] = \frac{k_1}{k_2 - k_1}(e^{-k_1 t} - e^{-k_2 t})[A]_0$$

$$[P] = \left(1 + \frac{k_1 e^{-k_2 t} - k_2 e^{-k_1 t}}{k_2 - k_1}\right)[A]_0$$

Let us consider the cases where the first reaction is much faster than the second reaction and vice versa.

$$[P]_{k_1 \gg k_2} = (1 - e^{-k_2 t})[A]_0$$
$$[P]_{k_2 \gg k_1} = (1 - e^{-k_1 t})[A]_0$$

We see that in sequential reactions, **the slowest step determines the overall rate of product formation**, and it is known as the **rate-determining step**. The slowest step limits the rate of the overall process as all products formed must pass through the slow step.

Parallel reactions refer to reactions that happen simultaneously. The reactant is able to form multiple different products through different pathways at different rates. We consider a sample reaction:

$$B \leftarrow A \rightarrow C$$

The rate constant to form B is k_1 while the rate constant to form C is k_2. We may express the rate of change of the 3 species as follows:

$$\frac{d[A]}{dt} = -k_1[A] - k_2[A] = -(k_1 + k_2)[A]$$

$$\frac{d[B]}{dt} = k_1[A]$$

$$\frac{d[C]}{dt} = k_2[A]$$

Using the initial condition that the system contains only A at an initial concentration $[A]_0$, we may solve the set of differential equations by separation:

$$[A] = [A]_0 e^{-(k_1+k_2)t}$$

$$[B] = \frac{k_1}{k_1 + k_2}(1 - e^{-(k_1+k_2)t})[A]_0$$

$$[C] = \frac{k_2}{k_1 + k_2}(1 - e^{-(k_1+k_2)t})[A]_0$$

We see that in parallel reactions, **the fastest step is the rate-determining step**. Most reactants will react through the faster path to form more of the product with a faster rate of formation.

The conceptual understanding about these 2 types of reaction mechanisms is important, however most reaction mechanisms are not as simple. They may contain elements of both types of reactions and involve many intermediates. It is much more challenging to solve differential equations to find the rate expression for such reactions. Thus, we must make reasonable assumptions.

The most important assumption that can be applied generally to most complex reaction systems is the **steady-state approximation (SSA)**. This assumption states that **all the intermediates are at a near-constant steady-state concentration** after a short induction period at the start. This is true when **the rate of intermediate consumption is much faster than intermediate production**. In such cases, the intermediate concentration is kept constant at a very low level.

Let us consider a complex reaction system with 4 elementary reactions. The overall reaction is:

$$H_2O_2 + 2H^+ + 2I^- \rightarrow I_2 + 2H_2O$$

This reaction proceeds in 4 elementary steps as shown in Table 2.20.

Table 2.20. Elementary steps of sample reaction.

Step number	**Elementary reaction**	**Rate constant(s)**
Step 1:	$H^+ + I^- \rightleftharpoons HI$	k_1, k_{-1}
Step 2:	$HI + H_2O_2 \rightarrow H_2O + HOI$	k_2
Step 3:	$HOI + I^- \rightarrow I_2 + OH^-$	k_3
Step 4:	$OH^- + H^+ \rightarrow H_2O$	k_4

We may apply SSA through 5 steps:

1. Using the definition of rate, determine the one that is easiest to solve.

   From the definition of rate, we may consider the overall reaction and write:

$$\text{Rate} = -\frac{d[H_2O_2]}{dt} = -\frac{1}{2}\frac{d[H^+]}{dt} = -\frac{1}{2}\frac{d[I^-]}{dt} = \frac{d[I_2]}{dt} = \frac{1}{2}\frac{d[H_2O]}{dt}$$

We may describe the rate from all the species shown in the overall reaction. However, it requires differing amounts of effort to solve the 5 expressions above. In this case, we see that H_2O_2 only appears in the first 2 steps. Thus, we only need to consider the first 2 steps to solve for rate as $-\frac{d[H_2O_2]}{dt}$.

2. List down all the intermediates and choose which to consider.

Frequently, we think of intermediates as species appearing in the elementary reactions but not appearing in the overall reaction. That is only partially correct, as catalysts will also appear in elementary reactions but not appear in the overall reaction. The difference between catalysts and intermediates is that catalysts are added to the reaction while intermediates are formed during the reaction. In the current case, there are no catalysts and the intermediates are HI, HOI and $\mathrm{OH^-}$. The only intermediate that appears in the first 2 reactions is HI.

3. Write $\frac{\mathrm{d[Intermediate]}}{\mathrm{d}t} = 0$ for intermediates in terms of rate constants and concentrations.

In this case, we only need to write this for HI:

$$\frac{\mathrm{d[HI]}}{\mathrm{d}t} = k_1[\mathrm{H^+}][\mathrm{I^-}] - k_{-1}[\mathrm{HI}] - k_2[\mathrm{HI}][\mathrm{H_2O_2}] = 0$$

4. Find the steady state concentrations for the intermediates by rearranging the equations above.

$$[\mathrm{HI}]_{SS} = \frac{k_1[\mathrm{H^+}][\mathrm{I^-}]}{k_{-1} + k_2[\mathrm{H_2O_2}]}$$

5. Substitute the steady state concentration into rate equation and solve for rate.

$$\begin{aligned}\mathrm{Rate} &= -\frac{\mathrm{d[H_2O_2]}}{\mathrm{d}t} = k_2[\mathrm{HI}][\mathrm{H_2O_2}] \\ &= k_2\left(\frac{k_1[\mathrm{H^+}][\mathrm{I^-}]}{k_{-1} + k_2[\mathrm{H_2O_2}]}\right)[\mathrm{H_2O_2}]\end{aligned}$$

This allows us to obtain the rate in terms of rate constants and starting material concentration.

Another approximation, which is just a special case of SSA, is known as the **pre-equilibrium hypothesis**. Let us just consider the system of equations earlier, and note that we only need to consider the first 2 elementary steps. In the pre-equilibrium hypothesis, we assume that the reversible step (step 1) is always at equilibrium. We may write:

$$k_1[\mathrm{H^+}][\mathrm{I^-}] = k_{-1}[\mathrm{HI}]$$

This allows us to find another expression for concentration of HI:

$$[\mathrm{HI}] = \frac{k_1}{k_{-1}}[\mathrm{H^+}][\mathrm{I^-}]$$

We may then find the overall rate to be:

$$\mathrm{Rate} = k_2\left(\frac{k_1}{k_{-1}}[\mathrm{H^+}][\mathrm{I^-}]\right)[\mathrm{H_2O_2}]$$

This method is much faster and the final rate equation is simpler. Now we need to understand the differences in these 2 assumptions and which is better.

SSA assumes that the rate of consumption of intermediate is much faster than the rate of production of intermediate. In this case, we are assuming that $k_{-1} + k_2 \gg k_1$. Pre-equilibria hypothesis assumes, on top of SSA, that the equilibrium is rapidly established before the intermediate reacts to form the product, that is $k_{-1} \gg k_2$. If we apply this assumption to our solution from SSA, we will obtain the solution from pre-equilibrium hypothesis.

If $k_{-1} \gg k_2$,

$$k_{-1} + k_2[\mathrm{H_2O_2}] \approx k_{-1}$$

$$k_2\left(\frac{k_1[\mathrm{H^+}][\mathrm{I^-}]}{k_{-1} + k_2[\mathrm{H_2O_2}]}\right)[\mathrm{H_2O_2}] \approx k_2\left(\frac{k_1}{k_{-1}}[\mathrm{H^+}][\mathrm{I^-}]\right)[\mathrm{H_2O_2}]$$

From the overall rate equation, we may determine the overall expression for activation energy from the Arrhenius equation when we have an effective rate constant. For example, we may simplify the rate equation above as:

$$\mathrm{Rate} = k_{eff}[\mathrm{H^+}][\mathrm{I^-}][\mathrm{H_2O_2}]$$

Where $k_{eff} = \frac{k_1 k_2}{k_{-1}}$ is the effective rate constant.

Since Arrhenius equation states that:

$$k = Ae^{-\frac{E_a}{RT}}$$

$$k_{eff} = \frac{k_1 k_2}{k_{-1}} = \frac{\left(A_1 e^{-\frac{E_{a,1}}{RT}}\right)\left(A_2 e^{-\frac{E_{a,2}}{RT}}\right)}{\left(A_{-1} e^{-\frac{E_{a,-1}}{RT}}\right)} = A_{eff}\, e^{-\frac{E_{a,eff}}{RT}}$$

$$E_{a,eff} = E_{a,1} = E_{a,2} - E_{a,-1}$$

The sign of the effective activation energy is able to provide information for the effect of temperature changes on the overall rate. In certain cases where the effective activation energy is negative, an increase in temperature will lead to a decrease in effective rate.

2.6.5 *Common reaction mechanisms*

For unimolecular reactions, the most common type of reaction mechanism is the **Lindemann-Hinshelwood mechanism**. Unimolecular reactions are not as simple as they seem. A single molecule is required to gain enough energy before it can

Table 2.21. Elementary reactions for unimolecular reactions.

Step number	**Elementary reaction**	**Rate constant(s)**
Step 1:	$A + A \rightleftharpoons A + A^*$	k_1, k_{-1}
Step 2:	$A^* \rightarrow P$	k_2

undergo the change, and this energy must come from collisions. Thus, the mechanism proposes a bimolecular collision with another reactant molecule to form the energised reactant (A^*). The energised reactant may either deactivate back to A through collision or form the product. The overall reaction is:

$$A \rightarrow P$$

The reaction may be split into 2 elementary steps as shown in Table 2.21.

We may apply SSA with A^* as the intermediate:

$$\frac{d[A^*]}{dt} = k_1[A]^2 - k_{-1}[A^*][A] - k_2[A^*] = 0$$

$$[A^*]_{SS} = \frac{k_1[A]^2}{k_{-1}[A] + k_2}$$

$$\text{Rate} = \frac{d[P]}{dt} = k_2[A^*] = \frac{k_1 k_2 [A]^2}{k_{-1}[A] + k_2}$$

If $[A]$ is high, we use the assumption from pre-equilibrium hypothesis that $k_{-1}[A] \gg k_2$,

$$\text{Rate} \approx \frac{k_1 k_2 [A]^2}{k_{-1}[A]} = \frac{k_1 k_2 [A]}{k_{-1}}$$

If $[A]$ is low, we may make the opposite assumption $k_2 \gg k_{-1}[A]$,

$$\text{Rate} \approx \frac{k_1 k_2 [A]^2}{k_2} = k_1[A]^2$$

We see that at high $[A]$, the reaction is first order with respect to $[A]$, while at low $[A]$, the reaction is second order with respect to $[A]$.

For chain reactions, which occur most commonly as radical reactions, the most common mechanism is the **Rice-Herzfeld mechanism**. For example, the overall reaction is:

$$CH_3CHO \rightarrow CH_4 + CO$$

Unlike other reactions seen thus far which are comprised of elementary steps, chain reactions consist of initiation, propagation and termination steps. As these intermediates may react in different ways to form many products, the overall reaction is not the sum of the 4 individual steps in this case. The overall equation

Table 2.22. Elementary steps for radical reaction.

Step	Elementary reaction	Rate constant(s)
Initiation	$CH_3CHO \rightarrow CH_3^{\bullet} + CHO^{\bullet}$	k_i
Propagation 1	$CH_3CHO + CH_3^{\bullet} \rightarrow CH_3CO^{\bullet} + CH_4$	k_p
Propagation 2	$CH_3CO^{\bullet} \rightarrow CH_3^{\bullet} + CO$	k_p'
Termination	$CH_3^{\bullet} + CH_3^{\bullet} \rightarrow C_2H_6$	k_t

instead describes the productive reactions that we are studying. The steps are shown in Table 2.22.

In this case, the method for solving is through SSA, and we consider all radical species as intermediates. Thus, the total radical concentration is treated as constant. This means that the rate of initiation is equal to the rate of termination.

$$k_i[CH_3CHO] = 2k_t[CH_3^{\bullet}]^2$$

$$[CH_3^{\bullet}] = \left(\frac{k_i}{2k_t}\right)^{\frac{1}{2}}[CH_3CHO]^{\frac{1}{2}}$$

The rate of the reaction may be described by the rate of formation of CH_4:

$$\text{Rate} = \frac{d[CH_4]}{dt} = k_p[CH_3CHO][CH_3^{\bullet}] = k_p\left(\frac{k_i}{2k_t}\right)^{\frac{1}{2}}[CH_3CHO]^{\frac{3}{2}} = k_{eff}[CH_3CHO]$$

We can see that the reaction order with respect to acetaldehyde is $\frac{3}{2}$.

2.6.6 *Enzyme catalysis and the Michaelis-Menten rate law*

A catalyst increases the reaction rate by providing an alternative mechanism through which the activation energy barrier is lower. It speeds up both the forward and backward reaction equally, thus there is no shift in equilibrium but the equilibrium will be established faster. Enzymes are natural catalysts that speed up reactions in our body. We will now take a detailed look at enzyme catalysis.

The general pathway for enzyme catalysis is for the enzyme (E) and substrate (S) to combine to form an enzyme-substrate complex (ES) before the product (P) is released from the enzyme. The reaction is shown below in Figure 2.6.1.

Figure 2.6.1. Reaction mechanism of an enzyme-catalysed reaction.

We will solve for the rate law of this reaction by using SSA.

$$\frac{\mathrm{d[ES]}}{\mathrm{d}t} = k_1[\mathrm{E}][\mathrm{S}] - k_{-1}[\mathrm{ES}] - k_2[\mathrm{ES}] = 0$$

$$[\mathrm{ES}] = \frac{k_1}{k_{-1} + k_2}[\mathrm{E}][\mathrm{S}]$$

For enzyme catalysis, we are concerned with the initial rate that may be determined from the total concentration of enzyme and substrate. By applying mass-balance, we have:

$$[\mathrm{E}] = [\mathrm{E}]_0 - [\mathrm{ES}]$$

$$[\mathrm{S}] = [\mathrm{S}]_0 - [\mathrm{ES}] - [\mathrm{P}]$$

We can express the steady-state concentration of $[\mathrm{ES}]$ as:

$$[\mathrm{ES}] = \frac{k_1}{k_{-1} + k_2}\big([\mathrm{E}]_0 - [\mathrm{ES}]\big)\big([\mathrm{S}]_0 - [\mathrm{ES}] - [\mathrm{P}]\big)$$

To simplify the expression, we must use 3 assumptions:

1. Initially, the amount of product is very little, thus $[\mathrm{P}] \approx 0$.
2. The concentration of substrate is much greater than enzyme, as enzyme is just a catalyst. Thus, $[\mathrm{S}]_0 \gg [\mathrm{E}]_0$.
3. The concentration of the intermediate enzyme-substrate complex is low, such that its quadratic term is negligible, $[\mathrm{ES}]^2 \approx 0$.

Using these assumptions, we may simplify our expression:

$$[\mathrm{ES}] = \frac{k_1}{k_{-1} + k_2}\big([\mathrm{E}]_0[\mathrm{S}]_0 - [\mathrm{ES}][\mathrm{S}]_0\big)$$

We have to solve for $[\mathrm{ES}]$:

$$[\mathrm{ES}] = \frac{k_1[\mathrm{E}]_0[\mathrm{S}]_0}{(k_{-1} + k_2)\left(1 + \frac{k_1}{k_{-1} + k_2}[\mathrm{S}]_0\right)}$$

$$[\mathrm{ES}] = \frac{k_1[\mathrm{E}]_0[\mathrm{S}]_0}{k_{-1} + k_2 + k_1[\mathrm{S}]_0}$$

We may define initial rate from the rate of formation of product:

$$\text{Rate}_0 = \frac{\mathrm{d}[\text{P}]}{\mathrm{d}t} = k_2[\text{ES}] = \frac{k_2 k_1 [\text{E}]_0 [\text{S}]_0}{k_{-1} + k_2 + k_1[\text{S}]_0}$$

Given a constant amount of enzyme, the maximum rate will be observed with an infinitely large substrate concentration, such that all enzymes are active in catalysis at all times.

$$\text{Rate}_{\text{max}} = \lim_{[\text{S}]_0 \to \infty} \frac{k_2 k_1 [\text{E}]_0 [\text{S}]_0}{k_{-1} + k_2 + k_1[\text{S}]_0} = k_2[\text{E}]_0$$

Expressing the initial rate in terms of the maximum rate, we have the **Michaelis-Menten rate equation**:

$$\text{Rate}_0 = \frac{\text{Rate}_{\text{max}} k_1 [\text{S}]_0}{k_{-1} + k_2 + k_1[\text{S}]_0} = \frac{\text{Rate}_{\text{max}} [\text{S}]_0}{\frac{k_{-1}+k_2}{k_1} + [\text{S}]_0} = \frac{\text{Rate}_{\text{max}} [\text{S}]_0}{K_M + [\text{S}]_0}$$

Where $K_M = \frac{k_{-1}+k_2}{k_1}$ is the Michaelis-Menten constant.

From the rate equation, we may draw a linear **Lineweaver-Burk** plot of $\frac{1}{\text{Rate}_0}$ against $\frac{1}{[S]}$:

$$\frac{1}{\text{Rate}_0} = \frac{K_M}{\text{Rate}_{\text{max}}} \frac{1}{[\text{S}]} + \frac{1}{\text{Rate}_{\text{max}}}$$

The parameters of the graph are as follows:

$$x - \text{intercept} = -\frac{1}{K_M}$$

$$y - \text{intercept} = \frac{1}{\text{Rate}_{\text{max}}}$$

$$\text{Gradient} = \frac{K_M}{\text{Rate}_{\text{max}}}$$

Using these parameters, we may plot the Lineweaver-Burk plot as shown in Figure 2.6.2:

It is important for us to interpret the physical meaning of K_M:

$\frac{1}{K_M} \propto$ Enzyme affinity to substrate

This is true because $\frac{1}{K_M}$ is the rate constant of ES formation over the rate constants of ES dissociation. The greater this value, the greater the formation rate of ES to dissociation rate of ES and this means that the formation of ES is more favourable and the enzyme will have greater affinity with the substrate.

We will now look at 3 different examples of enzyme inhibition that affect the activity of the enzyme:

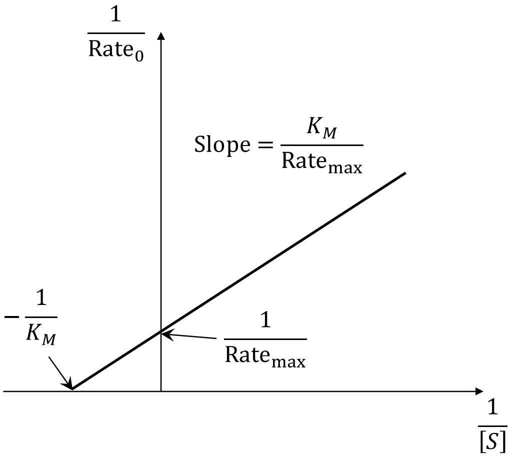


Figure 2.6.2. Lineweaver-Burk plot of Michaelis-Menten rate law.

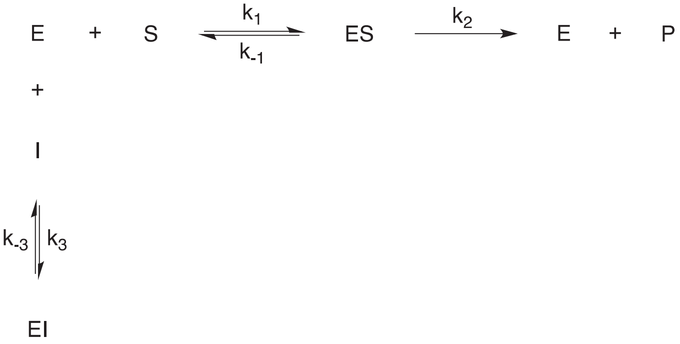


Figure 2.6.3. Modified rate mechanism for competitive inhibition.

1. Competitive inhibition
   A competitive inhibitor binds to the active site of the enzyme, in a sense competing directly with the substrate for the active site.
   The new rate mechanism is shown in Figure 2.6.3.
   Qualitatively, we can understand the following 2 properties:

   a. $\text{Rate}_{\max}$ does not change because when rate is maximum, all the enzymes are bound with substrate molecules rather than inhibitor. This is possible when the concentration of the substrate is very high compared to concentration of inhibitor.
   b. K_M will increase because the inhibitor lowers the enzyme's affinity towards the substrate by allowing the enzyme to also bind with the inhibitor instead of the substrate.

Using the new mechanism and steady state approximation, we can derive a modified rate law for such systems with competitive inhibitors as follows:

$$\text{Rate}_0 = \frac{\text{Rate}_{\max}[\text{S}]}{K_M\left(1+\frac{[\text{I}]}{K_i}\right)+[\text{S}]}$$

Where $K_i = \frac{k_{-3}}{k_3}$ which is the inhibitor constant.

2. Non-competitive inhibition

Contrary to competitive inhibitors, non-competitive inhibitors prefer to bind at allosteric sites (sites that are not the active site). This changes the shape of the active site and will make the enzyme binding more difficult.

The rate mechanism is given in Figure 2.6.4.

Qualitatively, we can understand the following 2 properties:

a. $\text{Rate}_{\max}$ will decrease because non-competitive inhibitor binds to the enzyme to change the shape of the active site to make the binding slower and less favourable.
b. K_M will not change significantly because although the change in shape of the enzyme will make its affinity for the substrate lower, there is an opposing effect where the inhibitor will provide the second pathway for the enzyme-substrate complex to form, increasing the affinity. Using Le Chatelier principle, since the inhibitor binds to both the enzyme and the enzyme-substrate complex equally, the equilibrium is maintained.

Using the new mechanism and steady state approximation, we can derive a modified rate law for such systems with non-competitive inhibitors as follows:

$$\text{Rate}_0 = \frac{\text{Rate}_{\max}[\text{S}]}{\left(1+\frac{[\text{I}]}{K_i}\right)\left(K_M+[\text{S}]\right)}$$

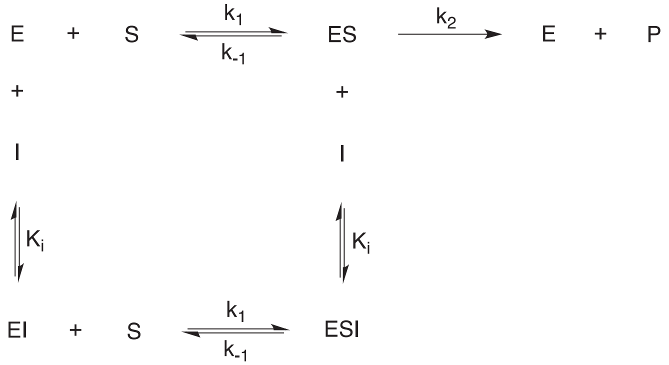


Figure 2.6.4. Modified rate mechanism for non-competitive inhibition.

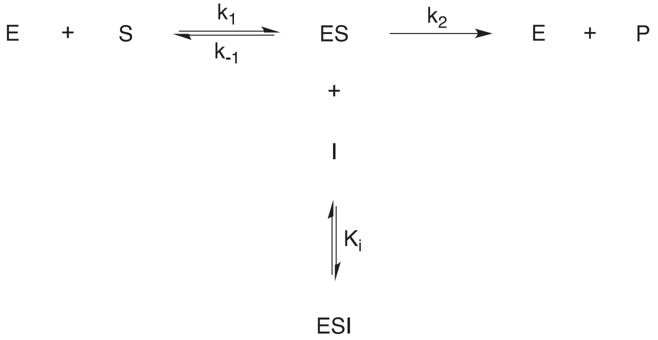


Figure 2.6.5. Modified rate mechanism for uncompetitive inhibition.

3. Uncompetitive inhibition

An uncompetitive inhibitor is the most interesting as it binds only to the enzyme-substrate complex, further slowing down the second step, the catalysis step.

The modified rate mechanism is shown in Figure 2.6.5.

Qualitatively, we can understand the following 2 properties:

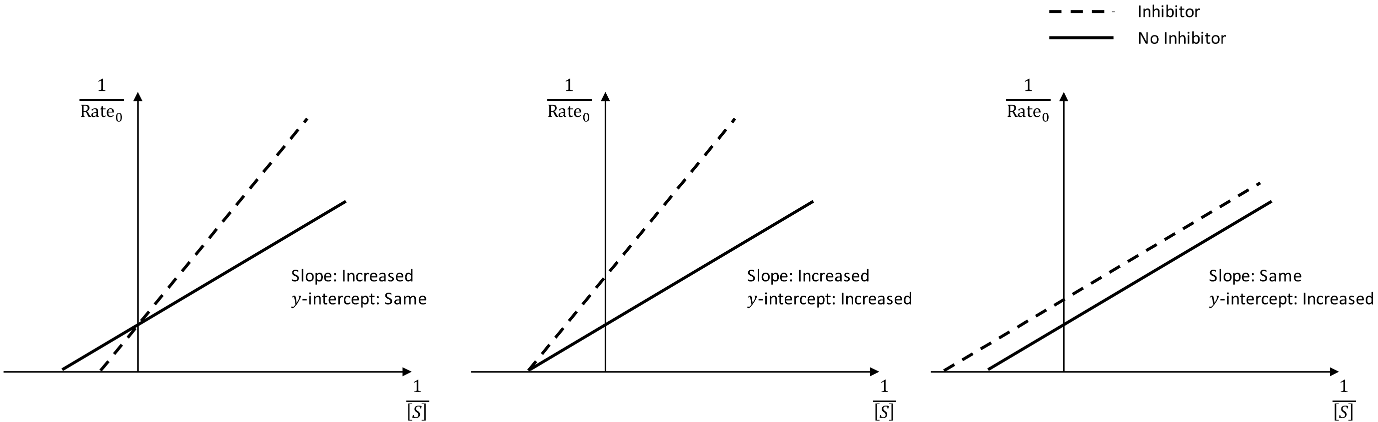
a. $\mathrm{Rate}_{\mathrm{max}}$ will decrease because uncompetitive inhibitor binds to the enzyme-substrate complex to slow down the second step, the catalytic step.
b. K_M will decrease for uncompetitive inhibitors because the formation of ESI complex will consume the ES complex such that the concentration of ES in solution is lower. By Le Chatelier's principle, this will shift the equilibrium of the first step (binding of substrate to enzyme) forward. This means that the enzyme's affinity to the substrate is effectively increased, thus K_M will decrease.

Using the new mechanism and steady state approximation, we can derive a modified rate law for such systems with uncompetitive inhibitors as follows:

$$\mathrm{Rate}_0 = \frac{\mathrm{Rate}_{\mathrm{max}}[\mathrm{S}]}{\left(1+\frac{[\mathrm{I}]}{K_i}\right)\left(\frac{K_M}{\left(1+\frac{[\mathrm{I}]}{K_i}\right)}+[\mathrm{S}]\right)}$$

We will now show how the Lineweaver-Burk plot changes with the 3 different types of inhibition in Figure 2.6.6.

By using the Lineweaver-Burk plots, we can understand how different types of inhibitors affect the rates of enzyme catalysis.



Competitive Inhibition

K_M: Increased
Rate_{max}: Unaffected

Non-Competitive Inhibition

K_M: Unaffected
Rate_{max}: Reduced

Uncompetitive Inhibition

K_M: Reduced
Rate_{max}: Reduced

Figure 2.6.6. Lineweaver-Burk plot for enzyme catalysis in the presence of inhibitors.

3. INORGANIC CHEMISTRY

Inorganic chemistry is the study of compounds formed from elements other than carbon, which includes the over 100 other elements in the periodic table. As a wide area, we are unable to go into detail regarding every element. In this chapter, we will start from the basics of atomic structure before moving onto the trends in the periodic table. Elements are classified based on block and group so that their properties can be discussed more systematically. There is also an introduction to crystal structures and coordination chemistry, which are advanced topics that are often explored in Chemistry Olympiad.

3.1 Atomic Structure and Quantum Theory

This chapter kicks off our discussion of inorganic chemistry by exploring the different theories and models for atomic structures. This involves detailed explanation of atomic orbitals and energy levels of electrons. The topics covered in this chapter will form the basis for future discussion into bonding in both inorganic and organic compounds.

3.1.1 *Bohr's theory of the atom*

The first modern theory of atomic structure was introduced by Bohr and Rutherford in 1913. It depicts the atoms as having a small, positively charged nucleus at the centre, surrounded by electrons in orbit around the nucleus, as shown in Figure 3.1.1.

The interaction between the nucleus and electron is treated as purely electrostatic. From experimental evidence at that time that atoms will only emit light at certain discrete wavelengths, Bohr suggested that electrons can only have certain classical motions, stably orbiting the nucleus in stationary orbits that do not radiate energy. By moving in circular motion, electrons possess certain amount of angular momentum. Bohr postulated that this angular momentum is quantised, implying that orbital radii are fixed to discrete values.

Bohr's model may only be applied accurately to one-electron systems, most notably the hydrogen atom. By accounting for the change in nuclear charge, Bohr's model may also be applied to other one-electron systems, such as He^{+} and Li^{2+}. We will now use Bohr's model to calculate properties of the hydrogen atom.

From Bohr's postulate that angular momentum is quantised, we have:

$$L = n\hbar = mvr$$

where:

$\hbar = \frac{h}{2\pi} = 1.055 \times 10^{-34}\ \mathrm{J \cdot s}$ is the reduced Planck's constant (Planck's constant h = $6.626 \times 10^{-34}\ \mathrm{J \cdot s}$).

$m = 9.109 \times 10^{-31}\ \mathrm{kg}$ is the electron mass.

v is the velocity of the electron.

r is the radius of the electron orbit.

From the electrostatic centripetal force allowing the electron to stay in orbit, we have:

$$F_C = \frac{ke^2}{r^2} = \frac{mv^2}{r}$$

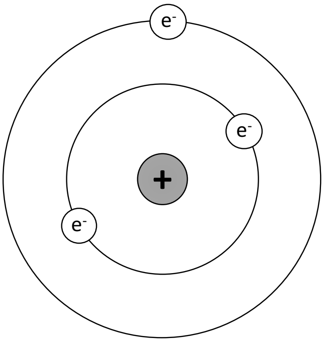


Figure 3.1.1. Bohr's model of the atom.

where $k = \frac{1}{4\pi\epsilon_0} = 8.99 \times 10^9\ \mathrm{N \cdot m^2 \cdot C^{-2}}$ is known as the Coulomb's constant ($\epsilon_0 = 8.854 \times 10^{-12}\,\mathrm{F \cdot m^{-1}}$ is the vacuum permittivity) and $e = 1.602 \times 10^{-19}\,\mathrm{C}$ is the electron charge.

Hence,

$$v^2 = \frac{ke^2}{mr}$$

$$v = \sqrt{\frac{ke^2}{mr}}$$

Substituting that into the expression for angular momentum, we have:

$$n\hbar = mr\sqrt{\frac{ke^2}{mr}} = \sqrt{mke^2 r}$$

$$mke^2 r = n^2\hbar^2$$

$$r = \frac{n^2\hbar^2}{mke^2} = \frac{n^2\left(\frac{h}{2\pi}\right)^2}{m\left(\frac{1}{4\pi\epsilon_0}\right)e^2} = \frac{n^2\epsilon_0 h^2}{\pi m e^2}$$

For a hydrogen atom at ground state, $n = 1$, the radius of the electron orbit is:

$$a_0 = \frac{\epsilon_0 h^2}{\pi m e^2} = 5.29 \times 10^{-11}\ \mathrm{m}$$

where a_0 is defined as the Bohr radius.

With the Bohr radius, we may proceed to calculate the energy of the electron orbit:

$$E_n = KE + PE = \frac{1}{2}mv^2 - \frac{ke^2}{r}$$

Since

$$\frac{mv^2}{r} = \frac{ke^2}{r^2}$$

We have

$$E_n = \frac{1}{2}\frac{ke^2}{r} - \frac{ke^2}{r} = -\frac{ke^2}{2r}$$

Substituting r into the expression, we have

$$E_n = -\frac{ke^2}{2r}$$

$$E_n = -\frac{1}{2}\frac{ke^2}{\frac{n^2\epsilon_0 h^2}{\pi m e^2}} = -\frac{1}{2}\frac{\left(\frac{1}{4\pi\epsilon_0}\right)e^4 \pi m}{n^2\epsilon_0 h^2}$$

$$E_n = -\frac{me^4}{8n^2\epsilon_0^2 h^2}$$

This allows us to calculate the energies of all possible orbits by substituting the appropriate n. To determine the wavelength of light that is released when an electron drops from one energy level to another, we must first write the energy of light as:

$$E = \frac{hc}{\lambda}$$

where $c = 3.00 \times 10^8\ \mathrm{m \cdot s^{-1}}$ is the speed of light and λ is the wavelength of light.

The energy difference between 2 energy levels n_1 and n_2 is:

$$E_{n_1 \to n_2} = -\frac{me^4}{8n_2^2\epsilon_0^2 h^2} - \left(-\frac{me^4}{8n_1^2\epsilon_0^2 h^2}\right)$$

$$E_{n_1 \to n_2} = \frac{me^4}{8\epsilon_0^2 h^2}\left(\frac{1}{n_1^2} - \frac{1}{n_2^2}\right)$$

Equating this with the energy of light released, we have:

$$\frac{hc}{\lambda} = \frac{me^4}{8\epsilon_0^2 h^2}\left(\frac{1}{n_1^2} - \frac{1}{n_2^2}\right)$$

$$\frac{1}{\lambda} = \frac{me^4}{8\epsilon_0^2 h^3 c}\left(\frac{1}{n_1^2} - \frac{1}{n_2^2}\right)$$

$$\frac{1}{\lambda} = R_\mathrm{H}\left(\frac{1}{n_1^2} - \frac{1}{n_2^2}\right)$$

where $R_\mathrm{H} = \frac{me^4}{8\epsilon_0^2 h^3 c} = 1.097 \times 10^7\ \mathrm{m}^{-1}$ is the Rydberg constant.

The equation that we arrived at is known as the Rydberg formula, which may be used to calculate the wavelengths of spectral lines of hydrogen.

3.1.2 *Schrödinger equation*

The Schrödinger equation forms the basis of quantum mechanics, and it was first published in 1926. This equation has allowed us to get a more accurate understanding of atomic structure, which we will proceed to describe. The equation itself looks deceivingly simple:

$$\hat{H}\Psi = E\Psi$$

In this equation, $\hat{H}$ is the Hamiltonian operator, which corresponds to the total energy of the system. E is the total energy, which is just a numerical value. The most important part of the equation is the wave function Ψ, which describes the possible space where an electron might be present.

As this book focuses on chemistry, the full solution of Schrödinger equation will not be described here. However, it is important to note that there are many wave functions Ψ that may fulfil the Schrödinger equation. To understand the solutions of the Schrödinger equation, we must first discuss **quantum numbers**, which may be described as the sets of numerical values which give acceptable solutions to the Schrödinger equation for hydrogen atom. Similar to the case of Bohr model, we will also limit our discussion of Schrödinger equation here to one-electron systems, as the Schrödinger equation has only been solved exactly for one-electron systems. The wave functions that are solutions of Schrödinger equation are known as **orbitals**. To describe an electron in an atom precisely, we must use 4 quantum numbers:

1. Principal quantum number (n)
We have previously encountered n in the Bohr's model, and it is a discrete variable that only takes on positive integer values. Each n gives rise to an electron shell, which may be interpreted as an orbit of the electron around the nucleus in Bohr's model. Thus, with higher n, the electron spends more time further from the nucleus and has higher energy.

2. Azimuthal quantum number (l)
Azimuth is an angular measurement in a spherical coordinate system, thus l is associated with the allowed angular momentum of an electron in an orbital. l describes the shape of the orbital, and takes on integer values starting from 0 to $n-1$ for any n.

3. Magnetic quantum number (m)
m is associated with the orientation of the orbital angular momentum, which corresponds to the orientation of the orbitals. It takes on integer values starting from $-l$ up to $+l$ for any l.

4. Spin quantum number (s)
s was first proposed after experimental evidence showed that lines in alkali metal emission spectra were doubled, as though the 2 electrons in the same orbital are at different energies. The small difference in energy was caused by spin-orbit coupling, as the 2 electrons possess different spin in the electrostatic field of the nucleus. The spin quantum number takes only 2 values: $+\frac{1}{2}$ and $-\frac{1}{2}$.

The 3 quantum numbers n, l and m are able to fully characterise the wave functions in Schrödinger equation. The wave function consists of 2 parts, the radial ($R_{n,l}(r)$) and angular ($Y_{l,m}(\theta, \phi)$) functions:

$$\Psi_{n,l,m}(r,\theta,\phi) = R_{n,l}(r)Y_{l,m}(\theta,\phi)$$

The wave function is a product of the radial and angular functions with the same l.

3.1.3 *Orbitals*

The wave functions that are solutions of the Schrödinger equation are also known as orbitals. The orbital energy, shape and orientation depends on the quantum numbers n, l and m. By convention, lower-case letters are used to designate l. This notation arose from description of alkali metal spectroscopic lines as sharp (s), principal (p), diffuse (d) and fundamental (f). For $l > 3$, the orbitals are named in alphabetical order. Table 3.1 shows the letter that corresponds to each l.

A different l corresponds to a different type of orbital, which we label based on the letter assigned to l. For example, an orbital with $n = 3$ and $l = 1$ will be a 3p-orbital. In general, for any n, there are a total of n^2 orbitals in that electron shell.

Table 3.1. Letters used to designate l.

l	**Letter**
0	s
1	p
2	d
3	f
4	g

Let us explore the shapes of different orbitals by analysing their wave functions. We will first look at the simplest orbital, the 1s-orbital ($n=1$, $l=0$, $m=0$). From solving the Schrödinger equation with this set of quantum numbers, we have:

$$\begin{aligned}\Psi_{100}(r,\theta,\phi) &= R_{10}(r)Y_{00}(\theta,\phi)\\ &= \left[a_0^{-\frac{3}{2}}2e^{-\frac{r}{a_0}}\right]\left[\frac{1}{2\sqrt{\pi}}\right]\\ &= \frac{1}{\sqrt{\pi}}a_0^{-\frac{3}{2}}e^{-\frac{r}{a_0}}\end{aligned}$$

Observe that the angular function is a constant, without the variables θ and ϕ. This means that the 1s-orbital is spherically symmetric. Looking at the function, we are unable to find any **nodes**. Nodes are regions where the **wave function passes through 0**. Nodes may be classified as radial nodes or angular nodes, depending on whether the radial or angular component of the wave function passes through 0. The 1s-orbital wave function is simply an exponential decay function in r and does not pass through 0, thus there are no nodes. We are able to plot the 1s-orbital wave function on a graph, or as a 3D electron cloud, shown in Figure 3.1.2.

Let us see how the wave function changes with n. Here is the wave function of 2s-orbital ($n=2$, $l=0$, $m=0$):

$$\begin{aligned}\Psi_{200}(r,\theta,\phi) &= R_{20}(r)Y_{00}(\theta,\phi)\\ &= \left[\frac{1}{2\sqrt{2}}a_0^{-\frac{3}{2}}\left(2-\frac{r}{a_0}\right)e^{-\frac{r}{2a_0}}\right]\left[\frac{1}{2\sqrt{\pi}}\right]\\ &= \frac{1}{4\sqrt{2\pi}}a_0^{-\frac{3}{2}}\left(2-\frac{r}{a_0}\right)e^{-\frac{r}{2a_0}}\end{aligned}$$

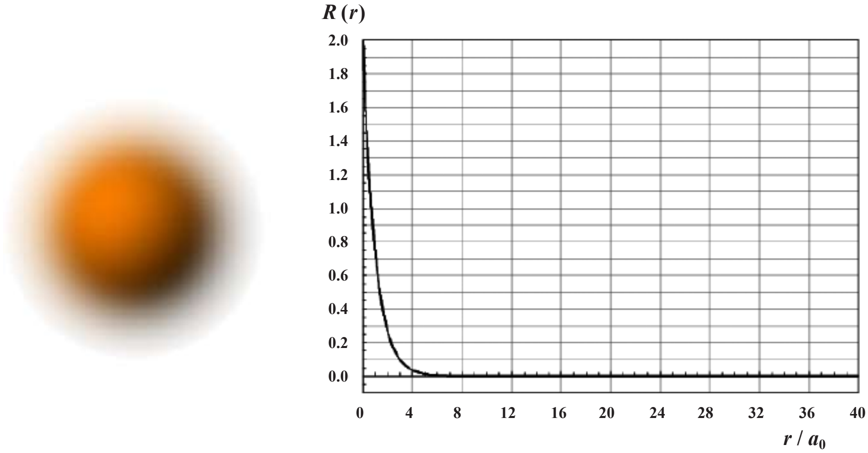


Figure 3.1.2. 2D and 3D plots of 1s-orbital wave function.

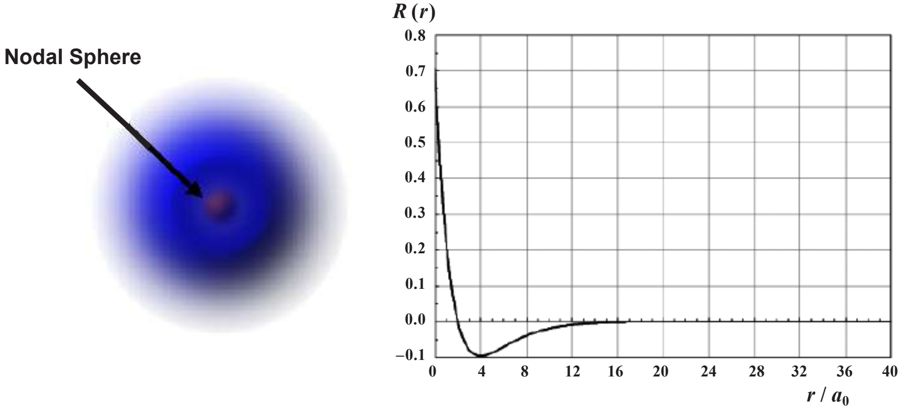


Figure 3.1.3. 2D and 3D plots of 2s-orbital wave function.

It has the exact same angular function as the 1s-orbital, thus the 2s-orbital is also spherically symmetric. However, in the 2s-orbital, there is a radial node, as the wave function passes through 0 when $2-\frac{r}{a_0}=0$. In 3D, the radial node is a nodal sphere at $r=2a_0$ from the nucleus. We may visualise the 2s-orbital wave function in a 2D graph and a 3D electron cloud, as shown in Figure 3.1.3.

As we move on to higher energy s-orbitals, the number of radial nodes increase. In general, a ns-orbital has $(\mathrm{n}-1)$ radial nodes. As the angular function is the same constant for all s-orbitals, s-orbitals are all spherically symmetric.

We move on to discuss 2p-orbitals $(n=2, l=1, m=-1,0,+1)$. There are 3 2p-orbitals along the 3-axes. The $2\mathrm{p}_z$-orbital is obtained when m = 0, with the wave function:

$$\psi_{210}(r,\theta,\phi)=R_{21}(r)Y_{10}(\theta,\phi)$$

$$=\left[\frac{1}{2\sqrt{6}}a_0^{-\frac{3}{2}}\left(\frac{r}{a_0}\right)e^{-\frac{r}{2a_0}}\right]\left[\frac{\sqrt{3}}{2\sqrt{\pi}}\cos\theta\right]$$

$$=\frac{1}{4\sqrt{2\pi}}a_0^{-\frac{3}{2}}\frac{r}{a_0}e^{-\frac{r}{2a_0}}\cos\theta$$

In the case of 2p-orbitals, the angular function contains the θ variable but not the ϕ variable. Thus, the 2p-orbital has cylindrical symmetry. There is no radial node in 2p-orbital, but there is an angular node when $\cos\theta=0$. The angular node is a nodal plane in the 3D electron cloud.

For the $2\mathrm{p}_x$ and $2\mathrm{p}_y$-orbitals, it is incorrect to assign the m values of +1 and −1 individually to the 2 orbitals. From the solution of Schrödinger equation, the angular functions corresponding to m values of +1 and −1 are complex functions. To obtain real electron wave functions for p_x and p_y-orbitals, we must perform

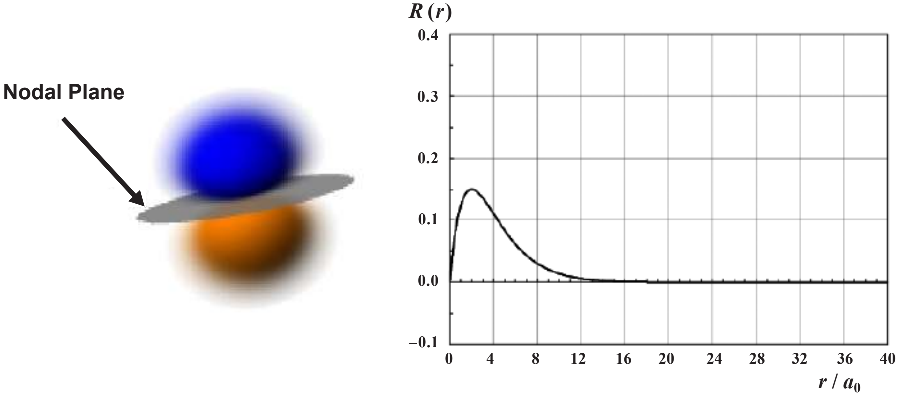


Figure 3.1.4. 2D and 3D plots of 2p-orbitals wave functions.

linear combination on the 2 complex functions. The real wave functions of $2\mathrm{p_x}$ and $2\mathrm{p_y}$ are given below:

$$2\mathrm{p_x} = \frac{1}{4\sqrt{2\pi}} a_0^{-\frac{3}{2}} \frac{r}{a_0} e^{-\frac{r}{2a_0}} \sin\theta\cos\phi$$

$$2\mathrm{p_y} = \frac{1}{4\sqrt{2\pi}} a_0^{-\frac{3}{2}} \frac{r}{a_0} e^{-\frac{r}{2a_0}} \sin\theta\sin\phi$$

The 2D graph and 3D electron cloud plots for the 2p-orbtials are shown in Figure 3.1.4.

Similar to s-orbitals, as n increases, there will be an increase in radial nodes in p-orbitals. For a np-orbital, it will have $(\mathrm{n}-2)$ radial nodes, which are nodal spheres. The analysis of wave functions may be extended to all orbitals, including d-orbitals $(l = 2)$ and f-orbitals $(l = 3)$. The electron cloud plot of the five d-orbitals and seven f-orbitals are shown in Figure 3.1.5.

Just like p-orbitals, $m = 0$ corresponds to the $\mathrm{d_{z^2}}$-orbital. The $\mathrm{d_{xz}}$ and $\mathrm{d_{yz}}$-orbitals are obtained through linear combination of $m = \pm 1$ functions and the $\mathrm{d_{xy}}$ and $\mathrm{d_{x^2-y^2}}$-orbitals are obtained through linear combination of $m = \pm 2$ functions.

Orbitals may be thought of as electron wave functions, and to determine the probability density of finding the electron, we must take the square of the modulus of the wave function:

$$\text{Probability Density}(r,\theta,\phi) \propto |\Psi(r,\theta,\phi)|^2$$

The probability density function has the same nodal and boundary surfaces as the orbital, just that all the negative signs in Ψ becomes positive in $|\Psi|^2$. The probability

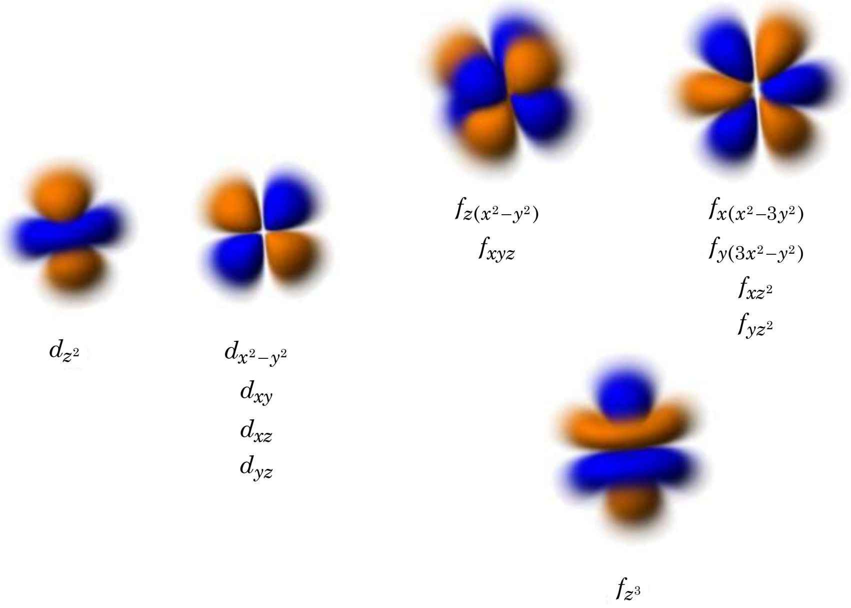


Figure 3.1.5. Electron cloud plots of d and f-orbitals.

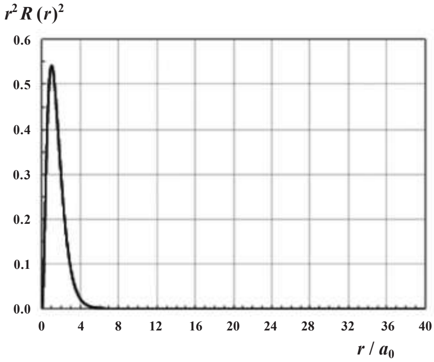
of finding the electron at a particular radius r away from the nucleus regardless of direction (θ,ϕ) is known as the radial distribution function:

$$\mathrm{Prob}(r) = r^2[R(r)]^2$$

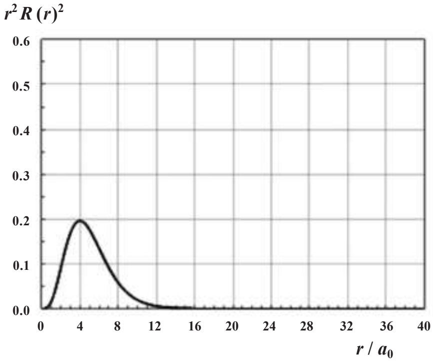
The plots of the radial distribution function correlate the Schrödinger wave model with Bohr's model. While Bohr's model postulates that electrons orbit the nucleus at fixed radius $r_n = n^2 a_0$ and are always found at exactly r_n, radial distribution functions derived from Schrödinger's wave model show that there is maximum probability of finding an electron at $r = r_n$. The radial distribution function is a smooth curve with peaks and nodes. Each curve decays smoothly to zero at large r, as we move further and further away from the nucleus. The graphs in Figure 3.1.6 show the radial distribution functions for common orbitals.

3.1.4 *Many-electron systems*

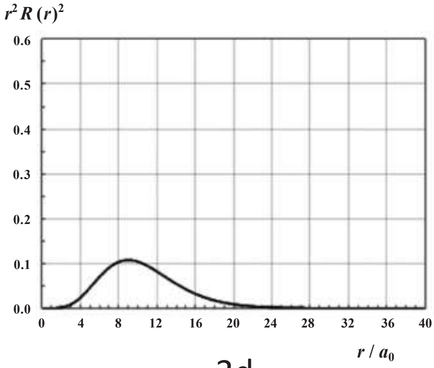
In the previous parts, we have only been solving the atomic structure for one-electron systems. If we were to add a second electron, 2 new interactions will come into existence. The second electron will experience attraction to the nucleus and repulsion from the first electron. This increases the degrees of freedom of the Schrödinger equation drastically, and it is impossible to solve for the exact wave function.



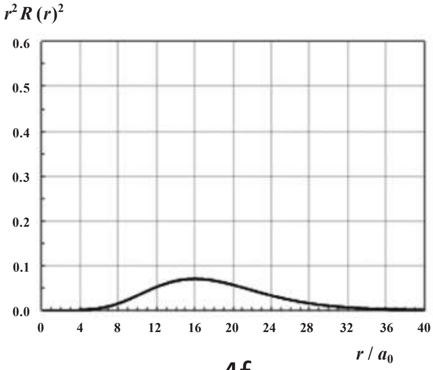
1s



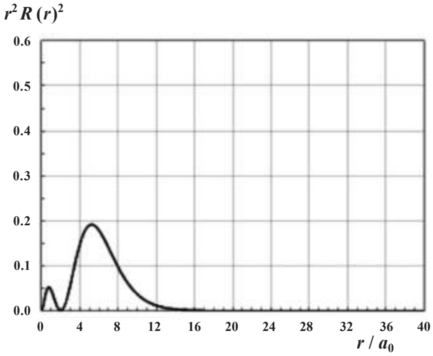
2p



3d



4f



2s

Note that for 1s, 2p, 3d and 4f orbitals, the radial distribution function peaks at $r = n^2 a_0$

Figure 3.1.6. Graphs of radial distribution functions for common orbitals.

If we first neglect the electron repulsion by applying the independent electron approximation, we are able to write the total wave function as a product of the individual wave functions. For a 2-electron helium atom,

$$\begin{aligned}\Psi(r_1,r_2) &\approx \Psi_{100}(r_1)\Psi_{100}(r_2)\\ &=\left[\left(\frac{a_0}{Z}\right)^{-\frac{3}{2}}2e^{-\frac{Zr_1}{a_0}}\right]\left[\left(\frac{a_0}{Z}\right)^{-\frac{3}{2}}2e^{-\frac{Zr_2}{a_0}}\right]\left(\frac{1}{2\sqrt{\pi}}\right)^2\\ &=\frac{Z^3}{\pi a_0^3}\left(e^{-\frac{Zr_1}{a_0}}\right)\left(e^{-\frac{Zr_2}{a_0}}\right)\end{aligned}$$

To account for the inter-electron repulsion, we must treat the electrons as independent waves. Assuming that the electronic charge is distributed around the nucleus, the other electrons will experience attractive force from the nucleus and an average repulsive force from the electronic charge. This repulsion that reduces the nuclear charge is known as shielding (S), and the electron will experience an effective nuclear charge (Z_{eff}) after subtracting the shielding(s) from the original nuclear charge (Z):

$$Z_{eff} = Z - S$$

By substituting the Z in the equation with Z_{eff}, the wave function for He atom may be written as:

$$\Psi(r_1,r_2) \approx \frac{Z_{eff}^3}{\pi a_0^3}\left(e^{-\frac{Z_{eff}r_1}{a_0}}\right)\left(e^{-\frac{Z_{eff}r_2}{a_0}}\right)$$

The shielding ability of electrons depends on the orbital they are in. The atomic orbitals have different wave functions and energies, and usually the inner-electrons are able to shield the outer-electrons from nuclear charge. For example, the 1s-electron is able to shield electrons in 2s, 2p and higher energy orbitals. However, as the 2s-orbital is lower in energy than the 2p-orbital, the 2s-orbital is more **penetrating** than the 2p-orbital. This means that there is a non-zero probability that the 2s-electron can be found closer to the nucleus than the 1s-electron and experience the full nuclear charge without being shielded by the 1s-electron.

To estimate the shielding effect an electron experiences from other electrons, we may employ **Slater's Rules**, which are empirically derived. The rules are as follows:

1. For an electron in (ns, np) orbital to be shielded by:

Other electrons in (ns, np) orbitals: $S = 0.35$

Other electrons in (n – 1) shell: $S = 0.85$

All other electrons (in (n – 2) shells or lower): $S = 1.00$

2. For an electron in (nd, nf) orbital to be shielded by:

Other electrons in (nd, nf) orbitals: $S = 0.35$

Other electrons in (ns, np) orbitals: $S = 1.00$

All other electrons (in (n – 1) shells or lower): $S = 1.00$

Let us use Slater's rules in an example to determine if the valence electron of potassium is in the 3d or 4s-orbital:

For the 4s-electron in the configuration $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 4s^1$: $S = 0.85 \times 8 + 1.00 \times 10 = 16.8$; $Z_{eff} = 19 - 16.8 = 2.2$

For the 3d-electron in the configuration $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 3d^1$: $S = 1.00 \times 18 = 18$; $Z_{eff} = 19 - 18 = 1$

Since the 4s-electron is under the influence of a greater Z_{eff}, the 4s-orbital is occupied in the ground state of potassium.

As a result of orbital penetration and shielding, the order of energies in a many-electron atom is typically $\mathrm{ns} < \mathrm{np} < \mathrm{nd} < \mathrm{nf}$ because in a given shell, s-orbitals are the most penetrating and f-orbitals are the least penetrating.

3.1.5 *3 Rules for electron filling*

We must apply 3 rules to determine the electron configuration of chemical species, which we will describe below:

1. Aufbau principle:

For ground state electron configurations, electrons fill the lower energy orbitals first before populating higher energy orbitals. The order of occupation follows: $1s$, $2s$, $2p$, $3s$, $3p$, $4s$, $3d$, $4p\ldots$

2. Hund's rule:
   a. Degenerate orbitals are always filled singly before any are doubly occupied as this minimises inter-electron repulsion.
   b. Electrons prefer to fill the separate orbitals with their spins aligned (same value of s). This is because electrons with aligned spin naturally keep further away from each other compared to electrons with opposite spins to further reduce electron-electron repulsion.
   c. Any state that does not satisfy both above but is permitted by Pauli exclusion principle is an excited state of the atom.

3. Pauli's exclusion principle:

No 2 electrons in any given atom can have exactly the same set of quantum numbers *n*, *l*, *m* and *s*. Any such state is forbidden.

There are exceptions to the first 2 rules stated above as half-filled and fully-filled subshells are more stable. As such, chromium has a $[\mathrm{Ar}]\ 3\mathrm{d}^5 4\mathrm{s}^1$ electron configuration (rather than $[\mathrm{Ar}]\ 3\mathrm{d}^4 4\mathrm{s}^2$) and copper has a $[\mathrm{Ar}]\ 3\mathrm{d}^{10} 4\mathrm{s}^1$ electron configuration (rather than $[\mathrm{Ar}]\ 3\mathrm{d}^9 4\mathrm{s}^2$). The other exception is when d-block metals form ions and complexes. For example, iron(0) atom usually has the $[\mathrm{Ar}]\ 3\mathrm{d}^6 4\mathrm{s}^2$ configuration, but in a complex, iron(0) has the $[\mathrm{Ar}]\ 3\mathrm{d}^8$ configuration. In addition, in transition metal cations such as Fe^{2+}, the 4s-electrons are lost first and the electron configuration of Fe^{2+} is $[\mathrm{Ar}]\ 3\mathrm{d}^6$.

3.2 Periodicity

The periodic table organises all known chemical elements in a systematic manner. In this chapter, we will explore the features of the periodic table that allow it to become arguably the most important tool for a chemist. The arrangement of elements in the periodic table follows periodic trends. Periodicity refers to these recurring trends that we will be discussing in this chapter.

3.2.1 *The periodic table*

In 1869 and 1870 respectively, Mendeleev and Lothar Meyer stated that properties of elements can be presented as periodic functions of their atomic weight. It is now recognised that periodicity is a consequence of the variation in ground state electronic configurations. Mendeleev's periodic table has 3 main features:

1. Allows us to interpret the periodic law in terms of the electronic structure of atoms.
2. Systematises trends in physical and chemical properties and detects possible anomalies.
3. Predicts the properties of new elements and compounds, leading to new areas of research.

The modern periodic table consists of 7 periods and 18 groups. A period is a horizontal row while a group is a vertical column. Elements are arranged in increasing atomic number, and the layout of the table reflects the electronic structure of the atoms of the elements. In the periodic table, hydrogen is usually placed in the first column, but it is not considered a group 1 element as it has unique properties. Excluding hydrogen, we may classify the periodic table into 4 sections:

1. s-block: Groups 1 and 2
2. p-block: Groups 13 to 18

3. d-block: Groups 3 to 12
4. f-block: Lanthanoids and Actinoids located in a separate section below the main table.

The naming of the block refers to the orbital that the valence electron occupies for elements in the block. The period number is the value of the principal quantum number, n, of the shell. A more general classification groups s-block and p-block elements together as main group elements, while d-block metals are known as transition metals. There is some controversy over whether group 12 metals are transition metals, as transition metals are defined as elements that have incomplete d-subshells in either the neutral atoms or ions. Previously, group 12 metals have never been known to exceed the +2 oxidation state, always leaving a full d-subshell. Recently, mercury (IV) fluoride has been reported, leaving mercury with an incomplete d-subshell. While the debates continue, it is generally easier to consider group 12 metals separate from transition metals as their properties differ. In the following chapters, we will delve deeper into the chemistry of main group and transition elements.

3.2.2 *Atomic radius*

Atomic radius, commonly understood as the size of the atom, is defined differently for covalent and metallic elements. For covalent molecules, the covalent radius is half of the inter-nuclear distance between neighbouring atoms of the same element in a molecule. For metals, the atoms are arranged in a solid lattice, and the metallic radius is defined as half the distance between the centres of neighbouring atoms in the solid lattice.

Atomic radius decreases across a period due to the increase in effective nuclear charge. The proton number increases while electrons are added to the valence shell. The poor shielding of nuclear charge by electrons in the same shell leads to overall increase in effective nuclear charge, pulling the valence electrons closer to the nucleus and decreasing the atomic radius.

Down a group, the atomic radius increases as the principal quantum number of the valence shell increases. The only anomaly is the **Lanthanide contraction**, where the metallic radii of the 6th-period transition metals are very similar to transition metals in the 5th-period and not significantly larger as might be expected given their considerably greater number of electrons. This is because the transition metals in the 6th-period are preceded by the lanthanoids, where the electrons occupy the 4f-orbitals. The f-electrons are poor at shielding and fail to compensate for the increasing nuclear charge, causing the effective nuclear charge to increase and the atom to be more compact.

3.2.3 *First ionisation energy*

The first ionisation energy is the energy required to remove the least tightly bound electron from the neutral atom in gas phase. The closer and more tightly bound an electron is to the nucleus, the more difficult it is to be removed, and the higher its ionisation energy will be. The first ionisation energy is mainly dependent on the energy of the highest occupied orbital of the ground-state atom.

Going across the period, ionisation energy increases as the effective nuclear charge experienced by the valence electrons increases. Going down the group, the valence electrons are located further and further from the nucleus while the effective nuclear charge it experiences increases only slightly due to the screening effect of extra electrons. Thus, ionisation energy decreases down the group.

Across the period, we observe 2 anomalies in the trend of ionisation energy. While the ionisation energy is supposed to increase across the period, it is observed that the ionisation energy of beryllium is higher than that of boron and that the ionisation energy of nitrogen is higher than that of oxygen. This trend across period 2 is also observed across the other periods.

To explain the anomalies, we must look at the valence shell electron configurations of the elements. Beryllium has the electron configuration $[\mathrm{He}]\ 2s^2$ while boron has the electron configuration $[\mathrm{He}]\ 2s^2 2p^1$. The valence electron of boron is in the higher energy 2p orbital, making the first ionisation energy of boron lower than that of beryllium. The electron configuration of nitrogen is $[\mathrm{He}]\ 2s^2 2p^3$ while the electron configuration of oxygen is $[\mathrm{He}]\ 2s^2 2p^4$. In nitrogen, the 2p subshell is relatively stable as it is half-filled with 3 electrons of the same spin. In oxygen, the fourth electron in the 2p subshell must have an opposite spin, paired with another electron in the same orbital. The inter-electron repulsion causes the fourth electron of oxygen to be at higher energy, making the ionisation energy of oxygen lower than that of nitrogen.

3.2.4 *Electron affinity*

Electron affinity is the difference in energy between the gaseous atom and the gaseous anion, measuring the ability for an atom to gain an electron to form an anion. Electron affinity is high when an electron can be added to an orbital that experiences a high effective nuclear charge. This is the case for elements at the top right of the periodic table. Electron affinity is negative when electrons are added to atoms with filled shells or subshells, as it costs energy to force an electron into a high energy orbital.

3.2.5 *Electronegativity*

Electronegativity is the power of an atom in a molecule to attract electrons to itself. There are a few definitions of electronegativity, and we will discuss 2 of the definitions here:

1. Mulliken electronegativity (χ_M)

By Mulliken definition,

$$\chi_M = \frac{1}{2}(\mathrm{IE}_1 + \mathrm{E}_\mathrm{a})$$

Where IE_1 is the first ionisation energy and E_a is the electron affinity.

If an atom has a high ionisation energy and high electron affinity, then it will be more willing to acquire electrons when it is part of a compound. Thus, it is classified as highly electronegative. On the other hand, if both values are low, the atom will tend to lose electrons and it is classified as electropositive.

2. Pauling electronegativity (χ_p)

Pauling observed in the 1930s that the bond dissociation energy (BDE) of heteronuclear bonds did not correlate well with a simple additive rule. For example, the expected BDE of $\mathrm{H{-}F}$ single bond is the average of the BDEs of H_2 and F_2:

$$\text{Expected BDE} = \frac{436 + 158}{2} = 297\ \mathrm{kJ\ mol^{-1}}$$

However, the experimental BDE of HF is $570\ \mathrm{kJ\ mol^{-1}}$. The difference in BDEs may be attributed to the ionic contribution of the bond. Thus, the greater the difference between the BDEs, the greater the ionic character of the bond and the greater the electronegativity difference between the 2 atoms. Pauling defined the difference in electronegativity between 2 atoms as the square root of the difference in BDEs:

$$\Delta\chi_p = \sqrt{\Delta \mathrm{BDE}}$$

To calculate an absolute value of electronegativity for all elements on the periodic table, Pauling fixed the electronegativity of hydrogen at 2.2 as an arbitrary reference and used it to determine the electronegativity of the other elements. Currently, Pauling electronegativity is the most commonly used electronegativity scale.

As a periodic trend, there is a general increase in electronegativity across a period and a general decrease down a group. Despite the different definitions, the trends in electronegativities are roughly in agreement.

3.3 Chemical Bonding

In this chapter, we will learn the geometries of molecules and their electronic structures. We will start by describing methods to draw molecular structures and predict their geometries. Then, we will move on to theories that describe the electronic properties of bonding. The theories covered in this chapter will be the cornerstone to understanding chemical and physical properties of molecules.

3.3.1 *Lewis structures*

Lewis structures may be proposed for covalent molecules, where all bonding involve the sharing of electrons between atoms. Only valence electrons are used to construct the Lewis structure of a molecule. Valence electrons may be used to form a covalent bond, or left unshared on the original atom. Unshared pairs of valence electrons are known as **lone pairs**, which do not contribute to bonding but influence the geometry of the molecule and its chemical and physical properties. A Lewis structure is complete when all atoms in the molecule are connected through covalent bonds and all valence electrons are distributed within the structure as either bonding electrons or lone pairs, such that all atoms obey the octet rule.

The **octet rule** states that atoms share electrons with neighbouring atoms to achieve a total of 8 valence electrons, known as an octet. This is based on the concept of fully filling the s and p subshells to achieve a stable electron configuration. Thus, the concept of octet rule is strictly limited to elements in the 2nd period. However, we usually generalise the octet rule and apply it to other main group elements in lower periods. For hydrogen, it only has a 1s-orbital, thus, it follows the duplet rule. For elements from the 3rd period onwards, it is possible for atoms to have more than 8 electrons in the valence shell, known as **hypervalence**.

To construct a Lewis structure, we may follow the 4 steps below:

1. Find the total number of valence electrons required for each atom to attain noble gas configuration.
2. Find the actual number of valence electrons present, accounting for the overall charge.
3. Subtract the actual number of valence electrons from the total number of valence electrons required to find the number of valence electrons that must be shared. The total number of bonds will be half the number of valence electrons to be shared.
4. After the bonds are drawn, add lone pairs to each atom until it has a full octet.

It is useful to note that the least electronegative element is usually the central atom of the molecule, but there are many well-known exceptions, such as H_2O and NH_3. Let us demonstrate how to apply these rules by drawing the Lewis structure of BF_4^-:

1. All 5 atoms require 8 electrons to achieve noble gas configuration, thus a total of $5 \times 8 = 40$ valence electrons are required.
2. Boron has 3 valence electrons while each fluorine has 7 valence electrons. Accounting for the overall −1 charge, there are a total of $3 + (4 \times 7) + 1 = 32$ valence electrons present.
3. The number of valence electrons that needs to be shared is $40 - 32 = 8$. 8 valence electrons correspond to $\frac{8}{2} = 4$ bonds.

4. After the 4 B–F bonds are drawn, boron already has a full octet. Each fluorine needs 6 more valence electrons, which should be added as 3 lone pairs.

As boron is the least electronegative atom, it is likely to be the central atom, and the final Lewis structure of BF_4^- may be given as shown in Figure 3.3.1.

There are certain important features that we must know about Lewis structures. Firstly, certain Lewis structures have many resonance forms. **Resonance** is to signify that there is more than one possible way in which the valence electrons can be arranged in a Lewis structure. For example, carboxylate anion has 3 resonance forms, as shown in Figure 3.3.2.

Resonance may be understood as a blending of structures, and the blended structure is known as a resonance hybrid. The resonance hybrid averages the bond characteristics over the molecule, resulting in it having a lower energy than any single contributing structure. This is in agreement with experimental results showing that all 3 C–O bonds in carboxylate are in fact equivalent. In this case, all 3 contributing structures are identical in energy and contribute equally to the resonance hybrid. Structures with different energies may also contribute to an overall resonance hybrid, but the higher-energy structure has a smaller contribution.

The second important feature in Lewis structures is **formal charge**, which is the apparent electronic charge of each atom in a molecule based on the Lewis structure. Formal charge on an atom is defined as the number of valence electrons in a free atom of the element minus the number of unshared electrons on the atom and the number of bonds to the atom. Formal charge is only a tool for assessing Lewis structures, not a measure of the actual charge on the atoms. Structures minimising formal charges, placing negative formal charges on the more electronegative elements and those with smaller separation of charges tend to be favoured as they have lower energy. As an example, we may assign formal charges to different resonance structures of SCN^-, as shown in Figure 3.3.3.

In A, the formal charge, –1, is placed on the most electronegative atom. In B, the –1 formal charge lies on the less electronegative sulfur. C has larger formal charges

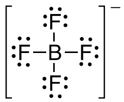


Figure 3.3.1. Lewis structure of BF_4^-.

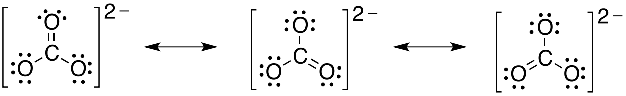


Figure 3.3.2. Resonance structures of carboxylate anion.

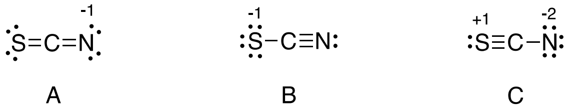


Figure 3.3.3. Different possible resonance structures of SCN^{-} with formal charges assigned.

and larger charge separation. Thus, resonance structure A is the most important, followed by B, and C is only of minor importance.

Finally, certain molecules with atoms beyond period 2 exhibit hypervalence. For example, the bonding in PCl_5 requires the P atom to have 10 electrons in the valence shell. Hypervalent species have Lewis structures that demand the presence of more than an octet of electrons around at least one atom.

The geometry of molecules may be predicted by **Valence Shell Electron Pair Repulsion (VSEPR)** theory. This approach allows us to find the approximate shapes of molecules for molecules with a central p-block atom. To determine the exact geometry of the molecule, we must use X-ray diffraction. VSEPR theory assumes that the regions with enhanced electron density, such as bonding and lone electron pairs, take up positions as far apart as possible to minimise the repulsions between them. This theory is a basic theory that does not account for steric factors and may not be used when the central atom is from the d-block.

The total number of electron regions refer to the sum of the number of atoms surrounding the central atom and the number of lone pairs on the central atom. When there are lone pairs, the lone pairs are considered regions of high electron density, affecting the geometry of the other atoms. We may determine the geometry of a molecule using VSEPR theory by counting the total number of electron region and number of lone pairs on the central atom. The predicted geometries are given in Table 3.2.

Table 3.2. Geometries based on VSEPR theory.

Number of lone pairs / Number of electron regions	**0**	**1**	**2**	**3**	**4**	**Ideal bond angles**
2	Linear					180°
3	Trigonal Planar	Bent				120°
4	Tetrahedral	Trigonal Pyramidal	Bent			109.5°
5	Trigonal Bipyramidal	See-saw	T-shaped	Linear		120° and 90°
6	Octahedral	Square Pyramidal	Square Planar	T-shaped	Linear	90°

When the number of electron regions increases beyond 6, VSEPR predictions may be substantially erroneous. When there are 7 electron regions, such as in IF_7 and $[TeF_7]^-$, VSEPR theory predicts pentagonal bipyramidal geometry, but experimental evidence shows that the equatorial F atoms are not co-planar. In this case, it is because lone pairs are stereochemically less influential when they belong to heavy p-block elements. In $[SeCl_6]^{2-}$, $[TeCl_6]^{2-}$ and $[BrF_6]^-$, the lone pair is stereochemically inactive and the molecules have regular octahedral structure.

Molecules may deviate from the ideal geometry as the repulsion between electron regions vary. Lone pair-lone pair repulsions are the strongest, followed by lone pair-bonding pair repulsions, and bonding pair-bonding pair repulsions are the weakest. Within bonding pair-bonding pair repulsions, repulsions between multiple bonds, with higher electron density, are stronger. This will cause the actual bond angles to deviate from the ideal bond angles, which assume that all repulsions are equally strong.

3.3.2 *Valence bond theory*

From the previous part, we have learnt the structure of molecules and the general concept of covalent bonding as the sharing of electrons between neighbouring atoms. In this part, we will discuss the valence bond theory, the basic theory reconciling covalent bonding with electron orbitals being wavefunctions.

In 1927, Heitler and London applied the independent particle model to H_2, calculating the energy of H_2 by treating the 2 atoms separately. Their calculation results differ significantly from experimental results. To improve their results, they have to consider the covalent bond between the 2 atoms, accounting for the sharing of electrons by the 2 nuclei. The exchange of electrons provides extra energy that gives rise to a deep minimum in the potential energy curve. The formation of a covalent chemical bond is fundamentally a quantum mechanical phenomenon.

Valence bond theory is the first quantum mechanical theory of bonding to be developed, where bonds are formed through the overlap of orbitals. We may write the bonding in a $H{-}H$ molecule as:

$$\Psi_{VB}(r_1, r_2) = \frac{1}{\sqrt{2}}[1s_{H_a}(r_1)1s_{H_b}(r_2) + 1s_{H_a}(r_2)1s_{H_b}(r_1)]$$

The first factor $\frac{1}{\sqrt{2}}$ is known as the normalisation factor, which is defined as

$$N = \frac{1}{\sqrt{C_1^2 + C_2^2 + C_3^2 + \cdots}}$$

where C is the coefficient of the atomic orbital.

Note that there are 2 terms in the bracket. The first term assumes that each electron stays with its own nucleus, applying the independent particle assumption.

Table 3.3. Hybridisations that correspond to the number of electron regions.

Number of electron regions	Hybridisation	Geometry
2	sp	Linear
3	sp^2	Trigonal Planar
4	sp^3	Tetrahedral
5	$sp^3d_{z^2}$	Trigonal Bipyramidal
6	sp^3d^2	Octahedral

The second term is the exchange term where each electron spends time with the other nucleus.

To account for the shape of molecules that we have determined from the VSEPR theory, Pauling came up with the theory of orbital hybridisation in 1931. **Orbital hybridisation** is the linear combination of certain atomic orbitals to obtain a set of hybrid orbitals. Depending on the number of electron regions, different orbitals are combined, as shown in Table 3.3.

As an example, we will examine sp^3-hybridisation, present in the central atom of tetrahedral molecules. By combining one s-orbital and three p-orbitals, we form four equivalent sp^3-orbitals. It is important to note that the number of hybrid orbitals formed must be equivalent to the number of atomic orbitals originally combined. The sp^3-hybrid orbitals wavefunctions are obtained through the linear combination of the wavefunctions of the atomic orbitals.

$$\Psi_{sp^3} = \frac{1}{2}(\Psi_{2s} + \Psi_{2p_x} + \Psi_{2p_y} + \Psi_{2p_z})$$
$$\Psi_{sp^3} = \frac{1}{2}(\Psi_{2s} + \Psi_{2p_x} - \Psi_{2p_y} - \Psi_{2p_z})$$
$$\Psi_{sp^3} = \frac{1}{2}(\Psi_{2s} - \Psi_{2p_x} + \Psi_{2p_y} - \Psi_{2p_z})$$
$$\Psi_{sp^3} = \frac{1}{2}(\Psi_{2s} - \Psi_{2p_x} - \Psi_{2p_y} - \Psi_{2p_z})$$

Each sp^3-hybrid orbital consists of a larger lobe pointing in the direction of one corner of a tetrahedron and a smaller lobe of the opposite sign, pointing in the opposite direction. Figure 3.3.4 shows the shapes of different hybrid orbitals, omitting the smaller lobe.

Hybrid orbitals are only able to form σ-bonds, which are formed from the head-on overlap of 2 orbitals. σ-bonds are defined based on their cylindrical symmetry about the inter-nuclear axis, which means that the wavefunction is unchanged through any amount of rotation about the inter-nuclear axis. All single bonds are σ-bonds, but multiple bonding involves another type of bond, the π-bond. π-bonds can only be formed by the sideways overlap of unhybridised orbitals. They are classified based on the interchange of sign when the bond is rotated 180° about the inter-nuclear axis. For double bonds, they generally consist of 1 σ-bond and 1 π-bond, while triple bonds consist of 1 σ-bond and 2 π-bonds. There is another type of rare bond known as the δ-bond, formed through the face-on overlap of d-orbitals. This bond is only encountered when discussing metal-metal multiple bonding and will not be explored extensively in this book. Figure 3.3.5 shows the different types of bonds discussed above.

As valence bond theory was the first theory to be proposed, detailed experimental studies found discrepancies. For example, calculations show that the energy of 3d-orbitals are too high to combine with s and p-orbitals in sp^3d and sp^3d^2-hybridisations. Also, it is unable to explain certain resonance structures, where the bond order may be a non-integer value, such as in ozone. The structure of ozone is shown in Figure 3.3.6.

In the case of resonance structures, the hybridisation of certain atoms are also not clearly defined. In the case of the terminal oxygens in ozone, they may be either sp^2 or sp^3-hybridised depending on the resonance structure considered. This causes confusion as it becomes impossible to assign the hybridisation certainly. Finally,

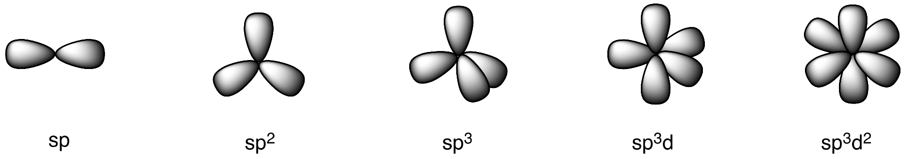


Figure 3.3.4. Shapes of different hybrid orbitals.

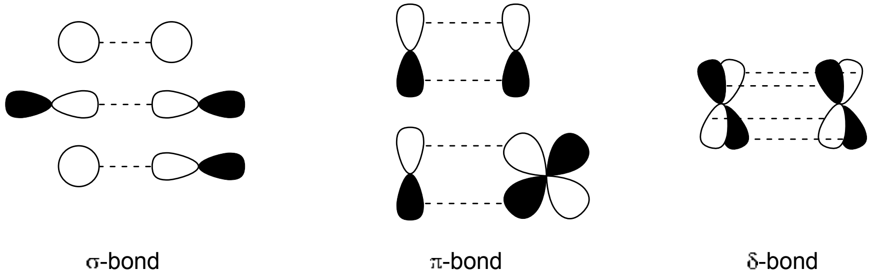


Figure 3.3.5. σ, π and δ-bonds.

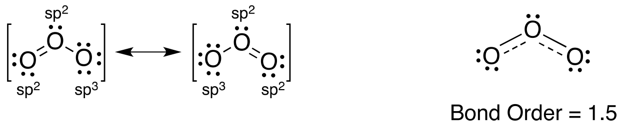


Figure 3.3.6. Resonance structures of ozone.

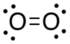


Figure 3.3.7. Lewis structure of O_2.

valence bond theory comes into clear contradiction with experimental results as liquid oxygen experiences an attractive force when passing through a powerful magnet. Valence bond theory and the Lewis structure of O_2 show that there are no unpaired electrons, as shown in Figure 3.3.7.

From the experimental observations, O_2 is a biradical, having 2 unpaired electrons. Thus it is paramagnetic and attracted to magnets. To overcome the limitations of valence bond theory, we will move on to discuss molecular orbital theory.

3.3.3 *Molecular orbital theory*

The **molecular orbital (MO)** is the regions of space spread across the entire molecule that a single electron might occupy. MOs may be obtained from linear combination of atomic orbitals, following the rule that the number of MOs that can be formed must equal the number of atomic orbitals of the constituent atoms. Since orbitals are essentially wave functions, 2 atomic orbitals may overlap either constructively or destructively to form the bonding and antibonding MOs respectively.

The interactions between atomic orbitals are only allowed when the orbitals have the same symmetry along the bond axis, such as σ and π-symmetry. Mathematically, the overlap integral between a σ-symmetric orbital and a π-symmetric orbital is 0. The overlap between atomic orbitals of the same symmetry is only efficient when the region of overlap between the 2 atomic orbitals is significant and the energies of the atomic orbitals are close. Mathematically, the wave functions of the MOs may be easily derived from the wave functions of the atomic orbitals:

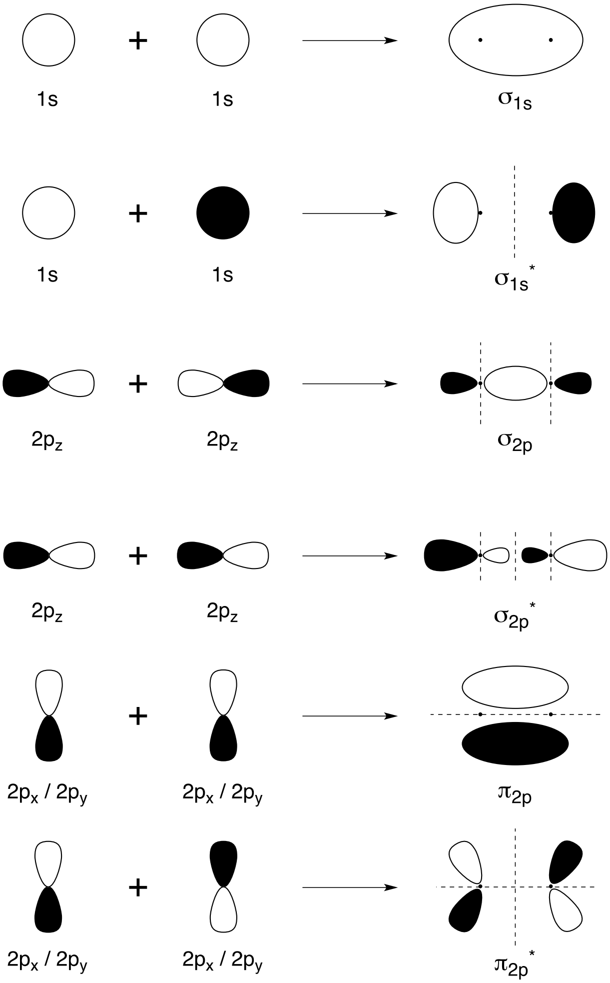
$$\Psi_{\text{Bonding MO}} = \Psi_{\text{MO}} = N(\Psi_1 + \Psi_2)$$

$$\Psi_{\text{Antibonding MO}} = \Psi^*_{\text{MO}} = N(\Psi_1 - \Psi_2)$$

where N is the normalisation factor and Ψ_1, Ψ_2 are wavefunctions of atomic orbitals. The antibonding MO is usually indicated with an asterisk *. Figure 3.3.8 shows the structures of MOs derived from s and p-atomic orbitals.

As a basic example, we will draw the MO diagram for O_2, which is a homonuclear diatomic molecule. To draw a MO diagram, we start by considering the valence orbitals of the atoms, and list them out according to their energies. Following that, the orbitals with the same symmetries and similar energies will overlap to form molecular orbitals. Finally, electrons may be filled into the MO diagram following the same principles of electron filling explained in 3.1.5. The MO diagram of O_2 is shown in Figure 3.3.9.

The atomic orbitals with identical energies may be represented by lines at the same horizontal level as per the example, or stacked on top of each other with a small gap in between (≡). The second representation allows the MO diagram to be more compact and it should not be misinterpreted as the 3 atomic orbitals having slightly different energies. The energy gap between σ and σ*-orbitals is larger than that between π and π*-orbitals as there is a larger region of head-on overlap in



No. of Nodes

	Perpendicular to bond axis	Along bond axis
σ_{1s}	0	0
σ_{1s}^*	1	0
σ_{2p}	2	0
σ_{2p}^*	3	0
π_{2p}	0	1
π_{2p}^*	1	1

Figure 3.3.8. Shapes of molecular orbitals arising from linear combination of identical orbitals.

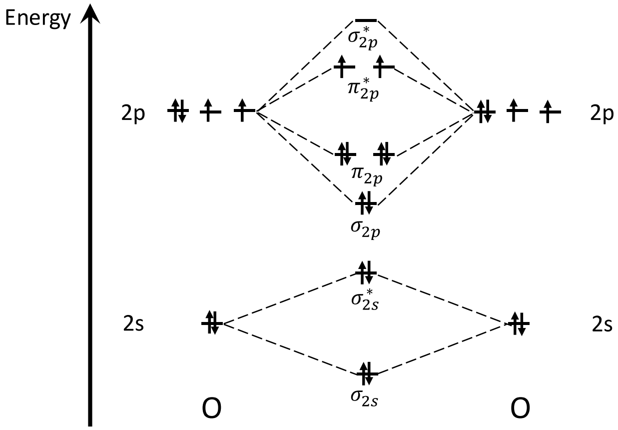


Figure 3.3.9. MO diagram of O_2.

σ-orbitals compared to side-on overlap in π-orbitals. Based on the MO diagram, we may write the O_2 electron configuration as:

$$(\sigma_{2s})^2(\sigma_{2s}^*)^2(\sigma_{2p})^2(\pi_{2p})^4(\pi_{2p}^*)^2$$

As there are 2 unpaired electrons in the π_{2p}^* orbital of O_2, O_2 is paramagnetic, which is in agreement with experimental observations. The bond order may be calculated from the MO diagram with the following equation:

$$\text{Bond Order} = \frac{1}{2}(\text{no. of electrons in bonding orbitals} \\ - \text{no. of electrons in antibonding orbitals})$$

For O_2, we may calculate its bond order as $\frac{1}{2}(8-4)=2$, agreeing with the double bond shown in the Lewis structure of O_2.

However, MO energy levels are not as straightforward for other period 2 diatomic molecules. As an example, the MO diagram of N_2 is shown in Figure 3.3.10.

We observe the **σ-π reversal**, where the energy of the σ_{2p}-orbital is higher than that of the π_{2p}-orbital. This is due to the small energy gap between 2s and 2p-orbitals, allowing 2s and $2p_z$ orbitals to interact as they are both of σ-symmetry. Thus, we may think of the four σ-orbitals (σ_{2s}, σ_{2s}^*, σ_{2p} and σ_{2p}^*) to be formed from the linear combination of the four 2s and $2p_z$ orbitals. From orbital energy calculations, s-p mixing is only significant for period 2 elements up to nitrogen, as the 2s-orbital energy decreases much more quickly with increasing nuclear charge than 2p-orbital energy. This is because the 2s-orbital is closer to the nucleus than the 2p-orbital. Thus, the σ-π reversal is present in the MO diagrams of all diatomic molecules consisting of at least one atom that comes before or is nitrogen.

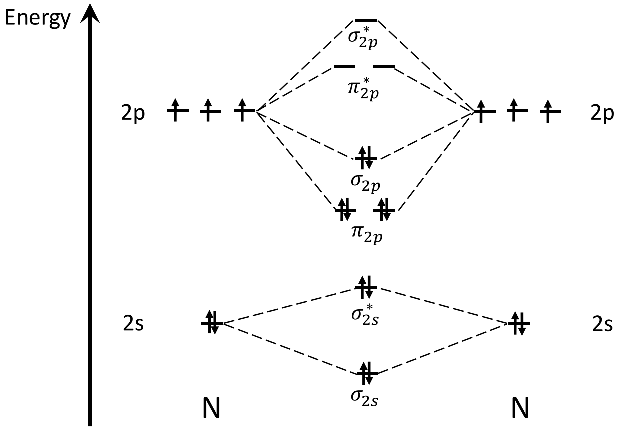


Figure 3.3.10. MO diagram of N_2.

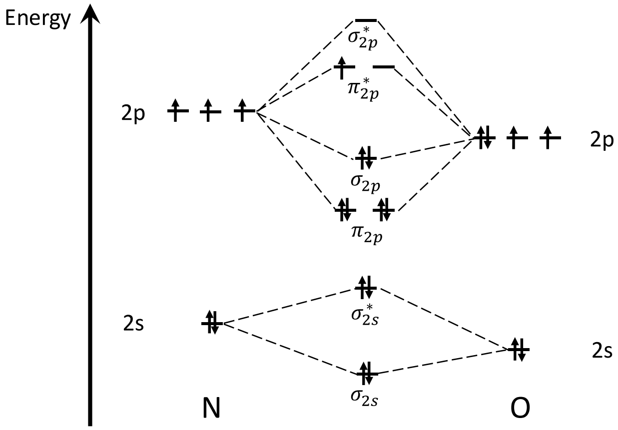


Figure 3.3.11. MO diagram of NO.

Now that we have described how to draw MO diagrams for homonuclear diatomic molecules, let us move on to the MO diagrams of heteronuclear diatomic molecules. For this example, we will look at the MO diagram of NO, which is shown in Figure 3.3.11.

As NO contains nitrogen, there is σ-π reversal, as shown in the MO diagram. The electron configuration is $(\sigma_{2s})^2(\sigma^*_{2s})^2(\pi_{2p})^4(\sigma_{2p})^2(\pi^*_{2p})^1$ and the bond order is 2.5. Note that the atomic orbitals of oxygen are slightly lower in energy than those of nitrogen due to the increase in nuclear charge. Thus, the shapes of the MOs are no longer symmetrical. The bonding MOs have higher coefficients on the more electronegative atom (oxygen) while the antibonding MOs have higher coefficients

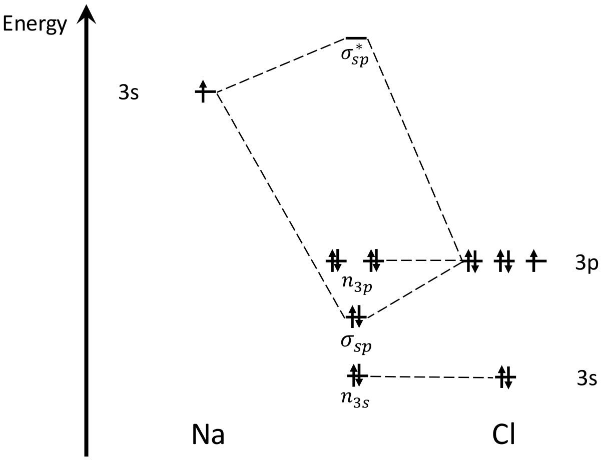


Figure 3.3.12. MO diagram of $NaCl$.

on the less electronegative atom (nitrogen). This is because electrons have a lower energy if they are near a more electronegative atom, and a bonding orbital would thus have a higher coefficient at the more electronegative atom to make it more stable.

The MO theory may be extended to discuss bonding in ionic molecules. The ionic bond is generally understood to be a charge interaction between 2 oppositely charged ions that are formed from an electron transfer from one atom to another. As an example, we will look at the MO diagram of $NaCl$ shown in Figure 3.3.12.

All the filled MOs in $NaCl$ are closer in energy to the AOs of the Cl atom. Thus, the Na–Cl bond is highly polarised, with most of the electron density on Cl. The only interaction is the σ-interaction between the 3s-orbital of Na and 3p$_z$-orbital of Cl, as the 3s-orbital of Cl is too low in energy to interact with the 3s-orbital of Na. The Cl atomic orbitals which are unable to interact with Na atomic orbitals will remain at the same energy level as non-bonding orbitals. These electrons do not contribute in any way to the bonding between Na and Cl.

Using MO theory, we may determine the reactivity of the molecule from its frontier orbitals. The **frontier orbitals** are the **highest occupied molecular orbital (HOMO)** and **lowest unoccupied molecular orbital (LUMO)**. As chemical reactions are generally electron transfers between molecules, the HOMO contains electrons with the highest energy that can be transferred to another molecule while the LUMO is the empty orbital with the lowest energy that can accept electrons from another molecule. Thus, the HOMO and LUMO energies play an important role in the reactivity of a molecule.

3.4 Acid-Base Chemistry

Acids and bases have been studied since ancient times due to their interesting properties and reactions, such as the sour taste of acids and the bitter taste of bases. Most importantly, they are known to be able to neutralise each other and form salts. Many chemists have proposed various definitions for acids and bases, and we will explore these definitions in this chapter, together with common acids and bases that fall under such definitions. At the end of the chapter, we will discuss the hard-soft acid-base theory, which is widely applied in explaining many chemical reactions.

3.4.1 *Acid-base theories*

While many acid-base theories have been proposed, we will focus on the 3 most widely accepted theories, and discuss them in chronological order:

1. Arrhenius theory (1887)

Arrhenius received the Nobel prize in 1903 for his acid-base theory, after establishing the presence of ions in aqueous solution. By Arrhenius definition, an acid is any species that forms H^+ in aqueous solution, and a base is any species that forms OH^- in aqueous solution. This allows us to explain the experimental observation that acid reacts with base to form salt and water. However, the Arrhenius theory is rather limited as it may only be applied to aqueous solutions, and the scope for acid and base is narrow, especially because OH^- is the only type of base.

2. Brønsted-Lowry theory (1923)

Brønsted-Lowry theory aims to generalise the Arrhenius definition by defining acids as H^+ donors and bases as H^+ acceptors. This allows us to define conjugate acids and bases, formed from the reactions between Brønsted-Lowry acids and bases. For example, if we look at the autoionisation of water:

$$\underset{\text{(Base)}}{\mathrm{H_2O}} + \underset{\text{(Acid)}}{\mathrm{H_2O}} \rightleftharpoons \underset{\text{(Conjugate Acid)}}{\mathrm{H_3O^+}} + \underset{\text{(Conjugate Base)}}{\mathrm{OH^-}}$$

After an acid donates a proton, it becomes a conjugate base, as the new species (OH^-) formed can now accept a proton. Similarly, a base becomes a conjugate acid after accepting a proton. As equilibrium is established by the acid with its conjugate base, and the base with its conjugate acid, the acid and base strengths are related to the strengths of the conjugate acid and base. The stronger the acid, the weaker its conjugate base, and similarly for the base. This is because a stronger acid is more willing to donate its proton to form the conjugate base, resulting in the conjugate base being less willing to accept a proton to regenerate the acid.

3. Lewis theory (1923)

Lewis theory defines an acid as an electron-pair acceptor and a base as an electron-pair donor. This further expands the list of acids to include metal ions and other molecules with empty orbitals. When such acids react with bases, the product is known as a **Lewis acid-base adduct**. Adducts involving metal ions as the Lewis acid are also known as coordination complexes, which will be discussed in greater detail in chapter 3.7. Lewis theory may be understood from a frontier orbital perspective, where the acid has a low-energy LUMO and the base has a high-energy HOMO, and the acid-base reaction involves the transfer of an electron pair from the HOMO of the base to the LUMO of the acid.

3.4.2 *Brønsted acids and bases*

There is a large variety of inorganic Brønsted acids and bases, and we will look at some characteristic examples, starting with Brønsted acids:

1. Hydrogen halides (HX)

Hydrogen halides are strong monobasic Brønsted acids, other than HF. HF is a weak acid due to the strong $\mathrm{H{-}F}$ bond, and the clustering of HF molecules. However, at high concentrations, HF undergoes homoassociation:

$$2\ \mathrm{HF} \rightarrow \mathrm{HF_2^-} + \mathrm{H^+}$$

This makes concentrated HF extremely corrosive and able to attack glass.

2. Oxoacids

Oxoacids are compounds with the acidic proton on a hydroxyl group with at least 1 oxo group attached to the same atom. The common oxoacids are phosphoric acid, nitric acid, sulfuric acid and perchloric acid. Pauling's rules provide a general guideline to calculate the first pK_a of oxoacids:

$$pK_{a1} = 8 - 5p$$

Where p is the number of oxo groups attached to the central atom.

The pK_as for subsequent dissociations in polyprotic acids increases by 5 with each dissociation. For example, sulfuric acid with 2 oxo groups ($p = 2$) and 2 hydroxyl groups bound to the central sulfur atom is predicted to have $pK_{a1} = 8 - 5(2) = -2$ and $pK_{a2} = -2 + 5 = 3$. It is found experimentally for sulfuric acid that its $pK_{a1} = -3$ and $pK_{a2} = 1.99$, which is slightly different from those predicted by Pauling's rules. However, Pauling's rules still serve as a simple way to approximate the pK_a values of oxoacids. Oxoacids are generally strong acids due to the inductive and resonance stabilisation of the conjugate base by the oxo groups.

3. Aquated cations ($[M(OH_2)_x]^{n+}$)
When metal cations with high charge density form aqua complexes, the $O–H$ bond in H_2O is highly polarised, with electron density drawn towards oxygen. This leaves the hydrogen with a partial positive charge, and it is now able to leave as a H^+ cation. Thus, aquated cations are considered Brønsted acids, with the acidity dependent mainly on the charge density of the central metal cation.

We will now look at common Brønsted bases:

1. Hydroxides (MOH)
Hydroxides are the most common inorganic bases, falling under all the 3 acid-base theories. The hydroxides are strong bases when they have high solubility in water, such as the group 1 hydroxides (other than $LiOH$, which has a significantly lower solubility).

2. Nitrogen bases (NR_3)
Nitrogen forms trivalent compounds with a lone pair of electrons on N. This allows the nitrogen atom to accept a H^+ cation and act as a Brønsted base.

3.4.3 *Lewis acids and bases*

Lewis theory is the most inclusive of the acid-base theories, allowing a large list of compounds to be classified as acids or bases. Unlike Brønsted acids, Lewis acids do not need to have an acidic proton. We will start by discussing the types of Lewis acids:

1. Incomplete octet
As Lewis acids are electron pair acceptors, any molecule with an incomplete octet can act as a Lewis acid. A common example would be boron trihalides (BX_3), as the central boron atom has an empty p-orbital that allows it to accept an electron pair from a Lewis base.

2. Metal cation
Metal cations can accept electron pairs from Lewis bases to form coordination complexes. The chemistry of coordination complexes will be discussed further in chapter 3.7.

3. Rearrangeable valence electrons
A molecule which already has a complete octet may be able to rearrange its valence electrons to accept an additional electron pair. For example, CO_2 is a Lewis acid as it is able to react with a hydroxide ion by breaking one $C–O$ bond to form the bicarbonate anion (HCO_3^-).

4. Expandable valence shells
Compounds with full octet configuration may be able to accept more electron pairs by expanding their octet. For example, SiF_4 is able to react with F^- anions to form SiF_6^{2-}, where the central Si atom is hypervalent.

Lewis bases include any molecule with a lone pair of electrons that can be donated to a Lewis acid. Thus, Lewis bases may either be anionic or neutral. When Lewis bases form dative bonds with metal cations in coordination complexes, they are known as ligands and have interesting chemical properties that will be described in chapter 3.7.

3.4.4 *Hard-soft acid-base (HSAB) theory*

Acids and bases may be classified into hard and soft acids and bases based on their **charge density** and **polarizability**. Hard acids and bases have high charge density and are not very polarisable. On the other hand, soft acids and bases have low charge density and high polarizability. Table 3.4 classifies the common acids and bases by the HSAB theory.

HSAB theory states that hard acids prefer hard bases while soft acids prefer soft bases. This is because hard acids and hard bases are able to form strong charge interactions, leading to strong ionic bonds. On the other hand, soft acids and soft bases have diffuse electron clouds and orbitals, forming strong covalent bonds. Compounds formed from hard-soft interactions are generally polar covalent and are highly reactive to form ionic and covalent compounds.

HSAB theory may be applied to solubility of salts. The hydration energy from dissolution comes from the interactions between water and the ions. As water is a hard acid and hard base, it forms strong interactions with hard cations and anions, and the hydration enthalpy is highly negative. However, the interactions between water and soft ions is weak. Thus, salts made up of soft acids and soft bases are generally insoluble as the soft acid-soft base interaction is strong but the soft acid-hard base and hard acid-soft base interactions after dissolution are weak. For example, soft acid halides ($AgCl$, $AgBr$, $CuBr$, $AuCl$) are insoluble in water.

Table 3.4. Classification of common acids and bases by HSAB theory.

	Hard	Borderline	Soft
Acid	H_2O, H^+, Li^+, Na^+, K^+, Be^{2+}, Mg^{2+}, Ca^{2+}, Sr^{2+}, BF_3, $B(OR)_3$, Al^{3+}, $AlCl_3$, AlH_3, Cr^{3+}, Mn^{2+}, Fe^{3+}, Co^{3+}, Ga^{3+}, Sc^{3+}, In^{3+}, All ions with oxidation state of $+4$ and higher	BMe_3, BBr_3, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Rh^{3+}, Ir^{3+}, Ru^{3+}, Os^{2+}	BH_3, Tl^+, Cu^+, Ag^+, Au^+, Cd^{2+}, Hg^{2+}, Pd^{2+}, Pt^{2+}, All metals with 0 oxidation state
Base	F^-, H_2O, OH^-, O^{2-}, ROH, RO^-, R_2O, CH_3COO^-, NO_3^-, ClO_4^-, CO_3^{2-}, SO_4^{2-}, PO_4^{3-}, NH_3, RNH_2, N_2H_4	Cl^-, Br^-, NO_2^-, N_3^-, SO_3^{2-}, $SC\underline{N}^-$, C_5H_5N	H^-, R^-, I^-, H_2S, HS^-, S^{2-}, R_2S, CN^-, CO, $S_2O_3^{2-}$, PR_3, $\underline{S}CN^-$, $P(OR)_3$, AsR_3

3.5 Main Group Chemistry

We have previously explored the periodic trends in chapter 3.2. We have noted that the main group elements, consisting of the s and p-block elements, have significantly different properties as compared to d and f-block metals. This chapter focuses on the properties of individual groups of main group elements, exploring common trends of compounds formed by elements in each group.

3.5.1 *Hydrogen*

Hydrogen is the most abundant element in the universe and forms more compounds than any other element. It is the lightest element with the proton number 1, and is not part of any group as it has properties unique to itself. There are 3 known isotopes of hydrogen: ^{1}H (99.9855%), ^{2}H (0.0145%) and ^{3}H (0.00001%). ^{2}H is known as Deuterium (D) and ^{3}H is known as Tritium (T).

Molecular hydrogen, H_2, is a colourless and odourless gas that is virtually insoluble in most solvents. It is relatively inert as the $H–H$ bond is strong with a bond enthalpy of $436\ kJ\ mol^{-1}$ and a short bond length of $74\ pm$. In a laboratory scale, hydrogen gas is easily prepared through 4 methods:

1. Metal with dilute acids

$$Zn_{(s)} + 2\ HCl_{(aq)} \rightarrow ZnCl_{2(aq)} + H_{2(g)}$$

2. Amphoteric metal with base

$$2\ Al_{(s)} + 2\ NaOH_{(aq)} + 6\ H_2O_{(l)} \rightarrow\ 2\ Na[Al(OH)_4]_{(aq)} + 3\ H_{2(g)}$$

3. Metal hydrides with water

$$CaH_{2(s)} + 2\ H_2O_{(l)} \rightarrow Ca(OH)_{2(aq)} + 2\ H_{2(g)}$$

4. Electrolysis of water

$$2\ H_2O_{(l)} \rightarrow 2\ H_{2(g)} + O_{2(g)}$$

Industrially, hydrogen gas is synthesised through the steam reforming of methane at 1200K with a nickel catalyst:

$$CH_{4(g)} + H_2O_{(g)} \rightarrow CO_{(g)} + 3\ H_{2(g)}$$

A similar process may be performed with carbon as the reagent, known as coal gasification:

$$C_{(s)} + H_2O_{(g)} \rightarrow CO_{(g)} + H_{2(g)}$$

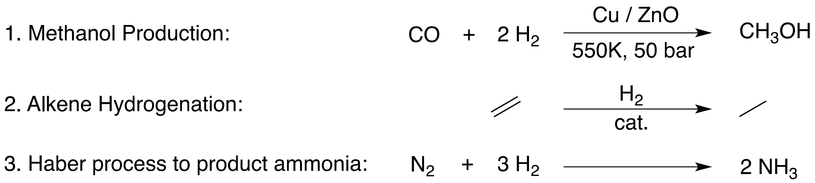


Figure 3.5.1. Industrial applications of H_2 gas.

The mixture of CO and H_2 gases is known as syngas and the CO gas may be further used to synthesise H_2 gas through the water-gas shift reaction at $700\ K$ with an iron or chromium catalyst:

$$CO_{(g)} + H_2O_{(g)} \rightarrow CO_{2(g)} + H_{2(g)}$$

The production of H_2 gas is important as H_2 gas has many industrial applications, as shown in Figure 3.5.1.

Hydrogen as an element may have the oxidation states of –1, 0 and +1. Hydrogen in oxidation state 0 is a radical, which is highly unstable. Its main chemistry is built upon loss of an electron to form a proton (H^+) or gaining an electron to form a hydride (H^-). When considering compounds of hydrogen, we may split up hydrides into 3 different categories:

1. Covalent Hydrides $(X–H)$

In order to form a covalent hydride, X must be a p-block element or beryllium. This makes the $X–H$ bonds a covalent bond, and the reactivity of the covalent hydride depends on the polarity of the $X–H$ bond.

When the electronegativites of X and H are similar, the $X–H$ bond may break homolytically, such as in the case of AsH_3 under heat:

$$2\ AsH_3 \rightarrow 2\ As + 3\ H_2$$

When the electronegativity of X is greater than that of H, the $X–H$ bond may break heterolytically, with the electrons going to X, forming a proton. These compounds are usually able to act as Brønsted acids, such as H_2O and HBr.

When the electronegativity of H is greater than that of X, the $X–H$ bond may break heterolytically, with the electrons going to H, forming a hydride ion. These compounds are good hydride-transfer reagents, acting as reducing agents, even though the $X–H$ bond is essentially covalent. The 2 most common examples are $LiAlH_4$ and $NaBH_4$, which may be prepared through the following reactions:

$$8\ LiH + Al_2Cl_6 \rightarrow 2\ LiAlH_4 + 6\ LiCl$$

$$2\ NaH + B_2H_6 \rightarrow 2\ NaBH_4$$

2. Saline Hydrides ($M–H$)

Saline hydrides are essentially salts as the interaction between the metal and the hydride has considerable ionic character. They are formed by reacting highly electropositive elements such as alkali and alkaline-earth metals directly with H_2 at high temperatures between 300 and 700°C:

$$\text{Alkali metals: } 2\ M_{(l)} + H_{2(g)} \rightarrow 2\ MH_{(s)}$$

$$\text{Alkaline-earth metals: } M_{(s)} + H_{2(g)} \rightarrow MH_{2(s)}$$

Due to the small size and high charge density of the smaller metals, their hydrides have higher covalent character, such as LiH and MgH_2. BeH_2 is considered a covalent hydride as it has a covalent polymeric structure with $Be–H–Be$ bridges.

Saline hydrides are highly reactive with water and air:

$$MH_{(s)} + H_2O \rightarrow H_{2(g)} + MOH_{(aq)}$$

They are also strongly basic and powerful hydrogen-transfer agents, reacting with Lewis and Brønsted acids:

$$NaH + B(OMe)_3 \rightarrow Na[HB(OMe)_3]$$

$$NaH + ROH \rightarrow NaOR + H_2$$

3. Transition Metal Hydrides

Hydrogen molecule (H_2) and hydride (H^-) can act as ligands to coordinate to transition metals, forming transition metal hydrides. We will discuss the bonding of these compounds in greater detail in chapter 3.7, coordination chemistry.

Other than conventional bonds, hydrogen is able to form strong intermolecular interactions known as hydrogen bonds. They are formed between a hydrogen atom attached to a highly electronegative atom and a lone pair of electrons on an electronegative atom, as shown in Figure 3.5.2.

Hydrogen bonds are largely due to electrostatic attraction of H and Y. The $X–H$ distance becomes slightly longer, but $X–H$ still remains essentially a normal 2-electron covalent bond. The $H–Y$ hydrogen bond distance is generally much longer than a covalent $H–Y$ bond. These are known as asymmetrical hydrogen bonds as the hydrogen atom is not midway between X and Y.

There are exceptions where the hydrogen bond is very strong, such as in the FHF^- ion. In such cases, the $X–Y$ distance becomes very short and $X–H$ and $Y–H$ distances are close to being equal. There are presumably both covalent and electrostatic interactions

$$\overset{\delta-}{X}-\overset{\delta+}{H}\text{----}:Y \qquad X = F, O, N, Cl$$

Figure 3.5.2. Depiction of the intermolecular hydrogen bond.

in both the X–H and Y–H bonds. This type of hydrogen bond is symmetrical and usually occur between like atoms $(X = Y)$.

Symmetrical hydrogen bonds are much stronger than asymmetrical hydrogen bonds, but they also occur rarely. While asymmetrical hydrogen bonds are weaker than conventional bonds, they are significant due to the large amount of hydrogen bonding interactions and are useful in biological structures such as DNA double helices and proteins.

3.5.2 *Group 1 elements*

Group 1 elements, also known as **alkali metals**, form +1 cations with low polarizability. Thus, the compounds formed are generally ionic salts, although there may be certain degree of covalent interactions, especially in Li^+ with the greatest polarising power.

The first 2 elements, lithium and sodium, are usually prepared through electrolysis of fused salts. The next 3 elements, potassium, rubidium and caesium, have low melting points and easily vaporise. They may be prepared by treating molten chlorides with sodium vapour.

Alkali metals have weak metallic bonding as there is only 1 valence electron per metal atom, leading to relatively weak lattice binding energies. Thus, alkali metals are soft with low melting points. They are highly electropositive and able to act as strong reducing agents as they are easily oxidised. The reactivity of the metals is generally very high, and increases down the group. For example, when in contact with water, lithium reacts slowly, sodium reacts vigorously, potassium inflames and the rest reacts explosively.

Due to the small size of Li^+ cation, it has very high charge density and its chemistry differs slightly from the rest of the group 1 metals. This is known as the **uniqueness principle**, which states that the first element in every group has properties that are slightly different from the rest of the group. The high charge density of Li^+ is due to its small size. It is thus able to polarise the electron cloud of the anion, allowing better orbital overlap and a higher covalent character of the bond. With its unique properties, lithium is able to react with nitrogen gas to form nitrides. The only other metal with this property is magnesium in group 2. The reactions of metals with nitrogen gas are given below:

$$6Li + N_2 \rightarrow 2Li_3N$$

$$3Mg + N_2 \rightarrow Mg_3N_2$$

The reaction of Li with N_2 is slow at room temperature and is usually carried out at 400°C, while the reaction of Mg with N_2 only occurs at high temperatures of around 800°C.

Alkali metals, and to a lesser extent Ca, Sr, Ba, Eu and Yb, are soluble in liquid ammonia, giving blue solutions of solvated electrons.

$$M + n\ NH_{3(l)} \rightarrow M^+ + e^-[NH_3]_n$$

The ammonia solvent forms a cavity where the electron has the highest probability to be found. This is experimentally justified as solutions are less dense than the pure solvent. If left at room temperature, the solution slowly decomposes to amide and hydrogen gas.

$$Na + NH_3 \rightarrow NaNH_2 + \frac{1}{2}H_2$$

At high concentration of metal ions ($[M^+] \geq 3\ mol \cdot dm^{-3}$), metal ion clusters are formed and the solution becomes copper-coloured with a metallic lustre.

Now, we will look at the compounds of alkali metals:

1. Oxides

There are 3 types of oxides formed by alkali metals: oxides, peroxides and superoxides. They can be obtained through the direct reactions of the metal with an excess of oxygen.

Oxide:	$4\ Li + O_2 \rightarrow 2\ Li_2O$
Peroxide:	$2\ Na + O_2 \rightarrow Na_2O_2$
Superoxide:	$K + O_2 \rightarrow KO_2$
	$Rb + O_2 \rightarrow RbO_2$
	$Cs + O_2 \rightarrow CsO_2$

Due to cation size, the metals down the group form higher order oxides.

2. Hydroxides

Alkali metal hydroxides are white, deliquescent solids. They are fully soluble in water and alcohol and may be used as strong alkali bases.

3. Ionic salts

Alkali metal salts are generally characterised by high melting points, electrical conductivity of the molten salt and ready solubility in water. Lithium, due to the uniqueness principle, form certain sparingly soluble salts due to the highly covalent nature of the lithium-anion bond. The important salts formed by alkali metals are the alkoxides, amides and hydrides. They are strong bases used in organic synthesis as we will discuss in the organic chemistry section. The preparation of such salts usually involve direct reaction with the alkali metal, as shown below:

Alkoxides:	$2\ t\text{-}BuOH + 2\ Na \rightarrow 2\ t\text{-}BuONa + H_2$
Amides:	$i\text{-}Pr_2NH + n\text{-}BuLi \rightarrow i\text{-}Pr_2NLi\ (LDA) + C_4H_{10}$
Hydrides:	$H_2 + 2\ Na \rightarrow 2\ NaH$

3.5.3 *Group 2 elements*

Group 2 elements, also known as **alkaline-earth metals**, form +2 cations. With an increased nuclear charge, they have a smaller ionic radius. The formal charge of +2 coupled with the smaller ionic radius causes alkaline-earth metal cations to have even higher charge density than alkali metals. This shows in physical properties as high densities, melting points and boiling points.

The alkaline-earth metals are widely distributed in minerals and in the sea. Beryllium occurs in the mineral beryl, $Be_3Al_2(SiO_3)_6$, while magnesium occurs in dolomite $(CaCO_3 \cdot MgCO_3)$ and carnallite $(KCl \cdot MgCl_2 \cdot 6H_2O)$. Calcium is most commonly found in limestone $(CaCo_3)$. The heavier elements are less abundant: strontium is found in strontianite $(SrCO_3)$ and barium in barytes $(BaSO_4)$.

Due to the uniqueness principle, the properties of Beryllium differ significantly from the rest of the group. With its exceptionally small ionic radius and high charge density, it forms compounds with high covalent character. As its charge density is greater than Li^+, beryllium compounds are more covalent and may be treated as covalent molecules.

Beryllium forms mainly linear BeX_2 molecules, but they are only stable in the gas phase due to unsaturated coordination of beryllium. In condensed phase, beryllium compounds generally form polymers or Lewis acid-base adducts. Depending on the steric bulk of X, a polymer, oligomer or a single molecule may be isolated. Examples are given in Figure 3.5.3.

It is common to form Lewis acid-base adducts with ethereal solvents.

$$BeCl_2 + 2\ Et_2O \rightarrow BeCl_2(OEt)_2$$

In water, beryllium molecules are hydrolysed to form the tetrahedral $[Be(H_2O)_4]^{2+}$ ion. This ion is acidic due to the high charge density of Be^{2+} polarising the H_2O molecules and weakening the $O–H$ bond.

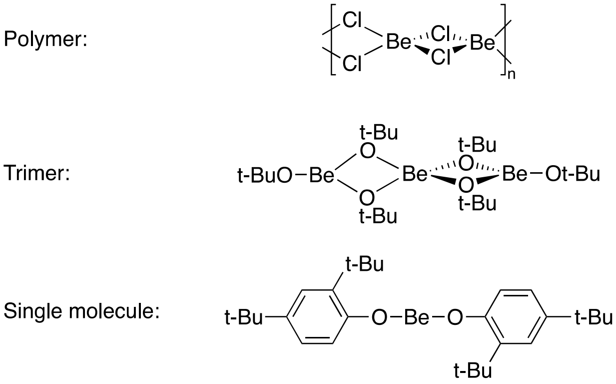


Figure 3.5.3. Structure of beryllium compounds.

Beryllium metal is relatively inert compared to other group 2 metal compounds. For example, beryllium does not react with hydrogen gas to form its hydride. Beryllium hydride must be prepared through less direct methods, such as reacting $BeCl_2$ with LiH. Similar to other BeX_2 compounds, BeH_2 forms a covalent polymer.

Similar to aluminium, beryllium forms the tetra-coordinate beryllate ion $[Be(OH)_4]^-$ when reacted with aqueous base. This property is not observed for the other group 2 metals. When beryllium or its compounds are burned in air, the white crystalline oxide BeO may be obtained.

Other group 2 metals are increasingly ionic in nature as we move down the group. Magnesium also has high charge density and form compounds with covalent character, but less so than beryllium. Its properties are similar to lithium from group 1. This trend is known as the **diagonal effect**, which states that there are significant similarities between lithium and magnesium, beryllium and aluminium, and boron and silicon. This is mainly due to the similar charge density of the ions as the ionic size and ionic charge increases proportional to each other.

The heavier group 2 metals have chemical and physical properties that change systematically with increasing size. They form only ionic salts due to their highly electropositive nature. Let us look at the characteristic salts that group 2 metals form:

1. Carbonates

Group 2 metal carbonates become more thermally stable down the group. This is because a smaller metal cation has a higher charge density that polarises the carbonate anion more, causing the weakening of the C–O bond and causes the carbonate to decompose more readily.

2. Oxides

Group 2 metal oxides are white, high-melting crystalline solids that can be prepared through thermal decomposition of the carbonate:

$$MCO_3 \rightarrow MO + CO_2$$

The basicity of the metal oxide increases down the group. While BeO is amphoteric and MgO is weakly basic, the rest of the oxides are strongly basic as they readily hydrolyse in water to form soluble hydroxides.

3. Hydroxides

Group 2 metal hydroxides are strong bases that become increasingly soluble down the group. The hydroxides may be prepared by reacting the metals with water.

$$M + 2\ H_2O \rightarrow M(OH)_2 + H_2$$

The reaction does not occur for Be due to the protective BeO coating formed on Be and reaction of Mg requires steam.

4. Halides

The group 2 metal halides readily absorb water to form hydrates, and dehydration may be carried out to obtain the anhydrous halide. As the hydration energy decreases more rapidly than the lattice energies with increasing ionic size, the ability to form hydrates and the solubility in water decrease down the group. The order is reversed for solubility of fluorides due to the exceptionally small size of fluorides.

5. Sulfates

The solubility of group 2 metal sulfates decreases down the group. Sr and Ba sulfates are completely insoluble in water, and the sulfate anion is commonly used as a qualitative method to detect Ba^{2+} ions in solution.

6. Hydrides

Group 2 metal hydrides may be prepared by direct reaction of the metal with hydrogen gas, other than for Be, which we have previously discussed.

$$\mathrm{M} + \mathrm{H_2} \rightarrow \mathrm{MH_2}$$

For Mg, the reaction requires high pressure, while for the heavier group 2 metals, the reaction requires high temperature. $\mathrm{MgH_2}$ is able to release $\mathrm{H_2}$ at a high temperature (>250°C), making it a useful metal for storage of $\mathrm{H_2}$. Mg also has a low molecular weight, increasing the weight percentage of $\mathrm{H_2}$. The hydrides react with water to form hydroxides through reactions less vigorous than that of group 1 hydrides.

3.5.4 *Group 13 elements*

Group 13 elements lie between metallic and covalent compounds, with group 1 and 2 elements being generally metallic and group 14 elements being generally covalent. Following the trend that we have observed from the previous groups, metallic character increases going down the group. For group 13, boron is a non-metallic element while the elements aluminium and below are metallic. This may also be attributed to the uniqueness principle, as boron is the first element in the group. As boron has a significantly different character compared to the rest of the group, we will start by discussing boron chemistry before moving on to the rest of the elements.

Boron may be naturally found in many ores which are borates, large covalent boron oxides that have diverse structures. As boron is non-metallic, no ionic salt containing B^{3+} can be formed. Boron oxides and hydroxides are acidic, as with the other non-metals. Boron is related to silicon through the diagonal principle, sharing many similarities, such as the variety of oxides formed.

Boron may be prepared mainly through 2 methods:

1. Reduction of boron oxide with magnesium:

$$B_2O_3 + 3\ Mg \rightarrow 2\ B + 3\ MgO$$

2. Reduction of boron halides with zinc or hydrogen:

$$2BX_3 + 3\ Zn \rightarrow 3\ ZnX_2 + 2\ B$$

$$2\ BX_3 + 3\ H_2 \rightarrow 6\ HX + 2\ B$$

Being non-metallic, boron is able to form a wide variety of covalent compounds:

1. Oxygen compounds of boron.

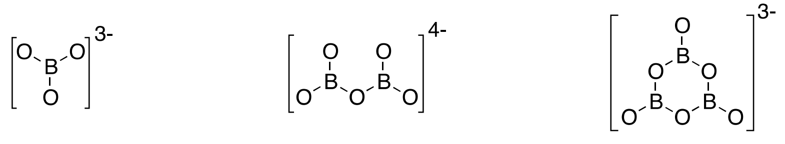
As mentioned previously, boron forms many oxides, known as borates. Borates are usually crystalline hydrates, the most common being borax ($Na_2[B_4O_5(OH)_4] \cdot 8H_2O$) and ulexite ($NaCa[B_5O_6(OH)_6] \cdot 5H_2O$). The elemental ratios do not reveal much about the structures of the borate anions, which are shown in Figure 3.5.4.

While the structures may be complicated, they are composed of trigonal planar BO_3 and tetrahedral BO_4 units, and structures may be proposed based on these units.

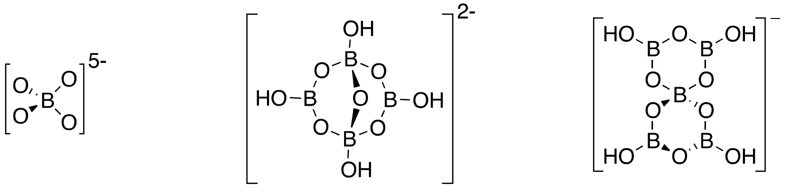
The simplest boron oxide is B_2O_3, which composes borosilicate glass (used in laboratory glassware) together with silica. Boron oxide may be prepared by dehydration of boric acid under heat:

$$2\ B(OH)_{3(s)} \rightarrow B_2O_{3(s)} + 3\ H_2O_{(g)}$$

Boric acid molecules are linked together by hydrogen bonds to form an infinite hexagonal 2-dimensional layer. The hydrogen bonds are asymmetrical, with the covalent bond length being $100\ pm$ and the hydrogen bond length being $170\ pm$. The structure formed is shown in Figure 3.5.5.



Monoborate, $[BO_3]^{3-}$ Diborate, $[B_2O_5]^{4-}$ Triborate, $[B_3O_6]^{3-}$



$[BO_4]^{5-}$ Tetraborate, $[B_4O_5(OH)_4]^{2-}$ Pentaborate, $[B_5O_6(OH)_4]^{-}$

Figure 3.5.4. Structures of selected borate anions.

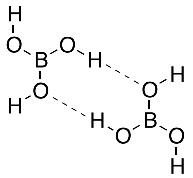
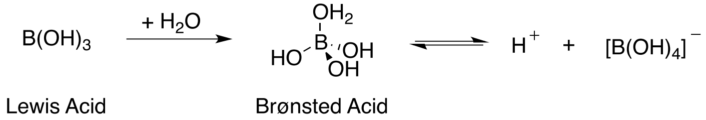


Figure 3.5.5. Hydrogen bonding in boric acid.

Boric acid is a weak Lewis acid:



2. Boron halides

Boron forms a variety of different halides. The most common type of boron halide is boron trihalide (BX_3). Boron trihalides have trigonal planar structure, and act as great Lewis acids. Unlike halides of other elements in group 13, BX_3 is monomeric in all phases.

BX_3 may be prepared by directly reacting boron with the halogen for all halides other than BF_3, as shown below:

$$B + \frac{3}{2}X_2 \rightarrow BX_3 \;\; (X = Cl, Br, I)$$

BF_3 can only be formed through the following reaction:

$$B_2O_3 + 3\ CaF_2 + 3\ H_2SO_4\ (conc.) \rightarrow 2\ BF_3 + 3\ CaSO_4 + 3\ H_2O$$

As good Lewis acids, boron trihalides react mainly with Lewis bases to form adducts. Note that the Lewis acidity follows the order $BI_3 > BBr_3 > BCl_3 > BF_3$. Although fluorine is the most electronegative, it is able to donate electrons into the vacant 2p-orbital of boron, forming a partial π-bond. While all the halogens are able to donate π-electrons to boron, the π-donation from fluorine is especially good due to the excellent 2p-2p overlap. As fluorine is the most electron-donating, BF_3 is the least Lewis acidic boron trihalide.

With BF_3 being the least Lewis acidic, we would expect it to form the least stable Lewis acid-base adducts. However, the stability of the adducts follows the order of $BF_3 > BCl_3 > BBr_3 > BI_3$. This is because boron adopts a tetrahedral geometry upon formation of the adduct, preventing any π-donation of electrons from halogen to boron. The stability of the adduct thus depends entirely on the electronegativity of the halide.

As strong Lewis acids, boron trihalides are easily hydrolysed by water:

$$BX_3 + 3\ H_2O \rightarrow B(OH)_3 + 3\ HX\ (X = Cl, Br, I)$$

BF_3 only hydrolyses partially in water:

$$4\ BF_3 + 3\ H_2O \rightarrow 3\ H^+ + 3\ BF_4^- + B(OH)_3$$

$$BF_4^- + H_2O \rightarrow [BF_3OH]^- + HF$$

Boron trihalides are able to undergo halogen exchange when mixed:

$$BCl_3 + BBr_3 \rightleftharpoons BCl_2Br + BBr_2Cl$$

The equilibrium is established rapidly, and only small amounts of the mixed boron trihalides are formed.

The other boron halides include:

i. Gaseous boron monohalides: BF and BCl
ii. Complex boron halides: B_nCl_n $(n = 8–11)$, B_nBr_n $(n = 7–10)$, B_nI_n $(n = 8–9)$
iii. Diboron tetrahalides: B_2X_4 $(X = F, Cl, Br, I)$
iv. Other boron fluorides: B_3F_5, B_8F_{12} and $B_{14}F_{18}$

These halides are less stable and highly reactive, usually requiring special synthetic techniques to prepare.

3. Hydrides

Boron forms an extensively series of molecular hydrides called boranes, such as B_2H_6, B_4H_{10}, B_9H_{15}, $B_{10}H_{14}$ and $B_{20}H_{16}$. BH_3 is rare and can only be isolated in gas phase, making B_2H_6 the simplest hydride of boron. B_2H_6 may be prepared by boron trihalides with hydride-transfer reagents:

$$4\ BX_3 + 3\ LiAlH_4 \rightarrow 2\ B_2H_6 + 3\ LiAlX_4$$

The bonding in boranes is interesting and different from conventional bonding patterns we have seen until now. In boranes, there are insufficient electrons for all bonds to be 2-centre-2-electron (2c-2e) bonds. Instead, **3-centre-2-electron (3c-2e) bonds** are formed, with 2 electrons being shared by 3 atoms. There are multiple types of 3c-2e bonds that are formed in boranes, as shown in Figure 3.5.6.

The hydrogen bridge bond is found in B_2H_6, and its orbital picture is shown in Figure 3.5.7.

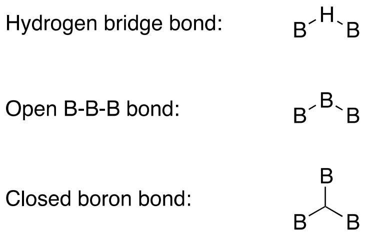


Figure 3.5.6. Examples of 3c-2e bonds found in boranes.

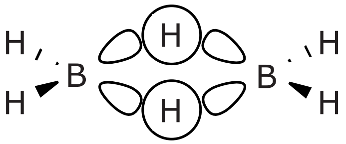


Figure 3.5.7. Orbital picture of 3c-2e hydrogen bridge bonds in B_2H_6.

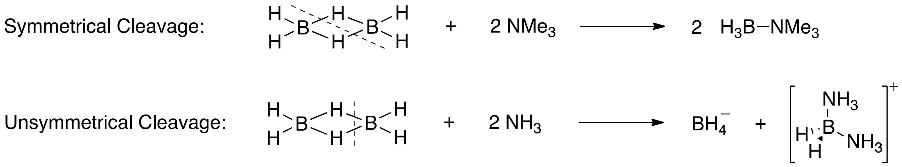


Figure 3.5.8. 2 types of cleavage reactions of B_2H_6.

B_2H_6 is a highly flammable and potentially explosive gas that participates in many reactions, which are listed below:

With oxygen: $B_2H_6 + 3\,O_2 \rightarrow B_2O_3 + 3\,H_2O$

With water: $B_2H_6 + 6\,H_2O \rightarrow 2\,B(OH)_3 + 6\,H_2$

With alcohols: $B_2H_6 + 6\,ROH \rightarrow 2\,B(OR)_3 + 6\,H_2$

With HCl: $B_2H_6 + HCl \rightarrow B_2H_5Cl + H_2$ (Cl replaces a terminal hydride)

With Cl_2: $B_2H_6 + 6\,Cl_2 \rightarrow 2\,BCl_3 + 6\,HCl$

3c-2e BHB bridges in B_2H_6 are electron deficient and susceptible to nucleophilic attack. There are 2 observed routes of cleavage: symmetrical and unsymmetrical. Symmetrical cleavage is the thermodynamic route, taken by large amine nucleophiles such as NMe_3 and pyridine. Unsymmetrical cleavage, being the kinetic route, occurs for smaller amines such as NH_3 and Me_2NH. The 2 types of cleavage reactions of B_2H_6 are shown in Figure 3.5.8.

In unsymmetrical cleavage, the tetrahydroborate (BH_4^-) anion is generated. This is the simplest borohydride anion and is an important source of H^- ion, acting as a reducing agent.

4. Boron-nitrogen compounds

The $B{-}N$ bond is isoelectronic with the $C{-}C$ bond, just that $B{-}N$ bonds are more polar. There are 3 main categories of boron-nitrogen compounds:

i. Amine boranes

Amine boranes are similar to alkanes, having a tetrahedral structure. They are Lewis acid-base adducts that can be formed by the symmetrical cleavage of B_2H_6, or by reaction of ammonium salts:

$$[H_3NR]Cl + LiBH_4 \longrightarrow RH_2N{\rightarrow}BH_3 + LiCl + H_2$$

The arrow in $RH_2N{\rightarrow}BH_3$ represents a dative bond, also known as a coordinate bond, where both electrons in the bond come from the same atom, which is N in this case.

ii. Aminoboranes

Aminoboranes are similar to alkenes, adopting a trigonal planar geometry. Aminoboranes may be prepared through dehydrohalogenation of amine boranes:

$$NHMe_2 + BCl_3 \longrightarrow Me_2HN{\rightarrow}BCl_3 \rightarrow Me_2\overset{+}{N}{=}\overset{-}{B}Cl_2 + HCl$$

The product may be modified through reaction with Grignard reagents:

$$Me_2\overset{+}{N}{=}\overset{-}{B}Cl + 2\ R'MgX \rightarrow Me_2N{-}BR'_2 + 2\ MgXCl$$

The $B{-}N$ bond in aminoborane has partial π-character formed by the 2p-2p orbital overlap.

Thus, the $B{-}N$ bond in these cases can be most accurately described as a resonance between a single bond and a double bond, and either representation is acceptable, as shown in Figure 3.5.9.

iii. Borazines

Borazine is the boron-nitrogen equivalent of benzene, with its structure shown in Figure 3.5.10.

Borazine has a fully delocalised π-system, resulting in all 6 bonds being equal in length ($144\ pm$). While borazine is physically similar to benzene, the partial positive boron atom is electrophilic and susceptible to nucleophilic attack while the partial negative nitrogen atom can act as a nucleophile to attack electrophiles. The distribution of electron density between boron and nitrogen atoms seems to contradict the formal charges on the atoms at first sight. However, we must realise that the π-electrons are fully delocalised and the electron density on nitrogen is greater due to the higher electronegativity of nitrogen. Thus, borazine readily undergoes addition, as shown in Figure 3.5.11.

The method for preparation of borazine is shown in Figure 3.5.12.

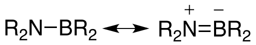


Figure 3.5.9. Resonance forms of aminoboranes.

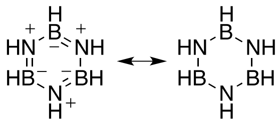


Figure 3.5.10. Structure of borazine.

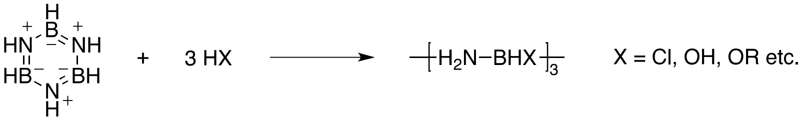


Figure 3.5.11. Addition reaction of borazine.

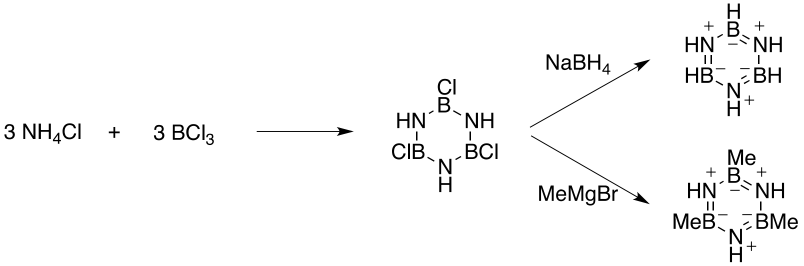


Figure 3.5.12. General scheme to prepare borazine.

The rest of the group 13 elements are metallic, forming ionic salts with +3 cations. As we move down the group, the +1 oxidation state becomes increasingly important. For thallium, the univalent Tl^+ ion is well-defined in solution. This is due to the **inert pair effect**, where the electrons in the outermost s-orbital remain unionised. This is because d and f-orbitals do not effectively shield the s-electrons; hence they are more tightly bound to the nucleus.

We will look at the properties of the compounds formed by the group 13 elements.

1. Oxides

The oxides generally have the formula M_2O_3. However, for thallium, Tl_2O_3 decomposes to Tl_2O at high temperatures. Aluminium and gallium are amphoteric, meaning that their oxides and hydroxides react with both acid and base:

With acid: $Al_2O_3 + 6\ H^+ \rightarrow 2\ Al^{3+} + 3\ H_2O$

$Al(OH)_3 + 3\ H^+ \rightarrow Al^{3+} + 3\ H_2O$

With base: $Al_2O_3 + 2\ OH^- + 3\ H_2O \rightarrow 2\ [Al(OH)_4]^-$

$Al(OH)_3 + OH^- \rightarrow [Al(OH)_4]^-$

Indium and thallium oxides are basic, and only react with acids. The elements are also able to form mixed oxides with other metals, such as spinel ($MgAl_2O_4$) and chrysoberyl ($BeAl_2O_4$).

2. Halides

Generally, the group 13 elements form trihalides (MX_3). The only exception is TlI_3, which isn't thallium(III) iodide but thallium(I) triiodide. The halides act as strong Lewis acids, with Lewis acidity decreasing down the group. The halides may exist as dimers (M_2X_6), such as Al_2Cl_6, which have bridging halogen atoms.

3. Aqueous complexes

In water the group 13 elements form well-defined octahedral aqua ions $[M(H_2O)_6]^{3+}$, which are quite acidic due to the high charge densities of M^{3+} ions.

$$[M(H_2O)_6]^{3+} \rightleftharpoons [M(H_2O)_5(OH)]^{2+} + H^+$$

4. Hydrides

Aluminium and gallium form tetrahydrido anions similar to boron, such as AlH_4^- and GaH_4^-. The stability order is $B > Al > Ga$. While BH_4^- is stable in water, AlH_4^- and GaH_4^- are rapidly hydrolysed in water:

$$MH_4^- + 4\ H_2O \rightarrow M(OH)_3 + OH^- + 4\ H_2$$

The tetrahydrido anions may be prepared by reacting the metal trihalide with lithium hydride:

$$MCl_3 + 4\ LiH \rightarrow LiMH_4 + 3\ LiCl$$

3.5.5 *Group 14 elements*

Group 14 elements contain carbon, which forms many organic compounds. While carbon is a non-metal, silicon and germanium are semi-metals and tin and lead are metals.

Carbon may be present in many different solid structures, such as diamond, graphite, fullerenes, nanotubes or amorphous structures. The properties of carbon allotropes are very different and will be briefly discussed.

1. Diamond

Diamond is the hardest substance on earth, and is a transparent electrical insulator. The carbons in diamond have tetrahedral geometry, forming a giant covalent 3D structure. Thermodynamically, diamond is less stable than graphite. However, diamond is considered metastable, which means that it exists without observable change although it is thermodynamically unstable with respect to another state. This is because the reaction of diamond to graphite is kinetically infinitesimally slow.

2. Graphite

Graphite is a soft and black electrical conductor, having largely different properties compared to diamond. In graphite, each carbon forms only 3 bonds, adopting a trigonal planar geometry. From each carbon, 1 electron is delocalised, forming a π-electron system in each sheet of graphene, allowing electricity to flow through.

Graphite consists of stacks of planar graphene layers held together by weak London dispersion forces.

3. Fullerene

Fullerenes may take the form of many shapes, such as hollow spheres and tubes. In all fullerenes, the carbon atoms are equivalent and covalently bonded to 3 other carbon atoms through 2 single bonds and 1 double bond. The most common fullerene is buckminsterfullerene (C_{60}), having a structure similar to a soccer ball.

The other aspects of carbon chemistry will be discussed in further detail in the next section on organic chemistry.

The other group 14 elements, other than silicon, are metals. They are able to form multiple bonds through p and d-orbitals. For the larger group 14 elements, multiple bonding is usually observed through pπ-dπ interactions. pπ-dπ interactions have been used to explain many unusual observations, which we will discuss here:

1. Trisilylamine vs. Trimethylamine

Trisilylamine is a weak base with trigonal planar geometry while trimethylamine is a strong base with pyramidal geometry. This is due to the pπ→dπ bonding between the 2p-orbital of N to the 3d-orbital of Si. This grants the N–Si bond partial double bond character, allowing $N(SiH_3)_3$ to be planar. $N(SiH_3)_3$ is also less basic at N as the lone pair of electrons on N is shared with the empty 3d-orbitals of Si.

2. Geometry of isocyanates

In the vapour phase, H_3SiNCO is linear while H_3CNCO is bent at N. This is explained by the partial double bond character of the Si–N bond due to pπ-dπ bonding.

3. Disilyl ether bond angle

Disilyl ethers ($R_3Si\text{-}O\text{-}SiR_3$) have exceptionally large bond angles at oxygen, ranging from 140° to 180°. The large bond angle improves the overlap between oxygen 2p-orbitals and silicon 3d-orbitals, allowing for pπ-dπ bonding.

4. Acidity of silanols

Silanols (e.g. Me_3SiOH) are stronger protonic acids than alcohols bonded directly to carbon, as the conjugate base anion may be stabilised through pπ-dπ interaction between the 2p-orbital of oxygen and the 3d-orbitals of silicon. This allows the negative charge on oxygen to be delocalised onto silicon, stabilising the conjugate base anion.

We will now continue to look at compounds formed by group 14 elements.

1. Hydrides

The hydrides have the general formula MH_4, and only monosilane (SiH_4) is of importance. It is spontaneously flammable and may be prepared through reduction

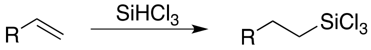


Figure 3.5.13. Examples of hydrosilation of alkenes.

of SiO_2 or $SiCl_4$ by $LiAlH_4$. Substituted silanes react with organic groups, such as in the hydrosilation of alkenes as shown in Figure 3.5.13.

2. Chlorides

The chlorides may be prepared by chlorination of hot group 14 elements. They have the general formula MCl_4, and are eventually hydrolysed by water to hydrous oxides through oxochlorides as intermediates. $SiCl_4$ and $GeCl_4$ are useful to prepare pure Si and Ge, while $SiCl_4$ and $SnCl_4$ are used in synthesis of organometallic compounds.

3. Oxygen compounds

The most common oxides of group 14 elements are their dioxides (MO_2). As we move down the group, the basicity of the dioxides increases: SiO_2 is acidic, GeO_2 is slightly acidic, SnO_2 is amphoteric, while PbO_2 is basic. Due to the inert pair effect, lead is able to form multiple types of oxides with different valences of +2 and +4, such as PbO and Pb_3O_4. Pure silica (SiO_2) occurs in 2 forms, quartz and cristobalite. In both structures, Si is tetrahedrally bound to 4 O atoms, and the difference is the presence of helices in quartz.

3.5.6 *Group 15 elements*

Group 15 elements consist of non-metals nitrogen and phosphorous, semi-metals arsenic and antimony and the metal bismuth. With a valence shell of ns^2np^3, the group 15 elements can lose up to 5 electrons or gain 3 electrons to achieve stable octet configuration. Thus, they are able to form compounds with formal oxidation states ranging from –3 to +5. Table 3.5 shows the different nitrogen compounds with different formal oxidation states.

Table 3.5. Examples of compounds with different formal oxidation states of nitrogen.

–3	–2	–1	0	+1	+2	+3	+4	+5
Li_3N, NH_3, NH_4Cl	N_2H_4	NH_2OH	N_2	N_2O	NO	N_2O_3, HNO_2	NO_2, N_2O_4	N_2O_5, HNO_3

We will start by discussing the properties and compounds of nitrogen first. Nitrogen occurs most commonly as N_2 gas, which is extremely stable and inert due to the strong $N{\equiv}N$ triple bond. Pure N_2 may be obtained through liquefaction and fractionation of air, and is commonly used to provide an inert atmosphere for air-sensitive reactions. At room temperature, the only reaction of N_2 is the slow reaction with Li metal to form $\mathrm{Li_3N}$. At elevated temperatures, $\mathrm{N_2}$ may react through the equations below:

$$\mathrm{N_{2(g)} + 3\ H_{2(g)} \rightarrow 2\ NH_{3(g)}}$$

$$\mathrm{N_{2(g)} + \ O_{2(g)} \rightarrow 2\ NO_{(g)}}$$

$$\mathrm{N_{2(g)} + \ 3\ Mg_{(s)} \rightarrow Mg_3N_{2(s)}}$$

$$\mathrm{N_{2(g)} + \ CaC_{2(s)} \rightarrow C_{(s)} + CaNCN_{(s)}}$$

Nitrogen has bonding features that differ significantly from carbon. $\mathrm{C{-}C}$ single bond ($\approx 346\ \mathrm{kJ\ mol^{-1}}$) is much stronger than $\mathrm{N{-}N}$ single bond ($\approx 160\ \mathrm{kJ\ mol^{-1}}$), while $\mathrm{N{\equiv}N}$ triple bond ($\approx 945\ \mathrm{kJ\ mol^{-1}}$) is much stronger than $\mathrm{C{\equiv}C}$ triple bond ($\approx 835\ \mathrm{kJ\ mol^{-1}}$). This is due to the short $\mathrm{N{-}N}$ bond length causing large lone pair-lone pair repulsion between the adjacent nitrogen atoms, weakening the bond. Thus, carbon is able to form more compounds compared to nitrogen. On the other hand, nitrogen compounds are usually explosive due to the large amounts of energy released in the formation of $\mathrm{N_2}$ and the large amounts of gaseous products that are formed.

Most nitrogen compounds are trivalent, forming pyramidal $\mathrm{NR_3}$ compounds with 1 lone pair. Due to the presence of lone pair, $\mathrm{NR_3}$ are Lewis bases. If all 3 substituents are different, pyramidal molecules are chiral. However, the energy barrier for inversion at the nitrogen centre is low ($\approx 24\ \mathrm{kJ\ mol^{-1}}$) and the optical isomers cannot be isolated. In rare cases, $\mathrm{NR_3}$ molecules may be trigonal planar, such as $\mathrm{N(SiMe_3)_3}$ due to the pπ-dπ bonding.

We will now look at some nitrogen compounds:

1. Nitrides ($\mathrm{N^{3-}}$)

Nitrides are usually only formed with highly electropositive metals and may be regarded as ionic salts. Nitrides may be directly prepared from reaction of metal with nitrogen, or through loss of ammonia during the heating of amides:

$$\mathrm{3\ Ba(NH_2)_2 \rightarrow Ba_3N_2 + 4\ NH_3}$$

Nitrides are readily hydrolysed to form metal hydroxides and ammonia:

$$\mathrm{Li_3N + 3\ H_2O \rightarrow 3\ LiOH + NH_3}$$

Transition metal nitrides are often non-stoichiometric with nitride ions in the interstices of metal atom arrays.

2. Hydrides

The most common hydride of nitrogen is ammonia ($\mathrm{NH_3}$), which is industrially produced through the **Haber process**:

$$\mathrm{N_2 + 3\ H_2 \rightleftharpoons 2\ NH_{3(g)}}$$

Ammonia is a colourless, pungent gas. At low temperatures, liquid ammonia may be used as a solvent with lower dielectric constant than water. When used to dissolve highly electropositive metals, solvated electrons may be formed. Ammonia burns in air to form nitrogen gas and forms NO under high temperature with a platinum or platinum-rhodium catalyst.

In air: $4\ \mathrm{NH_3} + 3\ \mathrm{O_2} \rightarrow 2\ \mathrm{N_2} + 6\ \mathrm{H_2O}$

With Pt/Rh catalyst at 750°C–900°C: $4\ \mathrm{NH_3} + 5\ \mathrm{O_2} \rightarrow 4\ \mathrm{NO} + 6\ \mathrm{H_2O}$

This provides us with a useful synthesis of NO. Upon further protonation, ammonium $(\mathrm{NH_4^+})$ ions may be formed, and a solution of $\mathrm{NH_4OH}$ is formed when ammonia is dissolved in water. While $\mathrm{NH_4OH}$ does not exist undissociated, ammonium forms many salts that are highly soluble and slight acidic.

Another less common nitrogen hydride is hydrazine, $\mathrm{N_2H_4}$. Hydrazine is a bifunctional base and a fuming colourless liquid which burns in air:

$$\mathrm{N_2H_4} + \mathrm{O_2} \rightarrow \mathrm{N_2} + 2\ \mathrm{H_2O}$$

Hydrazine may be prepared by the reaction of ammonia with sodium hypochlorite:

$$\mathrm{NH_3} + \mathrm{NaOCl} \rightarrow \mathrm{NaOH} + \mathrm{NH_2Cl}$$
$$\mathrm{NaOH} + \mathrm{NH_2Cl} + \mathrm{NH_3} \rightarrow \mathrm{N_2H_4} + \mathrm{NaCl} + \mathrm{H_2O}$$

Hydrazine is useful as a strong reducing agent in basic conditions as it can be easily oxidised to $\mathrm{N_2}$.

The last hydride of nitrogen of importance is hydroxylamine, $\mathrm{NH_2OH}$. It is a weaker base than $\mathrm{NH_3}$ due to the electronegative oxygen. It is useful in organic synthesis due to the presence of a weak $\mathrm{N{-}O}$ bond. It may be prepared through reduction of nitrites or nitrates either electrolytically or with $\mathrm{SO_2}$, under controlled conditions.

3. Azides $(\mathrm{N_3^-})$

The azide ion is linear symmetrical, acting as a pseudo-halide in reactions. Sodium azide may be prepared through the following reaction at 175°C:

$$3\ \mathrm{NaNH_2} + \mathrm{NaNO_3} \rightarrow \mathrm{NaN_3} + 3\ \mathrm{NaOH} + \mathrm{NH_3}$$

Azides are highly explosive and must be handled with care. Heavy metal azides have been used in detonation caps due to this property.

4. Oxides

Nitrogen forms a large variety of oxides with different formal oxidation states on nitrogen. We will look at the different nitrogen oxides by increasing nitrogen oxidation state. Figure 3.5.14 shows the Lewis structures of the nitrogen oxides that we will be discussing.

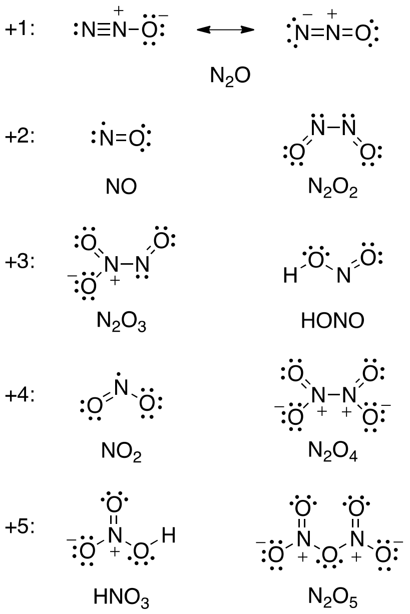


Figure 3.5.14. Lewis structures of nitrogen oxides.

i. +1 oxidation state

Dinitrogen monoxide (N_2O), also known as nitrous oxide, is obtained from the thermal decomposition of molten NH_4NO_3 at 250°C:

$$NH_4NO_3 \rightarrow N_2O + 2\ H_2O$$

N_2O is relatively unreactive at room temperature. At elevated temperatures, it reacts with alkali metals and many organic compounds. Upon heating, it decomposes into N_2 and O_2.

ii. +2 oxidation state

Nitrogen monoxide (NO), also known as nitric oxide, is a radical. It may be prepared by reduction of nitric acid:

$$8\ HNO_3 + 3\ Cu \rightarrow 3\ Cu(NO_3)_2 + 4\ H_2O + 2\ NO$$

It may also be prepared from nitrites:

$$2\ NaNO_2 + 2\ NaI + 4\ H_2SO_4 \rightarrow I_2 + 4\ NaHSO_4 + 2\ H_2O + 2\ NO$$

Industrially, NO may be prepared through direct reaction of NH_3 with O_2 at 1000°C with a platinum or ruthenium catalyst:

$$4\ NH_3 + 5\ O_2 \rightarrow 4\ NO + 6\ H_2O$$

Due to its radical structure, NO is rather unstable. It reacts readily with oxygen:

$$2\ NO + O_2 \rightarrow 2\ NO_2$$

Its radical electron is in the π^*-orbital and easily lost, allowing the formation of NO^+ ion. This allows it to react with halogens:

$$2\ NO + X_2 \rightarrow 2\ NOX$$

NOX are powerful oxidants that decompose on treatment with water. Under low temperatures, NO dimerises to forms N_2O_2, forming an extra $N-N$ single bond with the 2 unpaired electrons.

iii. +3 oxidation state
Dinitrogen trioxide (N_2O_3), is obtained through interaction of NO with NO_2:

$$NO_{(g)} + NO_{2(g)} \rightleftharpoons N_2O_{3(l)}$$

N_2O_3 is a dark blue liquid that is rather unstable due to the exceptionally long $N-N$ bond.

Nitrous acid (HNO_2) also has nitrogen in +3 oxidation state. It may be prepared by acidifying a cold solution of nitrite ions. Aqueous solutions are unstable and decompose rapidly:

$$3\ HNO_2 \rightarrow H_3O^+ + NO_3^- + 2\ NO$$

Nitrites of alkali metals may be prepared by reducing nitrates, and they are useful in organic reactions.

iv. +4 oxidation state
At +4 oxidation state, nitrogen dioxide (NO_2) and dinitrogen tetraoxide (N_2O_4) exists in a strongly temperature-dependent equilibrium both in liquid and gaseous phase:

$$2\ NO_2 \rightleftharpoons N_2O_4$$

NO_2 is a paramagnetic brown compound while N_2O_4 is colourless and diamagnetic. While the dimer is favoured by enthalpy, its dissociation is favoured by entropy. Thus, the dimer N_2O_4 is favoured at low temperatures. The oxides may be prepared by:

a. Heating metal nitrates
b. Oxidation of NO
c. Reduction of nitric acid or nitrates by metals and other reducing agents

They react with water following the disproportionation reaction below:

$$2\ NO_2 + H_2O \rightarrow HNO_3 + HNO_2$$

They are also good oxidising agents in aqueous solution:

$$N_2O_4 + 2\ H^+ + 2\ e^- \rightarrow 2\ HNO_2 \qquad E^0 = +1.07\ V$$

v. +5 oxidation state

Dinitrogen pentoxide (N_2O_5) exists as unstable colourless crystals, and may be prepared by the following reaction:

$$12\ HNO_3 + P_4O_{10} \rightarrow 6\ N_2O_5 + 4\ H_3PO_4$$

It is a strong oxidising agent that decomposes slowly at room temperature:

$$N_2O_5 \rightarrow N_2O_4 + \frac{1}{2}O_2$$

In the solid state, it exists as $NO_2^+\ NO_3^-$.

5. Halides

Nitrogen is able to form a large number of halides. We may generally classify them into 3 categories:

i. Binary halides: NF_3, NF_2Cl, NCl_2F, NCl_3
ii. Dinitrogen fluorides: N_2F_2, N_2F_4
iii. Halogen azides: XN_3 $(X = F, Cl, Br, I)$

The halides are mostly highly reactive or explosive, with the exception of NF_3. NF_3 is a stable gas that may be prepared by electrolysis of NH_4F in HF. NF_3 reacts with F_2 in the presence of a strong Lewis acid to from $NF_4{}^+$, one of the strongest known oxidants:

$$NF_3 + F_2 + BF_3 \rightarrow NF_4{}^+BF_4^-$$

As we move down group 15, the differences we observe between nitrogen and phosphorus is similar to differences between carbon and silicon. They may be mainly attributed to the diminished ability to form pπ-pπ bonds and the possibility of utilising d-orbitals for pπ-dπ interactions. Arsenic, antimony and bismuth increasingly form ionic salts as the metallic character increases.

Phosphorus is prepared by reduction of phosphate rock with coke and sand in an electric furnace:

$$2\ Ca_3(PO_4)_2 + 6\ SiO_2 + 10\ C \rightarrow P_4 + 6\ CaSiO_3 + 10\ CO$$

P_4 must be stored in water as it inflames in air. P_4 is known as white phosphorus, which may be converted to the amorphous red phosphorus by heating at 300°C in the absence of air. Black phosphorus is the most thermodynamically stable form of phosphorus at room temperature, which may be formed by heating white phosphorus at high pressures of 12000 atmospheres. Its structure is puckered sheets of hexagonally linked atoms, and has similar properties to graphite, such as being a conductor of electricity. Red and black phosphorus are stable in air but will burn on heating.

The other elements are obtained as metals by reduction of their oxides with carbon or hydrogen. We will now look at compounds formed by the rest of group 15 elements:

i. Hydrides (EH_3)

The hydrides become less stable going down the group, with SbH_3 and BiH_3 being very thermally unstable. Phosphine (PH_3) is the most chemically important hydride and it may be prepared by reacting zinc phosphide with acids. It is a very weak base, but a useful nucleophile in organic chemistry to prepare organophosphorus compounds.

ii. Halides (EX_3, EX_5) and oxohalides

All elements in group 15 other than nitrogen can form both trihalides and pentahalides through direct halogenation. The trihalide is formed by keeping the element in excess while the pentahalide may be formed by using the halogen in excess. Phosphorus trihalides are useful as halogenation agents, especially in organic synthesis. For the pentahalides, the fluorides PF_5, AsF_5 and SbF_5 are potent fluoride ion acceptors useful in preparing superacids. The most common oxohalide is $POCl_3$, which may be formed from the oxidation of PCl_3 in oxygen. $POCl_3$ has similar reactivity as PCl_3, and is a common chlorinating agent in organic chemistry.

iii. Oxides

Group 15 oxides follow the same trend that we have observed for oxides of the previous groups. As the elements become increasingly metallic going down the group, their oxides become increasingly basic. While nitrogen, phosphorus and arsenic form acidic oxides, antimony oxide is amphoteric and bismuth oxide is basic. Phosphorus is able to form many oxides of varying stoichiometry, but most commonly phosphorus(III) oxide (P_4O_6) and phosphorus(V) oxide (P_4O_{10}) are observed. P_4O_{10} is an effective drying agent that reacts with water to form a mixture of phosphoric acids.

iv. Sulfides

The other group 15 elements combine directly with sulfur to give several sulfides. For example, phosphorus forms P_4S_3, P_4S_5, P_4S_7 and P_4S_{10} by reacting stoichiometric quantities of red phosphorus with sulfur. The structures of the sulfides are similar to that of the oxides.

Other than compounds discussed above, phosphorus is able to form many strong oxoacids that we have previously discussed in chapter 3.4. Another class of interesting molecules are phosphorus-nitrogen compounds that contain $P{-}N$ single bonds and $P{=}N$ double bonds. These bonds give rise to a class of compounds known as phosphazenes.

3.5.7 *Group 16 elements*

Similar to the previous groups, the first element in group 16 has unique properties compared to the other elements. Oxygen is able to form compounds with every element except helium, neon and argon from group 18. The properties of oxides have been discussed with reference to each element or group. In this part, we will discuss some unique features of oxygen.

Oxygen has 3 isotopes: ^{16}O (99.759%), ^{17}O (0.0374%) and ^{18}O (0.2039%). It has 2 allotropes, dioxygen (O_2) and ozone (O_3). Dioxygen is a colourless gas, but has a pale blue colour in liquid and solid states. O_2 is a paramagnetic biradical that is thermodynamically unstable but kinetically inert. Simple valence bond theory is unable to account for the paramagnetism of O_2, thus it is important to give the electron configuration of O_2 using molecular orbital theory (chapter 3.3) to account for the triplet ground state.

Ozone (O_3) is a diamagnetic blue gas with a pungent odour. It occurs in the atmosphere at an altitude of 25 km, protecting the Earth's surface from excessive exposure to UV light. Ozone is a much stronger oxidising agent than O_2 and reacts with many substances, such as iodide:

$$O_3 + 2\ \mathrm{KI} + H_2O \rightarrow I_2 + 2\ \mathrm{KOH} + O_2$$

This reaction is quantitative and may be used for analysis. The oxidation mechanism most likely follows a radical pathway.

O_2 contains 2 unpaired electrons in the π^*-orbitals. The ground state is a triplet state, but 2 singlet excited states are available at higher energies. The electronic states and their energies relative to ground state are shown in Table 3.6.

The singlet excited state of oxygen $^1\Delta_g$ has sufficiently long lifetime to be used in specific oxidation reactions, such as [4 + 2]-cycloaddition, shown in Figure 3.5.15.

Singlet oxygen may be generated by photochemical or chemical means from triplet oxygen. Cycloadditions will be discussed in detail in chapter 4.14.

Oxygen is able to form weak O−O single bonds in peroxides, where the oxygen atoms have −1 oxidation state. Hydrogen peroxide decomposes easily to water and

Table 3.6. Ground and excited states of dioxygen.

State	π^*-orbital configuration	Energy relative to ground state (kJ mol^{-1})
$^1\Sigma_g^+$	↑ ↓	155
$^1\Delta_g^+$	↑↓ —	92
$^3\Sigma_g^+$	↑ ↑	0

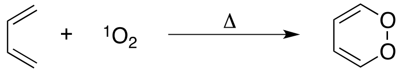


Figure 3.5.15. [4 + 2]-cycloaddition using singlet oxygen.

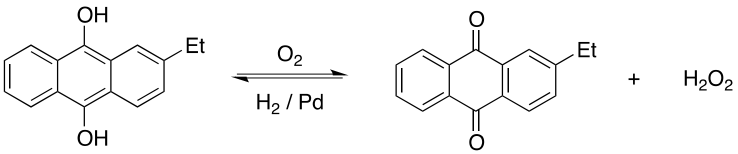


Figure 3.5.16. Example of industrial synthesis of H_2O_2 through autoxidation of anthraquinol.

oxygen, and the decomposition is catalysed by heavy-metal ions:

$$2\ H_2O_2 \rightarrow 2\ H_2O + O_2 \qquad \Delta H^0 = -99\ \text{kJ mol}^{-1}$$

Hydrogen peroxide may be produced by the 2 methods listed below:

1. Autoxidation of anthraquinol

Quinol may be oxidised to quinone in the presence of O_2, generating H_2O_2. The quinone may be reduced to quinol with H_2 gas. This cycle allows us to obtain a 20% aqueous solution of H_2O_2. An example of the process with 2-ethylanthraquinol is shown in Figure 3.5.16.

2. Electrolytic oxidation of sulfuric acid

Sulfuric acid or ammonium sulfate-sulfuric acid solution may be oxidised electrolytically to generate peroxodisulfuric acid ($H_2S_2O_8$), which may be hydrolysed to form H_2O_2.

$$2\ HSO_4^- \rightarrow H_2S_2O_8 + 2\ e^- \qquad \text{(electrolytic oxidation)}$$

$$H_2S_2O_8 + H_2O \rightarrow H_2SO_5 + H_2SO_4 \qquad \text{(fast)}$$

$$H_2SO_5 + H_2O \rightarrow H_2O_2 + H_2SO_4 \qquad \text{(slow)}$$

Fractional distillation may yield 90–98% H_2O_2.

Oxygen atom is easily reduced from −1 in H_2O_2 to −2 in H_2O, making H_2O_2 a good oxidising agent in both acidic and basic media. Peroxides are often used in organic chemistry to generate oxygen radicals due to the weak, non-polar $O-O$ single bond.

Oxygen is able to form compounds with fluorine. Since fluorine is more electronegative than oxygen, these compounds are best known as oxygen fluorides, with oxygen having a positive formal oxidation state. These compounds have been studied as rocket fuel oxidisers.

Oxygen difluoride (OF_2) may be prepared by:

i. Passing fluorine rapidly through a 2% $NaOH$ solution
ii. Electrolysis of aqueous $HF-KF$ solutions
iii. Reaction of fluorine with moist KF

OF_2 is a pale yellow, poisonous gas that is a strong oxidant. It is even able to oxidise xenon to give xenon fluorides and xenon oxide fluorides, which we will discuss in part 3.5.9.

Dioxygen difluoride (O_2F_2) is a yellow-orange solid made by a high-voltage electric discharge on mixtures of O_2 and F_2 at low temperature and pressure. It is highly reactive as a fluorinating and oxidising agent, which decomposes into gaseous elements at –50°C.

The other group 16 elements have properties that differ significantly from oxygen. They have lower electronegativities and tend to form covalent rather than ionic compounds. For sulfur, other than the possible $p\pi$-$d\pi$ interactions present for third-row elements, it is an element with high catenating ability, second to carbon. **Catenation** is the ability of an atom to bond to other atoms of the same element, usually through the formation of a single bond. In most groups, catenating ability decreases down the group, as the atomic size increases. In group 15 and 16, an anomaly is observed where phosphorus and sulfur have higher catenating ability than nitrogen and oxygen respectively. This is due to the lone pair-lone pair repulsion that weakens the $N-N$ and $O-O$ bonds.

Sulfur occurs widely in nature as S (with many different S_n allotropes), H_2S, SO_2, metal sulfides and sulfates. Selenium and tellurium are less abundant and occur as selenide and telluride minerals in ores. Polonium is radioactive and is found as the decay product of uranium and thorium.

We will now take a look at compounds formed by group 16 elements.

1. Hydrides (EH_2)

Group 16 hydrides may be obtained from reacting metal sulfides, selenides or tellurides with acid. The hydrides are poisonous gases with revolting odours. Going down the group, the acidity of the hydride in water increases while the thermal stability decreases. H_2S dissolves in water with a concentration of around $0.1\ mol \cdot dm^{-3}$ at $1\ atm$. As the second dissociation of H_2S is very limited, SH^- ions are most common in solutions. Due to the strong catenating ability of sulfur, compounds H_2S_2 to H_2S_6 can be prepared with S–S chains.

2. Halides

Sulfur is able to form a large family of halides. Direct fluorination of sulfur yields SF_6 with traces of S_2F_{10} and SF_4. SF_6 is very resistant to chemical attack due to the strong S–F bond, coordinative saturation and steric hindrance at sulfur. Chlorination of molten sulfur yields S_2Cl_2, an orange liquid with revolting odour. Sulfur oxochlorides are also synthetically useful chlorinating agents, such as thionyl chloride $(SOCl_2)$. It may be obtained from the following reaction:

$$SO_2 + PCl_5 \rightarrow SOCl_2 + POCl_3$$

3. Oxides and oxoacids

Sulfur forms a long list of oxoacids, which we have first discussed in chapter 3.4. The most common oxoacid, H_2SO_4, may be industrially produced through the contact process, described by the reactions below:

$$S_{(s)} + O_{2(g)} \rightarrow SO_{2(g)}$$

$$2\ SO_{2(g)} + O_{2(g)} \rightarrow 2\ SO_{3(g)}$$

$$H_2SO_{4(l)} + SO_{3(g)} \rightarrow H_2S_2O_{7(l)}\ (\text{oleum})$$

$$H_2S_2O_{7(l)} + H_2O_{(l)} \rightarrow 2\ H_2SO_{4(l)}$$

As seen above, the oxide first formed by burning S in air is SO_2. SO_2 dissolves in water to give acidic solutions. SO_3 may be formed from SO_2 and O_2, which is a thermodynamically favourable reaction that is kinetically slow. Thus, we make use of V_2O_5 catalyst, which is able to act as an oxidant for SO_2 before being oxidised back by air:

$$V_2O_5 + SO_2 \rightarrow V_2O_4 + SO_3$$

$$V_2O_4 + \frac{1}{2}O_2 \rightarrow V_2O_5$$

Similar to H_2SO_4, selenium forms H_2SeO_4, which is less stable and a strong oxidising agent. Telluric acid has a completely different structure of $Te(OH)_6$ in the crystalline form. It is a very weak acid that may also be used as an oxidiser. Sulfur may form oxides with multiple sulfur atoms, due to its strong catenating ability. Commonly, there is thiosulfate $(S_2O_3^{2-})$, which may be obtained by boiling solutions of sulfites with sulfur. Other sulfur oxides include dithionites, dithionates and polythionates. They all have $S–S$ bonds present in their structures. Generally, bridging S atoms may have linear geometry while S atoms bonded to oxygen have tetrahedral geometry.

3.5.8 *Group 17 elements*

Group 17 elements, also known as halogens, form compounds with all other elements in the periodic table other than He, Ne and Ar. In all the previous chapters, we have discussed halides formed by elements in each main group, which are easy to prepare and often are useful source materials for the synthesis of other compounds. These halides may be classified as ionic or covalent halides.

Fluorine occurs widely in ores such as CaF_2 (fluorite) and Na_3AlF_6 (cryolite). The pure element may be obtained from the electrolysis of molten fluorides. Fluorine is the most chemically reactive of all the elements and combines directly with most elements on the periodic table. The exceptionally high reactivity of F_2 may be attributed to the weak $F–F$ bond due to the lone pair-lone pair repulsion when the two F atoms are close together.

Chlorine occurs mainly in salts, such as $NaCl$, KCl, $MgCl_2$ and so on. Chlorine may be obtained as a pure element from electrolysis of brine, which is a highly concentrated salt solution. Similar, bromine occurs in salts and may be obtained from brines. However, bromine is much lower in abundance than chlorine. Iodine occurs as iodide in brines or iodate in Chile saltpetre. Iodine is concentrated by various forms of marine life. Iodine may be produced by oxidising I^-, usually with an acidic solution of MnO_2. Astatine is radioactive with no stable isotope, formed from the decay of uranium and thorium.

The most common compounds formed by halogens are the halides. As we have looked into halides in every other part of this chapter, we will not discuss the halides in detail here. Instead, we will look at other interesting compounds formed by halogens:

1. Halogen oxides

Oxygen fluorides have been discussed in part 3.5.7. Chlorine oxides are reactive and tend to explode. ClO_2 is a strong oxidising agent that may be used to bleach wood pulp. It may be generated from the reaction below:

$$2\ NaClO_3 + SO_2 + H_2SO_4 \rightarrow 2\ ClO_2 + 2\ NaHSO_4$$

Cl_2O is a selective and powerful chlorinating agent for organic compounds. For iodine, dehydration of iodic acid at an elevated temperature of 240°C generates I_2O_5:

$$2\ HIO_3 \rightarrow I_2O_5 + H_2O$$

I_2O_5 is an oxidising agent that can be used in the determination of CO through the reaction below:

$$5\ CO + I_2O_5 \rightarrow I_2 + 5\ CO_2$$

2. Oxoacids

Solutions of oxoacids and certain oxoanions may be obtained by interaction of the free halogens with water or aqueous bases. Fluorine forms only hypofluorous acid, HOF, which is explosive at room temperature:

$$2\ HOF \rightarrow 2HF + O_2$$

HOF is the only hypohalous acid that can be isolated as a solid and it may be prepared by passing F_2 over ice at –40°C:

$$F_2 + H_2O \rightarrow HOF + HF$$

The other halogens form a much larger variety of oxocompounds. We will look at the oxocompounds in ascending halogen oxidation state order:

i. +1 oxidation state: Hypohalous acid
The other halogens form hypohalous acids through interaction with mercury(II) oxide:

$$2\ X_2 + 2\ HgO + H_2O \rightarrow HgO \cdot HgX_2 + 2\ HOX$$

Hypohalous acids are very weak acids but good oxidising agents, especially in acidic medium. Hypohalite ions may be prepared by dissolving the halogens in base:

$$X_2 + 2\ OH^- \rightarrow XO^- + X^- + H_2O$$

However, hypohalite ions rapidly disproportionate in basic solution to form halate ions with +5 oxidation state:

$$3\ XO^- \rightarrow 2\ X^- + XO_3^-$$

For Cl, the disproportionation of ClO^- is slow below room temperatures. At high temperatures above 75°C, the disproportionation is accelerated and good yields of ClO_3^- may be obtained. For Br, BrO^- may be only prepared and kept around 0°C due to the increased rate of disproportionation. For I, IO^- disproportionates so quickly that no IO^- solution can be obtained.

ii. +3 oxidation state: Halous acid
The only certain halous acid is chlorous acid, $HClO_2$, which may be prepared by treating a suspension of barium chlorite with H_2SO_4, filtering away $BaSO_4$ precipitate formed. Chlorites $(MClO_2)$ are obtained by disproportionation of ClO_2 in solutions of bases:

$$2\ ClO_2 + 2\ MOH \rightarrow MClO_2 + MClO_3 + H_2O$$

Chlorous acid decomposes quickly in acidic medium through an autocatalytic pathway using Cl^-:

$$5\ HClO_2 \rightarrow 4\ ClO_2 + Cl^- + H^+ + 2\ H_2O$$

On the other hand, chlorites are stable in alkaline solutions, even upon boiling. They are applied as bleaching agents.

iii. +5 oxidation state: Halic acid
Chloric and bromic acids, $HClO_3$ and $HBrO_3$, are obtained in solution by treating the barium halates with H_2SO_4. Iodic acid, HIO_3, is a stable white solid that may be prepared by oxidising I_2 with concentrated HNO_3, H_2O_2, O_3 or others. Halic acids are strong oxidisers and strong acids. In basic medium, halate ions are formed instead. For Cl, ClO_3^- disproportionates into Cl^+ and ClO_4^- through a thermodynamically favourable process. However, this disproportionation is very slow in solution. For Br, the disproportionation of BrO_3^- is extremely unfavourable.

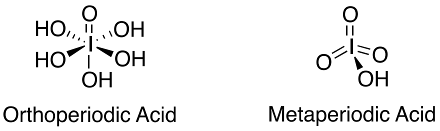


Figure 3.5.17. 2 different forms of periodic acid.

iv. +7 oxidation state: Perhalic acid

The +7 oxidation state is usually only obtainable through oxidation with strong oxidants. For Cl, $\mathrm{ClO_4^-}$ is prepared by electrolytic oxidation of solutions of chlorate. Perchloric acid, $\mathrm{HClO_4}$, may be formed by acidifying sodium perchlorate solution. For Br, $\mathrm{BrO_4^-}$ may be prepared by oxidising $\mathrm{BrO_3^-}$ with $\mathrm{F_2}$ in basic solution:

$$\mathrm{BrO_3^- + F_2 + 2\ OH^- \rightarrow BrO_4^- + 2\ F^- + H_2O}$$

Periodic acid, just like all periodates, exists in 2 forms as shown in Figure 3.5.17. At +7 oxidation state, the perhalides are rather unstable and strongly oxidising.

3. Interhalogen compounds

The halogens are able to form compounds and ions among themselves in binary and rarely ternary combinations. Neutral interhalogen compounds are of the type $\mathrm{XY_n}$, where n is odd. The heavier halogen is always X, being the central atom in the molecule. Interhalogen ions may be either cations or anions. Halogen fluorides react with fluoride ion acceptors:

$$\mathrm{2\ ClF + AsF_5 \rightarrow FCl_2^+ AsF_6^-}$$

The common triiodide ion, $\mathrm{I_3^-}$, may be formed by dissolving $\mathrm{I_2}$ in KI. Triiodide is able to form many salts.

3.5.9 *Group 18 elements*

Group 18 elements are also known as noble gases due to their low reactivity. They are all colourless, odourless, monoatomic gases under standard conditions as they have very weak dispersion forces between atoms. Their low reactivity is due to them having stable, filled octet electron configurations. They occur naturally as minor constituents of the atmosphere.

Helium is the second most abundant element in the universe, coming after hydrogen. It is mainly formed through radioactive decay, as α-particles are essentially helium nuclei. The other noble gases are obtained through the fractionation of liquid air. While the noble gases were originally thought to be completely inert, the heavier noble gases, especially xenon, show interesting chemistry. The lighter noble gases also find their application in many areas. Liquid helium is used in cryoscopy. Argon is used as an inert gas to protect sensitive reactions, in welding and in gas-filled electric light bulbs. Neon is used for discharge lighting tubes, giving off the characteristic red glow of neon lights.

The most chemically interesting noble gas is xenon, so we will focus our discussion on xenon chemistry. The first compound containing a noble gas was reported by Bartlett in 1962 as $[Xe^+][PtF_6^-]$. However, further studies showed that the structure is more complex, including salts such as $[XeF^+][PtF_5^-]$ and $[Xe_2F_3^+][PtF_6^-]$. Currently, many xenon compounds with $Xe–F$ and $Xe–O$ bonds are known, as we will discuss below:

1. Xenon fluorides

Xenon is able to form 3 different fluorides based on the reaction conditions through direct reaction of xenon with fluorine.

At 400°C, 1 atm, with xenon in excess:	$Xe + F_2 \rightarrow XeF_2$
At 600°C, 6 atm, with Xe:F_2 = 1:5 ratio:	$Xe + 2\ F_2 \rightarrow XeF_4$
At 300°C, 60 atm, with Xe:F_2 = 1:20 ratio:	$Xe + 3\ F_2 \rightarrow XeF_6$

These fluorides are usually synthesised in anhydrous nickel reaction vessels. XeF_2 is slowly hydrolysed in acid, but rapidly hydrolysed in base:

$$XeF_2 + 2\ OH^- \rightarrow Xe + \frac{1}{2}O_2 + 2\ F^- + H_2O$$

XeF_2 is a strong oxidiser, and may also be used as a mild fluorinating agent in organic synthesis. XeF_4 resembles XeF_2 in properties in being a strong oxidiser and mild fluorinating agent, however, it is easily hydrolysed in the presence of water:

$$3\ XeF_4 + 6\ H_2O \rightarrow\ XeO_3 + 2\ Xe + \frac{3}{2}O_2 + 12\ HF$$

XeF_6 is the most reactive xenon fluoride, reacting even with quartz.

$$SiO_2 + 2\ XeF_6 \rightarrow 2\ XeOF_4 + SiF_4$$

It is a strong acid by accepting oxide ions and inserting fluoride ions in its place. The structures of xenon fluorides generally follow VSEPR theory, with XeF_2 being linear and XeF_4 being square planar. XeF_6 has an interesting solid state structure with XeF_5^+ units linked by unsymmetrical and bent F^- bridges. In liquid and vapour phase, XeF_6 has a distorted octahedral structure due to a stereochemically active lone pair on Xe.

2. Xenon-oxygen compounds

XeO_3 may be formed from the hydrolysis of XeF_4 and XeF_6. XeO_3 is a white deliquescent solid that is dangerously explosive, forming colourless and odourless aqueous solutions. In basic solutions, the xenate(VI) ion is formed.

$$XeO_3 + OH^- \rightarrow HXeO_4^-$$

The xenate ion may be further oxidised through disproportionation or reaction with ozone to form the perxenate(VIII) ion, XeO_6^{4-}. Perxenate ions are yellow and strongly oxidising. Salts such as $Na_4XeO_6 \cdot 8\ H_2O$ are stable and sparingly soluble in water. The perxenate ion is slowly reduced by water in base while rapidly reduced in acid through hydroxyl radical intermediates:

$$H_2XeO_6^{2-} + H^+ \rightarrow HXeO_4^- + H_2O + \frac{1}{2}O_2$$

Lighter noble gases have higher ionisation energies and are therefore much less reactive. The only heavier noble gas, radon, is expected to be even more reactive than xenon, but radon is not well-studied due to its radioactivity.

3.6 Crystal Structure

In solid state chemistry, there are 3 types of solid structures: crystalline solids, amorphous solids and quasicrystals. Crystalline solids, simply known as crystals, have long-range order, meaning that the atoms or ions are arranged in an orderly array with a pattern that keeps repeating itself. Amorphous solids do not have a regular atomic arrangement and do not have a diffraction pattern. Quasicrystals have structures that are ordered but not periodic, lying somewhere between crystalline and amorphous. In this chapter, we will explore crystalline solid structures.

3.6.1 *Unit cell*

The long-range order of crystalline solids may be described by repeating patterns and motifs. The **unit cell** is the smallest repeating unit of a crystalline structure that shows the full symmetry of the structure. The full structure of the crystal must be obtained by repeating the unit cell structure without gaps in between, and all repeating unit cells must be identical. Figure 3.6.1 shows an example of unit cells in crystal lattices.

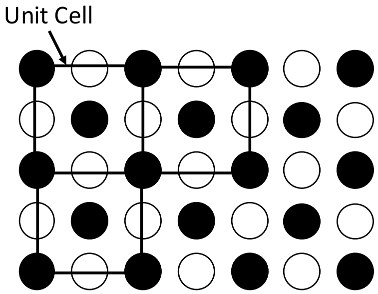
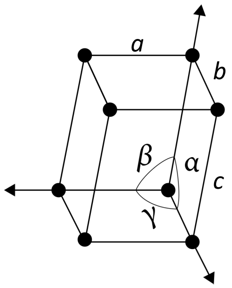


Figure 3.6.1. Example of unit cell in a simple crystal lattice.



7 Crystal Systems

Cubic	$a = b = c$	$\alpha = \beta = \gamma = 90°$
Tetragonal	$a = b \neq c$	$\alpha = \beta = \gamma = 90°$
Orthorhombic	$a \neq b \neq c$	$\alpha = \beta = \gamma = 90°$
Monoclinic	$a \neq b \neq c$	$\alpha = \gamma = 90°, \beta \neq 90°$
Triclinic	$a \neq b \neq c$	$\alpha \neq \beta \neq \gamma \neq 90°$
Hexagonal	$a = b \neq c$	$\alpha = \beta = 90°, \gamma = 120°$
Rhombohedral	$a = b = c$	$\alpha = \beta = \gamma \neq 90°$

Figure 3.6.2. 7 crystal systems.

There are 7 different crystal systems, characterised by different unit cell geometries, as shown in Figure 3.6.2.

We will focus on the most basic cubic crystal system, where there are 3 main unit cells:

1. Primitive cubic (Cubic-P, or simple cubic)

The primitive cubic structure is formed when atoms are layered directly above each other, and the unit cell is shown in Figure 3.6.3.

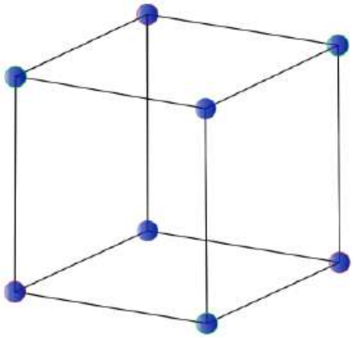


Figure 3.6.3. Primitive cubic unit cell.

It might appear that there are 8 atoms in the unit cell, but we must realise that the atom at the corner of the unit cell is shared by 8 unit cells. Thus, only $\frac{1}{8}$ of an atom at the corner is in the unit cell, and there is a total of $8 \times \frac{1}{8} = 1$ atom in each primitive cubic unit cell. For any lattice, we can represent every point in the lattice with a set of **lattice points** moving integer number of times in x, y or z-direction. For primitive cubic lattice, there is only 1 lattice point, which is the corner atom.

To calculate the packing efficiency, we must find the percentage of space occupied by atoms in the unit cell. As the atoms are packed directly touching each other, the unit cell is a cube with side length $2r$, where r is the radius of the atom.

The packing efficiency is:

$$\text{Packing Efficiency} = \frac{1 \text{ atom} \times \frac{4}{3}\pi r^3}{(2r)^3} = 52.4\%$$

2. Body-centred cubic (bcc)

The body-centred cubic structure is formed by 2 alternating layers of atoms, and the unit cell is shown in Figure 3.6.4.

In the body-centred cubic unit cell, other than the 8 atoms at the corner, there is another atom in the centre, fully within the unit cell. Thus, there are $8 \times \frac{1}{8} + 1 = 2$ atoms per unit cell. There are 2 lattice points, consisting of the corner atom and the atom in the centre.

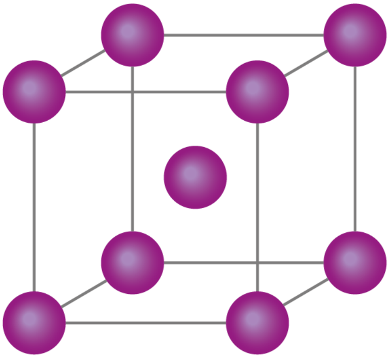


Figure 3.6.4. Body-centred cubic unit cell.

To calculate the packing efficiency, we must realise that the corner atoms are all in contact with the central atom, and that the body diagonal (bd) of the cube is $4r$. The bd is the distance between opposite corners of the cube. Meanwhile, face diagonal (fd) is the length of the diagonal across the face of the cube. We may express bd in terms of side length (a) by Pythagoras theorem:

$$\mathrm{fd} = \sqrt{a^2 + a^2} = \sqrt{2}a$$

$$\mathrm{bd} = \sqrt{a^2 + \mathrm{fd}^2} = \sqrt{a^2 + 2a^2} = \sqrt{3}a = 4r$$

$$a = \frac{4}{\sqrt{3}}r$$

$$\text{Packing Efficiency} = \frac{2 \text{ atoms} \times \frac{4}{3}\pi r^3}{\left(\frac{4}{\sqrt{3}}r\right)^3} = 68.0\%$$

3. Face-centred cubic (fcc)

The face-centred cubic structure is formed by 3 alternating layers of atoms, and the unit cell is shown in Figure 3.6.5.

There are atoms at each corner and atoms in the centre of each face. Each atom on the face is shared by 2 unit cells, and only $\frac{1}{2}$ of an atom on the face is in the unit cell. With 8 corner atoms and 6 face atoms, there are a total of $8\times\frac{1}{8}+6\times\frac{1}{2}=4$ atoms per unit cell. There are 4 lattice points, including a corner atom and 3 atoms on orthogonal faces.

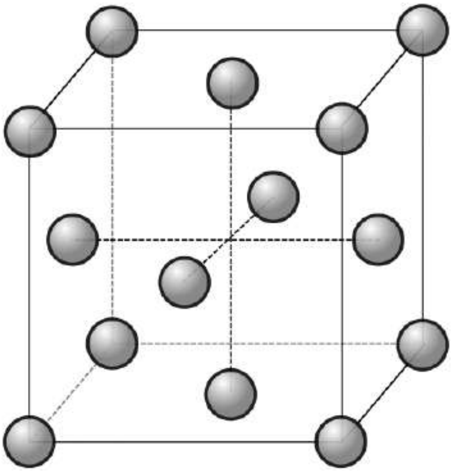


Figure 3.6.5. Face-centred cubic unit cell.

In a fcc lattice, the corner atoms are in contact with the atoms in the middle of the faces, and $\mathrm{fd}=4r$. We may use this relationship to determine the packing efficiency:

$$\mathrm{fd}=\sqrt{2}a=4r$$

$$a=\frac{4}{\sqrt{2}}r$$

$$\text{Packing Efficiency}=\frac{4\text{ atoms}\times\frac{4}{3}\pi r^3}{\left(\frac{4}{\sqrt{2}}r\right)^3}=74.0\%$$

It has been proven mathematically that the packing in fcc lattices is the densest possible, with a packing efficiency of around 74%. Lattices with the densest packing are known as close-packed structures. Thus, fcc is also known as cubic close-packed (ccp). Other than cubic close-packed, another close-packed structure is hexagonal close-packed (hcp), based on a hexagonal unit cell.

In an ionic salt, the larger anion forms a lattice while the smaller cation fills the holes of the lattice. As ions of the same charge repel each other, the holes must be filled with ions of the opposite charge. If the cation is too small and unable to fully fill the hole, the crystal lattice would be unstable as the anions are in contact with each other.

There are 3 types of holes in the cubic unit cells that we have previously discussed:

1. Cubic hole

Cubic holes are found in the centre of cubic-P unit cells. We will try to calculate the size of the cubic hole, by finding the bd:

$$a = 2r$$

$$\mathrm{bd} = \sqrt{3}a = 2\sqrt{3}r$$

$$r_{\text{hole}} = \frac{\mathrm{bd} - 2r}{2} = \frac{2\sqrt{3} - 2r}{2} = (\sqrt{3} - 1)r = 0.732r$$

2. Octahedral hole

Octahedral holes are found in the centre and edges of fcc unit cells. The size of the octahedral hole may be determined by considering the side length:

$$a = \frac{4}{\sqrt{2}}r$$

$$r_{\text{hole}} = \frac{\frac{4}{\sqrt{2}}r - 2r}{2} = (\sqrt{2} - 1)r = 0.414r$$

3. Tetrahedral hole

Tetrahedral holes may be found in fcc unit cells if we divide each unit cell into 8 smaller cubes. Tetrahedral holes are the smallest holes and we may determine their size by considering the bd of the smaller cube, which is half of the bd of the unit cell:

$$\mathrm{bd}_{\text{small cube}} = \frac{\mathrm{bd}}{2} = \frac{\sqrt{3}a}{2} = \frac{\sqrt{3}\left(\frac{4}{\sqrt{2}}r\right)}{2} = \sqrt{6}r$$

$$\mathrm{r}_{\text{hole}} = \frac{(\sqrt{6} - 2)r}{2} = 0.225r$$

We may count the number of holes in each unit cell the same way as we count atoms. For a fcc unit cell, there is 1 octahedral hole in the centre and on each of the 12 edges. Holes on the edge are shared between 4 unit cells, and only $\frac{1}{4}$ of the hole is in each unit cell. Thus, there are a total of $1 + 12 \times \frac{1}{4} = 4$ octahedral holes.

The 8 tetrahedral holes may be easily counted, since the 8 smaller cubes contains 1 tetrahedral hole each.

As the ions used to fill the holes must be at least the size of the hole, the radius range of atoms for each type of hole is listed in Table 3.7.

When discussing ionic lattices, we usually use coordination numbers to describe the positions of the ions in the lattice. We will discuss the coordination by using the notation: (x,y)-coordination, where x and y are the coordination numbers for the cation and anion respectively. From the size and radius range of the holes, we are able to predict the coordination number and lattice type by calculating the radius ratio, ρ:

$$\rho = \frac{\text{radius of cation}}{\text{radius of anion}} = \frac{r_+}{r_-}$$

Table 3.8 lists the coordination number and lattice structures for different ranges of ρ.

It is interesting to note that both square planar and octahedral coordination types are possible with $\rho = 0.414 - 0.732$, however, octahedral coordination is much more common in crystal lattices.

Table 3.7. Radius range of ion to fit in the different type of holes.

Type of hole	**Size of hole (*r*)**	**Radius range of ion (*r*)**
Cubic hole	0.732	0.732–0.999
Octahedral hole	0.414	0.414–0.732
Tetrahedral hole	0.225	0.225–0.414

Table 3.8. Radius ratios and their corresponding coordination types.

Radius ratio, ρ	**Coordination number**	**Coordination type**	**Sample compound**
<0.155	2	Linear	
0.155–0.225	3	Trigonal Planar	BN
0.225–0.414	4	Tetrahedral	ZnS
0.414–0.732	4	Square Planar	
0.414–0.732	6	Octahedral	NaCl
0.732–0.999	8	Body-centred Cubic	CsCl

3.6.2 *Common crystal structures*

There are some characteristic crystal lattices that most ionic salts fall under, and we will discuss 6 common structures below:

1. Rock salt ($NaCl$) structure:

The unit cell of $NaCl$ crystal lattice is shown in Figure 3.6.6.

$NaCl$ crystal lattice has (6,6)-coordination, and may be described as a fcc lattice of Cl^- anions with all the octahedral holes filled by Na^+ cations.

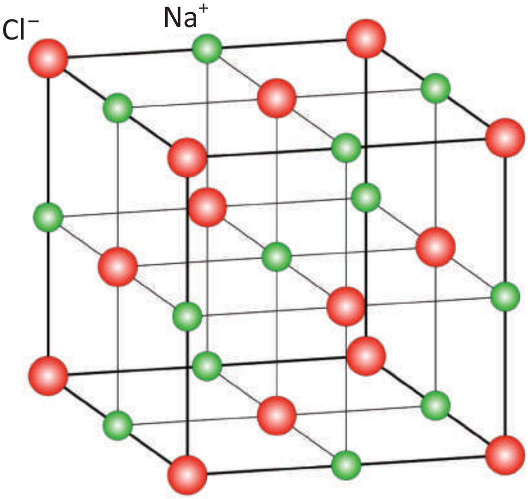


Figure 3.6.6. Unit cell of NaCl crystal lattice.

2. Caesium chloride ($CsCl$) structure:

The unit cell of $CsCl$ crystal lattice is shown in Figure 3.6.7.

$CsCl$ crystal lattice has (8,8)-coordination, and may be described as a primitive cubic lattice of Cl^- anions with the cubic holes occupied by Cs^+ cations.

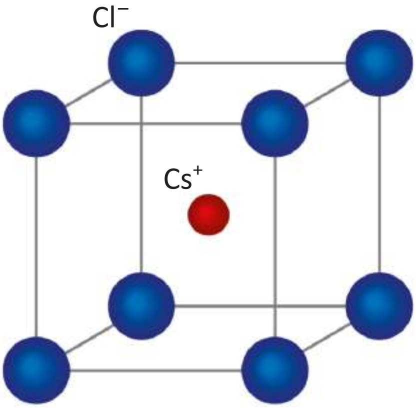


Figure 3.6.7. Unit cell of CsCl crystal lattice.

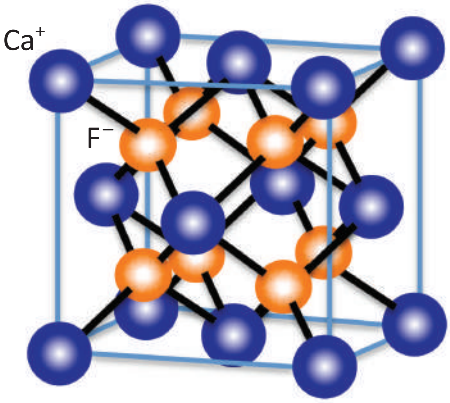


Figure 3.6.8. Unit cell of fluorite lattice structure.

3. Fluorite (CaF_2) and Antifluorite structure:
The unit cell of fluorite lattice structure is shown in Figure 3.6.8.

The fluorite lattice has (8,4)-coordination, and may be described as a fcc lattice of Ca^{2+} cations with all the tetrahedral holes occupied by F^- anions. As there are 8 tetrahedral holes per 4 calcium atoms in a fcc lattice, the ratio of the number of atoms of $Ca{:}F = 1{:}2$, which corresponds to the chemical formula of fluorite. Antifluorite has the opposite structure as fluorite: the anion forms the fcc lattice while the cation fills the tetrahedral holes. An example of an ionic salt with antifluorite lattice structure is Li_2O.

4. Zinc Blende (ZnS) structure:
The unit cell of zinc blende lattice structure is shown in Figure 3.6.9.

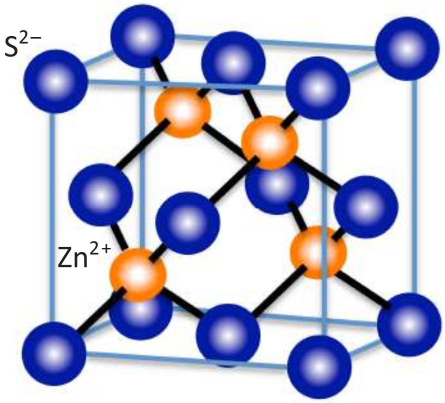


Figure 3.6.9. Unit cell of zinc blende lattice structure.

The zinc blende lattice has (4,4)-coordination, where S^{2-} anions form a fcc lattice and half of the tetrahedral holes are filled with Zn^{2+} cations. In this case, the Zn^{2+} cations are too small to fully occupy the octahedral holes, thus, half of the tetrahedral holes are filled up instead.

5. Rutile $(\mathrm{TiO_2})$ structure:

The unit cell of rutile lattice structure is shown in Figure 3.6.10.

The rutile lattice is not actually based on a cubic cell, instead, it is based on a tetragonal unit cell. The rutile lattice has (6,3)-coordination, with the Ti^{4+} cations forming a body-centred tetragonal lattice and the trigonal holes being occupied by O^{2-} anions. Although rutile is not a cubic cell, it is still an important structure to know as it is the prototypical structure for many metal dioxides and difluorides.

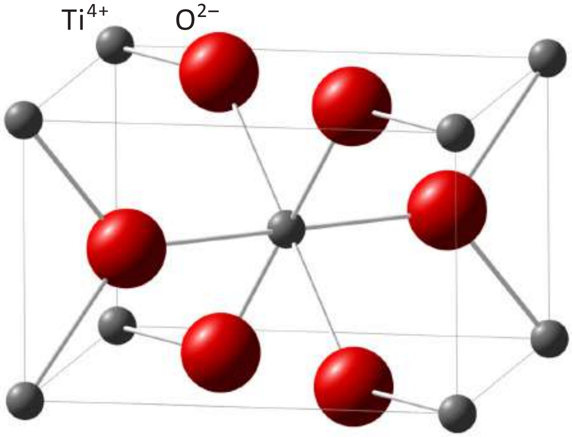


Figure 3.6.10. Unit cell of rutile lattice structure.

6. Spinel $(\mathrm{MgAl_2O_4})$ structure:

The unit cell of spinel lattice structure is shown in Figure 3.6.11.

The spinel lattice is the most complicated structure that we will discuss, with a general formula of $\mathrm{AB_2O_4}$, where A is a metal ion with oxidation state +2 and B is a metal ion with oxidation state +3. In a spinel lattice, O^{2-} anions form a fcc lattice and the A^{2+} and B^{3+} ions occupy the holes in the lattice. In a normal spinel lattice, the A^{2+} cations occupy $\frac{1}{8}$ of the tetrahedral holes while the B^{3+} cations occupy $\frac{1}{2}$ of the octahedral holes. However, certain compounds preferentially adopt the inverse spinel structure, $\mathrm{B[AB]O_4}$, where the A^{2+} cations occupy $\frac{1}{4}$ of the octahedral holes and B^{3+} cations occupy $\frac{1}{4}$ of the octahedral holes and $\frac{1}{8}$ of the tetrahedral holes. It is possible to determine if a compound prefers spinel or inverse spinel structure by considering the crystal field stabilisation energy from placing the cations in different holes, using the knowledge from chapter 3.7.

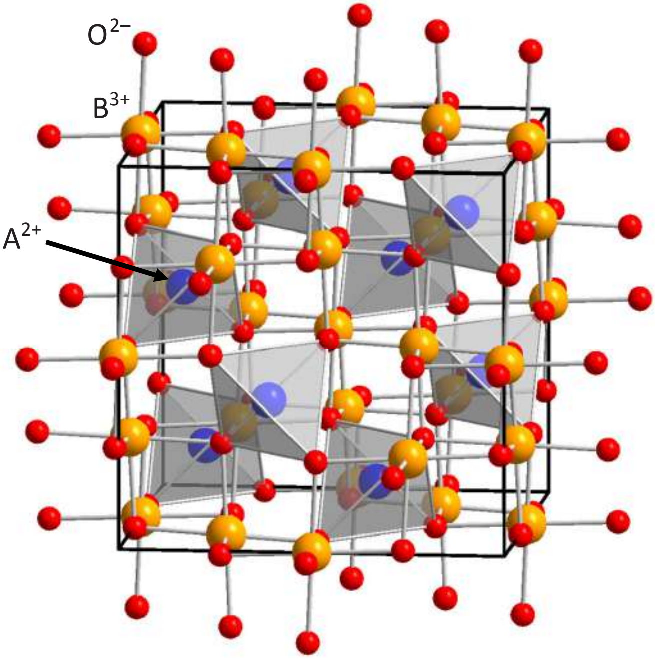


Figure 3.6.11. Unit cell of spinel lattice structure.

3.6.3 *Energetics of crystal lattices*

Lattice energy may be determined using the **Born-Lande equation**:

$$U = -\frac{N_A e^2}{4\pi\varepsilon_0}\left(\frac{|z_A z_B|}{d}\right)A$$

Where A is the Madelung constant.

Madelung constant is a property of the lattice type, and all lattices of the same type will have the same A. The Born-Lande equation is derived based on charge interactions between ions of opposite charges, and assumes that:

1. Bonds are purely ionic and there are no covalent interactions.
2. Repulsion arising from overlap of electron distributions of closed-shell ions in contact is negligible.

Due to the assumptions, the result calculated from Born-Lande equation may only be used as an estimate for the lattice energy. The key relationship shown by Born-Lande equation is:

$$U \propto \frac{1}{d} = \frac{1}{r_+ + r_-}$$

From this relationship, we may explain some properties of ionic solids:

1. Thermal stability of ionic solids

It is experimentally determined that ionic solids with a large difference in cation and anion sizes more readily decompose on heating. For example, the decomposition of group 2 carbonates:

$$\mathrm{MCO_{3(s)}} \rightarrow \mathrm{MO_{(s)}} + \mathrm{CO_{2(g)}}$$

For this reaction, $\Delta S > 0$ as $\mathrm{CO_2}$ gas is evolved but $\Delta H > 0$ as heat is absorbed. The smaller the ΔH, the easier it is for the carbonate to decompose. This depends on the relative stability of the metal oxide and metal carbonate. We may compare the thermal decomposition of $\mathrm{CaCO_3}$ to that of $\mathrm{BaCO_3}$ by calculating the percentage change in lattice energy for each carbonate.

$$\%\text{ change in } U = \frac{\Delta U}{U_i} \propto \frac{\frac{1}{d_f} - \frac{1}{d_i}}{\frac{1}{d_i}} = \frac{d_i - d_f}{d_f}$$

For $\mathrm{CaCO_3}$, $d_i = r_{\mathrm{Ca^{2+}}} + r_{\mathrm{CO_3^{2-}}}$ and $d_f = r_{\mathrm{Ca^{2+}}} + r_{\mathrm{O^{2-}}}$.

For $\mathrm{BaCO_3}$, $d_i = r_{\mathrm{Ba^{2+}}} + r_{\mathrm{CO_3^{2-}}}$ and $d_f = r_{\mathrm{Ba^{2+}}} + r_{\mathrm{O^{2-}}}$.

Thus, we have:

$$\%\text{ change in } U_{\mathrm{CaCO_3}} = \frac{r_{\mathrm{CO_3^{2-}}} - r_{\mathrm{O^{2-}}}}{r_{\mathrm{Ca^{2+}}} + r_{\mathrm{O^{2-}}}}$$

$$\%\text{ change in } U_{\mathrm{BaCO_3}} = \frac{r_{\mathrm{CO_3^{2-}}} - r_{\mathrm{O^{2-}}}}{r_{\mathrm{Ba^{2+}}} + r_{\mathrm{O^{2-}}}}$$

Comparing the percentage change in lattice energy for each carbonate, we have:

$$\frac{\%\text{ change in } U_{\mathrm{CaCO_3}}}{\%\text{ change in } U_{\mathrm{BaCO_3}}} = \frac{r_{\mathrm{Ba^{2+}}} + r_{\mathrm{O^{2-}}}}{r_{\mathrm{Ca^{2+}}} + r_{\mathrm{O^{2-}}}} > 1$$

As a larger percentage change in ΔU suggests a smaller ΔH, $\mathrm{CaCO_3}$ decomposes more readily than $\mathrm{BaCO_3}$, as $\mathrm{CaCO_3}$ has a larger difference in cation and anion sizes than $\mathrm{BaCO_3}$.

2. Solubility of ionic salts

As a consequence of lattice and hydration energies, dissolution is more favourable for compounds with cation and anion of very different sizes. We may express the changes in lattice and hydration energies in terms of ionic radii:

$$\Delta H_{\mathrm{LE}} \propto \frac{1}{r_+ + r_-}$$

$$\Delta H_{\mathrm{hyd}} \propto \frac{1}{r_+} + \frac{1}{r_-}$$

The process of dissolution consists of breaking up the crystal lattice and the hydration of the ions. While breaking up the crystal lattice is endothermic, the hydration of the ions is exothermic. Dissolution of the salt is favourable when the hydration energies of the ions is much greater than the lattice energy of the crystal. Mathematically, we may demonstrate that the hydration energy is much greater than the lattice energy when r_+ and r_- are very different. For example, if $r_+ = r_-$,

$$\frac{\Delta H_{\mathrm{hyd}}}{\Delta H_{\mathrm{LE}}} = 4$$

However, when r_+ and r_- are very different and $r_- = 10\, r_+$,

$$\frac{\Delta H_{\mathrm{hyd}}}{\Delta H_{\mathrm{LE}}} = 12.1$$

Thus, salts with a larger difference in cation and anion sizes are more soluble. This property may be used to explain solubility trends such as the solubility of group 2 sulfates. As sulfate is a large anion, the solubility of group 2 sulfates decreases going down the group as the cation size increases. This results in $\mathrm{MgSO_4}$ being soluble and $\mathrm{BaSO_4}$ being insoluble.

3.6.4 *Defects in crystal lattices*

While crystal lattices are thought to be perfectly ordered, in reality, there are crystal defects that cause slight changes in crystal structure. Defects may be classified as intrinsic or extrinsic, **intrinsic defects** being those that occur in pure lattices and **extrinsic defects** being those that are caused by inclusion of foreign species into the lattice.

We will first look at the 2 main types of intrinsic defects:

1. Schottky defect

Schottky defects arise from vacant lattice sites, but the stoichiometry and electrical neutrality of the crystal are maintained. Thus, the ratio of the number of cations lost to anions lost corresponds to the stoichiometry of the crystal. This causes the crystal to become less dense due to the lattice vacancies. Figure 3.6.12 shows an example of a Schottky defect.

Schottky defects occur mainly in highly ionic compounds, where the cations and anions are of similar size. Compounds affected by the Schottky defect generally have high coordination numbers, such as 6 or 8.

2. Frenkel defect

A Frenkel defect occurs when an ion is displaced into a vacant interstitial site. For example, a cation originally occupying an octahedral hole may be displaced into a tetrahedral hole. Figure 3.6.13 shows an example of the Frenkel defect.

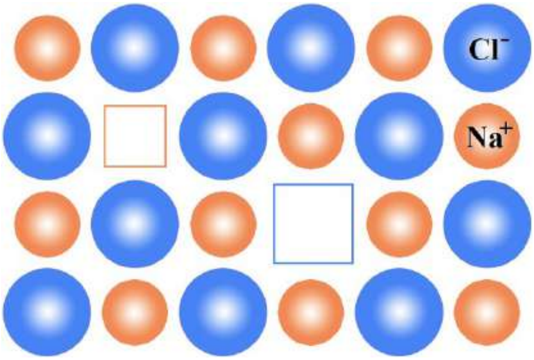


Figure 3.6.12. Example of Schottky defect.

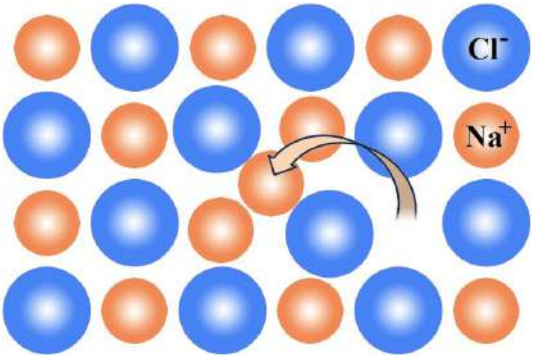


Figure 3.6.13. Example of Frenkel defect.

As the composition of the crystal does not change from a Frenkel defect, the stoichiometry and electrical neutrality are maintained. Frenkel defects usually occur when there is a significant difference in cation and anion size, and affected compounds have small coordination numbers, such as 4 or 6.

As the conditions for forming Schottky and Frenkel defects are very different, only one type of defect predominates in any given crystal. Intrinsic defects are often formed as a way for the crystal to absorb energy as the energy required to form a defect is much smaller than the lattice energy. For example, NaCl requires around $200\ \mathrm{kJ\ mol^{-1}}$ of energy to form a Schottky defect, compared to the lattice energy of around $750\ \mathrm{kJ\ mol^{-1}}$. Thus, it is much easier to form defects than to break the entire crystal lattice. Overall, the number of defects remains very small. For the NaCl crystal lattice, there is 1 defect in every 10^{15} lattice sites at room temperature, 1 defect in every 10^{6} lattice sites at 500°C and 1 defect in every 10^{4} lattice sites at 800°C.

Extrinsic defects are formed through introduction of a dopant into a crystal lattice. For example, we may introduce $\mathrm{Ca^{2+}}$ cations into a $\mathrm{ZrO_2}$ crystal, replacing

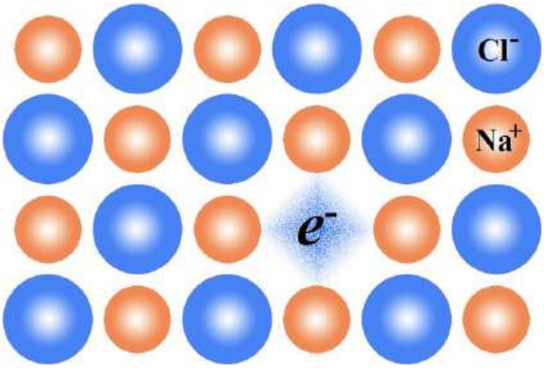


Figure 3.6.14. Example of a F-centre in a lattice.

some Zr^{4+} cations with Ca^{2+} cations, leading to O^{2-} vacancies to maintain charge neutrality. In certain cases, defects cause electrons to be trapped in a crystal lattice. These defects are known as F-centres, coming from the German word *Farbe* that stands for colour, as the presence of trapped electrons in a lattice causes colour changes. If we heat a $NaCl$ crystal in Na vapour, Na atoms will enter the lattice and be oxidised to Na^+ cations, leaving an electron in the lattice, filling the halide ion vacancy, creating a F-centre. Due to the presence of single, unpaired electrons, F-centres are paramagnetic. Figure 3.6.14 shows an example of a F-centre in a lattice.

The formation of metal alloys may be considered extrinsic defects in a metal lattice. There are 2 main types of metal alloys:

1. Substitution alloys

Substitution alloys are formed when some atoms in a metal lattice are substituted by other metal atoms. For example, in a $AuCu_3$ alloy, the fcc lattice of Au has its facial sites substituted by Cu.

2. Interstitial alloys

Interstitial alloys are formed when one metal fills holes in the interstitial sites of the other metal lattice. This usually occurs for metals with very different metallic radii, as the metal filling the interstitial sites must be significantly smaller than the metal forming the lattice.

3.7 Coordination Chemistry

Coordination chemistry is the study of metal complexes formed by mainly the d-block transition metals and f-block metals. In this chapter, we will look at the structure and properties of such complexes, explaining their stabilities and reactivities.

3.7.1 *Introduction to coordination chemistry*

Coordination complexes, as the name suggests, are compounds with coordination bonds, also known as dative bonds. These bonds are considered a special type of covalent bond where both the electrons in the bond come from one atom. Modern coordination chemistry started in the early twentieth century with the work of Alfred Werner, who was the first to propose the correct structure for coordination complexes.

In coordination chemistry, the central metal atom acts as the electron pair acceptor, with its surrounding species each bringing at least one pair of electrons to donate to an empty orbital on the central atom. These electron donors attached to the central atom are known as **ligands**. The formation of the complex follows the Lewis acid-base theory, where the central metal atom is a Lewis acid while the ligands are Lewis bases.

We will start by introducing complex nomenclature, including how to write both the complex formula and name. To write the formula for a complex, we write the complex in square brackets and the counterions outside. In the bracket, we always write the central atom first, and the oxidation number of the central atom may be indicated as an exponent after the central atom with Roman numerals. After the central atom, we list the anionic ligands before neutral ligands and observe alphabetical order within each ligand class. The alphabetical order is determined by how the ligand is represented, for example, if an abbreviation of the ligand is used, the first letter of the abbreviation should be used to determine the position of the ligand. Polyatomic ligands should be placed in round brackets.

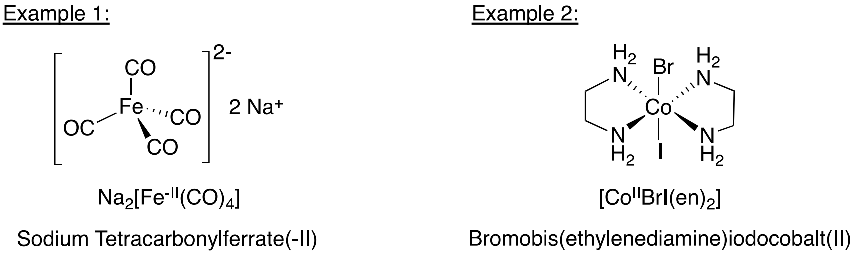
When naming coordination complexes, we put ligands in strict alphabetical order before the central atom regardless of whether the ligand is neutral or anionic. The oxidation state of the central atom is always indicated with Roman numerals in round brackets after the central atom, including the oxidation state of 0. Anionic ligands end with the letter "o" while neutral ligands are usually stated with their molecular names in round brackets, with exceptions of common neutral ligands. Table 3.9 shows a list of common ligands and their names.

We may count ligands using the prefixes "di-, tri-, tetra-…", but the first letter of the ligand should still be used to determine the order instead of the prefix. When ligand names are complicated and the above prefixes have already been used, we may avoid confusion by using the prefixes "bis-, tris-, tetrakis-…". The 2 classes of numerical prefixes should be alternated for the greatest clarity. When the charge of the complex is negative, the suffix "-ate" is added to the end, changing the name of the metal in certain cases. Figure 3.7.1 shows 2 coordination compounds with their formula and names.

In example 1, the complex is charged with sodium as the counter-cation. We may think of the species as an ionic salt, thus the sodium cation comes before the anionic complex. As we will learn later in this chapter, CO is a neutral ligand. Thus,

Table 3.9. Names of common ligands.

Formula	Ligand name	Formula	Ligand name
F^-	Fluoro	H_2	Dihydrogen
Cl^-	Chloro	O_2	Dioxygen
O^{2-}	Oxo	H_2O	Aqua
S^{2-}	Thio	H_2S	Sulfane, hydrogensulfide
$(C_2O_4)^{2-}$	Oxalato	CO	Carbonyl
$(SO_4)^{2-}$	Sulfoto	CS	Thiocarbonyl
$(CN)^-$	Cyano	N_2	Dinitrogen
$(NCO)^-$	Cyanato	NH_3	Ammine
$(NCS)^-$	Thiocyanato	$(CH_3)_3N$	Trimethylamine
$(NH_2)^-$	Amido	$(CH_3)_3P$	Trimethylphosphine
N_3^-	Azido	$HN = NH$	Diazene
$(NO_3)^-$	Nitrato	$HP = PH$	Diphosphene
$(NO_2)^-$	Nitrito-N or Nitrito-S	NO	Nitrosyl



$Na_2[Fe^{-II}(CO)_4]$

Sodium Tetracarbonylferrate(-II)

$[Co^{II}BrI(en)_2]$

Bromobis(ethylenediamine)iodocobalt(II)

Figure 3.7.1. 2 examples of complexes with their formulae and names.

the overall 2– charge of the complex must be due to the oxidation state of iron being –2. When writing the formula of the complex, the metal Fe comes first and its oxidation state is expressed as an exponent. CO, which is a polyatomic ligand, must be put within round brackets. The naming is rather straightforward, just that "iron" is changed to "ferrate" as the overall complex is anionic.

In example 2, the complex has an overall neutral charge. However, as Br and I are anionic ligands that carry one negative charge each, the metal must have the oxidation state of +2 for the complex to be overall neutral. When writing the formula, the complex must still be put within square brackets. The metal Co is first given with its oxidation state as an exponent, followed by the 2 anionic ligands Br and I, and finally the neutral ligand ethylenediamine, abbreviated as en. Common ligands such as en will be discussed in greater detail in the next part. When naming the complex, the ligands are placed in strict alphabetical order regardless of their charge, thus ethylenediamine is placed in front of the iodo ligand. As the numerical prefix "di-" has already been used in the name ethylenediamine, we use the numerical prefix "bis-" to indicate that there are 2 en ligands. As the complex is neutral, we do not have to include the suffix "-ate" and we may directly use the name of the metal, adding its oxidation state in round brackets behind.

To describe the bonding in complexes more accurately, there are 3 Greek letters that we use to indicate coordination modes:

1. Kappa $(\kappa^n - \mathrm{A,B,C})$

Kappa is used to describe the **denticity** of a ligand, which refers to the number and type of donor atoms in the ligand. Coordination modes may only be assigned to ligands in a complex, as the same ligand may exhibit different coordination modes in different complexes. The kappa notation indicates the number of donor atoms as a superscript after κ and the nature of the donor atoms behind a hyphen. It should only be used when the **donor atoms are not directly adjacent to each other**. It is most useful in describing the coordination mode of ligands with multiple donor atoms. Figure 3.7.2 shows a complex and the coordination mode of each ligand described with the kappa notation.

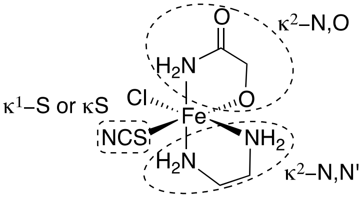


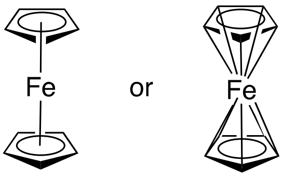
Figure 3.7.2. Example of using the kappa notation.

In the example, there are 2 ligands that bind to the metal through 2 donor atoms, which are glycinate and ethylenediamine. Thus, there is an exponent 2 behind κ. The 2 donor atoms are stated after the hyphen in no particular order. In the case of ethylenediamine, we indicate that the 2 nitrogens are different atoms by using an apostrophe. For the ligand NCS, it may either bind through N or S. When a ligand can bind through different donor atoms, it is known as **ambidentate**. In such cases, the kappa notation may be used to state specifically which atom is bound to the metal. Generally, κ^1 is assumed and the hyphen may be omitted for simple ligands. The last ligand, Cl, has the coordination mode of $\kappa^1\text{–}\mathrm{Cl}$, but it is rarely indicated as it is the only way for Cl to bind to the metal and there is no ambiguity.

2. Eta (η^n)

Eta indicates the **hapticity** of a ligand, which describes the **number n of donor atoms bonded to a metal centre which are directly connected to each other**. This is most commonly encountered in organometallic chemistry. Figure 3.7.3 shows an example of an organometallic compound showing the η space coordination mode.

In this example, the π-system of the aromatic ring acts as one ligand and donates electrons to the metal. Each cyclopentadienyl (Cp) ligand donates 6 electrons, and it may be visualised that iron is bonded to all the carbon atoms in Cp ligand, thus the coordination mode of the ligand is η^5.



$[\mathrm{Fe^{II}}(\eta^5\text{–}\mathrm{C_5H_5})_2]$

Ferrocene

Figure 3.7.3. Example of η^5-coordination of cyclopentadienyl ligand in ferrocene.

3. Mu (μ_n)

Mu is used to describe ligands that **bridge n metal centres**. When the ligand bridges 2 metal centres, the number 2 is often omitted, as μ-X is assumed to be μ_2-X. For complex bridging ligands, the μ notation may be used in combination with the κ and η-notations to indicate the coordination modes most accurately. An example is shown in Figure 3.7.4.

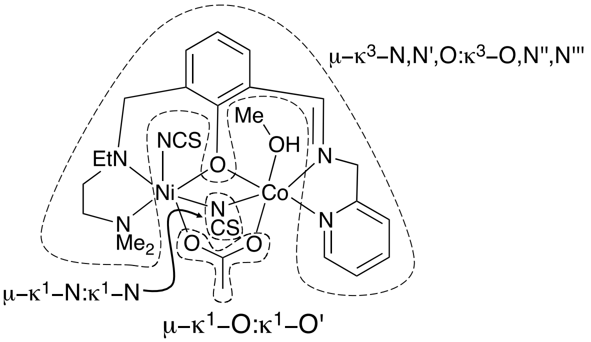


Figure 3.7.4. Example of bridging ligands and their coordination modes.

For the large bridging ligand, it bridges 2 metal centres, nickel and cobalt. Thus, we use the μ notation before using the κ notation to indicate how the ligand binds to each metal centre, separating the metal centres with a colon. The κ notation is used as the donor atoms are not directly connected, while the η notation should be used if the donor atoms are directly connected. The same logic is applied to assign the coordination modes of the other 2 bridging ligands.

3.7.2 *Ligand classification*

Ligands are electron donors that are able to form coordination bonds with the central metal, influencing the reactivity of the central metal ion. They are also able to undergo reactions of their own while still bound to the central metal ion. As ligands are an important aspect in coordination chemistry, they have been classified based on structural aspects, such as the nature and number of donor atoms and how these donor atoms bind to the metal centre.

For **non-bridging ligands**, they may be classified based on dentate nature as follows:

1. Monodentate ligands

Monodentate ligands are ligands with only one electron donor centre, such as the halides, H_2O, NH_3 and many others. In rare cases, polydentate ligands may also act as a monodentate ligand when only one of the donor atoms bind to a metal centre. This is known as **hypodentate** coordination, where the ligand binds using less than its full complement of donor atoms.

2. Polydentate ligands

When a ligand binds with more than one donor atom, it acts as a polydentate ligand. There are many types of polydentate ligands, which we will briefly discuss below:

i. Non-polypodal open-chain ligands

This is the largest class of polydentate ligands, which is usually further classified by their denticity. **Polypodal** is used to describe ligands where the donor groups are all bound to a central group, which we will see in the next group of polydentate ligands. **Open-chain** ligands are ligands where the donor atoms are not in a ring together with each other. Examples of non-polypodal open-chain ligands are shown in Figure 3.7.5, as classified by denticity.

Such non-polypodal polydentate ligands are usually **chelating ligands**, where the ligand atoms and metal centre forms a closed ring. The stability of the complex depends on the match between the ligand bite and metal size. Ligand bite consists of 2 factors, the length and angle, as described in Figure 3.7.6.

For the 1st row d-block metals, it has been experimentally determined that 5-membered chelate rings are the most stable. The 2nd and 3rd row d-block metals

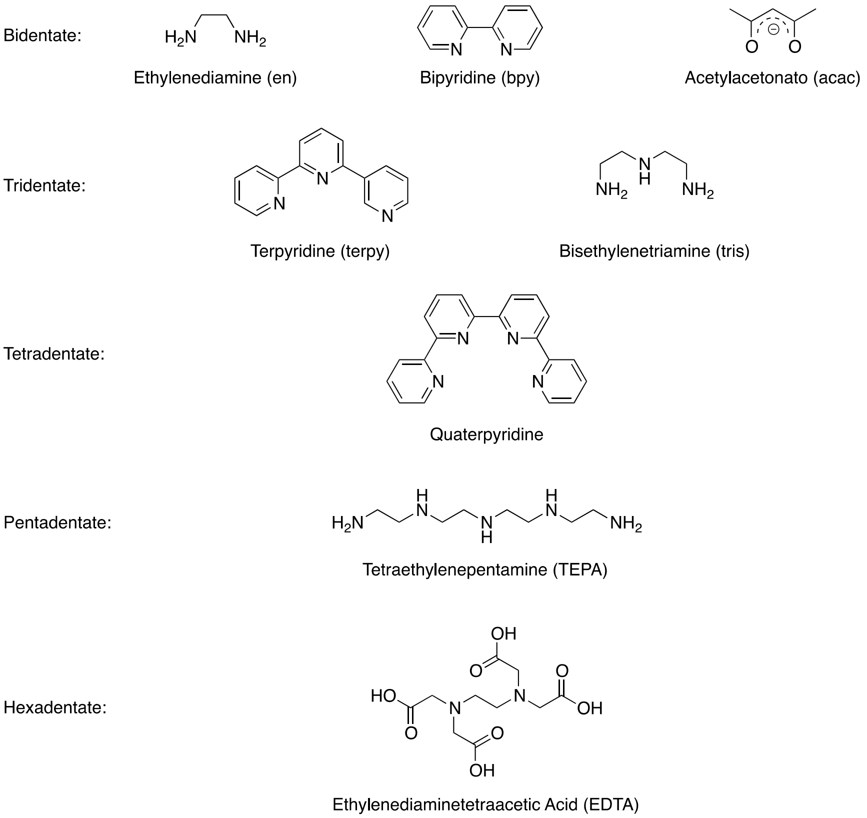


Figure 3.7.5. Examples of non-polypodal open-chain ligands.

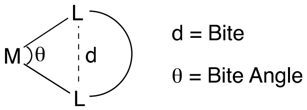


Figure 3.7.6. Description of ligand bite and bite angle.

are larger and may prefer a different ring size. For ligands with high denticity, such as EDTA, their coordination involves an aspect of "wrapping" around the metal ions, usually with gross rearrangement of ligand shape.

ii. Polypodal open-chain ligands

As explained previously, polypodal ligands have donor groups all bound to a central atom. The central atom may be either a donor atom, such as N, or a non-donor, such as C, and it generally has 3 or more arms. Polypodal open-chain ligands may be further sub-divided based on the central group, and examples are shown in Figure 3.7.7.

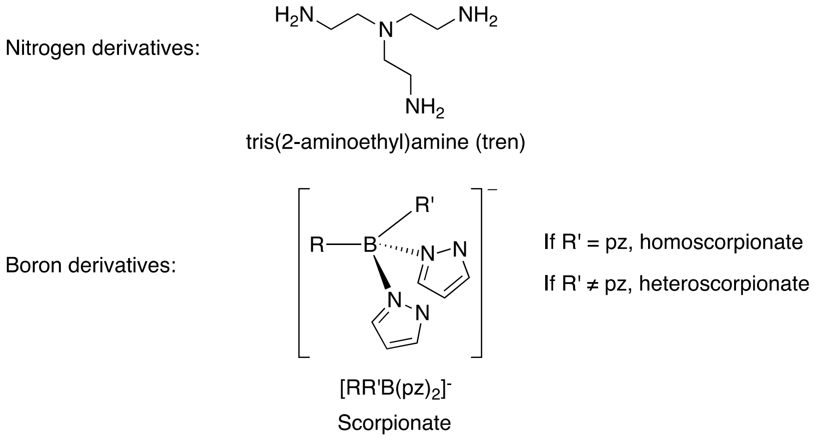


Figure 3.7.7. Examples of polypodal open-chain ligands.

Scorpionates have also been prepared with different central atoms, such as C, Al, In, Ga or Si. Modern research has also explored molecular derivatives, where the central group is not an atom but instead a molecule, such as benzene.

iii. Closed polydentate ligands: Macrocycles

Macrocycles are closed cyclic ligands with O, N, P or S donor atoms in a ring. The stability of complexes formed from their binding with metal cations depend mainly on the ion-hole fit. This allows macrocycles to selectively bind metal ions based on size. Examples of macrocycles are shown in Figure 3.7.8.

The non-systematic nomenclature of crown ethers comes from "ring size-crown-number of donor atoms", which is similarly used for nitrogenated non-aromatic macrocycles. Crown ethers are commonly used to coordinate alkali and alkaline-earth metals by the ion-hole size fit, and the O donor atoms may be substituted with N or S to modify the hard-soft nature of the crown ether. While the size fit affects the binding affinity, it is not true to say that metal cations larger than the hole are unable to be bound, as the cation can be outside of the cycle cavity, as shown in Figure 3.7.9.

Even for porphyrins, the metal ion may fit outside of the macrocycle, and large cations such as lanthanides, form double and triple layer sandwich complexes. For nitrogenated macrocycles with pendant donor groups, the pendant donor groups are able to coordinate to the metal cation from above and below the ring, encapsulating the metal cation. Macropolycyclic ligands are able to bind multiple metal ions in close proximity, allowing intermetallic interactions to be formed.

iv. Cryptands and encapsulating ligands

Cryptands and encapsulating ligands are able to fully surround the metal cation, forming extremely stable complexes. While the terms cryptand and encapsulating

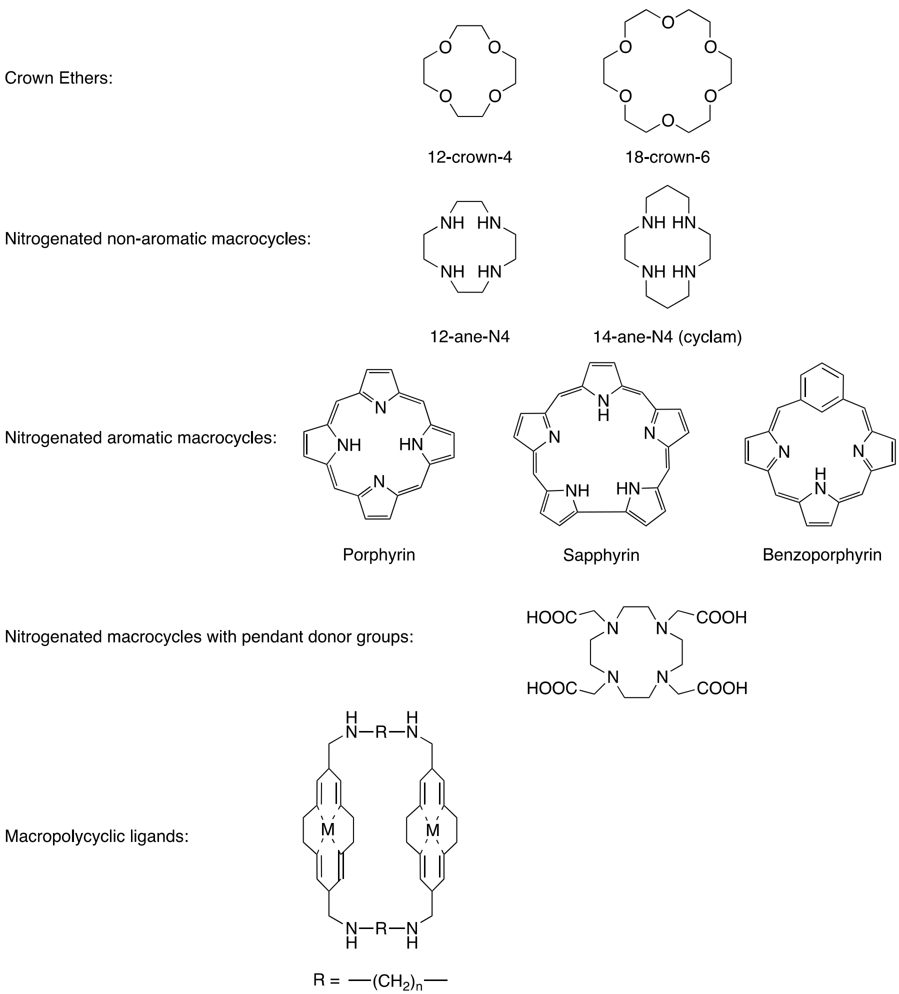
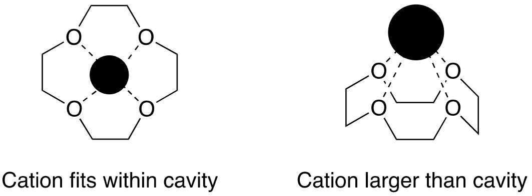


Figure 3.7.8. Example of macrocycles.



Cation fits within cavity Cation larger than cavity

Figure 3.7.9. Flexible coordination of cations of different sizes.

ligand have been used interchangeably, the 2 groups may be distinguished. Cryptands have a single atom (C or N) that closes the cage at both vertices of the 3-dimensional macrocycle, while encapsulating ligands have molecules to close the vertices of the cage. Examples of this class of ligands are shown in Figure 3.7.10.

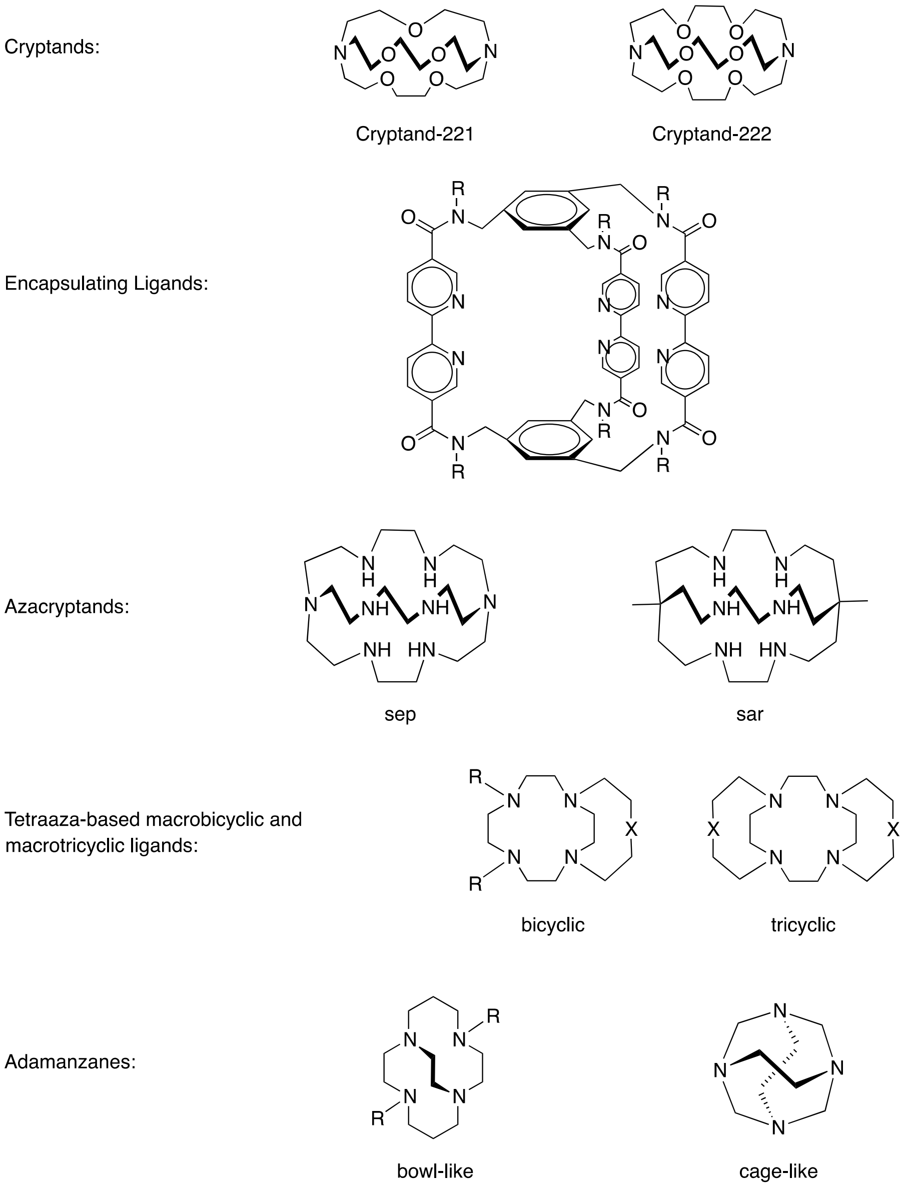


Figure 3.7.10. Examples of cryptands and encapsulating ligands.

The classifications that we have discussed up to now are for ligands that bind to only one metal centre. When a ligand binds to more than one metal centre, it is known as a bridging ligand. Complexes with more than one metal centre are known as polynuclear complexes, thus, bridging ligands are also known as polynucleating ligands. We will now discuss the classification of polynucleating ligands:

1. Monoatomic bridging ligand

Monoatomic bridging ligands are the simplest polynucleating ligands, with only one donor atom that binds to multiple metal centres simultaneously. Examples include O^{2-}, X^-, S^{2-} or RO^-. Such bridging ligands are good candidates for the preparation of metal clusters, as O^{2-} or X^- ligands are able to form bonds to 2, 3, or 4 metal atoms. Polyoxometalates $(POMs)$, which are large metal clusters, may be formed from only metals and oxido ligands with different coordination modes.

2. Polyatomic bridging ligands

Polyatomic bridging ligands are small versatile ligands that have multiple donor atoms. This allows them to form a large variety of complexes with different coordination modes, as shown in Figure 3.7.11.

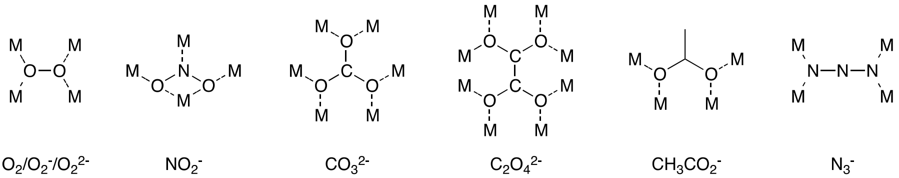


Figure 3.7.11. Example of polyatomic bridging ligands showing possible binding sites.

3. Polytopic ligands

Polytopic ligands are ligands that provide specific coordination sites for the metal, making it possible to predict the positions where the metal binds to the ligand. They have 2 major classes: compartmental and non-compartmental ligands. Compartmental ligands are polytopic ligands where metal ions share at least 1 donor atom, which acts as a bridge. This allows metal ions to be bound in close proximity in different compartments. The design of such ligands allows us to modulate the type and extent of intermetallic interactions between metal ions in adjacent chambers. Non-compartmental ligands contain multiple separate coordination sites linked by bridging units, such that there is no sharing of any donor atom. Examples of polytopic ligands are shown in Figure 3.7.12.

It is more favourable to form heterodinuclear complexes with 2 different metals in asymmetric systems. For example, in the Schiff base derivative on the right, there is haptoselectivity. **Haptoselectivity** refers to the preferential binding of a different metal to each separate subunit, which occurs when the coordination sites are different.

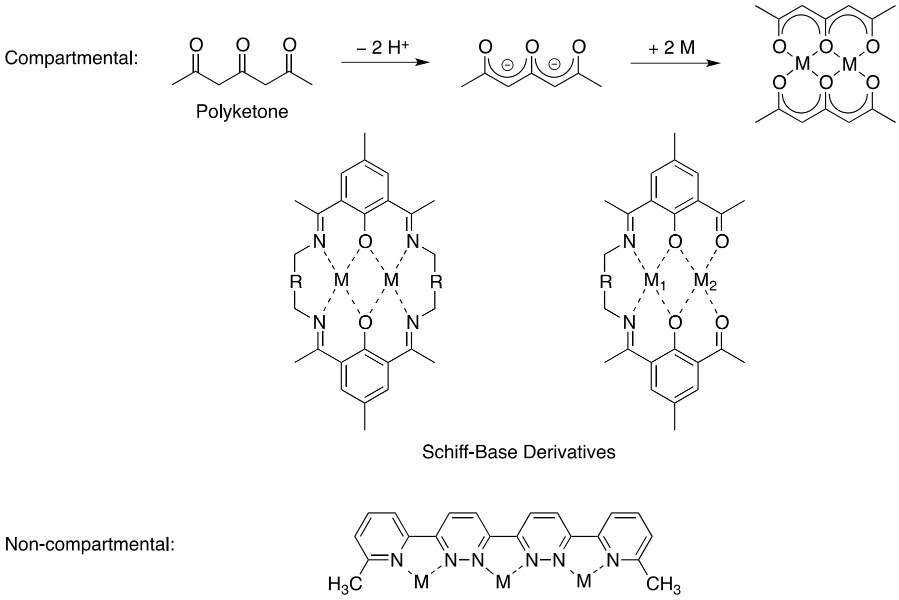


Figure 3.7.12. Examples of polytopic ligands.

3.7.3 *Isomerism in coordination chemistry*

Isomers are defined as compounds with the same molecular formula, but different structures. As a result, isomers differ in physical and chemical properties. There are 2 broad types of isomers: **constitutional isomers** with different connectivity of atoms and **stereoisomers** with the same connectivity of atoms but different arrangement of atoms in 3D space.

We will first look at different types of constitutional isomerism:

1. Linkage isomerism

Linkage isomerism occurs in ambidentate ligands such as SCN^- and NO_2^- as they can coordinate to the metal centre in more than one way. An example of linkage isomerism is shown in Figure 3.7.13.

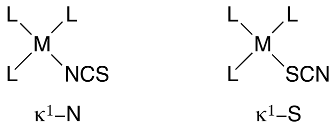
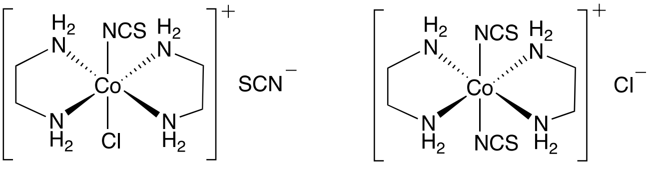


Figure 3.7.13. Example of linkage isomerism.

2. Ionisation isomerism

As most complexes are positively charged, they have counter-anions to balance the charge. Counter-anions, being negatively charged with an electron pair, may also act as a ligand. Ionisation isomers produce different ions in solution as one of the ligands is exchanged with the counter-anion. This exchange is often accompanied by a distinct colour change, and an example is provided in Figure 3.7.14.



Blue

Red

Figure 3.7.14. Example of ionisation isomerism.

3. Coordination isomerism

Coordination isomerism occurs when ligands are exchanged between the metal centres in salts that consist of complex cations and complex anions. An example is given below:

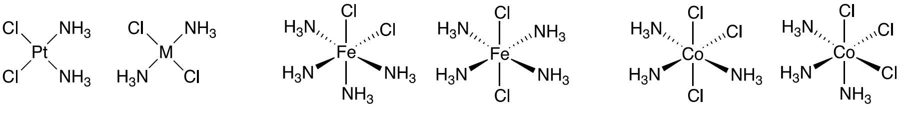
$$[Co(NH_3)_6]^{3+}[Cr(CN)_6]^{3-} \text{ and } [Cr(NH_3)_6]^{3+}[Co(CN)_6]^{3-}$$

In this example, a different coordination isomer may be obtained with every exchange of NH_3 and CN^-, such as

$$[Co(CN)(NH_3)_5]^{2+}[Cr(CN)_5(NH_3)]^{2-} .$$

Stereoisomers may be divided into geometric and optical isomers. Geometric isomers differ in the spatial arrangements of ligands about the metal ion. For MA_2B_2 and MA_4B_2 complexes, they have cis-trans isomers, while MA_3B_3 complexes have meridional-facial (mer-fac) isomers, as shown in Figure 3.7.15.

There are, of course, many other types of geometrical isomers for other complexes. For example, square planar $MABCD$ has 3 geometric isomers. When listing



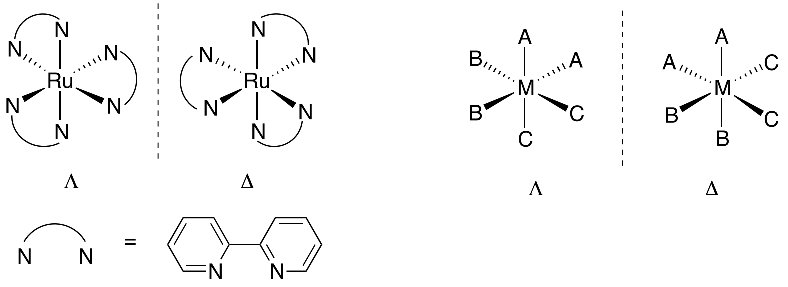
cis trans cis trans mer fac

MA_2B_2 MA_4B_2 MA_3B_3

Figure 3.7.15. Examples of geometric isomerism.

geometric isomers, a tip would be to observe which ligands are trans to each other, to avoid double counting the same isomers.

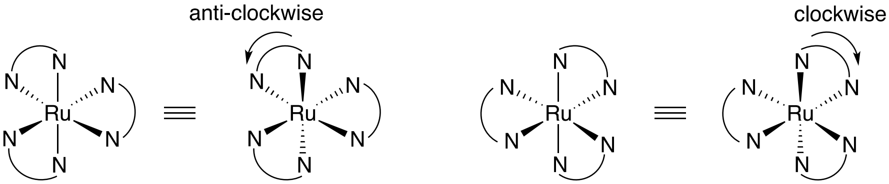
Optical isomers are compounds with non-superimposable mirror images. In tris-chelate octahedral complexes, there is $\Lambda - \Delta$ isomerism. $\Lambda - \Delta$ isomerism is also referred to as helicity, and examples are shown in Figure 3.7.16.



Λ Δ Λ Δ

Figure 3.7.16. Examples of $\Lambda - \Delta$ isomerism.

To assign Λ and Δ to the isomers, we must visualise the octahedral complex as a metal cation between 2 planes, each containing 3 donor atoms. When moving from the top to bottom plane across a ligand, if we move clockwise, we have the Δ-isomer, and if we move anticlockwise, we have the Λ-isomer. This is demonstrated in Figure 3.7.17.



Λ Δ

Figure 3.7.17. Method to assign Λ/Δ descriptors to octahedral coordination complexes.

$\Lambda - \Delta$ isomerism is also present in $MA_2B_2C_2$ complexes, and the Λ/Δ-descriptors may be assigned by considering the rotation direction from A in the top plane to A in the bottom plane, even if the 2 A atoms are not part of a bridging ligand.

Tetrahedral complexes are generally highly labile and *R*/*S*-optical isomers for $MABCD$ complexes are rarely isolated. However, when tetrahedral complexes have 2 unsymmetrical bidentate ligands, they also exhibit $\Lambda - \Delta$ isomerism, as shown in Figure 3.7.18, and their chirality may be assigned in the same way as for octahedral complexes.

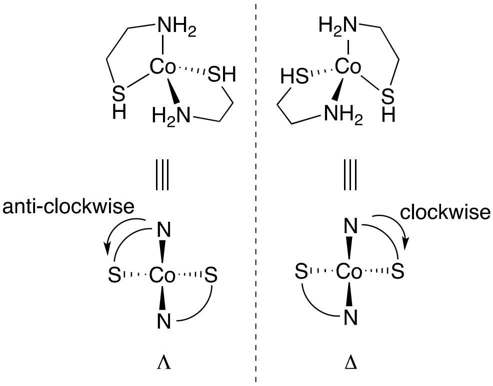


Figure 3.7.18. Λ – Δ isomerism in tetrahedral complexes.

3.7.4 *Crystal field theory and ligand field theory*

To describe the bonding in metal complexes, the crystal field theory and ligand field theory were developed. We will start by explaining the more basic crystal field theory. Crystal field theory is a purely electrostatic model that considers the ligands as point charges that create an electric field around the metal centre. As we move on to ligand field theory, we will start to consider the metal-ligand covalent interactions.

Consider a first-row metal cation with five valence 3d-orbitals. Originally, the five 3d-orbitals are degenerate and at ground state. As we add in ligands, which are treated as negative point charges, the energies of the 3d-orbitals would be raised due to electrostatic repulsion. If the electrostatic field, also known as crystal field, is spherical, the energies of the five 3d-orbitals would be raised by the same amount and they would still be degenerate. However, the crystal field is never spherical in reality and it follows the geometry of the complex. For an octahedral complex, the crystal field is octahedral and the energies of the 3d-orbitals would be split depending on the proximity of the ligands to the orbitals. In an octahedral crystal field, the ligands are placed along the *x*, *y* and *z* axes. As the $3d_{z^2}$ and $3d_{x^2-y^2}$ orbitals point directly at the ligands, their energies are raised with respect to the spherical field. The $3d_{xy}$, $3d_{xz}$ and $3d_{yz}$ orbitals point between the axes, and their energies are lowered with respect to the spherical field. The 3d-orbital energies in the spherical field is known as the **barycentre**, and the average energy of the 3d-orbitals will always be the barycentre regardless of the geometry and splitting. Figure 3.7.19 shows the different energies of the d-orbitals in the scenarios described.

As indicated in Figure 3.7.19, the Δ_O represents the octahedral crystal field splitting parameter. The value of Δ_O varies depending on the metal cation and ligands, and must be determined experimentally. e_g^* and t_{2g} are the symmetry labels for the higher energy and lower energy groups of orbitals, respectively. In complexes of other

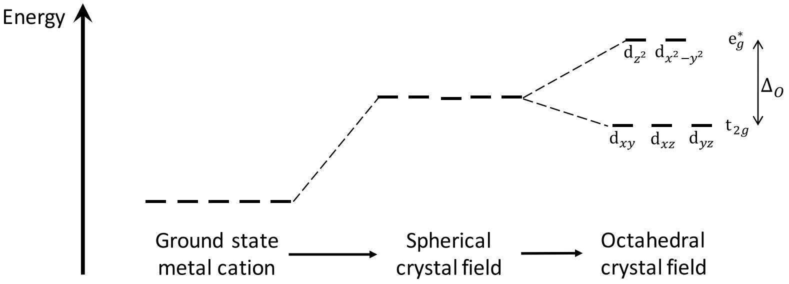


Figure 3.7.19. Change in d-orbital energies due to different crystal fields.

geometries, the crystal field splitting pattern is different and may be determined similarly by considering the proximity of the d-orbitals to the ligands. Figure 3.7.20 shows crystal field splitting patterns for common complex geometries with reference to Δ_O.

The crystal field splitting parameter differs for every metal complex, depending on a large range of factors. As seen from Figure 3.7.20, the geometry of the complex greatly affects the amount of splitting. A useful approximation to remember is:

$$\Delta_T = \frac{4}{9}\Delta_O$$

where Δ_T is the tetrahedral crystal field splitting parameter.

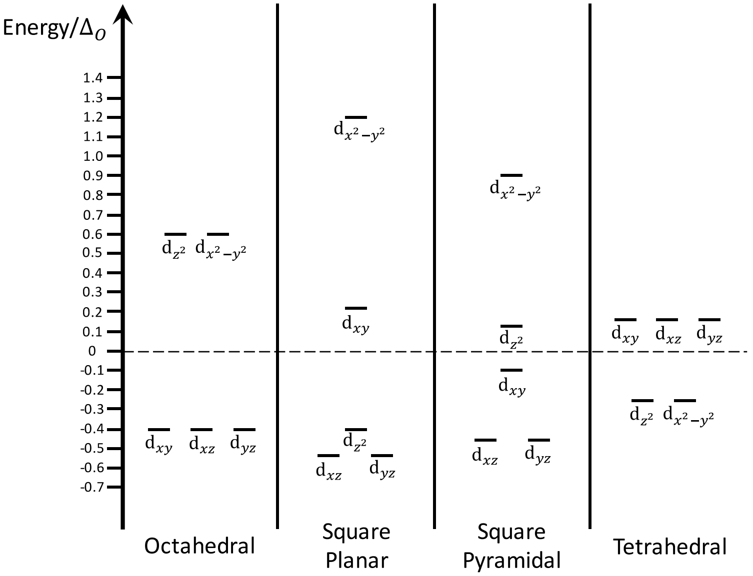


Figure 3.7.20. Crystal field splitting patterns for common geometries with respect to Δ_O.

The crystal field splits less in tetrahedral complexes than in octahedral complexes as the ligands in tetrahedral complexes do not point directly at the d-orbitals from both sides and the difference in repulsions between d-orbitals and the ligands is small.

Other than complex geometry, both the metal and ligand properties affect the degree of crystal field splitting. For the metal, crystal field splitting parameter increases with the oxidation state and period of the metal. As the oxidation state of the metal increases, the ligands are pulled closer to the metal due to the stronger attraction and the crystal field splitting increases. Moving down the period, the principal quantum number of the valence d-orbital increases, leading to a larger and more diffuse orbital that interacts more with the ligands.

The easiest way to modify the crystal field splitting is through selection of ligands. Ligands may be arranged by magnitude of crystal field splitting energy, known as the **spectrochemical series**:

$$I^- < Br^- < S^{2-} < \underline{S}CN^- < Cl^- < N\underline{O}_2^- < N^{3-} < F^- < O^{2-} < OH^- < C_2O_4^{2-} < H_2O$$

$$< \underline{N}CS^- < CH_3CN < py < NH_3 < en < bipy < phen < \underline{N}O_2^- < PPh_3 < CN^- \approx CO$$

The trends in the spectrochemical series will be explained using ligand field theory, which we will briefly discuss later.

The crystal field splitting parameter is important as it affects the electron configuration for certain octahedral complexes. For d^4, d^5, d^6 and d^7 metals in octahedral complexes, there are 2 different ways to fill the metal d-electrons, known as low spin and high spin. **Low spin** is the arrangement where all the lower energy t_{2g}-orbitals are filled before electrons are filled into the higher energy e_g^*-orbitals. **High spin** is the arrangement where each d-orbital is singly occupied before electrons are paired in the lower energy t_{2g}-orbitals. Table 3.10 shows the low spin and high spin electron configurations for d^4, d^5, d^6 and d^7 octahedral metal complexes.

Table 3.10. Low spin and high spin electron configurations for d^4, d^5, d^6 and d^7 octahedral metal complexes.

	Low spin	**High spin**
d^4	— — ⇅ ↑ ↑	↑ — ↑ ↑ ↑
d^5	— — ⇅ ⇅ ↑	↑ ↑ ↑ ↑ ↑
d^6	— — ⇅ ⇅ ⇅	↑ ↑ ⇅ ↑ ↑
d^7	↑ — ⇅ ⇅ ⇅	↑ ↑ ⇅ ⇅ ↑

The electron configuration is determined by comparing the magnitudes of Δ_O and pairing energy. Pairing energy is the energy penalty from inter-electron repulsion when placing 2 electrons in the same orbital. Low spin electron configuration is preferred when Δ_O is larger than pairing energy as it requires less energy to place another electron in a $\mathrm{t_{2g}}$-orbital than to promote it to an $\mathrm{e_g^*}$-orbital. High spin electron configuration is preferred when Δ_O is smaller than pairing energy as it requires less energy to promote an electron to an $\mathrm{e_g^*}$-orbital than to pair the electron with another electron in the $\mathrm{t_{2g}}$-orbital. As the pairing energy is similar across all complexes, the electron configuration depends mainly on Δ_O. Although there are also 2 energy levels in tetrahedral complexes, tetrahedral complexes are generally all high spin as Δ_T is much smaller than Δ_O. The electron configuration of the complexes changes their properties. For example, $[\mathrm{Fe(H_2O)_6}]^{2+}$ is a high spin d^6-complex that is strongly paramagnetic with 4 unpaired electrons $(\mathrm{S} = 2)$ while $[\mathrm{Fe(CN)_6}]^{4-}$ is a low spin d^6-complex that is diamagnetic with no unpaired electrons $(\mathrm{S} = 0)$. S is the total spin quantum number, the sum of all the electron spins.

To better understand the bonding in metal complexes, ligand field theory was developed using a molecular orbital approach. While the molecular orbital theory we learnt up to now can only be applied to diatomic molecules, molecular orbital theory may be extended to polyatomic molecules by considering their symmetries. This approach is known as **symmetry-adapted linear combination of atomic orbitals**. In the case of metal complexes, the ligands may be considered together as a set of ligand group orbitals. The MO diagram may be constructed by matching

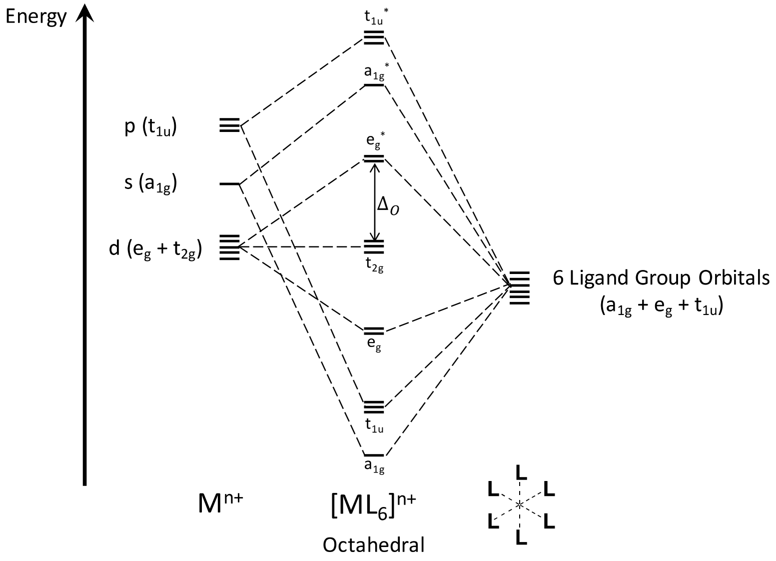


Figure 3.7.21. MO diagram for the metal-ligand σ-bonding in octahedral metal complex.

the symmetries of the metal orbitals and the ligand group orbitals, as shown in Figure 3.7.21.

The MO diagram provides us with a more complete picture of the bonding in such octahedral complexes. From the MO diagram, we are able to identify Δ_O as the energy difference between t_{2g} and e_g^*-orbitals. For many ligands, their interactions with the metal are not limited to σ-donation. Ligands with filled p-orbitals are able to donate their p-electrons to metal d-orbitals through a π-bond. Such ligands are known as π-donor ligands. Ligands with low energy antibonding orbitals are able to accept d-electrons from the metal. This is known as π-backbonding and such ligands are known as π-acceptor ligands.

The MO diagram may be expanded to consider metal-ligand π-interactions by including ligand π-orbitals. As ligand π-orbitals are of t_{2g}-symmetry, they are able to interact with metal t_{2g}-orbitals. Figure 3.7.22 shows the partial MO diagram that take into consideration metal-ligand π-interactions.

Due to the π-interactions changing the energy of the t_{2g}-orbital, the Δ_O magnitude changes with π-donor and π-acceptor ligands. For π-donor ligands, the Δ_O energy is defined as the energy difference between the t_{2g}^* and e_g^*-orbitals as the π-electrons from the ligands will fill the t_{2g}-orbital, leaving the empty t_{2g}^* and e_g^*-orbitals for the metal d-electrons. The energy of the t_{2g}^*-orbitals is raised and closer to the energy of the e_g^*-orbital, making the Δ_O magnitude smaller. Thus, π-donor ligands form complexes with smaller Δ_O compared to purely σ-donor ligands. On the other hand, for π-acceptor ligands, the vacant ligand π*-orbitals are very high in energy. Thus, the t_{2g}^*-orbital energy is higher than that of the e_g^*-orbital and Δ_O remains as the energy difference between t_{2g} and e_g^*-orbitals. As the t_{2g}-orbital changes from a non-bonding orbital to a bonding orbital, its energy is lowered and the energy gap between t_{2g} and e_g^*-orbitals is increased. Thus, π-acceptor ligands form complexes with larger Δ_O than σ-donor ligands. This explains the spectrochemical series as we

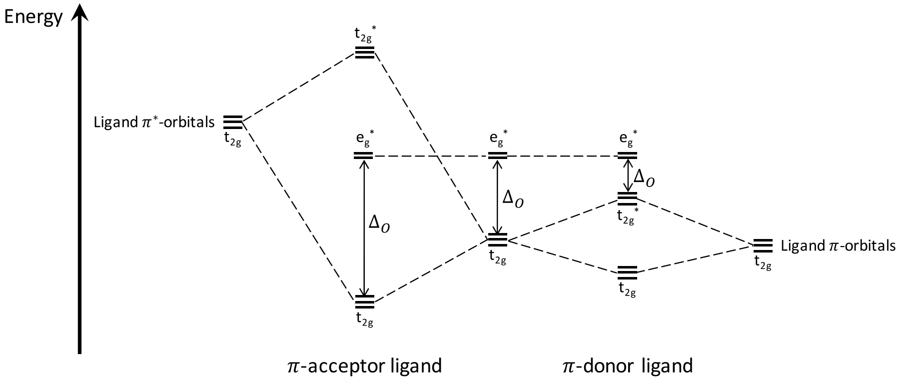


Figure 3.7.22. Partial MO diagram for π-donor and π-acceptor ligands.

could roughly classify the ligands into 3 groups based on their π-interactions with the metal:

π–donor ligands	σ–donor ligands	π–acceptor ligands
(e.g. I^-, Br^-, Cl, $\underline{S}CN^-$)	(e.g. H_2O, NH_3)	(e.g. CO, CN^-, PPh_3, bipy)

$$\longrightarrow$$

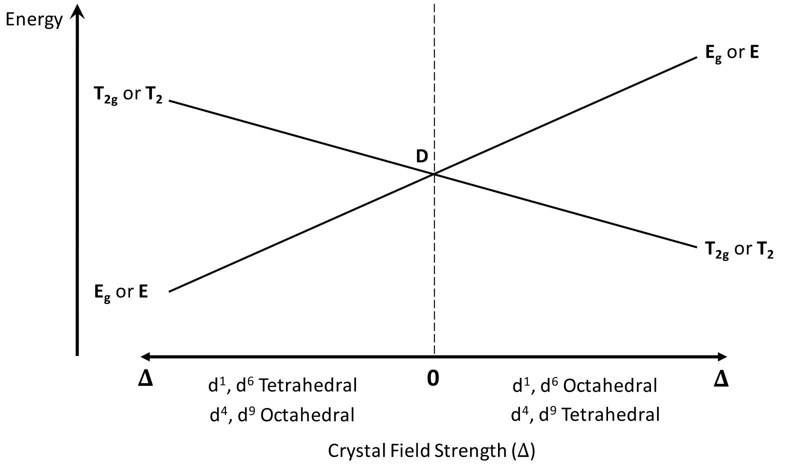
Increasing Δ_o

Transition metal complexes are often colourful due to the d-orbitals having different energies. Electrons in d-orbitals absorb light to move from one energy level to another, in what is known as **d-d transitions**. As the light absorbed is of specific wavelengths corresponding to the energy gaps, these wavelengths are usually within the visible light spectrum, light corresponding to specific colours will be absorbed and the complex will display the complementary colours.

For most complexes, the d-d transition wavelengths do not directly correspond to Δ_o as inter-electron repulsions between d-electrons affect the energy of the states. In a multi-electron system, inter-electron repulsions cause microstates with identical electron configurations to have different energies. A **microstate** is a specific arrangements of valence electrons in valence orbitals. Microstates with the same total angular momentum L and total spin S may be grouped into **terms**. For each specific number of d-electrons, there is a series of terms used to describe all the possible microstates. Terms are represented by term symbols $^{(2S+1)}L$, depending on the S and L of the microstates that make up the term. $2S+1$ is known as the spin multiplicity of the term. The letter used to represent L follows exactly the letter used to designate the orbital that corresponds to L except that it is in capital letter. As an example, the term containing microstates with $S=1$ and $L=2$ is known as the $^3\mathrm{D}$ term.

Such terms will be split when in a crystal field, similar to how orbitals split into different energy levels. The details in obtaining the terms and determining the splitting are beyond the coverage of the book. However, we provide the results, as shown in the Orgel diagrams in Figure 3.7.23.

Orgel diagrams show the possible d-d transitions for high-spin complexes that do not involve changing electron spin. Absorptions of transitions that do not conserve spin multiplicity are extremely weak and may be usually disregarded. To consider such d-d transitions, we must use the Tanabe-Sugano diagrams. From the Orgel diagrams, we note that d^1, d^4, d^6 and d^9 complexes have only one spin-allowed d-d transitions from ground-state while d^2, d^3, d^7 and d^8 complexes have 3 spin-allowed d-d transitions from ground-state. d^5 high spin configuration involves filling every d-orbital with 1 electron, making it impossible for any electronic transition without changing the spin of the electron. The d-d transition energies increase together with Δ_o, as seen from the Orgel diagram. Experimentally, UV-vis spectroscopy may be performed on transition metal complexes to obtain absorption spectra with peaks that correspond to the d-d transitions.



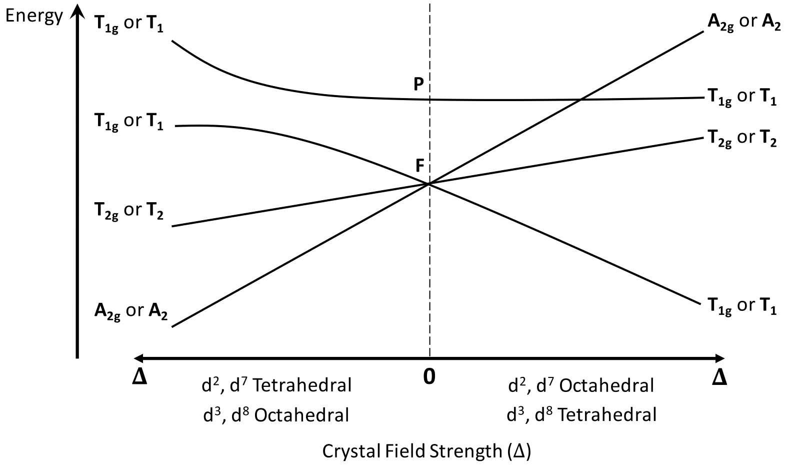


Figure 3.7.23. Orgel diagrams for d-d transitions.

However, an anomaly was observed in the UV-vis absorption spectra of octahedral d^1-complexes. Applying what we have learnt, the single d-electron could only have 1 possible d-d transition from t_{2g} to e_g^* energy levels. As it is not a multi-electron system, there is no need to consider the effects of inter-electron repulsion. While it seems that only 1 d-d transition is possible, 2 peaks similar in energy were observed in the absorption spectra. This suggests that there are more than 2 energy levels (t_{2g} and e_g^*), and it must be explained by Jahn-Teller theorem.

Jahn-Teller theorem states that "any non-linear molecular system in a degenerate electronic state will be unstable and will undergo distortion to form a system of lower symmetry and lower energy, thereby removing the degeneracy". When applied to octahedral complexes, the Jahn-Teller effect refers to the distortion

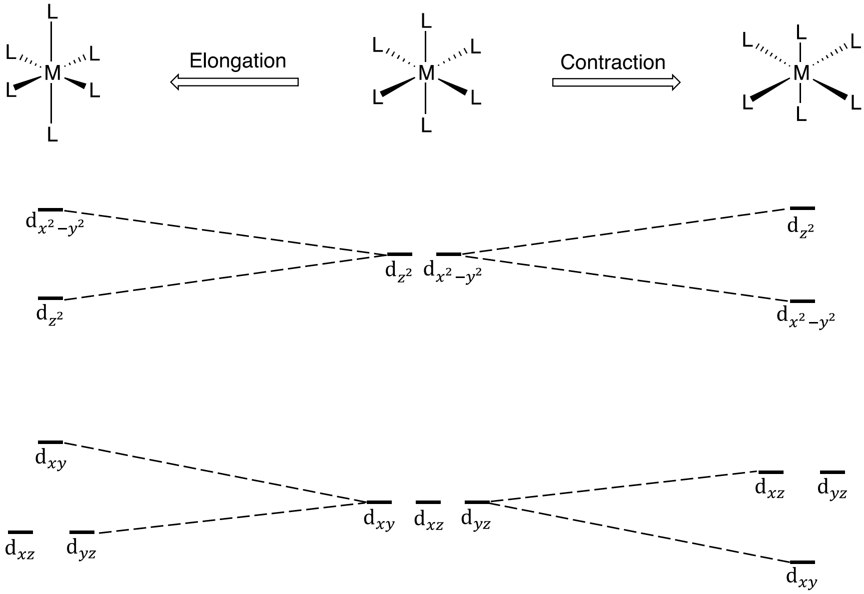


Figure 3.7.24. Jahn-Teller distortions and associated changes in d-orbital energies.

of octahedral geometry either by elongation or contraction along the z-axis. An energy level is degenerate if it corresponds to two or more different electron configurations. For example, a d^4 high spin complex is in a doubly degenerate electronic state as the electron in e_g^* energy level may be placed in either d_{z^2} or $d_{x^2-y^2}$ orbital. By distortion of the octahedral geometry, the energies of d_{z^2} and $d_{x^2-y^2}$ orbitals are no longer equivalent and the degeneracy is removed in the new electronic state of lower energy. As the barycentre must remain the same for any distortion, for elongation, the 2 ligands along *z*-axis moving away from the metal is accompanied by the 4 ligands on the *xy*-plane moving closer to the metal. Similarly, for contraction, the 2 ligands along *z*-axis moving closer to the metal is accompanied by the 4 ligands on the *xy*-plane moving away from the metal. The distortions and associated changes in d-orbital energies are shown in Figure 3.7.24.

The changes in d-orbital energies may be easily explained with crystal field theory. For elongation, the ligands on the *z*-axis are further away from the metal and the ligands on the *xy*-plane are closer to the metal. Thus, d-orbitals pointing along the *z*-axis will have their energies lowered while d-orbitals lying on the *xy*-plane will have their energies raised. The opposite change is observed for contraction. By removing the degeneracy through Jahn-Teller distortion, the new energy of the complex is lower, and an example is shown in Figure 3.7.25.

As seen from the example, the energy of the e_g^* electron is lowered through elongation, as it may be placed in lower energy d_{z^2}-orbital after elongation.

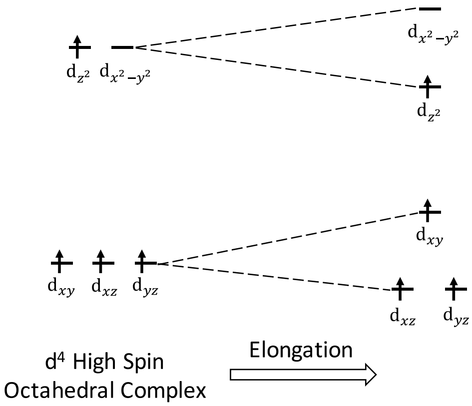


Figure 3.7.25. Elongation of a d^4 high spin octahedral complex.

Theoretically, any system with a degenerate electronic state may undergo Jahn-Teller distortion. However, the distortion is most significant for systems with degeneracy in the e_g^*-energy level, as the orbitals in e_g^* energy level point directly to the ligands and the associated energy change from distortion is greater. Thus, strong Jahn-Teller effect is observed for d^4 high spin, d^7 low spin and d^9 octahedral complexes. While the Jahn-Teller theorem is unable to accurately predict whether the distortion is an elongation or contraction, it has been experimentally observed that most distortions are elongations while contractions are rarely observed.

3.7.5 *Electron counting and the 18-electron rule*

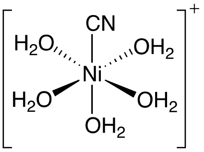
For any metal complex, it is possible to count the electrons surrounding the central metal atom using 2 methods:

1. Neutral method

In the neutral method, the metal and ligands are treated as neutral species. Thus, anionic ligands are treated as single-electron neutral radicals and the oxidation state of the metal is not considered when counting the metal electrons. If the overall complex is charged, the charge must be accounted for after summing up the electrons contributed by the metal and ligands.

2. Ionic method

In the ionic method, the metal and ligands may be charged species. The oxidation state of the metal must be accounted for when counting the number of electrons on the metal. All ligands, regardless of their charge, are electron pair donors. As the charges have been considered in the number of electrons from the metal and ligands, the overall charge of the complex need not be considered.



Neutral:		Ionic:	
Ni^0 :	10 e^-	Ni^{2+} :	8 e^-
$CN^\bullet$:	1 e^-	6 ligands :	6 x 2 = 12 e^-
5 H_2O :	5 x 2 = 10 e^-		
+1 charge :	-1 e^-		
Total :	20 e^-	Total :	20 e^-

Figure 3.7.26. Example of electron counting using the 2 methods.

Figure 3.7.26 shows an example of performing electron counting on a complex using the 2 methods.

The significance of electron counting is that it allows us to apply the 18-electron rule to complexes. The 18-electron rule is analogous to the octet rule, except that 18 electrons are required to complete the valence of a transition metal in a complex ($d^{10}s^2p^6$). The 18-electron rule may be applied for 2 different purposes:

1. Determining the stability and redox activity of metal complexes

Metal complexes want to become stable 18-electron complexes just as how main group elements want to achieve octet configuration. Thus, complexes with less electrons are good oxidisers as they are willing to gain electrons to achieve 18-electron configuration. Similarly, complexes with more electrons are good reductants. For example, the 18-electron $[Fe^{II}(CN)_6]^{4-}$ complex is redox stable while the 17-electron $[Fe^{III}(CN)_6]^{3-}$ complex is a good oxidiser.

2. Predicting the presence of metal-metal bonds

In polynuclear complexes, metal-metal bonds may be formed to allow the metal centres to achieve 18-electron configuration. Such predictions using the 18-electron rule are most accurate for metal-carbonyl complexes. For example, $[Fe_2(CO)_9]$ originally has a total of 34 electrons, averaging to give 17 electrons around each Fe metal. To achieve 18-electron configuration for both Fe metal centres, a $Fe{-}Fe$ metal-metal bond is formed.

However, the 18-electron rule is not as absolute as the octet rule. For example, low spin d^8 square planar complexes are most stable with a 16-electron configuration. This is due to the square planar crystal field having a high energy $d_{x^2-y^2}$ orbital that is more stable when left empty.

3.7.6 *Ligand substitution reaction mechanisms*

Ligand substitution reactions involve the exchange of one ligand for another in a metal complex. Generally, ligand substitution mechanisms may be classified into 3 types:

1. Dissociative (D)

The leaving group is removed before the entering group is attached to the metal, thus the intermediate has a lower coordination number than the reactant and product.

2. Associative (A)

The entering group is attached to the metal before the leaving group is removed, thus the intermediate has higher coordination number than the reactant and product.

3. Interchange (I)

In the interchange mechanism, no intermediate is formed. Instead, the reaction proceeds through a transition state where bond formation and breaking take place simultaneously. The interchange mechanism may be further divided into associative and dissociative interchange. In associative interchange, bond formation dominates over bond breaking while the opposite holds true for dissociative interchange.

To determine if the reaction pathway is associative or dissociative, we may study the rate of the reaction to see if it depends on the entering group. A large dependence on the nature and concentration of entering group will suggest an associative mechanism. However, it is difficult to differentiate between associative and associative interchange mechanisms, or between dissociative and dissociative interchange mechanisms through rate studies. These mechanisms may only be distinguished by checking for the presence of a long-lived intermediate.

In this section, we will mainly focus on the ligand substitution reactions in square planar complexes, as they have been well-studied. It is found that substitutions at square planar metal complexes are generally associative, suggesting a trigonal bipyramidal intermediate or transition state. As the entirely dissociative and associative mechanisms are rarely observed experimentally, most ligand substitution reactions at square planar metal complexes follow an associative interchange mechanism, which is shown in Figure 3.7.27.

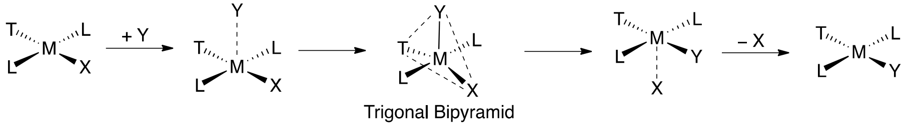


Figure 3.7.27. Mechanism of associative ligand substitution at square planar metal complexes.

In the trigonal bipyramidal transition state, the trans ligand (T), leaving group (X) and entering group (Y) make up the trigonal plane. Thus, ligand substitution reactions at square planar metal complexes are stereoretentive. This means that the entering group takes up exactly the same spot left by the leaving group.

The factors that affect the rate of ligand substitution are discussed below:

1. Nature of entering group

The rate of ligand substitution depends largely on the affinity of the entering ligand to the metal. Small changes to the entering group may result in large changes to the rate of ligand substitution. The most important factor to consider is the donor atom on the entering ligand. The affinity of the ligand to the metal may be analysed using hard-soft acid-base theory, as hard metal cations prefer hard donor atoms while soft metal cations prefer soft donor atoms.

2. The effect of other ligands in the complex

The ligand trans to the leaving group plays a big part in the rate of ligand substitution, through the **trans-influence** and **trans-effect**. The trans-influence is a thermodynamic effect, where the trans ligand affects the ground state properties of the leaving ligand, such as the energy and length of the metal-leaving group bond.

The trans-influence is most pronounced for strong σ-donor ligands, as the 2 ligands trans to each other share the p_x and $d_{x^2-y^2}$ orbitals of the metal. When the trans ligand is a strong σ-donor, a large coefficient of the metal p_x and $d_{x^2-y^2}$ orbitals is used for bonding with the trans ligand, and a smaller coefficient of the orbitals is left for bonding with the leaving ligand. Thus, a strong σ-donor is able to destabilise the ground state, decreasing the activation energy and increasing the rate of substitution.

However, the thermodynamic trans-influence must not be confused with the kinetic trans-effect. The trans-effect is a kinetic effect that is based on the stabilisation of the transition state by the trans ligand. The trans-effect may be explained with both σ and π-interactions. The σ-trans effect may be discussed using the Langford-Gray model, which is shown in Figure 3.7.28.

From the model, we see that both the entering and leaving groups are pointing between the p_x and p_y ligands in the trigonal bipyramidal transition state. A strong σ-donor ligand will be able to take advantage of the partially vacated p_x-orbital to stabilise the trigonal bipyramidal transition state.

The π-trans effect may be explained by the Chatt-Duncanson model, shown in Figure 3.7.29.

Unlike the trans-influence, trans-effect is also affected by the π-interactions of the trans ligand with the metal. The associative transition state is a high energy transition state due to the additional electron density from the entering group. Thus, π-acceptor ligands are able to stabilise the transition state by removing electron density from it.

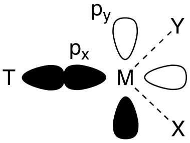


Figure 3.7.28. Langford-Gray model for σ-trans effect.

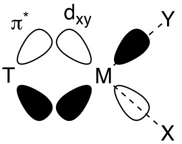


Figure 3.7.29. Chatt-Duncanson model for π-trans effect.

More accurately, the charge from the entering and leaving ligands may be delocalised into the π^*-orbital of the trans ligand through the d_{xy}-orbital.

π-donor ligands are also able to stabilise the transition state by forming a weak metal-ligand bond, but this stabilisation is much less significant than that of the π-acceptor ligands. Thus, the experimentally determined trans effect series is:

$$H_2O < OH^- < NH_3 \approx RNH_2 < \text{pyridine} < Cl^- < Br^- < I^-$$
$$< C_6H_5^- < CH_3^- < PR_3 \approx H^- < CO \approx C_2H_4 \approx CN^-$$

If we look at the activation energy of the reaction, we see that the trans-influence and trans-effect work together to reduce the energy gap between the reactant and transition state. This is because the trans-influence increases the energy of the reactant and the trans-effect lowers the energy of the transition state. Together, the 2 effects are able to speed up ligand substitution reactions.

Cis ligands are also able to change the rate of ligand substitution reactions through the steric effect. Steric blocking by a ligand is more significant when it is cis to the leaving group. This is because cis ligands form a 90° angle with the entering and leaving groups while the angle is 120° for trans ligands in the trigonal bipyramidal transition state. If the bulky ligand is the trans ligand, it will lie on the trigonal plane and be further from the entering and leaving groups. In the case where cis ligands are extremely bulky, ligand substitution may proceed through a dissociative mechanism with a transition state that has a lower coordination number.

3. Influence of the leaving group

The bond strength between the metal and leaving group affects the rate of ligand substitution reactions, and may be predicted using hard-soft acid-base theory. It is also noted that strong trans-effect ligands are replaced very slowly due to their strong σ and π-interactions with the metal. Overall, the effect of leaving group on the rate of ligand substitution is smaller than the factors discussed previously due to the largely associative mechanism.

4. Influence of central metal

While the factors discussed previously are mainly studied on Pt(II) square planar complexes, the nature of the central metal also affects ligand substitution rates significantly. In isovalent ions, the order of reactivity is: $Ni(II) > Pd(II) >> Pt(II)$. This follows the tendency for metals to form pentacoordinate complexes, due to the trigonal bipyramidal transition state. As the additional ligand increases the electron density on the metal, metals with higher charge density are able to better stabilise the ligands and will thus have a higher rate of ligand substitution.

4. ORGANIC CHEMISTRY

In the previous chapter, we mentioned the high catenating ability of carbon. Indeed, carbon is able to form such a wealth of compounds that an entire area in chemistry is devoted to the study of carbon-based molecules. Organic compounds are especially important as they are the building blocks of life. In the past 50 years, there has been tremendous progress in the area of organic chemistry, allowing us to synthesise almost any molecule we desire. This chapter starts from the basics of organic molecules before moving on to explore organic reactions by the different types of mechanism. We hope that students are able to develop a keen sense for the logic behind organic reactions by understanding reactions by their mechanisms. At the end, we include a few advanced areas that have been gaining popularity, and a discussion on retrosynthesis to show reactions from a different perspective.

4.1 Introduction to Organic Chemistry

Organic Chemistry started off as a study of chemicals in life, but has slowly grown as a field that covers mainly compounds built from carbon skeletons. While carbon is only one element on the periodic table, it forms large and complicated biomolecules that are the basis of life. The great diversity of organic chemicals makes the study of organic chemistry extremely interesting, as we unravel the mysteries behind the reactions of such compounds.

4.1.1 *Organic structures and drawings*

Previously in inorganic chemistry, we have discussed about how to draw Lewis structures from simple molecules. However, Lewis structures are inefficient and difficult to draw for large organic molecules. Thus, we will draw organic compounds using **skeletal structure**, which we will be explaining now.

Consider a simple organic compound, ethyl acrylate. Do not mind the naming first as we will be discussing that in a while. The Lewis structure is shown in Figure 4.1.1.

We can change this to a skeletal structure by only showing the **heteroatoms**, which are atoms that are not carbon or hydrogen. We can draw the skeletal structure of ethyl acrylate as shown in Figure 4.1.2.

Note that we have kept the carbon skeleton from the Lewis structure, but the carbon and hydrogen atoms are not shown anymore. We may summarise drawing the skeletal structure into 3 simple steps:

1. Draw the carbon skeleton (all the carbon atoms and their connectivity) using zig-zag lines. Each kink on the zig-zag line represents a carbon atom.
2. The hydrogens connected to carbon are omitted in the drawing, but all carbon are treated as tetravalent unless otherwise indicated (such as in the case of cations).
3. All heteroatoms must be shown, and hydrogen atoms in functional groups must be shown.

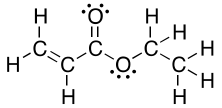


Figure 4.1.1. Lewis structure of ethyl acrylate.

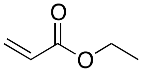


Figure 4.1.2. Skeletal structure of ethyl acrylate.

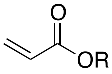


Figure 4.1.3. Simplified structure of ethyl acrylate.

In skeletal structures, we may use **the letter R to represent any organic group**. It is usually used in the case when the group represented in R is not important and to keep the structure simple. In the case of acrylates, we may simplify the structure as shown in Figure 4.1.3.

The R group may refer to the ethyl group in ethyl acrylate, or any other organic moiety. It is used to prevent confusion and draw the viewer's attention to the functional groups that are shown, as the group represented by R does not participate in the reaction. As we learn about functional groups later, we will see different simpler methods to represent common functional groups and how to name compounds.

Tip 4a. Drawing organic structures clearly

It is important to draw organic structures in a way that emphasises the reacting functional groups and shows the formation of new bonds clearly. A short excerpt from a synthesis of strychnine by Rawal in 1994 is shown in Figure 4.1.4.

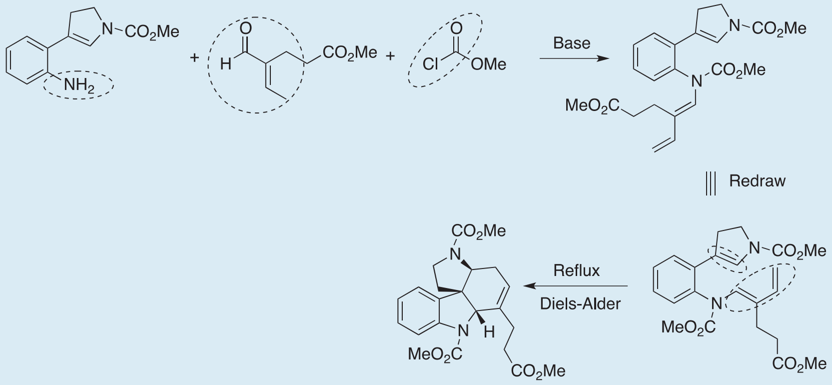


Figure 4.1.4. Excerpt of strychnine synthesis.

In these reactions, the circled functionalities are reacting. These functionalities are drawn out in full, while the other functionalities in the molecule are condensed (such as the ester Co_2Me). Since the second reaction is a Diels-Alder cyclisation, we want to draw the diene and dienophile facing each other so that we can clearly visualise the formation of the new bonds. By developing a good habit of drawing molecules clearly, it prevents any unnecessary mistakes when we try to rotate and bend the molecule in our head.

4.1.2 *Functional groups and nomenclature*

Before we start introducing the functional groups, we will look at the basics of naming organic compounds. Organic compounds are usually named systematically following the International Union of Pure and Applied Chemistry (IUPAC) convention, and such names are known as **IUPAC names**. It is important to understand IUPAC naming well as a skilled chemist should be able to interconvert easily between IUPAC names and structures of compounds for simple compounds, as IUPAC naming is the unambiguous way to name compounds. However, for large molecules, their IUPAC names may be complex and difficult to decipher, thus commonly used compounds may be referred to by their **trivial names**, which are usually simpler than their IUPAC names and passed down from the older days before the IUPAC nomenclature system was derived. Trivial names are still used widely and it is good to know them well. In this chapter, we will cover IUPAC naming, but across the book we will use trivial names where appropriate to expose you to trivial names.

For simple compounds, we may name them based on the number of carbon atoms they contain and their functional groups. The number of carbon atoms is given as a **prefix**, as listed in Table 4.1:

Table 4.1. Prefixes for different numbers of carbon atoms.

Number of Carbon Atoms	Prefix
1	Meth-
2	Eth-
3	Prop-
4	But-
5	Pent-
6	Hex-
7	Hept-
8	Oct-
9	Non-
10	Dec-
11	Undec-
12	Dodec-

The ending is usually determined by the **functional group**. The carbon backbone supports the functional groups, which give the molecule its characteristic reactivity. We will now look at the common functional groups, their structural properties and how to identify and name them.

Alkanes are the simplest organic compounds that contain no functional groups. Due to the lack of functional groups, alkanes are unreactive and usually used as non-polar solvents in organic synthesis. They may be burned in air to generate energy

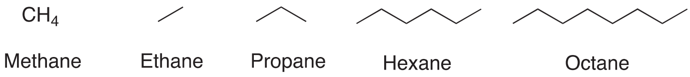


Figure 4.1.5. Examples of straight chain alkanes.

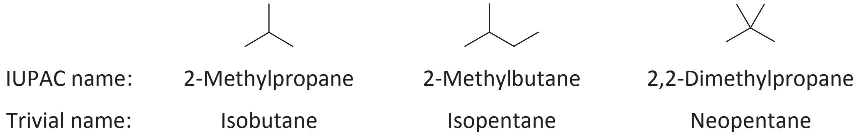


Figure 4.1.6. Examples of branched alkanes, with their IUPAC and trivial names.

and make up petrol. They consist of carbon and hydrogen atoms only and do not contain multiple bonds. They may be represented by the chemical formula C_nH_{2n+2}. Alkanes are named with the **suffix –ane**. There are 2 types of alkanes: straight chain alkanes and branched alkanes. Straight chain alkanes are just a continuous chain of carbon atoms, as shown in Figure 4.1.5.

Branched alkanes may have more complex structures, and they may be named by IUPAC convention or trivial names. Simple examples of branched alkanes are shown in Figure 4.1.6.

From this example, we will look at how to use IUPAC naming to describe branching groups. Note that we always find the parent chain first. For alkanes, the parent chain is the longest carbon chain as there are no functional groups. In other types of compounds, the highest priority functional group must be included in the parent chain. The alkyl substituents on the parent chain may be named with a **–yl** ending. **Numbers** are used to specify which carbon on the parent chain the substituent is attached on. While we may start counting the parent carbon chain from either side, the convention states that we must choose the name where the number used is the **smallest**. For example, 2-methylbutane may also be known as 3-methylbutane if we count the carbons on the parent chain starting from the other side. However, we must use the name with the smallest number (e.g. 2-methylbutane) and 3-methylbutane is not an acceptable name for the compound. When there are replicate substituents in a molecule, we add prefixes to indicate the number of such substituents in the whole molecule, as listed in Table 4.2.

Table 4.2. Prefixes of different numbers of substituents.

Number of such substituents	Prefix
1	Mono- (usually omitted)
2	Di-
3	Tri-
4	Tetra-
5	Penta-

(*Continued*)

Table 4.2. (*Continued*)

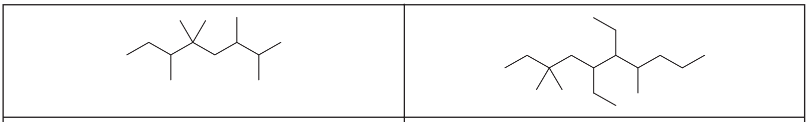
Number of such substituents	**Prefix**
6	Hexa-
7	Hepta-
8	Octa-
9	Nona-
10	Deca-
11	Undeca-
12	Dodeca-

Note that counting from five onwards is the same as the numerical prefixes used for counting carbon atoms, just with an extra –a at the back.

Two examples of alkanes with replicate substituents are shown in Figure 4.1.7. Note that replicated groups attached on the same carbon must be written for the correct number of times and the parent chains are numbered so that the first substituent has the smallest possible locant number. In this example, 2,3,5,5,6-pentamethyloctane should not be wrongly named as 2,3,5,6-pentamethyloctane or 3,4,4,6,7-pentamethyloctane. Last but not least, if there are more than one type of substituents in the molecule, the substituents are written in alphabetical order. For example, in 5,6-diethyl-3,3,7-trimethyldecane, "ethyl" appears before "methyl" since "ethyl" starts with "e" whereas "methyl" starts with "m". Do not consider the numerical terms into the "alphabetical ranking". In this case, "di" and "tri" are not considered in determining which substituent comes first in the naming.

Straight chain substituents are easily named by taking the prefix for the number of carbon atoms and adding the –yl ending. There are some branched substituent groups that have common names using the **prefixes *iso* and *tert*** and their structures are shown in Figure 4.1.8.

When drawing structures, the common alkyl substituent groups may be represented by a shorthand notation to keep the structure compact. The shorthand may be derived by taking the **first two letters** of the name of the substituent. In the case of branched substituents, we add the letters *i* and *t* to represent iso and tert respectively. While there are many rules to follow, they will become straightforward once we look at more examples going down the book.



2,3,5,5,6-pentamethyloctane

5,6-diethyl-3,3,7-trimethyldecane

Figure 4.1.7. Examples of alkanes with replicate substituents.

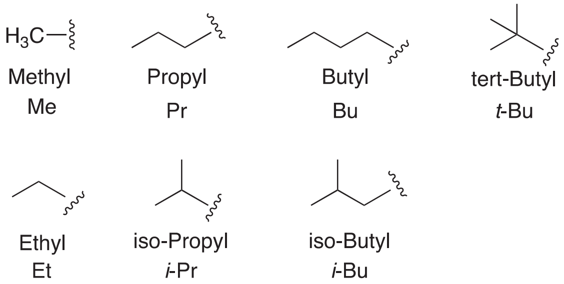


Figure 4.1.8. Branched substituent groups and their common names.

Cycloalkanes are a special type of alkanes that are cyclic in structure. They start from a minimum of three carbons. Since they adopt a cyclic structure, they have two less hydrogens than normal alkanes and have the general formula C_nH_{2n}. Cyclic compounds are very common in organic chemistry and their cyclic structure gives them more rigidity, which we will discuss in detail in the later chapters. They may be named easily by adding the prefix **cyclo-** before the original name of the alkane, as shown in Figure 4.1.9.

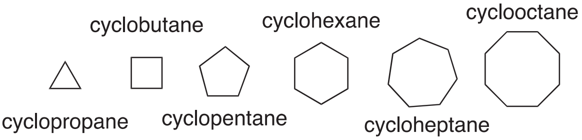


Figure 4.1.9. Examples of cycloalkanes.

Alkenes, also known as **olefins**, contain **C=C double bonds**, which imparts reactivity to the molecule, as we will see later. For simple alkenes with only one C=C double bond, their chemical formulae follow C_nH_{2n}. Alkenes are named similarly to alkanes, just that they end with the **suffix –ene**. Before the suffix, we may add a number to specify the position of the C=C double bond in the alkene. Note that the double bond bridges two carbon atoms, but we will always label it with the smaller number following IUPAC convention. In the case of terminal alkenes (the double bond is between the first and second carbon), the number 1 may be omitted. Alkenes may also be branched, or contain multiple double bonds in one single molecule. The structures and names of simple alkenes are shown in Figure 4.1.10.

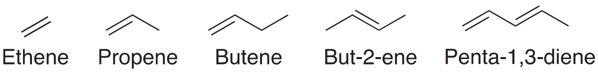


Figure 4.1.10. Examples of alkenes.

Alkynes contain C≡C triple bonds. Alkynes have similar reactivities as alkenes, but alkynes are not as common as alkenes in nature. Alkynes are drawn as linear molecules due to the sp-hybridization of carbon orbitals and they are named with the **suffix –yne**. Alkynes with one triple bond have the general formula of C_nH_{2n-2}. They may be numbered in the same way alkenes are numbered. Examples of alkynes are given in Figure 4.1.11.

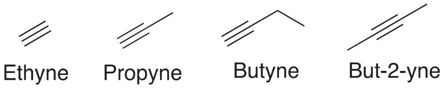


Figure 4.1.11. Examples of alkynes.

Alkenes and alkynes may also be in cyclic rings, however the ring strain will be greater due to the bond angles, and smaller rings may be very unstable. We will come back to them later, and now we will move on to functional groups containing heteroatoms.

Alcohols contain the **hydroxyl group**, written as $R\text{-}OH$. Alcohols may be classified as Primary (1°), Secondary (2°) or Tertiary (3°) alcohols based on the carbon next to the $-OH$ functionality, as shown in Figure 4.1.12.

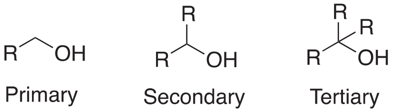


Figure 4.1.12. Classification of alcohols.

We classify alcohols based on the **carbon neighbouring the OH group**. If the carbon has one organic group and two hydrogens attached, the alcohol is primary. If the carbon has two organic groups and one hydrogen attached, the alcohol is secondary. If the carbon has three organic groups and no hydrogens attached, the alcohol is tertiary. Depending on the nature of the alcohol, it will have different reactivity and products of oxidation. Alcohols may be named with the **suffix –ol**. The position of the alcohol may be indicated by locant numbers before –ol. Due to their high polarity, alcohols usually have good solubility in water and can act as polar solvents.

Ethers also contain oxygen, but instead contain an **alkoxy group**, written as $R\text{-}OR$. The oxygen bridges two organic groups and is not bonded to any hydrogens. Ethers are named with the smaller of the two organic groups treated as a substituent alkoxy group, ending with the **suffix –oxy**, onto the parent chain.

Note that cyclic ethers are named differently as it is impossible to clearly name the substituent and parent chain, and we will only review the naming of heterocycles when we discuss their chemistry. Ether is also the common name for ethoxyethane (diethyl ether), a highly flammable solvent. Ethers are less polar than alcohol and more volatile, thus they are often used as a solvent for less polar compounds. Common ethers are shown in Figure 4.1.13.

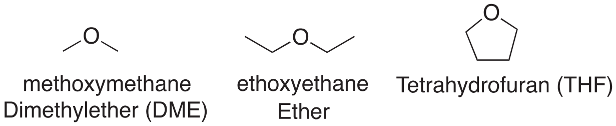


Figure 4.1.13. Examples of ethers.

Amines are the nitrogen equivalents of alcohols, containing the **amino group**, $R\text{-}NR_2$. Amines may also be classified as primary, secondary or tertiary depending on the number of organic groups **connected to the nitrogen atom**, as shown in Figure 4.1.14.

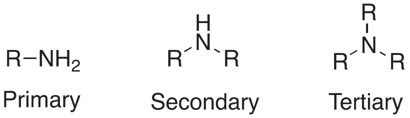


Figure 4.1.14. Classification of amines.

Amines may be named with the **suffix –amine** when there are no other functional groups present in the molecule, if not they are usually named as substituents and referred to as **amino** groups. When the amine is secondary or tertiary, the other organic groups on the nitrogen may be named using **"*N*-" as the locant "number"** to indicate that they are directly attached to the nitrogen atom. Amines usually have pungent fishy smells as some of them are formed during meat decay.

Alkyl halides contain halogens (fluorine, chlorine, bromine or iodine) bonded to organic groups. Due to their high electronegativity, halogens withdraw electron density from neighbouring carbon atoms to make the carbon electrophilic. However, the reactivity of alkyl halides follows an increasing trend as we move down the group, with alkyl fluorides being the least reactive and alkyl iodides being the most reactive. The halogen atoms may be treated as substituents and named using **prefixes of fluoro-, chloro-, bromo- and iodo-**. Since alkyl halides have similar properties, we may use X to represent any halogen such that $R\text{-}X$ is an alkyl halide.

Nitro compounds contain the **nitro functional group**, and are written as $R\text{-}NO_2$. Nitro groups are named as substituents using the **prefix of nitro-**. Nitro

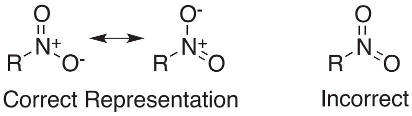


Figure 4.1.15. Representation of the nitro group.

groups are strongly electron withdrawing. They can be drawn as a zwitterion that is stabilised by resonance and not as a structure with 5 bonds to nitrogen, as shown in Figure 4.1.15.

Nitriles, also known as cyanides, contain the **cyano group** and can be represented as $\mathrm{R\text{-}C{\equiv}N}$. Nitriles may be named systematically with the **suffix –nitrile**, but there is a myriad of common names for nitriles. Nitriles are also electron-withdrawing groups and may react as an electrophile at the carbon.

Aldehydes and **ketones** contain the **carbonyl group (also known as oxo group)**, which is the $\mathrm{C{=}O}$ group. They are the oxidised products from alcohols. Aldehydes ($\mathrm{R\text{-}CHO}$) are found at the ends of carbon chains and have at least one hydrogen attached to the carbonyl carbon. Aldehydes are named with the **suffix –al** and the simplest aldehyde having two hydrogens attached to the carbonyl carbon is known commonly as formaldehyde. When writing aldehyde in condensed form, it is important to write it as $\mathrm{R\text{-}CHO}$ and not $\mathrm{R\text{-}COH}$ to avoid confusion with alcohols. Ketones ($\mathrm{R_2C{=}O}$) are found in the middle of carbon chains and have organic groups attached to both sides of the carbonyl carbon. They are named with the **suffix –one** The general structures of aldehydes and ketones are shown in Figure 4.1.16.

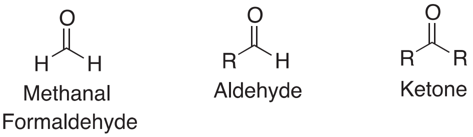


Figure 4.1.16. Examples of aldehydes and ketones.

Carboxylic acids contain the **carboxyl group**, and are written as $\mathrm{R\text{-}COOH}$ or $\mathrm{R\text{-}CO_2H}$. They are formed from the oxidation of aldehydes and can be named with the **suffix –oic acid**. As the name suggests, carboxylic acids are acidic and react with bases to form carboxylate salt. Many functional groups are known as carboxylic acid derivatives as they are on the same oxidation level as carboxylic acids. **Esters** contain a carboxyl group with an extra organic group and are written as $\mathrm{R^1\text{-}COOR^2}$ or $\mathrm{R^1\text{-}CO_2R^2}$. Esters are usually fragrant, with fruity scents. They may be named by treating the organic group directly bonded to oxygen as a substituent, and the parent chain ending with the **suffix –oate**. **Amides** are found in proteins, and are formed by the condensation of carboxylic acids with amines. They have the structure $\mathrm{R\text{-}CONR_2}$ and are named with the **suffix –amide**, and substituents on the nitrogen may be indicated using N-. **Acyl chlorides** are highly reactive compounds that have the structure $\mathrm{R\text{-}COCl}$. They may be named with the **suffix –oyl chloride**. Similarly, there are **acyl bromides** with the structure $\mathrm{R\text{-}COBr}$ and named with the **suffix –oyl bromide**. The last common carboxylic acid derivative is **acid anhydrides**, with the structure $\mathrm{(R^1CO)O(COR^2)}$. If the two organic groups are the same, the acid anhydride is classified as symmetric. As anhydride is the condensation product of two carboxylic acids, we may name them based on their parent carboxylic acids, adding the **suffix –oic anhydride**. For example, an anhydride formed by condensation of methanoic acid and propanoic acid will be known as methanoic propanoic anhydride (the order of acids follows alphabetical order). Structures and examples of carboxylic acid and its derivatives are shown in Figure 4.1.17.

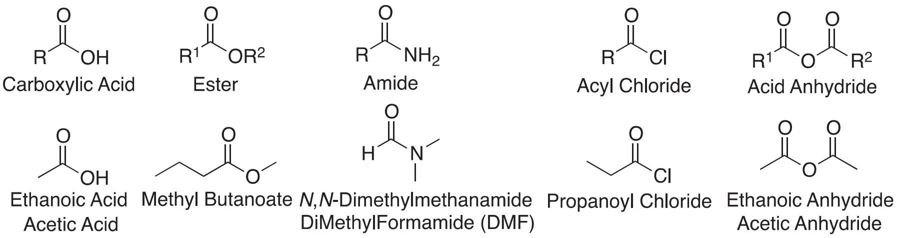


Figure 4.1.17. Examples of carboxylic acids and its derivatives.

Tip 4b. Naming molecules with multiple functional groups

Since almost all functional groups can be written as the parent chain (using suffixes) or substituents, in molecules where there are multiple functional groups, we need to determine the priority of functional groups when naming, such that the longest chain with the highest priority functional group may be named as the parent chain. The priority of functional groups from highest to lowest, together with their suffixes and prefixes, are listed in Table 4.3.

Table 4.3. Priorities of the different functional groups and their suffixes and prefixes.

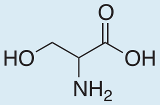
Functional group	Suffix (as the parent chain)	Prefix (as the substituent)
Carboxylic Acid	-oic acid	carboxy-
Ester	-oate	R-oxycarbonyl-
Acyl Chloride	-oyl chloride	chlorocarbonyl
Amide	-amide	carbamoyl-
Nitrile	-nitrile	cyano-
Aldehyde	-al	formyl-
Ketone	-one	oxo-
Alcohol	-ol	hydroxy-
Amine	-amine	amino-
Alkene	-ene	alkenyl
Alkyne	-yne	alkynyl
Alkane	-ane	alkyl

(Continued)

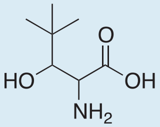
Tip 4b. (*Continued*)

Ethers, alkyl halides and nitro groups are of lower priority than alkanes, so they are always named with the suffix –ane and named with prefixes.

When naming compounds with multiple substituents, we follow **alphabetical order** to arrange the substituents. Let's review the naming of a simple amino acid, serine.



We first identify the highest priority functional group present to be carboxylic acid. Thus, we may name the parent chain together with the carboxylic acid as **propanoic acid**. Next, we see that there are two substituents, an amine and an alcohol. For amine, the prefix used is **–amino** while the prefix is **–hydroxy** for alcohol, thus by alphabetical order, the amine will be written first in the name. Finally, to number the functional groups, we must assign 1 to the highest priority functional group, which is the carboxylic acid. Thus, the amine group is attached to carbon **2** and the alcohol is attached to carbon **3**. Thus, the systematic IUPAC name for serine is **2-amino-3-hydroxypropanoic acid**. Let us modify this structure slightly by adding a tert-butyl group:



With an extra tert-butyl group on carbon 3, the parent chain of the molecule is extended and the new name would be **2-amino-3-hydroxy-4,4-dimethylpentanoic acid**. Note that all of the same functional group is numbered together and the numerical prefixes are used to specify the number of such functional groups. A small point to keep in mind is that numbers are separated by commas (,) while number and words are separated by hyphens (-).

4.2 Optical Activity and Stereochemistry

Chemical molecules are three-dimensional and we need to study their stereochemical properties. This is because most molecules have many **stereoisomers** which have the same **connectivity of bonds** but **different spatial arrangement of atoms**. When we analyse stereochemistry, we need to be clear of the difference between **configuration** and **conformation**. If we say that 2 molecules have two different **configurations**, the two configurations refer to **stereoisomers** of the molecule. It is **not possible to interconvert between two configurations without cleaving old covalent bonds and forming new covalent bonds**. Since bond breaking requires a lot of energy, stereoisomers are considered different molecules and it often requires a few reaction steps to change the configuration of a molecule. On the other hand, **conformations** of a molecule are structures with different spatial arrangement of atoms that can **easily interconvert through rotation of single bonds**. Thus, the **same molecule may have multiple conformations**. In this chapter, we will be dealing with stereoisomers, which are molecules with different configurations. **Chiral molecules** are molecules with a **non-superimposable mirror image**. This means that the mirror image of the molecule has a different configuration with the original molecule. The simplest example would be our left and right hands, which are mirror images and non-superimposable. This is why chirality may also be referred to as "handedness" in layman terms.

We may draw and show 3D features of a molecule by using **wedges and dashes**. A wedge bond (◢) indicates the substituent to be coming forward and out of the plane of the drawing while a dash bond (⋰) indicates the substituent to be going backward and into the plane of the drawing. While the wedge and dash notation gives us clear information of the stereochemistry, it may be difficult to draw for biological molecules with multiple consecutive chiral centres. In this case, we use the **Fischer projection**, which is commonly used for carbohydrates. Fischer projections are drawn with intersecting vertical and horizontal lines. The groups on the horizontal lines point forward and out of the plane of the drawing while the groups on the vertical lines point backward and into the plane of the drawing. We may understand Fischer projections by the method shown in Figure 4.2.1.

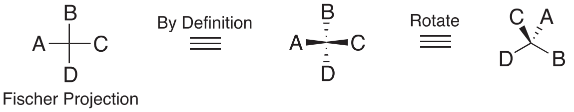


Figure 4.2.1. Visualisation of the Fischer projection.

It is important to study stereochemistry because chiral isomers may have different chemical and physical properties. We need to classify stereoisomers into two different types, **enantiomers** and **diastereomers** (or **diastereoisomers**).

The **enantiomer** of a molecule is the non-superimposable mirror image of the molecule. Thus, all chiral molecules exist as a **pair of enantiomers**. The **diastereomers** of a molecule are the other stereoisomers of the molecule that are not the enantiomer of that molecule. Note that diastereomers may also exist as pairs of enantiomers.

The criteria for a molecule to be chiral is that the molecule has **no plane of symmetry**. Any molecule with a plane of symmetry has a mirror image that is superimposable on the original molecule and is achiral. However, a molecule with a plane of symmetry may still have diastereomers but it does not have an enantiomer.

The most common type of chirality is chirality at a **chiral centre**, which is usually a **carbon centre that has four different substituents attached**. We may apply IUPAC convention to assign *R* or *S* configuration at such centres based on priorities from the Cahn-Ingold-Prelog Rules (CIP Rules):

1. Compare the atomic number of the atoms directly attached to the chiral centre. The priority of the groups follows the order of the atomic numbers from the highest to the lowest.
2. If there is a tie, we will consider the subsequent atoms bonded to those directly attached to the chiral centre, at a distance of two covalent bonds from the chiral centre, and compare their atomic numbers one by one. If there is a double or triple bond, we consider them as two or three single covalent bonds to the same atom.
3. This process is repeated until the tie is broken, and we assign the priorities of the different groups.

After applying the CIP rules to find the priorities of the substituents attached to the chiral centre, we may assign the *R* or *S* configuration by **rotating the lowest priority substituent to the back** and checking if the other three substituents go from **highest to lowest priority** in a **clockwise (*R*)** or **anticlockwise (*S*)** direction. We will demonstrate how to apply the rules using the sample molecule in Figure 4.2.2.

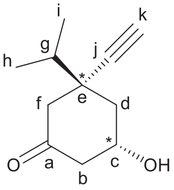


Figure 4.2.2. Sample molecule for assignment of chiral centres.

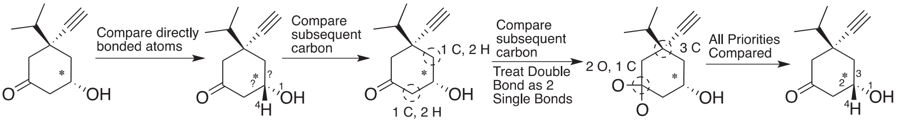


Figure 4.2.3. Process of assigning priorities to the different substituent groups for carbon *c*.

In the sample molecule, the two carbons *c* and *e* are chiral centres as they have four different substituents attached. Let's start with the chiral centre *c* connected to the hydroxyl group. We may rank the priorities of the group based on CIP rules, as shown in Figure 4.2.3 and explained below:

1. Comparing the atoms directly bonded to the carbon *c*, we have 1 oxygen (atomic number 8), 2 carbons (atomic number 6) and 1 hydrogen (atomic number 1). From comparing the atomic numbers, it is clear that the group with oxygen is the highest priority while the hydrogen is the lowest priority. However, we are unable to determine the priority of the two carbon substituents without further comparison, since there is a tie as both carbons *b* and *d* have equal atomic numbers.

2. Next we compare the atoms further bonded to the two carbons *b* and *d*. Carbon *b* has one carbon (carbon *a*) and two hydrogens attached. Carbon *d* also has one carbon (carbon *e*) and two hydrogens attached. Hence, it is still a tie for carbon *b* and carbon *d*.
3. We have to move on to compare the substituents one more covalent bond away from the chiral centre. This is done by following the highest priority atom, which is carbon in this case. We need to compare the atoms connected to the carbon two bonds away from the chiral centre, which refers to atoms on carbon *a* and carbon *e*. We see that carbon *a* is connected to oxygen by a double bond and carbon *f*. Meanwhile, carbon *e* is connected to 3 carbons *f*, *g* and *j*. We may treat the double bond to oxygen as being connected to 2 oxygens. Thus carbon *b* bonded to carbon *a* with oxygen is of higher priority.

After the priorities are ranked, we have to rotate the molecule such that the lowest priority group, hydrogen, is facing the back. Then, we may consider if the other groups go from highest to lowest priority in a clockwise or anticlockwise fashion to assign *R* or *S* configuration to the chiral centre.

After rotating hydrogen to the back as shown in Figure 4.2.4, we see that the groups with priorities 1, 2 and 3 rotate in an anticlockwise direction. Thus we may assign *S* configuration to this chiral centre. Since it is difficult to visualise rotation of the molecule, we may consider the original molecule with the **lowest priority group facing the front**. In this case, we assign *S* configuration for clockwise rotation and *R* configuration for anticlockwise rotation.

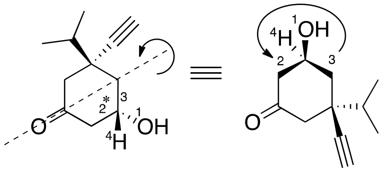


Figure 4.2.4. Assigning the absolute configuration by pushing hydrogen to the back.

We proceed to the other chiral centre on carbon *e*. We will assign priorities to the four substituents following the CIP rules, as shown in Figure 4.2.5 and explained below:

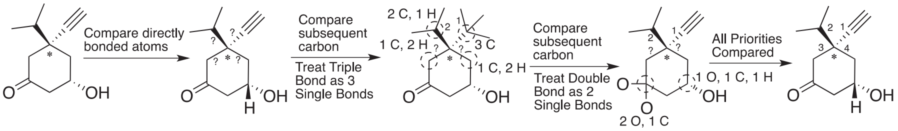


Figure 4.2.5. Process of assigning priorities to the different substituent groups for carbon *e*.

1. Comparing directly bonded atoms, all four atoms are carbons (*d*, *f*, *g* and *j*), thus we are unable to rank the priorities at this stage.
2. We move on one more carbon and compare the substituent atoms. We treat multiple bonds as multiple single bonds to the same atom. Thus, carbon *j* is attached to CCC, carbon *g* is attached to CCH, carbon *d* is attached to CHH, and carbon *f* is attached to CHH. Hence, carbon *j* has priority 1 and carbon *g* has priority 2. The other two carbons *d* and *f* are still in a tie at this level.
3. Moving one bond further, we see carbon *c* from carbon *d* singly bonded to oxygen and carbon *a* from carbon *f* doubly bonded to oxygen. Since double bonds may be treated as 2 imaginary single bonds, the doubly bonded oxygen takes higher priority.

Placing the lowest priority group at the back, we view the molecule from the left side to see that the priorities 1, 2 and 3 follow a clockwise sequence, thus this chiral centre is assigned as *R* configuration. This compound is thus named as (3*R*,5*S*)-3-ethynyl-5-hydroxy-3-isopropylcyclohexanone. Note that the *R* or *S* configuration is placed in front of the name and numbers are used to specify the carbon centre assigned.

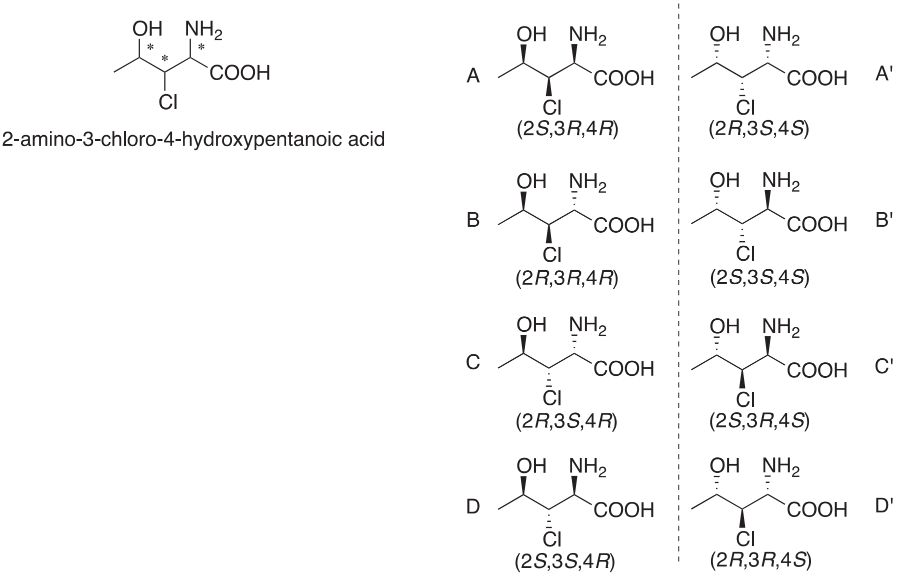


Figure 4.2.6. Example of diastereomers and enantiomeric pairs for a sample compound.

We will now look at examples of stereoisomers and how the *R* and *S* configurations relate to the different stereoisomers. When discussing stereochemistry, it is important to first **identify all the chiral centres** on the compound, and check if the compound has a **plane of symmetry**. For a compound with no plane of symmetry, the **total number of stereoisomers will be 2^n**, where *n* is the number of chiral centres, as each chiral centre may be of *R* or *S* configuration. These stereoisomers will come as enantiomeric pairs, which are mirror images of each other. Enantiomeric pairs have **opposite configuration of each other at every chiral centre in the compound**. Let's take a look at an example in Figure 4.2.6.

The compound has 3 chiral centres and no plane of symmetry, thus it has a total of $2^3 = 8$ stereoisomers. These 8 stereoisomers are 4 pairs of enantiomers (A and A′, B and B′, C and C′, D and D′) with opposite configuration on every chiral centre. To elaborate on the concept of enantiomer and diastereomer, we may consider compound A. The enantiomer of compound A is A′. The diastereomers of compound A is B, B′, C, C′, D and D′.

Now, what if a compound has not only chiral centres, but also a plane of symmetry? Such compounds are known as **meso compounds**, and they have less stereoisomers than expected from the 2^n rule because certain isomers are achiral.

In Figure 4.2.7, the compound has 2 chiral centres, but only 3 stereoisomers. This is because B has a plane of symmetry and thus is achiral and identical to its mirror image. The other stereoisomer A does not have a plane of symmetry and is chiral with an enantiomer A′.

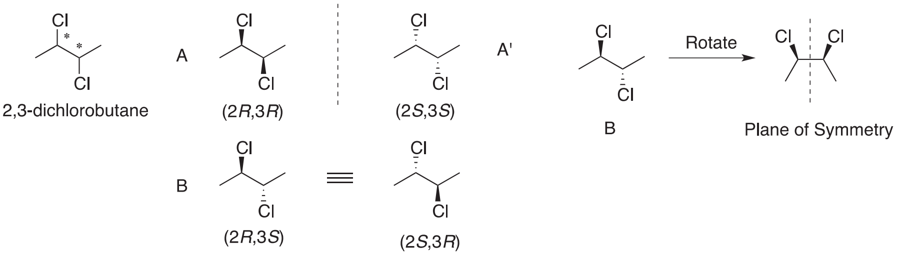


Figure 4.2.7. Example of a meso compound.

Chiral molecules do not necessarily possess a chiral centre. A different type of chirality that is less commonly encountered is **planar chirality**. Planar chirality exists when there are non-coplanar rings that are unable to freely rotate. A common example used in asymmetric catalysis is Fu's planar chiral 4-(dimethylamino)pyridine (DMAP) catalyst, which has no mirror planes and is able to differentiate left from right and top from bottom. This catalyst has been used in the kinetic resolution of amines, and its structure is shown in Figure 4.2.8.

Axial chirality is observed when molecules do not have a chiral centre, but instead have an axis of chirality, usually due to restriction in single bond rotation by steric bulk. This is common in biphenyl or binaphthyl compounds due to the restriction of rotation of aryl-aryl single bonds (atropisomerism). The most common compound with axial chirality is a chiral phosphine catalyst, 2,2′-bis(diphenylphosphino)-1,1′-binaphthalene (BINAP), and it has been widely used in asymmetric catalysis.

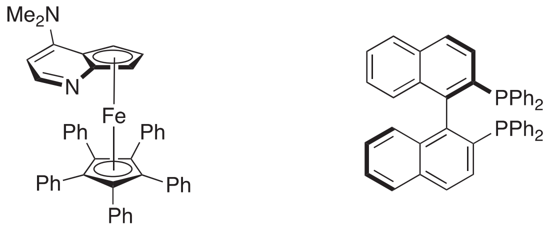


Figure 4.2.8. Fu's planar chiral DMAP (left) and chiral phosphine BINAP (right).

The physical difference in stereoisomers is their **optical activity**, which is the **ability to rotate plane-polarised light**. Molecules with a plane of symmetry are achiral and not optically active, which means that they do not rotate plane-polarised light. Chiral molecules that rotate plane-polarised light to the right are known as dextrorotatory (+) and those that rotate plane-polarised light to the left are known as laevorotatory (–). This property is **unrelated to the *R* and *S* assignments of chiral centres**, as this is a property of the entire molecule, which may be attributed to multiple different chiral centres with different configurations. The angle in which the plane of polarised light is rotated can be described by **specific rotation α**. The value of α is positive for a rotation towards the right and negative for a rotation towards the left. This angle depends on the following factors:

1. Identity of the chiral molecule
2. Concentration of the solution of chiral molecule
3. Path length: The length of solution that the light passes through

To characterise the optical activity of a molecule, we may use the specific rotation $[\alpha]_{\mathrm{D}}^{20}$ value. The subscript D represents the D-lines of a sodium lamp, which is light of wavelength 589 nm. The superscript 20 indicates that the specific rotation is measured at a temperature of 20°C. This value is experimentally determined by shining light of wavelength 589 nm through a solution of the chiral molecule with known concentration (c) and length (l) and measuring the angle of rotation α at 20°C. We then calculate $[\alpha]_{\mathrm{D}}^{20}$ as follows:

$$[\alpha]_{\mathrm{D}}^{20} = \frac{\alpha}{cl}$$

It is important to note that **a pair of enantiomers rotate the plane of polarised light by the same amount, but to opposite directions**. Thus, for a molecule with $[\alpha]_{\mathrm{D}}^{20} = x$, its enantiomer will have $[\alpha]_{\mathrm{D}}^{20} = -x$.

In synthesis, we are usually concerned with making a single enantiomer, as stereochemistry can change the way that the molecule interacts with other chiral compounds. A sample with only one enantiomer is known as **enantiomerically pure**. A sample with both enantiomers in equal proportions is known as a **racemic**

mixture. Any other sample with both enantiomers present but not in equal proportion is known as **enantiomerically enriched**.

We may use **enantiomeric ratio (*er*)** or **enantiomeric excess (*ee*)** to describe enantiomerically enriched mixtures. For a mixture with 98% (*S*)-isomer and 2% (*R*)-isomer, the *er* is 98:2, while the *ee* is $98\% - 2\% = 96\%$. Using *ee* is more common now, as *ee* tells us how much of the pure enantiomer we have in the mixture, treating the rest as a racemic mixture. Mixtures can be analysed for optical purity by using the specific rotation method as enantiomeric pairs have opposite optical rotations, and we may compare the optical rotation to the known enantiomerically pure sample. However, this method may have large deviations for other impurities in the mixture. In modern research, it is more common to use chiral chromatography to separate the enantiomers and measure their amounts.

Other than chiral centres, we are also interested in achiral carbon centres and their properties depending on whether there is a chiral centre adjacent. These carbon centres may be known as **homotopic**, **enantiotopic** or **disasterotopic**. In the example shown in Figure 4.2.9, we will look at carbon centres with two hydrogens and two other groups.

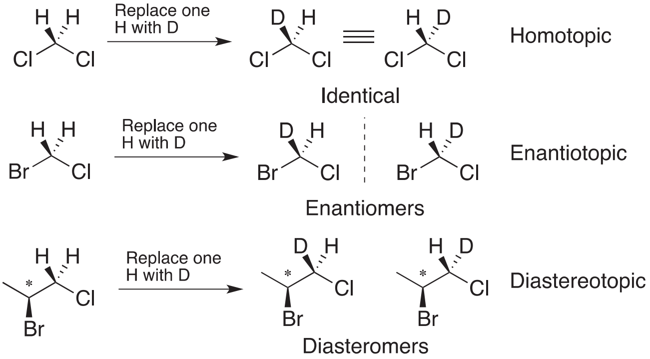


Figure 4.2.9. Types of achiral carbon centres adjacent to chiral centres.

We may check if the hydrogens are homotopic, enantiotopic or diastereotopic by replacing one hydrogen with deuterium ($^2\mathrm{H} = \mathrm{D}$) and checking if the two resulting compounds are identical, enantiomers or diastereomers. **Homotopic groups** are chemically identical and cannot be differentiated in any way. **Enantiotopic groups** can only be distinguished in chiral environments, and chiral reagents, auxiliaries or catalysts may be used to control reactions on enantiotopic groups to generate only one enantiomer preferentially. **Diastereopic groups** are chemically different even in achiral environments due to the adjacent chiral centre. In the example in Figure 4.2.9, the hydrogen pointing out of the page will be closer to the bromine than the hydrogen pointing behind the page, resulting in different properties that can be differentiated by analytical methods such as Nuclear Magnetic Resonance (NMR) spectroscopy. While the chiral centre may be anywhere along the molecule and not necessarily directly adjacent for the two hydrogen groups to be considered diastereotopic, the effects of the chiral centre on the carbon centre is much more significant when it is adjacent and decreases as it gets further from the carbon centre.

Carbons that can be converted into a chiral centre directly in a single step are known as **prochiral carbons**. In the example in Figure 4.2.10, both the carbon with enantiotopic groups and the carbon with diastereotopic groups are prochiral, as substituting one hydrogen for another substituent results in the carbon centre becoming chiral. The two equivalent groups (in this case the two hydrogens) may be described as *pro-R* or *pro-S*. If we promote the *pro-R* group to a higher priority than the other identical group, the resulting chiral centre has a *R*-configuration, and similarly for the *pro-S* group.

More commonly, sp^2-carbons may be prochiral carbons, such as carbonyl carbons. Since they are planar, they have two faces, which may be homotopic, enantiotopic or diastereotopic. When the faces are homotopic, addition of a nucleophile to the carbonyl group does not turn the carbon centre to a chiral centre, thus the carbon centre is not considered prochiral. The difference between enantiotopic faces and diastereotopic faces is whether there are other chiral centres in the carbonyl compound.

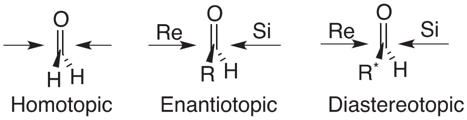


Figure 4.2.10. Faces of sp^2-carbons. R^* is an organic group containing at least 1 chiral centre.

The enantiotopic and diastereotopic faces of the aldehyde may be assigned as *Re* or *Si*, depending on whether the three substituents have priorities 1, 2 and 3 that follow the clockwise order (*Re*) or anticlockwise order (*Si*) when viewed from that face. It is impossible to predict the configuration of the product formed as it depends on the priority of the incoming group in relation with the other groups on the molecule.

The concepts discussed above are important fundamentals in asymmetric synthesis. When reacting at a carbon with diastereotopic groups or faces, we may be able to achieve a certain level of diastereoselectivity depending on the properties of the existing chiral centre. On the other hand, achieving enantioselectivity for a carbon with enantiotopic groups or faces would require chiral induction from a chiral reagent, auxiliary or catalyst. While such syntheses are interesting, they are beyond the scope of the Olympiad and will not be covered further in this book. You may look up university level organic chemistry texts to explore more on stereoselective synthesis.

4.3 Conjugation and Aromaticity

Conjugation refers to double bonds that are joined up such that there is a series of **alternating single and double bonds**. We have previously discussed hybridization and bonding. Let's review it for ethene to understand carbon-carbon double bonds. Carbon has one 2s and three 2p orbitals in its valence shell. A double bond consists of a σ-bond and a π-bond. The π-bond is formed by the sideway overlap of 2p orbitals. Thus the carbon atoms keep one 2p orbital for the π-bond while hybridising the three other valence orbitals to form three sp^2-hybrid orbitals. The C-C σ-bond is formed by the head-on overlap of two sp^2-hybrid orbitals, and the C-H σ-bond is formed by the head-on overlap of the sp^2-hybrid orbital of C with the 1s orbital of H. The orbital bonding picture of ethene is shown in Figure 4.3.1.

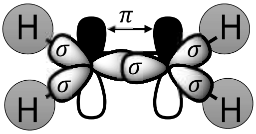


Figure 4.3.1. Orbital bonding picture of ethene.

When double bonds and single bonds alternate, we have a conjugated π-system where the π-electrons are **delocalised over the whole conjugated system**, since every carbon atom has a 2p orbital that can overlap (sideways) with each other to form a continuous π-electron cloud. The important properties of π-systems are:

1. The π-system must be completely planar. This is to allow for the 2p orbitals to overlap effectively, because each 2p orbital is perpendicular to the same plane of the π-system.
2. The carbon atoms are all sp^2-hybridised. This means that the C-C-C bond angles are roughly 120°.
3. The π-orbital is formed by the in-phase combination of the 2p orbitals, and the π*-orbital is formed by the out-of-phase combination of the 2p orbitals.

For more extended π-systems, we recall the rule that the number of molecular orbitals is equal to the number of linearly combined atomic orbitals. We may apply this rule to analyse the bonding in hexa-1,3,5-triene, and its MO diagram is shown in Figure 4.3.2.

The three lower energy molecular orbitals (Ψ_1,Ψ_2, and Ψ_3) are bonding π-orbitals, which account for the three π-bonds in the molecule. The three empty molecular orbitals of higher energy (Ψ_4, Ψ_5 and Ψ_6) are π*-antibonding orbitals. When light shines onto the molecule, the electrons from the HOMO (Ψ_3) may be excited to the LUMO (Ψ_4), absorbing a certain wavelength of light. If the wavelength of light

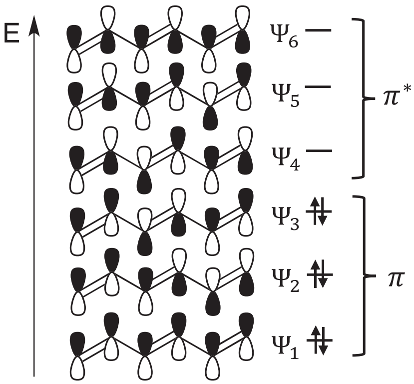


Figure 4.3.2. Frontier orbital picture for π-system of hexatriene.

absorbed lies in the visible range, the molecule will display the complementary colour of that being absorbed. With more extensive conjugation, the **energy of the HOMO is increased** and the **energy of the LUMO is decreased** such that the energy gap of $\pi \rightarrow \pi^*$ electronic transition is smaller. Thus, **highly conjugated compounds are often coloured**. Compounds which have a smaller number of double bonds in conjugation have a larger $\pi \rightarrow \pi^*$ energy gap and absorb in the ultraviolet (UV) range, being **UV active**.

Double bonds are stereochemically rigid due to the π-bond, leading to isomers when the double bond has different substituents. It is possible to interconvert between the two isomers of alkenes using light to promote one electron from $\pi \rightarrow \pi^*$ orbital, essentially breaking the π bond and allowing free rotation of the single bond. The more stable isomer (usually trans) will be formed as the major product from such an isomerisation.

Background 4a. Double bond isomers of alkenes

Disubstituted alkenes may be classified as cis or trans depending on whether the two substituents are on the same side (cis) or different sides (trans). Figure 4.3.3 demonstrates the classification using butene as an example.

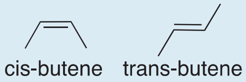


Figure 4.3.3. Examples of cis and trans alkenes.

Cis and trans may be easily assigned for disubstituted alkenes, but we need a more systematic nomenclature system for all alkenes, even for those that are tri- or tetra-substituted. IUPAC convention employs the *E*–*Z* convention, where *E* stands for *entgegen* (German for "opposite") and *Z* stands for *zusammen* (German for "together"). These rules may be applied on any general alkene (Figure 4.3.4) using the method below.

(*Continued*)

Background 4a. (*Continued*)

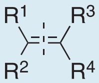


Figure 4.3.4. Sample alkene for assignment of *E*–*Z* configuration.

1. Divide the alkene into half through the double bond.
2. Compare the two substituents on each sp^2-carbon and assign their priorities according to Cahn-Ingold-Prelog priority rules. In this case, compare R^1 with R^2 on the left sp^2-carbon. Likewise, compare R^3 with R^4 on the right sp^2-carbon.
3. If the higher priority groups are on the same side of the double bond (for example, R^2 and R^4), the alkene is a (*Z*)-alkene, as the higher priority groups are together (both below the double bond in this case). On the other hand, if the higher priority groups are on opposite sides (for example, R^1 and R^4), the alkene is an (*E*)-alkene, since R^1 is above the double bond but R^4 is below.

Note that alkenes with two identical substituents on either one of the two sp^2-carbons ($R^1 = R^2$ and/or $R^3 = R^4$) do not have stereoisomers. Double bond isomers of alkenes are considered **stereoisomers** due to restricted rotation along the double bond, and since each double bond may have either *E* or *Z* configuration, each double bond generates **a pair of stereoisomers**, similar to a chiral centre.

Background 4b. Position descriptors for carbons near multiple bonds

Since the presence of multiple bonds affects the reactivity characteristics at the carbon atoms nearby, we assign names to the different carbon positions relative to the multiple bond to generalise their properties. The sp^2-carbon within a C=C double bond is known as a **vinylic** carbon while the sp^3-carbon next to C=C double bond is known as an **allylic** carbon. The sp^3-carbon next to a C≡C triple bond is known as a **propargylic** carbon. The sp^3-carbon directly adjacent to a carbonyl group (C=O) is known as the α-carbon, and as we move further away from the carbonyl group, we continue labelling the carbons as β-carbon, γ-carbon, δ-carbon, and so on. As we will see later, benzene rings are aromatic systems and have extended conjugation, and the position next to a benzene ring is known as **benzylic**. Figure 4.3.5 shows the different positions described using sample molecules.

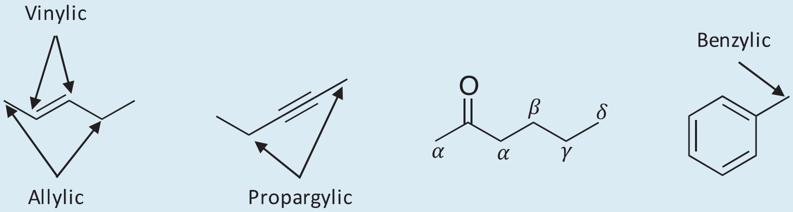


Figure 4.3.5. Diagram with arrows to show the different positions.

We may continue to look into allylic systems. Charged species, especially with charges on carbon, are usually unstable and may be stabilised by conjugation. **Carbocations** have a positive charge on carbon and **carbanions** have a negative charge on carbon. These charged carbon species are common intermediates in organic reactions, as will be discussed in later chapters. Conjugation is able to stabilise charges at allylic, propargylic and benzylic positions. We will use allylic systems as an example to discuss how conjugation affects charge distribution along the system. Allylic systems contain three p-orbitals that are able to overlap to form three molecular orbitals, and their π-systems are shown in Figure 4.3.6 for the allyl cation and allyl anion:

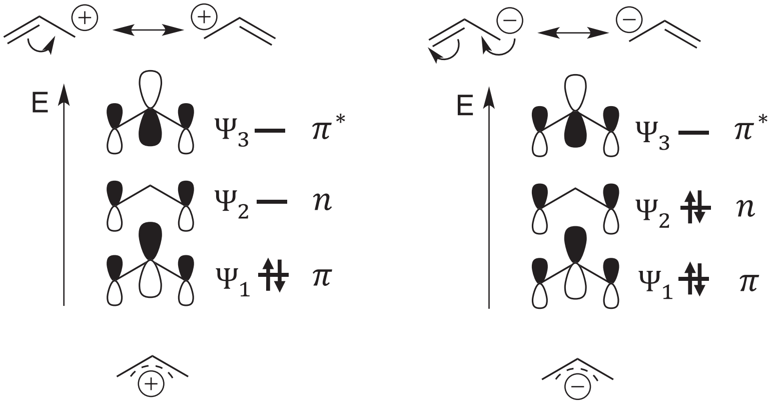


Figure 4.3.6. Frontier orbital picture for allylic cation and anion.

The three molecular orbitals formed include a π-bonding orbital, a non-bonding orbital (the p-orbital of the central carbon contributes zero coefficient) and a π^*-antibonding orbital. The coefficient of the central p-orbital is larger than the other two p-orbitals as it is only distributed in Ψ_1 and Ψ_3. Note that the delocalisation in allylic systems may be represented by resonance structures or by showing that the charge is delocalised over all three carbons, as shown in Figure 4.3.6. Both representations have their advantages and disadvantages, and we will use the frontier orbital diagram to explain their drawbacks. Looking at the allyl cation, we see that the two electrons are both in the Ψ_1 orbital. Since it is a cation, we are interested to find where the deficit in electron density is present. Since the coefficient of the p-orbital is greatest in the central carbon, the central carbon has the greatest electron density and the least positive charge. Thus, it is true that the positive charges are more significant at the two end carbons, but there is still a smaller coefficient of positive charge on the central carbon. The most accurate representation will be a hybrid of the two, but usually we will use one of the resonance structures to draw mechanisms. For the allyl anion, we see that both Ψ_1 and Ψ_2

are filled. In this case, since Ψ_2 has no contribution from the central p-orbital, the p-orbitals at the end carry greater electron density and thus the negative charges are more significant on the end carbons. Similarly, the accurate representation for the allylic anion is a hybrid of the two diagrams, but the resonance structures are used more commonly for the ease of drawing mechanisms.

Since we have discussed about allylic systems, we may have to redefine the concept of conjugation. No doubt that **alternating single and double bonds** build up a conjugated system, but a conjugated system is not limited to that. For example, an allylic cation or anion (with only one double bond) is also a conjugated system. The requirement of a conjugated system is just effective sideway overlap of three or more p-orbitals, so that electrons can be delocalized in these p orbitals. In hexa-1,3,5-triene, 3 pairs of electrons are delocalised in 6 p-orbitals (hence 6 molecular orbitals, which can accommodate a maximum of 12 electrons). In an allylic anion, 2 pairs of electrons are delocalised in 3 p-orbitals (hence 3 molecular orbitals, which can accommodate a maximum of 6 electrons).

Similar to the allylic system, many functional groups feature delocalisation of electrons over three atoms, such as amides, carboxylate and nitro groups. The structural feature of conjugated systems is that the system must be **planar** for all the p-orbitals to overlap effectively. This means that all atoms must be sp^2-hybridised, including the N in amides, unlike N in amines that are sp^3-hybridised. The three systems shown in Figure 4.3.7 are also conjugated systems with only one double bond.

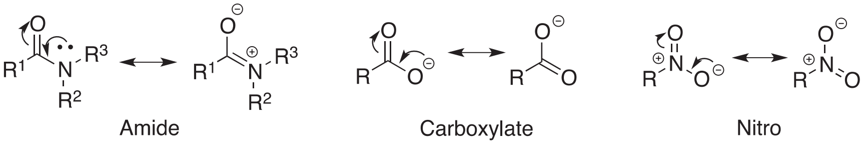


Figure 4.3.7. Conjugation in various functional groups.

Aromatic systems are special **conjugated systems that are cyclic**, such that the π-electrons are delocalised in a ring. The most frequently encountered aromatic system is **benzene**. All 6 carbon atoms in benzene are sp^2-hybridised such that benzene has a fully conjugated and planar system with parallel p-orbitals that can overlap effectively in a ring. Figure 4.3.8 shows the bonding in benzene and the MO diagram of benzene.

The MO diagrams of benzene and other conjugated hydrocarbons have been proposed by Erich Hückel and are known as **Hückel Molecular Orbitals**. By this method, all molecular orbitals for **conjugated cyclic systems** may be determined by the **polygon with the apex facing downwards**. The apex faces downwards because there is always one non-degenerate orbital with lowest energy, which is when all p-orbitals overlap in phase. This applies to any *n*-sided polygon as shown in Figure 4.3.9.

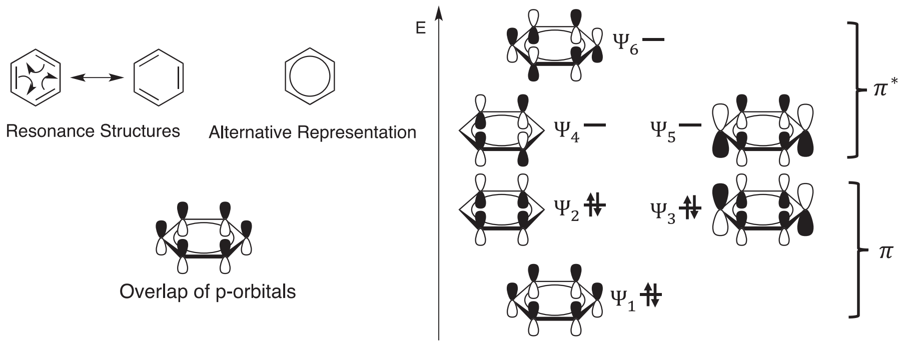


Figure 4.3.8. Bonding in benzene and frontier orbital picture of benzene.

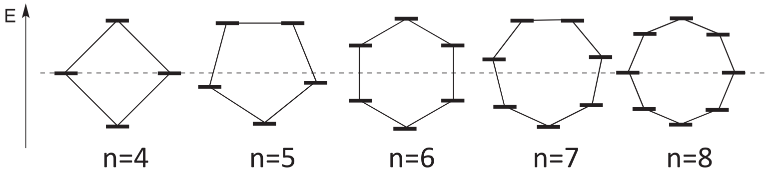


Figure 4.3.9. Hückel's MO diagrams for conjugated cyclic polygons.

A ring may be **aromatic**, **anti-aromatic** or **non-aromatic**. To determine the aromaticity, we may apply **Hückel's rule**, which states that an aromatic ring must fulfil all the following criteria:

1. **Monocyclic**: This rule is only theoretically justified for systems without fused rings, though we will discuss how to apply it to fused rings later.
2. **Planar**: The ring must be completely flat for the p-orbitals to overlap effectively
3. **Fully-conjugated**: Every atom in the ring must participate in the sharing of π-electrons.

We will look at 3 single rings in Figure 4.3.10 and derive the last condition for aromaticity.

Using Hückel's molecular orbitals, we may derive the molecular orbital diagram for the cyclic, fully-conjugated rings shown above. We see that benzene has a **closed shell structure**, which means that no molecular orbitals are half-filled. Thus, benzene is **aromatic** and exceptionally stable. On the other hand, cyclobutadiene and cyclooctatetraene both have 2 unpaired electrons in their nonbonding orbitals. These electrons are reactive and thus destabilise the molecules. This is the case in highly unstable and reactive cyclobutadiene, which is **anti-aromatic**. This gives us the last condition of aromaticity, which is that systems that satisfy the above three conditions with **(4n+2) π-electrons are aromatic** and those with **4n π-electrons are**

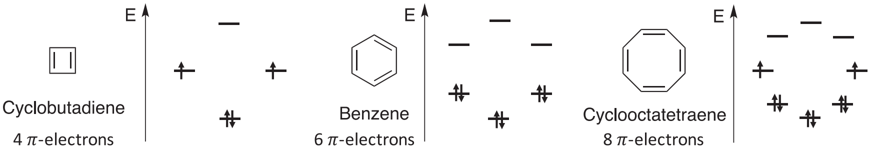


Figure 4.3.10. Applying Hückel's molecular orbitals to 3 sample conjugated rings.

anti-aromatic. Since anti-aromatic compounds are unstable, many compounds may adopt distorted shapes to avoid being aromatic. This is the case of cyclooctatetraene. It adopts a tub-shaped structure that is non-planar such that the p-orbitals cannot effectively overlap, and is **non-aromatic**.

As mentioned in Hückel's rule, it is only theoretically justified for monocyclic compounds. Many other compounds with fused rings or multiple connected rings may be aromatic as well, however their aromaticity is harder to determine. We have to **apply Hückel's rule to each individual ring**, and only when **there is a resonance structure where every ring fulfils Hückel's rule** then the compound is aromatic. We will look at some fused ring molecules in Figure 4.3.11.

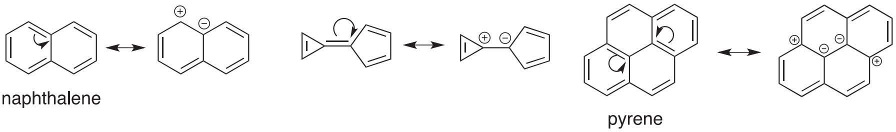


Figure 4.3.11. Fused ring molecules and their aromatic resonance structure.

Naphthalene has a total of 10 π-electrons, satisfying Hückel's rule to have $(4n+2)$ π-electrons, but this is the incorrect justification for its aromaticity. Instead, it is worthy to note that it has resonance structures where both six-membered rings have 6 π-electrons, thus it is aromatic. For the other two molecules, they have 8 and 16 π-electrons respectively, and would be anti-aromatic if we were to apply Hückel's rule directly. However, we may draw resonance structures for these molecules such that each ring will have $(4n+2)$ π-electrons. Thus, these molecules are also aromatic and follow reaction patterns of aromatic compounds. Hückel's rule works the best in monocyclic system, but becomes less clear with some polycyclic systems. Nevertheless, chemists can always rely on experimental results to prove whether a compound is aromatic or not, which is usually clear and unambiguous.

Aromatic compounds are not limited to hydrocarbons. Many heterocycles, rings that contain heteroatoms, are also aromatic, as long as they satisfy Hückel's rule. A few common examples are listed in Figure 4.3.12.

The heteroatoms have lone-pairs of electrons that may occupy either p-orbitals or sp^2-orbitals. Thus, these heteroatoms contribute 1 or 2 electron(s) to the π-electron system and help to fulfil Hückel's rule.

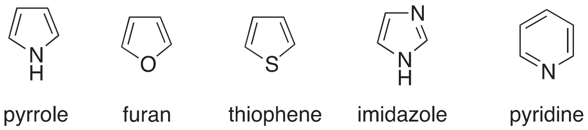


Figure 4.3.12. Common aromatic heterocycles.

Aromaticity is an important feature in organic compounds, as we will see in subsequent chapters. It is a strong driving force for some reactions to occur, while many reaction pathways do not proceed if they will cause a molecule to lose aromaticity. All in all, we must be able to immediately identify aromatic molecules and analyse their different reaction patterns as compared to non-aromatic molecules.

4.4 Acidity, Basicity, Nucleophilicity and Electrophilicity of Organic Compounds

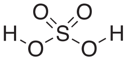
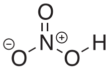
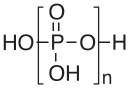
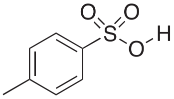
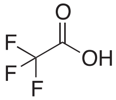
Organic reactions are mostly nucleophile-electrophile interactions driven by acids or bases. It is important to be able to immediately recognise the **role of a reagent** to predict the product of reactions. In the huge spectrum of organic reactions, there are way too many reagents and it is impossible to remember each reaction condition by heart. Instead, we must analyse the purpose of each reagent so that we are able to fine-tune reaction conditions by varying the reagents to fit the same role. In this chapter, we will introduce the common acids and bases, their differing strengths and applications, before defining nucleophiles and electrophiles and comparing them with acids and bases.

4.4.1 *Acids and bases*

In organic chemistry, the Brønsted-Lowry definition of acids and bases is most commonly applied. Thus, acids are proton donors while bases are proton acceptors. Recall that the stronger the acid, the weaker its conjugate base and vice versa. We will first take a look at common acids used in organic synthesis and common acidic protons in organic compounds.

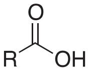
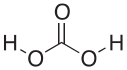
The first category of acids is **strong acids**, many of which are common inorganic acids. Strong acids are often used in acidic hydrolysis and are considered harsh conditions that may cause the compound to react at other undesired sites, thus the reaction conditions must be carefully controlled. Since many of the inorganic acids are interchangeable, we may sometimes write H_3O^+ to refer to a general aqueous acid. For strong acids, the pK_a is usually very small and we may consider the first proton to be fully dissociated. A list of strong acids is given in Table 4.4.

Table 4.4. Table of strong acids.

Strong acids	**Formula**	**Structure**	**Remarks**
Hydrochloric Acid	HCl	H−Cl	
Sulfuric Acid	H_2SO_4		Slightly oxidising
Nitric Acid	HNO_3		Strongly oxidising, used as a reagent for nitration
Polyphosphoric Acid	PPA		Strong acid, useful in cyclisation reactions
p-Toluenesulfonic Acid	TsOH		Organic sulfonic acids are strong organic acids that are useful for their high solubility in organic solvents
Trifluoroacetic Acid (TFA)	CF_3COOH		TFA is a strong organic acid, its high acidity comes from the inductive effect of 3 fluorine atoms

The next category of acids are **weak acids** that are commonly employed as acidic buffers. They can provide an acidic environment to speed up reactions but are not too strong to cause undesirable hydrolysis. The acidity is measured by it pK_a value, and the **lower the pK_a, the stronger the acid**. A list of weak acids is given in Table 4.5.

Table 4.5. Table of weak acids.

Weak acids	**Formula**	**Structure**	pK_a	**Remarks**
Carboxylic Acids	RCO_2H		For $R = Et$, $pK_a = 4.76$	Useful for amines reacting with carbonyl group
Carbonic Acid	H_2CO_3		$pK_{a1} = 6.37$ $pK_{a2} = 10.32$	Bicarbonate (HCO_3^-) and carbonate (CO_3^{2-}) are useful as slightly basic buffers

Lastly, we will compare **acidity of organic protons**. This is very important as we must be able to determine which proton(s) will be preferentially deprotonated on the addition of base. These protons can be deprotonated to generate reactive anions. Such protons may be generally classified into two categories, **protons bonded to heteroatoms** and **protons bonded to carbon**. Generally, protons bonded to heteroatoms are more acidic because heteroatoms are more electronegative and better at stabilising the negative charges.

Table 4.6 shows the acidity of protons bonded to heteroatoms:

Table 4.6. Table of acidic protons bonded to heteroatoms.

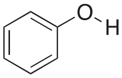
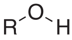
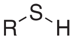
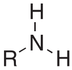
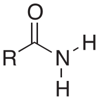
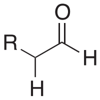
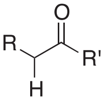
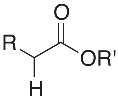
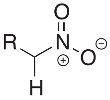
Acidic protons	**Formula**	**Structure**	pK_a	**Remarks**
Phenol	PhOH		9.95	Exceptionally acidic as an alcohol due to negative charge stabilised by resonance in benzene ring
Alcohols	R-OH		16–18	Water also falls into this category, with $pK_a = 15.7$
Thiols	R-SH		10.5	Thiols are more acidic than alcohols
Amines	R-NH$_2$		36	Amines usually act as bases
Amides	R-CONH$_2$		15	Amide protons are more acidic than most α-protons and are preferentially deprotonated

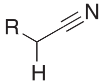
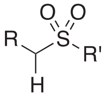
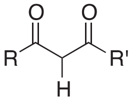
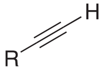
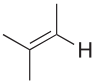
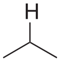
Table 4.7 shows the acidity of protons bonded to carbon:

Table 4.7. Table of acidic protons bonded to carbon.

Acidic protons	**Structure**	pK_a
α-proton of aldehyde		17 (Aldehyde proton –CHO is not acidic)
α-proton of ketone		20
α-proton of ester		25
α-proton of nitro		9

(*Continued*)

Table 4.7. (*Continued*)

Acidic protons	**Structure**	pK_a
α-proton of nitrile		25
α-proton of sulfone		30
α-proton of 1,3-dicarbonyl compounds		9–13
Alkyne (sp) proton		26
Alkene (sp^2) proton		45
Alkane (sp^3) proton		50

After seeing all the pK_a values, we have a good idea of the varying acidity of protons. It is handy to keep the relative acidity of protons in mind when attempting to solve organic chemistry problems. Now we will proceed to consider the **factors that affect acidity**:

1. **Bond strength** of H-X:

Since electronegativity decreases down the group as the atoms get bigger, it may seem that acidity should decrease going down the group. However, acidity actually **increases down the group**, which means that it must have increased due to a different reason. Down the group, the size of the atom increases significantly due to the increase in number of electron shells, which leads to an increase in the H-X bond length and a corresponding decrease in H-X bond strength. Thus, it is easier to break the H-X bond for the proton to dissociate and HX is more acidic. A comparison of thiol (R-S-H, $pK_a = 10.5$) with alcohol (R-O-H, $pK_a = 16–18$) is a good example.

2. **Electronegativity** of the atom which carries the negative charge:

Electronegativity measures how much an atom is willing to accept an extra electron and to become negatively charged. Thus, the negative charge is more stable on heteroatoms such as chlorine, oxygen or nitrogen rather than on carbon. When comparing acidity of protons directly bonded to heteroatoms, we see that the ability to stabilise a negative charge **increases across the period**. If the negative charge is more stabilised, dissociation of the proton is more favourable and acidity is higher.

3. **Inductive Effect**:

Other than electronegativity, there are other effects that contribute to the stabilisation of the negative charge that increases the acidity. The inductive effect stabilises the negative charge by having **electron-withdrawing substituents** near the negative charge, such that the charge is spread across more atoms and less concentrated. Inductive effects are σ-effects that happen through the **polarisation of σ-bonds**, as electronegative atoms pull electron density in the σ-bonds towards them. This effect is obvious in trifluoroacetic acid (TFA), which is a strong acid due to the strongly electron-withdrawing nature of CF_3 group that gives it a pK_a of −1 as compared to acetic acid with pK_a of 4.76.

4. **Resonance Effect**:

Just as how inductive effect is a σ-effect, the **resonance effect is a π-effect**. The resonance effect comes from conjugation, as the negative charge can be delocalised over a π-system. This is significant in highly conjugated molecules, such as aromatic compounds, and explains why phenol is a lot more acidic than normal alcohols. Carboxylic acids are also acidic due to the resonance splitting the negative charge between the 2 oxygens. α-protons of electron-withdrawing groups are slightly acidic due to the negative charge on carbon being stabilised through resonance into the electron-withdrawing group.

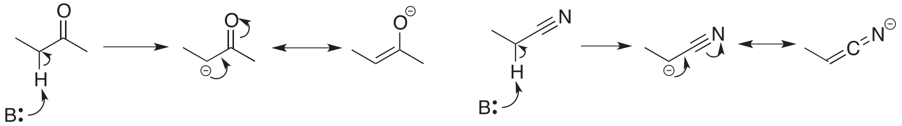


Figure 4.4.1. Deprotonation of α-proton and stabilisation of anion by conjugation.

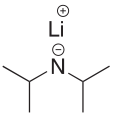
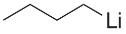
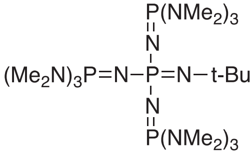
Figure 4.4.1 shows α-protons being deprotonated to generate unstable carbanions that can be stabilised by resonance to adjacent electron-withdrawing groups. These groups have electronegative atoms that can stabilise the negative charge.

5. **Hybridisation** of atom carrying the negative charge:

We discuss hybridisation when we consider a carbon atom to carry the negative charge, as carbon atoms may be sp, sp^2 or sp^3-hybridised. The new hybrid orbital will have different properties depending on how the original atomic orbitals are mixed. For example, an sp-orbital will have 50% s-character and 50% p-character, while an sp^3-orbital will have 25% s-character and 75% p-character. Since s-orbitals are held closer to the nucleus than p-orbitals, s-electrons have greater penetrating power than p-electrons. This means that the extra electron from the anion will be more stable in an s-orbital rather than p-orbital. By this logic, the anion is most stabilised on an sp-hybridised carbon and least stabilised on an sp^3-hybridised carbon, which explains the trend of acidities of alkyne, alkene and alkane protons. Generally, alkene and alkane protons are extremely difficult to remove due to their high pK_a, but deprotonation of alkyne protons provide useful synthetic possibilities.

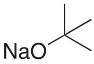
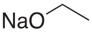
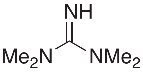
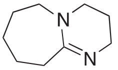
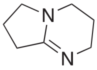
Now that we have discussed the common acids encountered in organic chemistry, we will move on to the bases. Since bases are proton acceptors, we must consider not only their electronic properties (strength and basicity) but also their steric properties to determine whether they are able to approach certain protons. When discussing the strength of bases (B^-), we consider their pK_{aH}, which is the pK_a of the conjugate acid (HB) of the base. The weaker the conjugate acid, the greater the pK_{aH} and the stronger the base. Bases may either be anionic or neutral. We will first look at commonly used bases that are very strong.

Table 4.8. Table of very strong bases.

Very strong bases	**Formula**	**Structure**	**Remarks**	pK_{aH}
Lithium Diisopropylamide (LDA)	$LiN(i\text{-}Pr)_2$		Extremely bulky base commonly used to prepare enolates	36
Alkali Metal Hydrides	NaH KH	$M^+ H^-$	Small and versatile	35
Butyllithium	BuLi		Small base that may also act as a nucleophile	60
Phosphazene Base	$P_4\text{-}t\text{-}Bu$ (one example)	 $(Me_2N)_3P{=}N{-}P(=N{-}P(NMe_2)_3)_2{=}N{-}t\text{-}Bu$	Strong neutral base that is non-nucleophilic	30

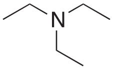
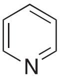
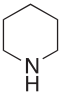
The very strong bases listed in Table 4.8 can easily pick off acidic protons from molecules, even those only weakly acidic. However, with very strong bases, the reactions may end up being kinetically controlled instead of thermodynamically controlled, and the selectivity may be undesirable. Table 4.9 shows other basic conditions that are not too strong which allow for better thermodynamic control. Alkoxides are common bases in this category and their properties depend largely on the group connected to the oxygen atom.

Table 4.9. Table of strong bases.

Strong bases	**Formula**	**Structure**	**Remarks**	pK_{aH}
Sodium Hydroxide	NaOH	Na$^+$ OH$^-$	Usually used in aqueous conditions for hydrolysis. May often act as a nucleophile	157
Sodium tert-Butoxide	NaOt-Bu		Bulky base used to selectively deprotonate the most accessible proton	16–18
Sodium Methoxide Sodium Ethoxide	NaOMe NaOEt	 	Used in their corresponding alcoholic solvents and may act as nucleophiles as well	
Tetramethylguanidine (TMG)	$HNC(NMe_2)_2$		Neutral non-nucleophilic base that may be used for alkylations	13
Bicyclic Nitrogen Bases	DBU and DBN	 DBU  DBN	Neutral non-nucleophilic bases that are useful for simple elimination reactions	14

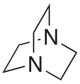
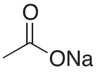
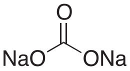
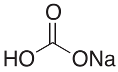
Strong bases (and strong acids) are more difficult to employ in organic chemistry as they are highly reactive and usually lead to unnecessary side reactions. Thus, we tend to choose reagents that are as mild as possible. Weak bases are usually neutral amine bases. Table 4.10 shows the common weak bases used to generate a mild basic environment.

Table 4.10. Table of weak bases.

Weak bases	**Formula**	**Structure**	**Remarks**	pK_{aH}
Triethylamine (TEA)	Et_3N		Bulky non-nucleophilic amine base	11
Pyridine	C_5H_5N		Heterocyclic aromatic amine base	5.2
Piperidine	$C_5H_{11}N$		Saturated heterocyclic amine base	11

(*Continued*)

Table 4.10. (*Continued*)

Weak bases	**Formula**	**Structure**	**Remarks**	pK_{aH}
Quinuclidine	$C_7H_{13}N$		Bridgehead compound with higher availability of nitrogen lone pair	11
1,4-Diazobicyclo [2.2.2]octane (DABCO)	$C_6H_{12}N_2$		Presence of another nitrogen reduces the basicity of DABCO	8.8 (3.0)
Sodium Acetate	NaOAc		Conjugate base of acetic acid that can be used together to create a buffer	4.8
Sodium Carbonate Sodium Bicarbonate	Na_2CO_3 $NaHCO_3$	 	Useful in various reactions and during work-up to neutralise any acid generated	10.3 (6.3)

Trends in basicity are exactly opposite the trends in acidity, since the basicity depends entirely on the acidity of the conjugate acid. Thus, the conjugate base of a weak acid will be a strong base and the conjugate base of a strong acid is a weak base. This is easy to rationalise since a strong acid is willing to let go of its proton and thus its conjugate base will not have a large tendency to gain back that proton. On the other hand, it is difficult to remove a proton from a weak acid and thus the conjugate base will have a large tendency to gain back the proton.

4.4.2 *Nucleophiles and electrophiles*

Arguably, the most important concept in organic chemistry is the concept of nucleophiles and electrophiles, as organic reactions are mostly reactions between them. The concept of nucleophiles and electrophiles is similar to acids and bases, in the sense that nucleophiles and electrophiles react with each other to form stable chemical species. However, instead of talking about proton affinity, the concept of nucleophiles and electrophiles deal with **electron affinity**. **Nucleophiles are "nucleus-loving" species that are electron donors** while **electrophiles are "electron-loving" species that are electron acceptors**.

To understand the concept of nucleophiles and electrophiles fully, we must understand the concept of organic reactions. With the exception of special reactions (radical reactions, pericyclic reactions), most organic reactions are polar reactions between nucleophiles and electrophiles. These reactions primarily occur through **charge interactions** and **orbital interactions**, as shown in Figure 4.4.2.

Attraction between opposite charges

Attraction between lone pair and dipole

Figure 4.4.2. Charge interactions bring nucleophiles and electrophiles together to react.

Charge interactions are electrostatic attractions between opposite charges. They do not refer only to ionic interactions between ions, but more commonly dipole-dipole interactions. Due to electronegativity differences, carbon-heteroatom bonds are usually polarised. Dipole-dipole interaction between electron-rich species (nucleophiles) and electron-deficient species (electrophiles) bring these species together to react.

Orbital interactions refer to the favourable orbital overlap between molecules that allow them to react. Bond formation and cleavage are due to electrons being transferred between different orbitals, as electrons in antibonding orbitals break bonds while electrons in bonding orbitals form bonds. For example, the reaction of alkenes with bromine happen entirely by the orbital interaction between the π-orbital of the alkene and the σ^*-orbital of bromine. The donation of electrons from the π-orbital of the alkene removes electrons from the bonding orbital of the alkene, breaking the π-bond of the alkene. The electrons enter the σ^*-orbital of bromine, breaking the σ-bond in bromine. This forms a new bond between an alkene carbon and a bromine atom. In this case, both reactants are neutral and do not have a dipole. The reaction occurs entirely based on orbital interactions.

Most reactions are a combination of charge and orbital interactions. The charge interactions bring the reactants together for orbital overlap, leading to the breaking and forming of bonds. Through the interactions, electrons flow between the reactants, from nucleophile to electrophile. Thus, a **nucleophile reacts using its Highest Occupied Molecular Orbital (HOMO)** while **an electrophile reacts using its Lowest Unoccupied Molecular Orbital (LUMO)**.

The effectiveness of orbital overlap depends on how close the energies of the overlapping orbitals are. Usually, the LUMO of a molecule is an antibonding orbital while the HOMO of a molecule is a bonding orbital. Energies of antibonding orbitals are usually a lot higher than bonding orbitals. Thus, a **good nucleophile should have a high energy HOMO** while a **good electrophile should have a low energy LUMO**.

Let us first consider examples of electrophiles. Electrophiles are species that accept electrons, so they must have a low energy **empty orbital**. The electrophilicity, or strength of an electrophile, is determined by the energy of the empty orbital, with a lower energy indicating a better electrophile.

Electrophiles may be positively charged to indicate an empty orbital (such as carbocations), or neutral with an empty orbital (such as BR_3). Carbon atoms may also be electrophilic if they are bonded to highly electronegative heteroatoms through single or double bonds. For such species, a bond with the heteroatom will break when a nucleophile attacks it.

Now, we will look at nucleophiles and their strength. Since nucleophiles are electron donors, they must have a **lone pair of electrons** to donate to the electrophile. Nucleophiles may be either anionic or neutral. We will now look at a few factors that determine the strength of a nucleophile, known as nucleophilicity:

1. Charge

Generally, anionic nucleophiles are stronger nucleophiles than neutral nucleophiles, since their negative charge means that they are more willing to give away their extra lone pair of electrons compared to a neutral species. However, it is incorrect to say that any anionic nucleophile is stronger than neutral nucleophiles as we will see that there are many other factors that affect nucleophilicity. What we can say is that for any neutral nucleophile, its corresponding anionic nucleophile is definitely a stronger nucleophile. For example, $\mathrm{OH^-}$ is a stronger nucleophile than $\mathrm{H_2O}$ and $\mathrm{NH_2^-}$ is a stronger nucleophile than $\mathrm{NH_3}$.

2. The element that carries the lone pair of electrons

The general trend is that **nucleophilicity decreases across a period and increases down a group**. For example, if we look at the first period, the nucleophilicity trend is:

$$\mathrm{CH_3^-} > \mathrm{NH_2^-} > \mathrm{OH^-} > \mathrm{F^-}$$

This follows the trend of increasing electronegativity across the period, which means that the negative charge is increasingly more stable. A more stable negative charge corresponds to a lower energy HOMO which means lower nucleophilicity. Going down a group, the nucleophilicity increases. Considering group 17, the nucleophilicity trend is:

$$\mathrm{I^-} > \mathrm{Br^-} > \mathrm{Cl^-} > \mathrm{F^-}$$

This follows the trend in electronegativity as well, as larger ions hold on less tightly to their lone pair of electrons and are more willing to donate them to electrophiles. This trend is also dependent on the solvent used in the reaction.

Background 4c. Solvents in organic chemistry

Solvents are an essential part in organic synthesis as they provide the medium for the reaction to take place. Generally, we classify solvents into three categories: **Non-polar solvents**, **polar aprotic solvents** and **polar protic solvents**.

The polarity of solvents follows a continuous trend and it is important to choose the right polarity of solvent to use for each reaction. Non-polar solvents are usually hydrocarbons such as hexane, benzene and toluene. Most other organic solvents contain heteroatoms which makes them polar solvents.

(*Continued*)

Background 4c. (*Continued*)

Polar solvents can be further classified into protic and aprotic solvents. Protic solvents have labile hydrogen atoms (usually bonded to electronegative atoms such as oxygen and nitrogen) that can form hydrogen bonds with the species in the reaction, especially ions. This allows better solvation of ions that can stabilise them and reduce their reactivity. Examples of polar protic solvents include alcohols, carboxylic acids and water. Polar aprotic solvents include acetone, ethyl acetate and acetonitrile.

In polar protic solvents, the trend holds true since larger ions are less solvated than smaller ions which leave them more reactive. However, in polar aprotic solvents, the nucleophilicity trend may be reversed to follow the trend in basicity.

4.4.3 *Nucleophilicity versus basicity*

As we have seen above, nucleophilicity parallels basicity most of the time. This is understandable as the strength of a base is determined by how well it can abstract a proton, which is dependent mainly on how much its lone pair of electrons is willing to accept a proton. However, we must take note that nucleophilicity is not the same as basicity, and there are situations where the trends are reversed.

Nucleophiles are species that attack electrophiles, which are electron deficient centres, while bases only abstract protons. Protons are small atoms usually sticking out of molecules that make them easy to abstract, thus we have large bulky strong bases such as LDA. These bases are designed to be bulky so as to reduce their nucleophilicity, as it is much harder to approach an electrophilic carbon centre than to abstract a proton. Thus, a key consideration when comparing basicity and nucleophilicity is the **steric property of the molecule**.

We will look at some examples of nitrogen compounds to see if they are good nucleophiles or bases. We may measure nucleophilicity from the rate of reaction with methyl iodide and basicity using pK_{aH} values, and we will compare the 3 nitrogen-containing molecules shown in Figure 4.4.3.

All 3 molecules are tertiary amines, but their basicity and nucleophilicity differ significantly. Quinuclidine is the most basic as well as most nucleophilic as the cyclic

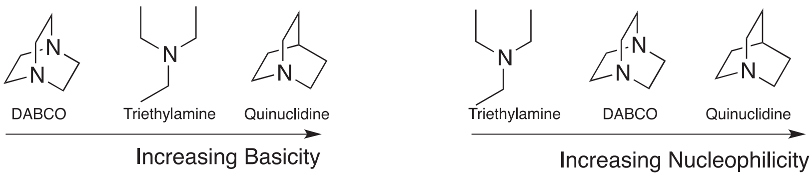


Figure 4.4.3. Basicity and nucleophilicity comparisons for 3 amine bases.

structure ties all three alkyl groups together at the back, exposing the nitrogen lone pair to make it more reactive.

Comparing DABCO with trimethylamine, we see that DABCO is less basic as the two nitrogen atoms withdraw electron density from each other. However, for nucleophilicity, the trend is reversed. This is because triethylamine has 3 free ethyl groups that make it very bulky and hinder it from approaching electrophilic centres. However, triethylamine is good at abstracting small protons as a base. On the other hand, DABCO is similar to quinuclidine as the alkyl chains are tied behind by the cyclic structure, and its lone pair is not sterically hindered to act as a nucleophile. DABCO is still a weaker nucleophile than quinuclidine due to the nitrogen atoms withdrawing electron density from each other. The special property of DABCO makes it a non-basic nucleophile that is especially useful in nucleophilic catalysis.

4.5 Radical Chemistry

Most organic reactions are polar reactions, reactions where electron pairs move and transfer between molecules. However, in special cases, bonds are broken such that a single electron from the bond goes to each one of the two fragments. This causes the products of bond cleavage to be radicals, which are molecules with an unpaired electron. Unpaired electrons are very reactive, and in this chapter, we will look at how they react and how to control their reactivity to obtain our desired product.

4.5.1 *Radical structure and stability*

Radicals are molecules or ions with an **unpaired electron**. In general, they may be **classified by structure** into 2 categories: σ-radicals and π-radicals, depending on whether their unpaired electron lies in an orbital with s-character or a p-orbital.

In Figure 4.5.1, the benzene radical is a σ-radical because the single electron lies in a sp^2-hybrid orbital while the *tert*-butyl radical is a π-radical as the single electron lies in a p-orbital. From the structure, it can be seen that π-radicals are much more stable than σ-radicals due to their stabilization from hyperconjugation. We will look further into the stability of radicals later in this section.

Figure 4.5.1. Examples of σ-radical and π-radical.

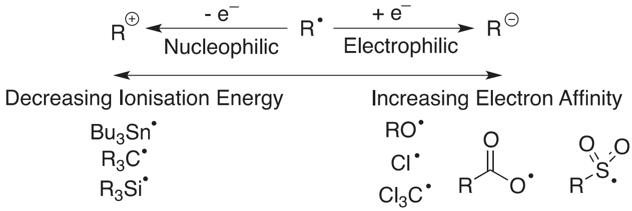


Figure 4.5.2. Comparison of nucleophilic and electrophilic radicals and some examples.

Radicals may also be **classified by reactivity** into 2 categories: electrophilic and nucleophilic radicals. Unlike polar reagents, radicals are **ambiphilic**, having the ability to act as both nucleophiles and electrophiles. This is because radicals can gain greater stability either by acting as a nucleophile (losing the unpaired electron) or by acting as an electrophile (gaining an electron to form a lone pair). By reacting as a nucleophile or an electrophile, the radical ends up as a cation or an anion respectively. Depending on the stability of the cation and the anion, the radical will have a greater tendency to react as either a nucleophile or an electrophile, which allows us to classify them into nucleophilic and electrophilic radicals, as shown in Figure 4.5.2.

While radicals are highly reactive and unstable species, there are still many factors that contribute to their stability. By comparing their stability, we are able to predict the feasibility of reactions. Note that radical stability is similar to carbocation stability as they are governed by a similar set of factors.

1. Thermodynamic stability

Thermodynamic stability comes from the combination of all the factors that will be mentioned below, and is a simple way to quantitatively examine radical stability. Radicals are always generated by a homolytic bond dissociation to form 2 radicals. Thermodynamically, the bond strength will determine the feasibility of the reaction and how stable the radical is, as a weak bond would mean that it is easier to form the radicals and that the radicals will not recombine as readily to form a molecule.

2. Hyperconjugation

Hyperconjugation is the **donation of electron density from a parallel σ-bond** to the p-orbital containing the single electron. This effect is weaker than conjugation as electrons in σ-orbitals are held tighter than electrons in π-orbitals. Figure 4.5.3 shows a *tert*-butyl radical being stabilised by hyperconjugation.

In the case of the *tert*-butyl radical shown above, every methyl group can be rotated such that one C-H bond is parallel to the p-orbital containing the unpaired electron. Thus there can be 3 hyperconjugation interactions to stabilise the radical. This explains the trend for the radical stability to be: Methyl<Primary<Secondary< Tertiary, due to the greater amount of stabilisation from hyperconjugation.

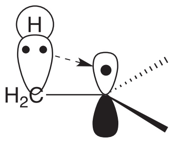


Figure 4.5.3. Hyperconjugation in *tert*-butyl radical.

3. Conjugation

Conjugation is the donation of electron density from an adjacent π-bond, and it can also be referred to as resonance. The effect has been extensively discussed in chapter 4.3, and it is able to stabilise the radical by providing additional electron density to the radical such that the effects of the unpaired electron is shared across all the atoms in the conjugated system and not localised on one atom. This effect commonly applies to allylic and benzylic radicals.

4. Adjacent lone-pair donating heteroatom

A lone-pair donating heteroatom may donate electron density from its lone pair to stabilise the radical, such that the effect of the unpaired electron is shared with the heteroatom. The effectiveness of stabilisation depends on how willing the heteroatom is to donate its lone pair to the radical. The stabilities of carbon radicals next to heteroatoms are arranged in increasing order as shown in Figure 4.5.4.

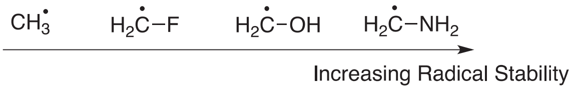


Figure 4.5.4. Stability series of radicals by adjacent heteroatom.

5. Electronegativity of the atom with unpaired electron

The electronegativity of the atom where the unpaired electron is situated will affect the stability of the radical. The higher the electronegativity, the less stable the radical. This is because the atoms with high electronegativity are the most prone to gaining an additional electron to become more stable. Radicals with the unpaired electron on different atoms are listed in decreasing order of stability in Figure 4.5.5.

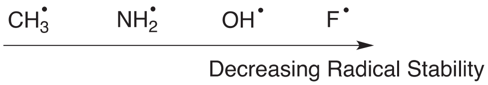


Figure 4.5.5. Stability series of radicals due to electronegativity of atom with unpaired electron.

6. Hybridisation of atom with lone electron

The original hybridisation of the atom before the homolytic bond cleavage will determine how easy it is to break the bond and remove an electron. This is easiest for an sp^3-orbital, followed by an sp^2-orbital and most difficult for an sp-orbital. This is because the electrons in orbitals with higher s-character are held closer to the nucleus and tighter than electrons in orbitals with higher p-character, as s-orbitals are closer to the nucleus than p-orbitals. It is important to note that forming a radical from an sp^3-orbital will cause the atom to change to sp^2-hybridisation with the single electron in the p-orbital such that it is a π-radical, which is stabilised by hyperconjugation. However, radicals generated from sp^2 and sp-orbitals will stay as σ-radicals, which are much less stable.

Since radicals are ambiphilic, they may be stabilised by both electron-donating and electron-withdrawing substituents. This important property of radicals may be demonstrated by the MO diagram in Figure 4.5.6.

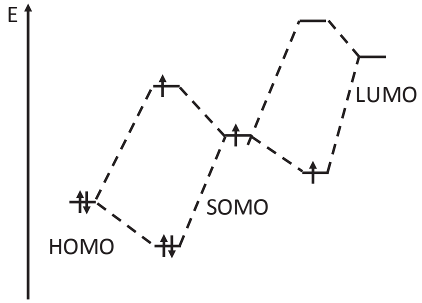


Figure 4.5.6. The stabilisation shown on a MO diagram through interaction with HOMO and LUMO.

As we can see from the MO diagram, the SOMO (Singly-Occupied Molecular Orbital) electron can be stabilised and moved to a MO with lower energy, regardless of whether the stabilisation is from an electron-donating or electron-withdrawing group.

Despite stabilising effects, radicals are still generally highly unstable and reactive species that have a very short life span. However, there exists a special class of radicals known as **persistent radicals** that can prevent self-termination through kinetic and

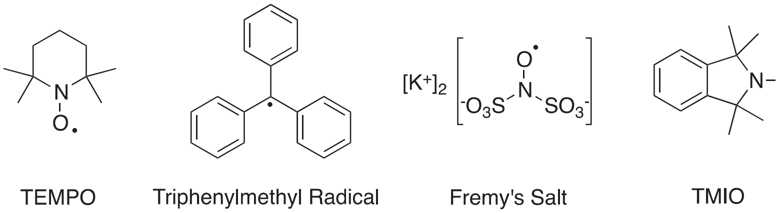


Figure 4.5.7. Examples of persistent radicals.

thermodynamic factors. As they do not self-terminate, they are able to participate in cross-coupling reactions to generate the major product. Some of these radicals are also important organic reagents, such as (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl (TEMPO), which is a commonly used oxidising agent. These radicals are thermodynamically stabilised by hyperconjugation, conjugation and adjacent lone pair effects, and are kinetically inert due to steric crowding at the radical site. Examples of persistent radicals are shown in Figure 4.5.7.

4.5.2 *Radical initiation*

We need to generate radicals reliably to kick off radical chain reactions. Generally, radicals may be generated through 3 methods: thermolysis, photolysis, and redox processes. **Thermolysis** is the homolytic bond cleavage driven by **heat**. **Photolysis** is the homolytic bond cleavage driven by **energy from light**. Bond cleavage may also be driven by γ-rays in the case of radiolysis and ultrasound in the case of sonolysis, but applications of such methods are limited. **Redox processes** involve electron transfer to molecules and ions such that radicals may be formed by heterolytic cleavage too.

The key factor in homolytic cleavage is the strength of the bond to be cleaved. We choose molecules with **weak covalent bonds** such that these bonds may be cleaved easily without use of harsh reaction conditions. We will look at some of such compounds useful for radical reactions:

1. Peroxides and Diacylperoxides

Peroxides have a weak $O{-}O$ bond with a bond energy of around $150\ \mathrm{kJ/mol}$. This makes such bonds easily cleaved by heat or light to generate radicals. Common peroxides used as initiators are *tert*-butyl peroxide and di-*tert*-butyl peroxide, as the *tert*-butyl group is able to stabilise the product radical through both inductive and steric factors. The homolytic cleavage of $O{-}O$ bonds in *tert*-butyl peroxide and di-*tert*-butyl peroxide is shown in Figure 4.5.8.

Diacylperoxides form resonance stabilised radicals, thus the bond dissociation energy of $O{-}O$ bonds in diacylperoxides are even weaker, usually around 125 kJ/mol.

The R group of the diacylperoxide does not significantly affect the dissociation, and the common R groups are phenyl and *n*-nonadecyl.

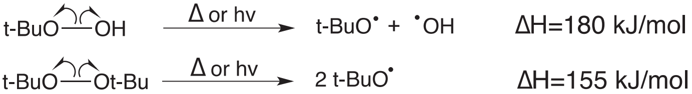


Figure 4.5.8. Radical formation through homolysis of $O{-}O$ bond of peroxides and their bond energies.

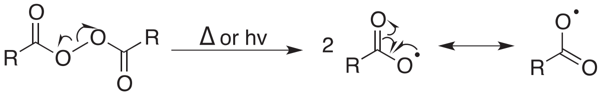


Figure 4.5.9. Radical formation through homolysis of $\mathrm{O{-}O}$ bonds of diacylperoxides and the stabilisation of such radicals by conjugation.

2. Azocompounds

Azocompounds contain a $\mathrm{N{=}N}$ double bond in the centre of the molecule that can leave as nitrogen gas, generating 2 radicals in the process. Due to the exceptional stability of nitrogen gas and the favourable entropy change from gas formation, the reaction is highly favourable. The most commonly used radical initiator 2,2′-azobisisobutyronitrile (AIBN) falls in this category. The reaction scheme to generate radicals from AIBN is shown in Figure 4.5.10.

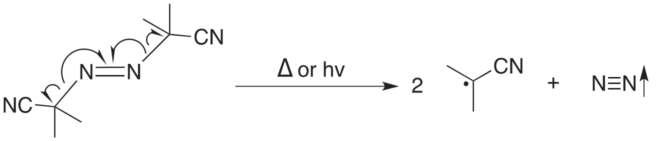


Figure 4.5.10. Decomposition of AIBN to form 2 radicals and nitrogen gas.

3. Halogens and Halides

Halogen compounds have weak covalent bonds in general. In particular, iodine has a bond dissociation energy of $150\ \mathrm{kJ/mol}$, similar in strength to $\mathrm{O{-}O}$ bonds in peroxides. This makes iodine compounds unstable in light and they are usually stored in dark containers to prevent decomposition. This property makes them good radical initiators as they decompose in heat or light to generate 2 radicals readily. Carbon-halogen bonds are also relatively weak and may be broken using ultraviolet light, but this process is more difficult.

4. Nitrites

Organic nitrites have a weak $\mathrm{N{-}O}$ bond that may be cleaved homolytically by ultraviolet light to yield an oxygen radical and a nitrogen monoxide radical, as shown in Figure 4.5.11.

Figure 4.5.11. Generation of radicals from nitrite.

5. Organometallic Compounds

Metal-metal and metal-carbon bonds may be cleaved homolytically by light to form metallic radicals. Common metal-metal bonds that may be cleaved include $\mathrm{Sn{-}Sn}$, $\mathrm{Se{-}Se}$ and $\mathrm{Mn{-}Mn}$ bonds. Common metal-carbon bonds that can be cleaved come from organocobalt and organomercury compounds.

Other than breaking weak bonds homolytically, we may generate radicals through redox processes, as shown in Figure 4.5.12.

The oxidising and reducing reagents are usually metals. Alkali metals, Sm, Cu, Ru and Fe are reducing while Ag^{2+}, Pb^{4+}, Ce^{4+} and Mn^{3+} are oxidising. These metals may react with many common functionalities such as carbonyls, alcohols, carboxylic acids and aromatic compounds to generate radicals.

$$\text{Reduction:}\quad R{-}X + e^- \longrightarrow [R{-}X]^{\ominus\bullet} \longrightarrow R^\bullet + X^\ominus$$

$$R^\oplus + e^- \longrightarrow R^\bullet$$

$$\text{Oxidation:}\quad R{-}X - e^- \longrightarrow [R{-}X]^{\oplus\bullet} \longrightarrow R^\bullet + X^\oplus$$

$$R^\ominus - e^- \longrightarrow R^\bullet$$

Figure 4.5.12. Generation of radicals through redox processes.

4.5.3 *Radical reaction pathways and mechanisms*

Radicals react through **chain reactions**, which are reactions that proceed to generate reactive species that can further react, leading to a chain of reactions. Once radicals are generated through initiation, they propagate by reacting with other non-radical species to form new radicals. Through the chain reaction, the product is generated. In radical reaction mixtures, the concentration of radicals is always very low such that the rate of self-coupling of the radicals is very low. This means that termination steps where two radicals meet to generate a non-radical product are unlikely and most of the products are generated through **propagation**.

Here we will state some of the common radical reaction pathways:

1. Radical Abstraction

Radical abstraction is the most common reaction pathway for radicals. It is the reaction where a radical removes an atom from a molecule. The radical becomes a stable molecule after gaining the atom while the molecule becomes the new radical. Usually, the atoms that are abstracted are halogen and hydrogen atoms. The general mechanism is shown in Figure 4.5.13.

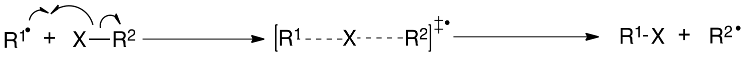


Figure 4.5.13. General mechanism for radical abstraction.

This is a **bimolecular homolytic substitution** reaction, that we may abbreviate as **S_H2 reaction**. The transition state is a linear transition state where the entering group and leaving group lie on the same line as the central atom.

2. Radical Addition

This involves the addition of the radical to a multiple bond. The multiple bond is most commonly a C=C double bond that can be found in alkenes. However, there may also be radical addition to alkynes, benzenes, carbonyls and oxygen.

The regioselectivity of radical addition to multiple bonds follows **anti-Markovnikov rule** as shown in Figure 4.5.14, which makes it a useful complementary reaction to normal electrophilic addition. This reaction is thermodynamically favourable due to the breakage of a weaker π-bond to form a stronger σ-bond. The regioselectivity is such that the radical will add to the less substituted side of the alkene as it forms a more stable radical intermediate with more substituents groups and the radical faces less steric hindrance. The reaction of alkynes is slower than alkenes as the intermediate sp^2-radical is much less stable than the sp^3-radical formed from reaction of alkene. The rate of the reaction depends on electronic factors, where nucleophilic radicals react faster with electron-deficient alkenes and electrophilic radicals react faster with electron-rich alkenes. The steric effects, especially the bulkiness of the radical, may also affect the rate. The polarity of carbonyls decides its reactivity with electrophilic and nucleophilic radicals, as shown in Figure 4.5.15.

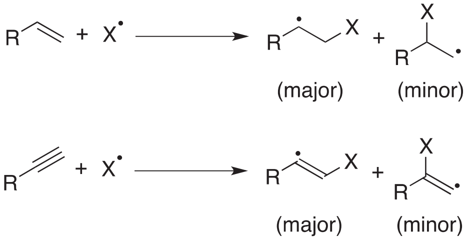


Figure 4.5.14. Addition of radicals to alkenes and alkynes.

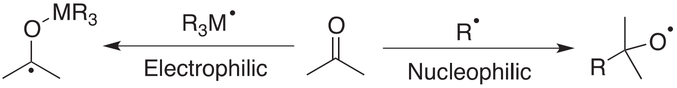


Figure 4.5.15. Radical addition to carbonyls depending on the radical polarity.

3. Aromatic Homolytic Substitution

The general scheme for aromatic homolytic substitution is shown in Figure 4.5.16.

While the reaction of a radical with the aromatic ring usually ends up as a substitution to preserve the aromaticity of the ring, the mechanism starts with a radical addition to alkene. The intermediate radical may be oxidised to a cation and eliminated to regenerate aromaticity or the elimination may occur through a radical pathway, known as fragmentation.

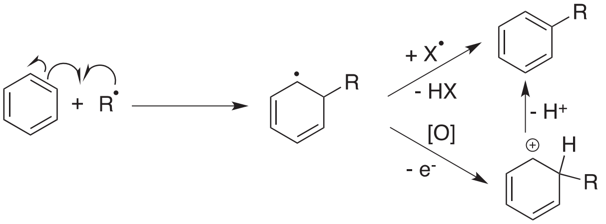


Figure 4.5.16. Aromatic homolytic substitution of radical to aromatic ring.

4. Fragmentation Reactions

Fragmentation is the reverse reaction of addition where a particle leaves as a radical, and the general scheme is shown in Figure 4.5.17.

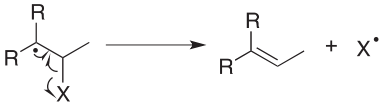


Figure 4.5.17. A common fragmentation reaction known as the β-elimination.

β-elimination occurs when the leaving group is in β-position to the radical. A similar reaction where the leaving group is directly on the radical carbon is known as α-elimination. A lot of fragmentation reactions involve the leaving of a gas such that the reaction may be driven by entropy, and examples are given in Figure 4.5.18.

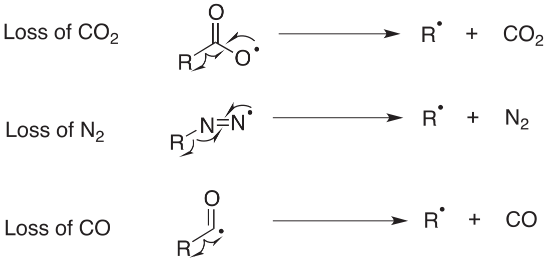


Figure 4.5.18. The mechanisms of common fragmentations that involve the release of a gas.

Note that the loss of CO_2 and N_2 are β-eliminations while the loss of CO is an α-elimination.

5. Rearrangement Reactions

Radicals may be controlled better than cations due to their difficulty in rearrangement. Most free radicals do not rearrange as it is almost impossible for hydrogen or alkyl migration in free radical chemistry. However, it is possible to have **aryl and halogen migrations**. Most of such migrations proceed through cyclic intermediates, as shown in the mechanism in Figure 4.5.19.

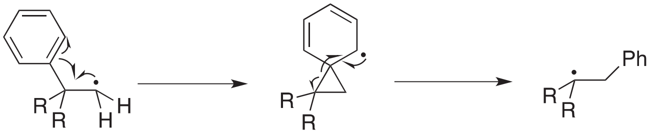


Figure 4.5.19. The mechanism for a 1,2-aryl shift.

4.5.4 *Important radical reactions*

We have spent so much time discussing radical reaction patterns because radicals are highly useful in synthesis. In this section, we will cover the important radical reactions that are commonly used in synthesis.

The most common radical reactions are based upon stannane chemistry, in the use of organotin hydrides as reducing agents. The most common organotin hydride used is tributyltin hydride, written as Bu_3SnH. The reaction follows a general pathway as shown in Figure 4.5.20.

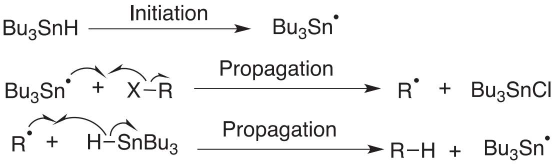


Figure 4.5.20. Scheme for organostannane reactions.

As per most radical chain reactions, the initiation step creates a small amount of radical in the solution, which propagates to form the product and is regenerated to react again. The leaving group X may be halides (such as Cl, Br, I), chalcogenides (SR, SeR), isocyanindes, nitro and xanthates. The rate of reaction depends on the $R–X$ bond strength and stability of the $R^{\bullet}$ radical. Generally, since $C–X$ bond strength decreases down a group, the reactivity follows the order of iodides > bromides > chlorides, and alkyl radicals are much more stable than vinyl radicals. Due to these factors, the organotin reduction on complicated moieties can be highly chemoselective for the most reactive functionality on a molecule, as shown in Figure 4.5.21.

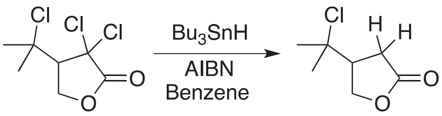


Figure 4.5.21. Chemoselective reduction by organotin hydrides.

In the example above, the α-carbonyl position is much more reactive due to the radical stabilisation by conjugation with adjacent carbonyl group. The other chlorine and the ester are less reactive functionalities and they are not reduced.

When alcohols are reduced with this method, we make use of **Barton-McCombie deoxygenation**, which converts the poor hydroxyl leaving group to a much better leaving group xanthate. The xanthate may then be reduced easily by organotin hydrides. The reaction scheme for Barton-McCombie deoxygenation is shown in Figure 4.5.22.

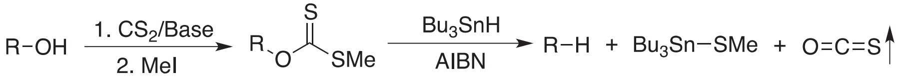


Figure 4.5.22. General reaction scheme for Barton-McCombie deoxygenation.

The mechanism for both the formation of xanthate and reduction of xanthate by tributyltin hydride is provided in Figure 4.5.23.

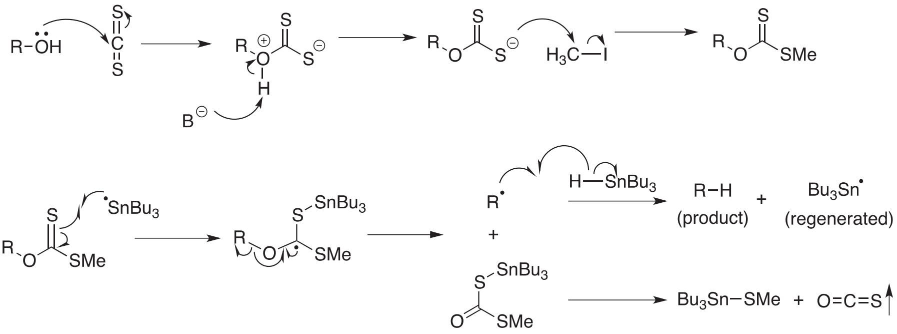


Figure 4.5.23. Mechanism for the formation of xanthate and its reduction by Bu_3SnH.

This is a general method to reduce alcohols to alkanes directly. A similar method is used to reduce carboxylic acids, known as the **Barton-McCombie decarboxylation**. The general scheme for Barton-McCombie decarboxylation is shown in Figure 4.5.24.

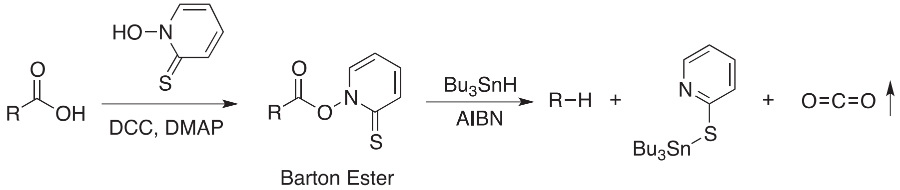


Figure 4.5.24. General method for decarboxylation via Barton ester intermediate.

In the diagram, the first step is Steglich esterification using coupling agent *N*,*N*′-dicyclohexylcarbodiimide (DCC) and nucleophilic catalyst DMAP to form the Barton ester (the mechanism of coupling agents and nucleophilic catalysts will be explained in subsequent chapters). The Barton ester is designed to be easily reduced by tributyltin hydride as there is a C=S double bond that reacts readily with the tributyltin radical and the intermediate immediately forms aromatic pyridine, driving the reaction to the right. The mechanism for the reduction of Barton ester is shown in Figure 4.5.25.

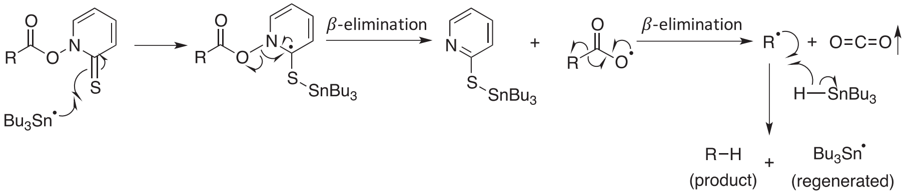


Figure 4.5.25. Mechanism for the reduction by tributyltin hydride followed by β-elimination in the reduction of the carbonyl functional group.

The mechanism is similar to the case of alcohols where the tributyltin radical reacts as an electrophilic radical with the C=S double bond to form a radical. The radical undergoes fragmentation through β-elimination driven by the formation of aromatic pyridine ring and the resulting carboxyl radical is resonance-stabilised. The carboxyl radical then proceeds to undergo further entropy-driven fragmentation to generate carbon dioxide gas and the alkyl radical that can abstract a proton to form the product.

Another important radical reduction uses free electrons in solution for reduction of benzene, known as **Birch reduction**. The stability of benzene due to its aromaticity makes benzene a very difficult target compound to reduce, requiring harsh hydrogenation conditions. The general reaction for Birch reduction is shown in Figure 4.5.26.

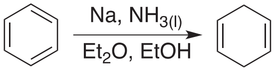


Figure 4.5.26. General reaction of Birch reduction.

The alkali metal is dissolved in liquid ammonia to generate free electrons that participate in the reaction. The solvated electrons give an intense blue solution that slowly decomposes into a colourless solution due to the reduction of ammonia by the free electron. The generation of solvated free electrons and the decomposition of this solution are shown in Figure 4.5.27.

The mechanism of Birch reduction is given in Figure 4.5.28.

$$\mathrm{Na} + n\,\mathrm{NH_3} \xrightarrow{\text{fast}} \mathrm{Na}^{\oplus} + e^{\ominus}\,[\mathrm{NH_3}]_n \qquad \text{Blue solution of solvated electrons}$$

$$\mathrm{NH_3} + e^{\ominus} \xrightarrow{\text{slow}} \mathrm{NH_2}^{\ominus} + 1/2\ \mathrm{H_2}\uparrow \qquad \text{Colourless solution}$$

Figure 4.5.27. Generation of solvated free electrons and the decomposition of the solution.

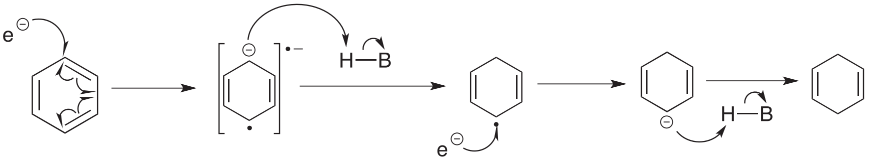


Figure 4.5.28. Mechanism of Birch reduction.

Notice that the intermediates formed are a radical and an anion, which means that electron-withdrawing substituents that are able to stabilise the anion will make the reduction more favourable. This leads us to the substituent effects of Birch reduction:

Electron-withdrawing substituents promote *ipso-para* Birch reduction.
Electron-donating substituents promote *ortho-meta* Birch reduction.

We can understand the stabilisation effect mechanistically, as shown in Figure 4.5.29.

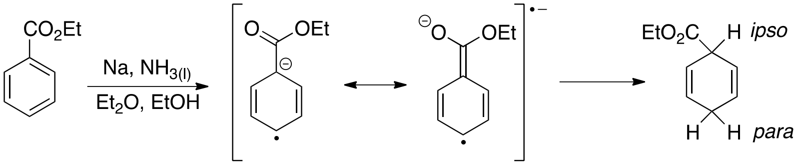


Figure 4.5.29. Resonance-stabilisation of intermediate by electron-withdrawing group.

For electron-donating groups, they destabilise the anion intermediate and slow down the reaction. Thus, it is best not to put the anion directly adjacent to them, which leads to *ortho-meta* Birch reduction, as shown in Figure 4.5.30.

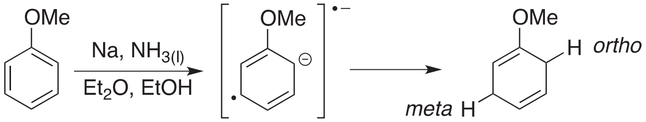


Figure 4.5.30. Anions avoid the electron-donating substituent.

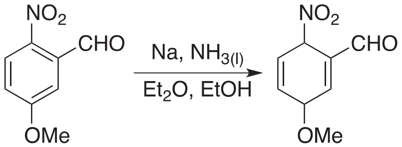


Figure 4.5.31. Example of benzene with multiple substituents undergoing Birch reduction.

In the case of competing substituents, the major product is formed through the fastest reaction pathway, thus the most electron-withdrawing substituent controls the reduction pattern. An example of a multi-substituted benzene ring undergoing Birch reduction is shown in Figure 4.5.31.

In the example, the nitro group is the strongest electron-withdrawing group that controls the reduction pattern to be *ipso-para* to it. Although both the aldehyde and alkoxy groups direct the reduction *ortho-meta* to the nitro group, they are not as activating as the nitro group and the reaction pathway with the anion stabilised by the nitro group is still the fastest.

Other than reductions, radicals react in addition and substitution reactions. While alkanes may undergo free radical substitution, the selectivity is usually poor and multiple products are formed simultaneously. However, free radical substitutions at allylic positions are highly selective and synthetically useful. Such reactions make use of the fact that radicals formed at allylic positions are more stable than normal alkane radicals. The halogen most easily substituted is bromine, and the reaction is known as **Wohl-Ziegler bromination**. The reaction scheme for Wohl-Ziegler bromination is shown in Figure 4.5.32.

We can see from above that the benzylic position reacts similarly to an allylic position for the bromination. The reagent used is *N*-Bromosuccinimide (NBS), together with a radical initiator in tetrachloromethane solvent. NBS is an excellent source of bromine, which generates the bromine radical in-situ when combined with a radical initiator. Its advantages over liquid Br_2 is its higher selectivity and ease of handling, as NBS is a white crystalline solid. The mechanism for Wohl-Zieger bromination is shown in Figure 4.5.33.

NBS may react in many ways, but its role in this reaction is to provide a bromine radical. In certain bromination reactions, NBS may also be used to generate bromine.

The last radical reaction that we will discuss in this chapter is the **Sandmeyer reaction**. This is a synthetically useful reaction to perform substitution on aromatic rings. We will focus on the transformation from a diazoarene to a substituted arene, as shown in Figure 4.5.34.

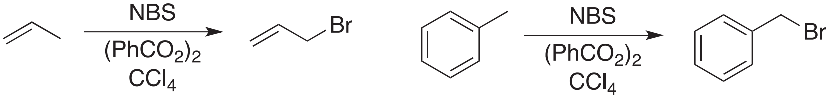


Figure 4.5.32. General reaction of Wohl-Ziegler bromination.

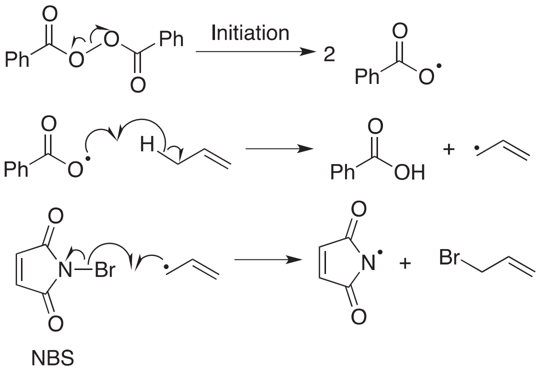


Figure 4.5.33. Simplified mechanism for Wohl-Ziegler reaction.

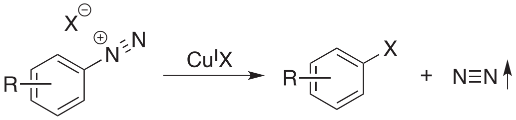


Figure 4.5.34. General scheme for Sandmeyer reaction.

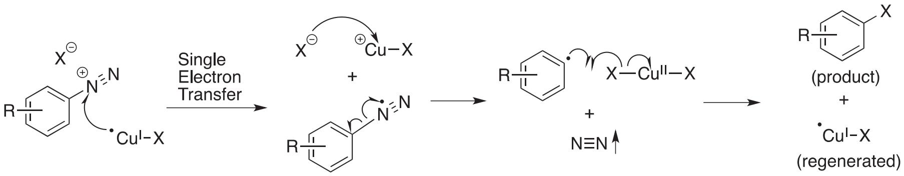


Figure 4.5.35. Reaction mechanism for Sandmeyer reaction.

The mechanism, shown in Figure 4.5.35, involves a single electron transfer (SET) by copper(I) to generate the diazo radical that decomposes to form an arene radical and give off nitrogen gas. The unstable sp^2-radical can be formed due to the entropic driving force from the release of nitrogen gas. This radical reacts rapidly to generate the product.

4.6 Nucleophilic Addition

As we have previously learnt, polar organic reactions are usually driven by nucleophiles and electrophiles. These reactions occur at specific functional groups. In this book, we will not consider reactions based on functional groups, instead, we will consider reactions based on their reaction type. In this chapter, we will discuss nucleophilic addition reactions, where a nucleophile adds to an electrophile.

4.6.1 *Nucleophilic addition to carbonyl carbon*

The carbonyl group is polarised towards the oxygen such that the carbon atom holds a partial positive charge while the oxygen atom holds a partial negative charge. This makes the carbonyl carbon electron-deficient, and an excellent electrophile. It is able to accept a pair of electrons from a nucleophile to form a carbon-nucleophile bond, while breaking the carbon-oxygen π-bond. The general reaction is given in Figure 4.6.1.

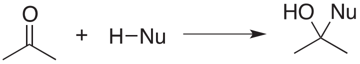


Figure 4.6.1. General reaction of nucleophilic addition to carbonyl carbon.

The mechanism of this reaction is straightforward and shown in Figure 4.6.2.

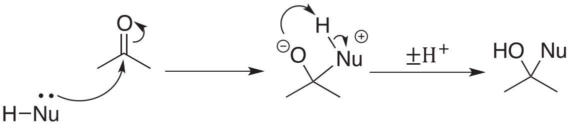


Figure 4.6.2. Mechanism of nucleophilic addition to carbonyl carbon.

The first step is the **direct attack of nucleophile on the carbonyl carbon**. The nucleophilic attack is driven by charge and orbital interactions. Charge interactions involve the electrostatic attraction between the negatively-charged nucleophile and the electrophile with a partial positive charge. Orbital interactions involve the electron pair moving from the HOMO of the nucleophile to the LUMO of the electrophile. Through crystallography and computational calculations, Bürgi and Dunitz determined the angle of nucleophilic attack to be 107° to the C=O double bond. The orbital picture in Figure 4.6.3 shows the approach of a nucleophile to the carbonyl.

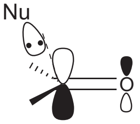


Figure 4.6.3. Orbital picture of nucleophilic attack at carbonyl carbon.

The second step involves the **protonation of the oxygen anion formed**. When the nucleophile is neutral, this step is a proton transfer, which is commonly written as $\pm H^+$. For an anionic nucleophile, the protonation of the oxygen anion formed may take place through the solvent or any acid present in the system. In this case, a stoichiometric amount of acid is required for the reaction. In the mechanism

Tip 4c. Proton transfer reactions and how we may represent them

Proton transfer reactions are extremely common in organic chemistry. However, they are usually treated as the less important areas of reaction mechanisms since they are treated as basic knowledge that any organic chemist should know. In reality, proton transfers occur through many pathways and any of the pathways are acceptable when writing a mechanism. We will give a simple discussion regarding these mechanisms, which are shown in Figure 4.6.4.

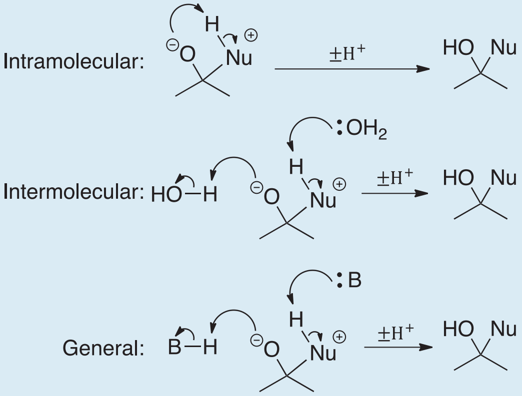


Figure 4.6.4. Different mechanisms for proton transfer.

The intramolecular mechanism may occur without the presence of any other chemical species, as the proton is transferred directly to the oxygen anion. The intermolecular mechanism is constructed assuming that water is the solvent, and water assists the proton transfer by acting both as an acid and a base to provide a proton to the oxygen anion and to remove a proton from the nucleophile. In the general case, we are not concerned with the exact nature of the acid and base, just that we know that there exist such species in solution. We may represent a general acid as H-B and a general base as B. In this case, another molecule of the intermediate may also act as an acid or base. The intermolecular proton transfer mechanism is usually drawn as separate protonation and deprotonation steps, in any order.

Each mechanism has its advantages. Intramolecular reactions are usually faster than intermolecular reactions since they do not require molecules to encounter each other. However, the concentration of solvent in a reaction is usually high and reactant molecules are surrounded by solvent molecules, such that the intermolecular reaction is also highly feasible and may be preferred over the intramolecular reaction since the molecule need not twist itself to the correct conformation to react. The proton transfer may take place through a combination of the mechanisms, but we are not concerned as the reaction is very fast.

detailed in Figure 4.6.2, an intramolecular proton transfer is shown. In reality, the proton transfer may be completed through solvent-assisted intermolecular reactions, where the solvent acts as both acid and base.

Now that we understand the mechanism of nucleophilic addition to carbonyl compounds, we will move on to discuss certain common reactions that involve this mechanism.

When an aldehyde or ketone is placed inside water, water may act as a nucleophile to perform nucleophilic addition. This forms **geminal diols** which are compounds with 2 hydroxy groups bonded to the same carbon. In this case, they are formed through the addition of water and may also be known as hydrates. They are in rapid equilibrium with the corresponding carbonyl compound, as shown in Figure 4.6.5.

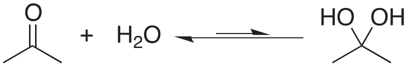


Figure 4.6.5. Equilibrium between carbonyl and hydrate in the presence of water.

The position of the equilibrium depends on the properties of the carbonyl compound. Generally, the carbonyl compound is more stable than the hydrate due to the hydrate being tetrahedral while the carbonyl compound is trigonal planar, keeping the two R-groups further from each other and reducing the steric strain. Thus, ketones form hydrates less readily compared to aldehydes. In the special case of formaldehyde, the hydrate is greatly favoured over the aldehyde due to its high electrophilicity and the small hydrogen atoms that do not sterically interact with each other. In other cases, such as 1,1,1-trifluoroacetone, high electrophilicity due to electron-withdrawing substituents on the alkyl groups can also increase the concentration of hydrate. In special cases of strained cyclic systems, such as cyclopropanone, the hydration of the carbonyl compound may help to release ring strain. These examples are illustrated in Figure 4.6.6.

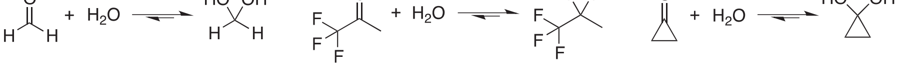


Figure 4.6.6. Some special carbonyl compounds that favour hydrated form.

One of the most reliable nucleophilic addition reactions is the **nucleophilic addition of cyanide** to form cyanohydrins. This reaction is reversible, and the reaction scheme for both forward and reverse reactions are shown in Figure 4.6.7.

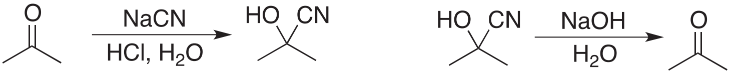


Figure 4.6.7. Addition of cyanide to carbonyl group and the reverse reaction.

In this reaction, cyanide anion acts as the nucleophile. The addition of acid is to protonate the oxygen anion after the nucleophilic attack. The reverse reaction may be carried out by using base to deprotonate the hydroxyl group such that the cyanide leaves to regenerate the carbonyl compound. The mechanism is given in Figure 4.6.8.

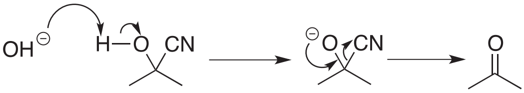


Figure 4.6.8. The mechanism of the decomposition of cyanohydrin to carbonyl compound.

Reduction of carbonyl compounds is the **nucleophilic addition of hydride** to the carbonyl compound. Hydride anion (H^{-}) is an extremely strong base that does not act as a nucleophile. This is because the electron pair resides in the 1s orbital of hydrogen and interacts best with the 1s orbital of a proton that is similar in size and energy. The 2p orbital of carbon is a lot larger and more diffuse, rendering the orbital overlap ineffective. Instead, when we wish to reduce carbonyl compounds, we need to use a nucleophilic hydride. One such example is sodium borohydride $(\mathrm{NaBH_4})$. In the chapter on oxidation and reduction, the various oxidising and reducing agents will be examined in detail. Here we will only discuss the reduction reaction with regards to sodium borohydride. Unlike hydrides, the borohydride ion is much less basic and reactive due to its larger size to stabilise the negative charge. This makes sodium borohydride stable in alcoholic solvents and a solid reagent that is easy to handle. Note that while boron carries the negative charge, it does not have a lone pair of electrons. Instead, the pair of electrons from one $\mathrm{B{-}H}$ covalent bond will attack the electrophile, which is the carbonyl compound. The mechanism is shown in Figure 4.6.9.

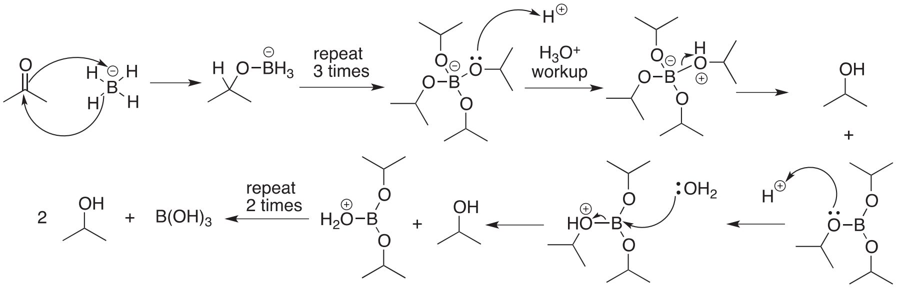


Figure 4.6.9. Mechanism for reduction of carbonyl compound by $\mathrm{NaBH_4}$.

In this reaction, each molecule of sodium borohydride can donate all four hydrides, ending up as a boric acid side product. This allows us to theoretically reduce 4 equivalents of carbonyl compound, but practically, we will use an excess of reducing agent to ensure a complete reduction and a good yield. The chelation of the boron to oxygen is essential in ensuring that the boron is still negatively charged and the reagent can continue to act as a hydride donor.

Background 4d. Reaction workup

In organic reactions, workup is often required after the reaction to remove the remaining reagents and to purify the product from the reaction mixture. In most organic reactions, the workup step is implied and need not be specified. Acid or base may be used during workup.

Organometallic reagents may act as a carbanion and perform nucleophilic attack on the carbonyl group. This reaction is synthetically useful as it can help us extend the carbon chain and form carbon-carbon bonds. While carbon can form bonds with many different metals, organolithium and organomagnesium compounds are the most useful nucleophiles in nucleophilic addition reactions.

These compounds are prepared by the addition of metal to alkyl halide, as shown in Figure 4.6.10.

Organolithium	$R{-}X + 2\,Li \longrightarrow R{-}Li + Li{-}X$
Organomagnesium	$R{-}X + Mg \longrightarrow R{-}MgX$

Figure 4.6.10. Preparation of organometallic compounds from alkyl halides.

The mechanism for the formation of organomagnesium compounds are complex radical reactions that are not essential to the understanding of their use in organic chemistry. These organomagnesium compounds are more commonly known as **Grignard reagents**. Nucleophilic addition to carbonyl carbon can be performed by both organolithium and organomagnesium reagents, but the use of organomagnesium Grignard reagents are more common. This is because there is a greater electronegativity difference between carbon and lithium than between carbon and magnesium. This makes organolithium reagents more reactive than organomagnesium reagents, and more basic. Thus, organolithium reagents are more difficult to handle and commonly used as strong bases instead of nucleophiles. Organolithium reagents can also undergo **Lithium-Halogen exchange**, as shown in Figure 4.6.11.

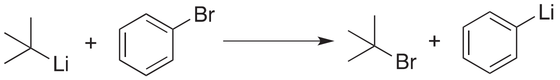


Figure 4.6.11. Lithium-halogen exchange reaction example.

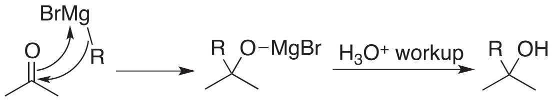


Figure 4.6.12. Reaction mechanism for nucleophilic addition of organometallic compounds to carbonyl carbon.

The general reaction mechanism for the nucleophilic addition of Grignard reagents to carbonyl carbon is shown in Figure 4.6.12.

The oxygen-metal affinity accelerates the reaction by bringing the reagents together quickly for reaction. The organometallic reagent can be treated almost like an ionic compound with a metal cation and carbanion due to the large electronegativity difference leading to a highly polarised metal-carbon bond.

Next, we will look at **nucleophilic addition by alcohols to the carbonyl carbon** (Figure 4.6.13). This reaction is interesting as it proceeds through 2 stages and the intermediate is stable. The first stage is similar to addition of water to form hydrate, just that the alcohol adds to the carbonyl compound to form a hemiacetal. Historically, the term hemiacetal is used specifically for products formed from aldehydes and hemiketal is used for products formed from ketones. However, the chemical difference between them is small and in modern context, it is common to refer to all such compounds as hemiacetals. Similar to the formation of hydrates, the reaction is an equilibrium depending on the alcohol and the carbonyl compound. The second stage involves the substitution of the carbonyl oxygen by another alcohol to form an acetal. The formation of acetal follows an addition-substitution pathway and may be classified under both nucleophilic addition and substitution reactions.

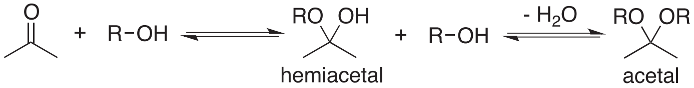


Figure 4.6.13. Nucleophilic addition of alcohol to form hemiacetal, followed by acetal.

We can vary the reaction conditions to have the reaction stop at the hemiacetal or for it to proceed all the way to form the acetal. Under basic conditions, the reaction stops at the hemiacetal stage while the reaction proceeds to form the acetal under acidic conditions. We shall examine the mechanisms of the transformation in base and in acid to explain the difference, starting with the base-catalysed reaction shown in Figure 4.6.14.

When base is used to catalyse the reaction, it is able to deprotonate the alcohol to generate the alkoxide, which is a strong nucleophile that can attack the carbonyl carbon. The oxygen anion formed in the product is stable under basic condition and may not be quickly protonated. This stops the reaction from proceeding further. Upon workup, protonation occurs and the hemiacetal is formed as the product.

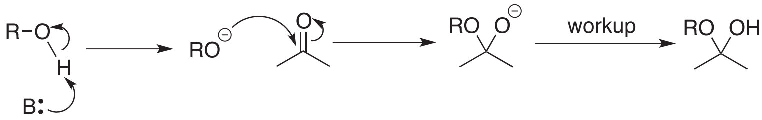


Figure 4.6.14. Reaction mechanism for base-catalysed formation of hemiacetal.

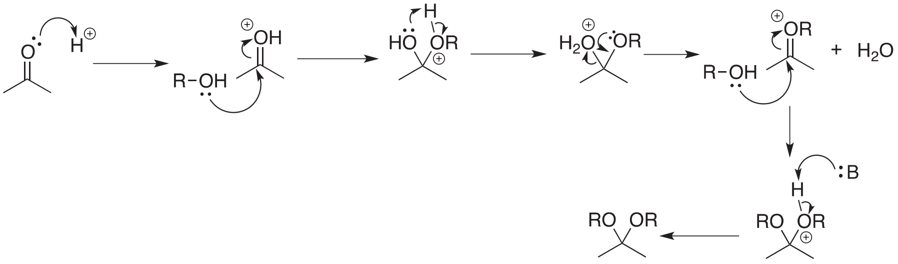


Figure 4.6.15. Reaction mechanism for acid-catalysed formation of acetal.

We will proceed to analyse the acid-catalysed formation of acetal, with the reaction mechanism shown in Figure 4.6.15.

When acid is used to catalyse the reaction, the carbonyl compound is protonated to form an oxonium ion that makes the carbonyl carbon more electrophilic. This allows the alcohol to attack as a neutral nucleophile to form the hemiacetal intermediate. In acid, the hydroxyl group in the hemiacetal can be protonated and leave as a molecule of water. The carbocation formed can be stabilised by the neighbouring oxygen lone pair to form an oxonium ion. This can be attacked by another molecule of alcohol to give the acetal product. Note that acetal formation is an equilibrium that favours acetal at high concentration of alcohol and favours carbonyl compound at high concentration of water. Thus, acetals can undergo acidic hydrolysis following the reverse mechanism in excess of water, but they are stable towards base as they do not have any acidic proton.

When the alcohol is replaced by amines and other nitrogen nucleophiles, similar reactions can take place, as shown in Figure 4.6.16.

The mechanism for such reactions is similar to the formation of acetal, just that the second equivalent of amine acts as a base rather than nucleophile. A sample mechanism for the formation of imine is shown in Figure 4.6.17.

There is a small difference in this mechanism compared to that of acetal formation: the carbonyl group is not protonated by acid before the nucleophilic attack by amine. This is because amines are better nucleophiles than alcohols, and the nucleophilic attack takes place without the need to activate the carbonyl group. When forming imines, the pH of the reaction is generally maintained at a slightly acidic level of pH 5-6, which is inefficient at protonating the carbonyl group. A pH lower than 5-6 is not ideal because amines are basic and will be protonated at higher acidity, before the carbonyl group does, and the ammonium cation is no longer nucleophilic. The slight acidic environment is still required to protonate the hydroxyl group to leave as water.

The mechanism is the same for oxime and hydrazine formation, but for enamine formation, there is one extra step. When a secondary amine is used as the nucleophile, the iminium ion can no longer be deprotonated. The only way is to remove the proton from the α-carbon, as shown in Figure 4.6.18.

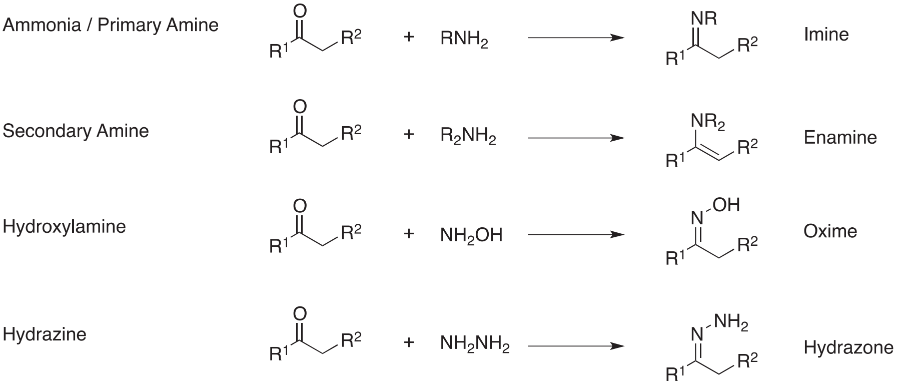


Figure 4.6.16. Reactions of nitrogen nucleophiles with carbonyl compounds.

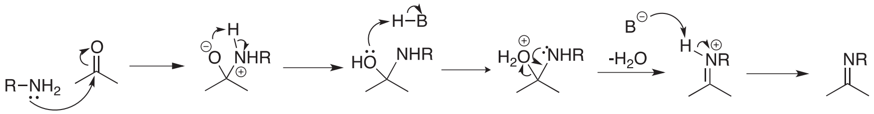


Figure 4.6.17. Mechanism for formation of imine.

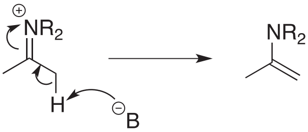


Figure 4.6.18. Mechanism for deprotonation at α-carbon to generate enamine.

An interesting application of hydrazones is the **Wolff-Kishner reduction**, where the hydrazone can be removed under basic environment. This reaction is useful to remove carbonyl groups, which are often added in synthesis to help form carbon-carbon bonds.

The mechanism of the reaction is just the repeated deprotonation of hydrazone until it is finally released as nitrogen gas, as shown in Figure 4.6.19. The driving force of the reaction is the formation of nitrogen gas due to its exceptional stability and the positive entropy of generating gaseous products.

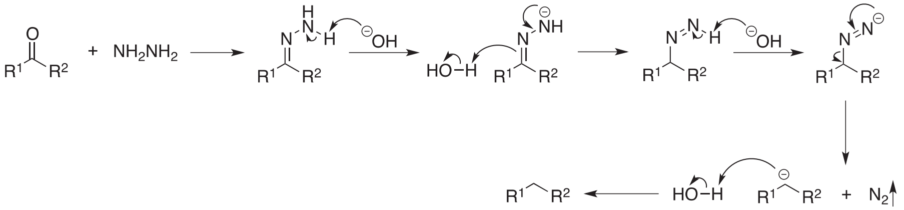


Figure 4.6.19. Reaction mechanism for Wolff-Kishner reduction.

4.6.2 *Nucleophilic conjugate addition to alkenes*

While alkenes are generally electron-rich species, they can act as electrophiles when conjugated to electron withdrawing groups. This is due to the resonance electron-withdrawing effect from the conjugating group, as shown in Figure 4.6.20.

Any nucleophile can add to electrophilic alkenes following the general reaction shown in Figure 4.6.21.

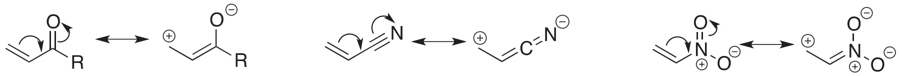


Figure 4.6.20. Resonance structures of conjugated alkenes to show its electrophilicity.

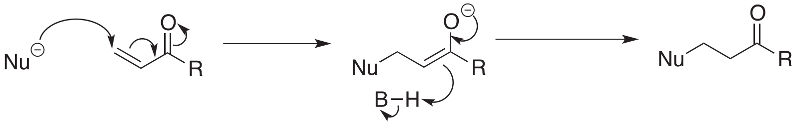


Figure 4.6.21. General reaction mechanism for addition of nucleophile to electrophilic alkene.

The nucleophilic addition to a conjugated alkene is a named organic reaction called **Michael addition**. Similar to nucleophilic addition to carbonyl compounds, the nucleophilic addition to electrophilic alkenes can be catalysed by either acid or base. The challenge of performing such reactions is to control their selectivity between direct (1,2) and conjugate (1,4) addition. While the alkene is electrophilic, the carbonyl carbon is also electrophilic. Table 4.11 compares the properties of direct and conjugate addition to understand the methods to control the reaction.

We have already learnt about hard-soft acid-base (HSAB) theory, and the concept applied here is similar. However, many carbanion nucleophiles are organometallic reagents, which have a selectivity preference for conjugate or direct addition. We have just seen organolithium and Grignard reagents used for direct addition, and they are excellent for direct addition as the metal is able to chelate to the carbonyl oxygen to activate the carbonyl group and increase the electrophilicity of the carbonyl carbon.

Table 4.11. Conjugate addition versus direct addition.

Conjugate addition	Direct addition
Thermodynamic Control: Favoured under high temperature and long reaction time. This is because conjugate addition product is more stable ($\mathrm{C{=}O}$ double bond is stronger than $\mathrm{C{=}C}$ double bond).	Kinetic Control: Favoured under low temperature and short reaction time. This is because carbonyl carbon is closer to electronegative oxygen with more $\delta+$ charge and greater electrophilicity.
Irreversible: After long time, equilibrium will favour the formation of conjugate addition product.	Reversible: Tetrahedral intermediate can collapse to regenerate the starting materials.
Favoured by unreactive carbonyl groups that are less electrophilic, such as esters, amides and carboxylic acids.	Favoured by reactive carbonyl groups that are more electrophilic, such as acyl chlorides, acid anhydrides and aldehydes.
Favoured by unhindered β-carbon such that there is less steric hindrance for nucleophilic attack at β-carbon.	Favoured by hindered β-carbon such that there is more steric hindrance for nucleophilic attack at β-carbon.
Favoured by soft nucleophiles that have low charge density as well as large and highly polarisable electron clouds. This is because conjugate addition is controlled by orbital overlap.	Favoured by hard nucleophiles that have high charge density as well as small and highly polarising electron clouds. This is because direct addition is controlled by charge interactions.

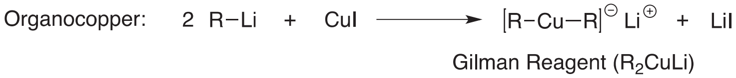
While such activation will increase the electrophilicity of the conjugated alkene as well, the increase is less significant since the β-carbon is 4 bonds away from the metal. Organolithium and Grignard reagents are also highly basic and hard nucleophiles, which prefer to attack the carbonyl carbon directly. This leaves us to think about how we can apply other organometallic carbanions to perform conjugate addition.

In fact, copper(I) reagents are excellent for conjugate addition. Unlike lithium or magnesium, copper is a relatively soft Lewis acid that interacts better with alkene than carbonyl oxygen. Thus, the alkene can act as an organometallic ligand to interact with the copper(I) metal, and it is activated electronically while the nucleophilic carbanion is positioned appropriately for the attack.

Organocopper reagents are usually prepared from transmetallation of organolithium or Grignard reagents. The most common organocopper reagent is known as **Gilman reagent**, and its preparation is shown in Figure 4.6.22.

Organocopper reagents are highly selective for conjugate addition due to their soft nature and the coordination of the alkene to the copper metal. The mechanism for conjugate addition with organocopper reagents is shown in Figure 4.6.23.

We will consider an interesting reaction example of conjugate nucleophilic addition, **nucleophilic epoxidation**. The overall reaction is given in Figure 4.6.24.



$$\text{Organocopper:}\quad 2\ R{-}Li + CuI \longrightarrow \underset{\text{Gilman Reagent }(R_2CuLi)}{[R{-}Cu{-}R]^{\ominus}\,Li^{\oplus}} + LiI$$

Figure 4.6.22. Preparation of Gilman reagent by transmetallation of organolithium reagents.

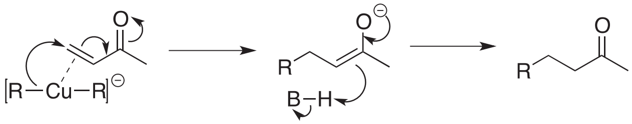


Figure 4.6.23. Mechanism for conjugate addition of Gilman reagent.

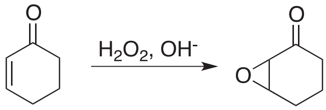


Figure 4.6.24. Overall reaction of nucleophilic epoxidation of cyclohexenone.

The nucleophile in this reaction is the hydroperoxide anion, HOO^-. This nucleophile is less basic and more nucleophilic than OH^-. This is because the presence of the extra oxygen is electron-withdrawing, reducing its basicity, but the energy of the HOMO is increased through the alpha effect. The alpha effect is caused by the overlap of 2 oxygen sp^3-orbitals containing lone pairs of electrons. This overlap raises the energy of the HOMO and causes the HOMO orbital to become larger. HOO^- is thus a very soft nucleophile due to the large electron cloud that would perform conjugate addition.

The mechanism of the reaction involves the conjugate addition of hydroperoxide anion followed by the leaving of OH^-, as shown in Figure 4.6.25. Although OH^- is rather basic and a poor leaving group, the reaction is possible due to the very weak peroxide $O{-}O$ bond that is broken.

In cases when the $C{=}C$ double bond has multiple substituents attached and the product has stereochemical isomers, nucleophilic epoxidation is not stereospecific and may not retain the original stereochemistry. This is because the π-bond is broken to form the carbanion intermediate, and the single bond is able to rotate to assume the most stable conformation before the epoxide is formed.

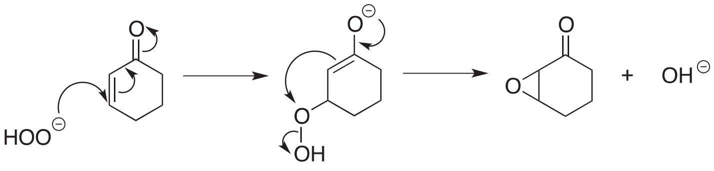


Figure 4.6.25. Mechanism of nucleophilic epoxidation of cyclohexenone.

4.7 Nucleophilic Substitution

After nucleophilic addition has been covered in the previous section, we will move on to nucleophilic substitution. Both reaction types start with an attack from a nucleophile, but during substitution, a group that was originally present is replaced by the nucleophile, essentially leaving the compound. Such a moiety is known as the **leaving group**. In this chapter, we will explore the different mechanisms for nucleophilic substitution.

4.7.1 *Aliphatic nucleophilic substitution*

Aliphatic compounds are essentially organic compounds that are not aromatic, and they are most commonly encountered. In this part, we will look at nucleophilic substitutions on a saturated carbon centre. On saturated centres, it is not possible to perform nucleophilic addition as carbon cannot form 5 bonds. Instead, nucleophilic substitution will occur as the nucleophile replaces the leaving group at the carbon centre. In the reaction shown in Figure 4.7.1, the incoming nucleophile (Nu^-) will replace the leaving group (X^-).

There are 2 different mechanisms for nucleophilic substitution at saturated carbon centres. The mechanisms are the **bimolecular nucleophilic substitution** $(\mathbf{S_N2})$ and the **unimolecular nucleophilic substitution** $(\mathbf{S_N1})$. The mechanisms are shown in Figure 4.7.2.

When referring to the reaction as bimolecular or unimolecular, we are actually specifying the order of the rate-determining step. The rate determining step in the $\mathrm{S_N2}$ mechanism involves the nucleophile attacking the substrate whereas the rate determining step in the $\mathrm{S_N1}$ mechanism involves the decomposition of the substrate without participation from the nucleophile.

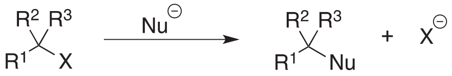


Figure 4.7.1. General reaction for aliphatic nucleophilic substitution.

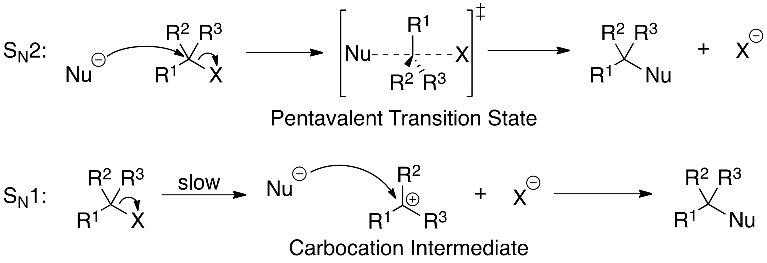


Figure 4.7.2. 2 mechanisms for nucleophilic substitution.

One main difference in the 2 mechanisms is the stereochemistry of the product. The S_N2 reaction is **stereospecific**. That means the stereochemistry of the product is dependent entirely on the stereochemistry of the substrate. Since the S_N2 reaction proceeds in a one-step fashion with a backside nucleophilic attack, there is an **inversion in stereochemistry**. The backside attack is due to the lone pair of electrons from the nucleophile donating into the σ^*-orbital of the $C{-}X$ bond, where X is the leaving group. On the other hand, the S_N1 reaction is not stereoselective at all as it passes through a planar carbocation intermediate that may undergo nucleophilic attack from both sides with equal probability. Thus, an S_N1 reaction causes **racemisation**, forming an equal mixture of both enantiomers, known as a **racemic mixture**.

Background 4e. Selectivity in organic chemistry: "Specific" vs. "Selective"

In organic chemistry, we are always concerned about the selectivity of the reactions. This is because organic reactions may generate multiple products, but only one is the product we want. There are 3 main types of selectivity that we are concerned with:

1. **Chemoselectivity**: The preference for a reaction to occur at one **functional group** as opposed to another.
2. **Regioselectivity**: The preference for a reaction to occur at a certain **position** as opposed to another.
3. **Stereoselectivity**: The preference for a reaction to form a certain **stereoisomer** as opposed to another. This can be further divided into **diastereoselectivity** (stereoselective between diastereomers) and **enantioselectivity** (stereoselective between enantiomers).

Selectivity usually results from a series of effects, such as electronic effects and steric effects. These effects are able to guide reactions to proceed with high selectivity, which means that one isomer is formed in large excess of the others. However, there are certain reactions that are specific. **Specific reactions** only form one isomer due to the **mechanism of the reaction**, such that other isomers are not formed at all. The product of specific reactions is dependent entirely on the properties of the substrate.

In Figure 4.7.3, we show an example to demonstrate the stereochemical preference of nucleophilic substitutions using the 2 mechanisms.

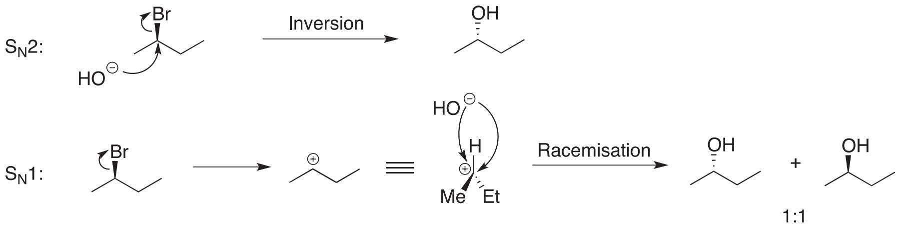


Figure 4.7.3. Stereochemical preference of S_N2 and S_N1 reaction mechanisms.

Since the stereochemistry of the product is different depending on the mechanism, we need to look at the factors that govern which mechanism is more likely to proceed. To determine the reactivity of compounds for nucleophilic substitution reactions, we need to consider the following factors:

1. Substrate

When looking at any organic reaction, we have to consider both the electronic and steric factors. For nucleophilic substitutions, the electronic factor comes from the ability for the substrate to form a stabilised carbocation as the intermediate. The steric factor determines the rate of nucleophilic attack on the substrate. These 2 factors must be considered for each substrate to determine the mechanistic pathway that the reaction will follow. Electronically, we consider the **stability of the carbocation** that will be formed without the leaving group. There are 5 factors for this, which are **conjugation**, **hyperconjugation**, **hybridisation of empty orbital**, **presence of adjacent electron pair donating heteroatom** and the **change in geometry due to change in hybridisation**. Since the carbocation is electron-deficient, any electron-donating effect will stabilise it. The factors above have been discussed in part 4.5.1, and their effects with respect to carbocations have been summarised in Table 4.12.

Table 4.12. Factors affecting stability of carbocation.

Effect	Description	Stability trend
Hyperconjugation	Stabilisation of cation through donation of electrons from adjacent $C{-}H$ σ-bonds.	Tertiary > Secondary > Primary > Methyl Carbocation
Conjugation	Stabilisation of cation through donation of electrons from adjacent $C{=}C$ π-bonds.	Benzylic > Allylic > Unconjugated Carbocation
Hybridisation of empty orbital	The empty orbital must have greatest p-character for the carbocation to be most stable as the p-orbital has the highest energy.	p > sp^2 (phenylic/vinylic) > sp
Presence of adjacent electron-pair donating heteroatom	Stabilisation of cation through the donation of a lone pair of electrons from the heteroatom to the cation.	$C{-}S > C{-}N > C{-}O$
Change in geometry due to change in hybridisation	This applies to sp^3-carbon centres that adopt sp^2-hybridisation when forming carbocations such that the empty orbital is a p-orbital. This increases the bond angles from 109.5° to 120°, releasing steric strain.	The formation of carbocation will be more favourable for carbon centres with multiple bulky substituents.

Steric effects affect the rate of nucleophile approaching the electrophilic carbon. We are concerned about the groups directly adjacent to the electrophilic carbon that may shield it from nucleophilic attack. The rate of the bimolecular reaction of nucleophile attacking the carbon centre follows the steric trend in ascending order from tertiary to secondary to primary and methyl carbon centres, where the direct nucleophilic attack on a methyl carbon is fastest.

Thus, the **formation of a stable carbocation favours S_N1 mechanism** while **an unhindered electrophilic carbon centre favours S_N2 mechanism**.

2. Nucleophile

We have discussed nucleophiles and their relative strength in part 4.4.2. Since this reaction starts with a nucleophilic attack, we would like to believe that nucleophile strength is critical for the reaction. In fact, this is true for the S_N2 mechanism, where the strength of nucleophile plays a critical role in the rate of the bimolecular nucleophilic attack. However, nucleophile strength is irrelevant in the S_N1 mechanism, as the rate determining step is the unimolecular decomposition of the substrate to form the carbocation intermediate. The addition of nucleophile to a positively charged, reactive carbocation is very fast and much faster than the formation of carbocation regardless of the nucleophile used. Thus, **S_N2 reactions are driven by strong nucleophiles** while **S_N1 reactions are unaffected by nucleophile strength** (thus, S_N1 reactions are usually carried out with weak nucleophiles).

When carrying out S_N2 reactions, we have to increase the strength of our nucleophile to improve the efficiency of the reaction. One method is to trap the counteraction through the use of crown ethers. For example, cyanide is a nucleophile commonly used as KCN salt. The crown ether is able to trap the potassium cation, leaving the free cyanide anion with greater nucleophilicity. The concept of solvation will be discussed in further detail when we look at solvent effects below.

3. Leaving group

The presence of leaving group is the main difference between addition and substitution reactions. It is important to identify the presence of a leaving group and its ability to act as a leaving group. Since the **S_N1 reaction is rate-determined by the decomposition of the substrate, the leaving group ability is especially important**. Leaving group ability depends on how well it can stabilise the negative charge after leaving. The most important character of leaving groups is that they are not basic. The common leaving groups are ranked by leaving ability in Figure 4.7.4.

Basic anions such as OH^- are bad leaving groups and need to be converted into better leaving groups before nucleophilic substitution can occur. Here we will discuss

$$\underset{\text{Increasing leaving group ability}}{\xrightarrow{H_2O < Cl^- < Br^- < I^- = OTs^-}}$$

Figure 4.7.4. Leaving group ability trend for common leaving groups.

reactions to convert hydroxide into better leaving groups for substitution. Firstly, we will discuss the methods to convert hydroxides into halides.

Appel reaction uses triphenylphosphine together with a halogenating agent. The common reaction conditions involve using PPh_3 together with CX_4 $(X = Cl, Br)$ to form chlorides and bromides and using PPh_3 together with I_2 and imidazole to form iodides. The general scheme for Appel reaction is shown in Figure 4.7.5.

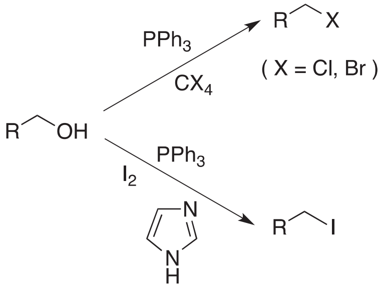


Figure 4.7.5. General scheme for Appel reaction.

The mechanism of the Appel reaction, shown in Figure 4.7.6, involves the nucleophilic attack of phosphine on the halogenating agent to form the intermediate that is attacked by the alcohol. The alcohol oxygen becomes a better leaving group when it is bonded to triphenylphosphine as the $P{=}O$ double bond formed in the side product $(Ph_3P{=}O)$ is very stable.

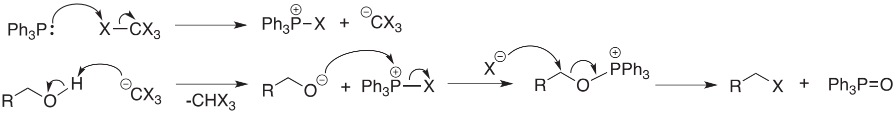


Figure 4.7.6. Mechanism of the Appel reaction.

In the reaction with iodine, the mechanism is similar, but iodide is a poor base and imidazole is added to speed up the reaction.

There are other reagents that may be used to convert alcohols to halides. To convert alcohols into chlorides, we may use PCl_5, PCl_3 or $SOCl_2$. To convert alcohols into bromides, we usually use PBr_3. The reactions are shown in Figure 4.7.7.

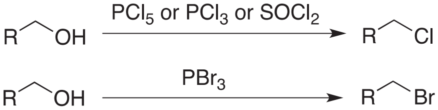


Figure 4.7.7. Reactions to convert alcohols into alkyl halides.

The reaction mechanisms are similar, so only the mechanism with PBr_3 is shown in Figure 4.7.8. It is a simple reaction that involves the nucleophilic attack of the alcohol on the halogenating agent, generating the halide and making the alcohol a better leaving group. The idea is very similar to that of Appel reaction.

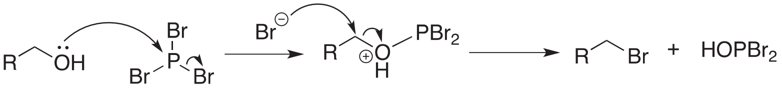


Figure 4.7.8. Mechanism of the conversion of alcohols to halides.

These reactions involve the alcohol acting as a nucleophile to attack the halogenating agents, and are more efficient with primary and secondary alcohols. Tertiary alcohols are poor nucleophiles due to steric hindrance. Instead, we may convert tertiary alcohols to halides with **strong acids** through a S_N1 reaction, as shown in Figure 4.7.9.

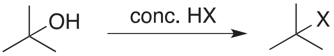


Figure 4.7.9. General scheme for conversion of alcohol to halide with strong acid.

The mechanism, shown in Figure 4.7.10, involves the protonation of alcohol to generate water, which is a good leaving group. The tertiary carbocation formed is stable and may be attacked by the halide anion to form the alkyl halide.

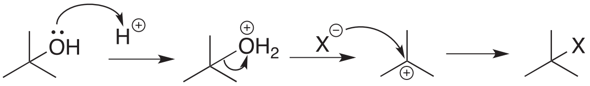


Figure 4.7.10. Mechanism for conversion of alcohol to halide with strong acid.

Halides are not the only good leaving groups that we may convert alcohols into. It is often more convenient to convert alcohols into **tosylates and mesylates**. These are sulfone compounds that can stabilise the negative charge on the oxygen when it leaves. The reagents used are readily available sulfonyl chloride compounds. Their structures and abbreviations are described in Figure 4.7.11.

Figure 4.7.11. Common reagents and their abbreviations.

The alcohol may attack the sulfonyl chloride in a nucleophilic substitution reaction. In this case, the negative charge may be stabilised by the sulfone, following a similar reaction mechanism as the nucleophilic substitution of carboxylic acid derivatives (part 4.7.3). In Figure 4.7.12, we will show the reaction mechanism of an alcohol with mesyl chloride, but this mechanism is the same as with tosyl chloride.

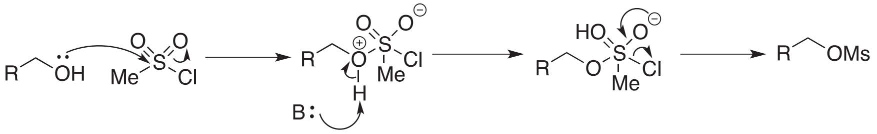


Figure 4.7.12. Mechanism for conversion of alcohol to mesylate.

Finally, we will discuss the most famous named reaction for nucleophilic substitution of alcohols, the **Mitsunobu reaction**. The general scheme for Mitsunobu reaction is shown in Figure 4.7.13.

The mechanism, shown in Figure 4.7.14, involves the nucleophilic attack of phosphine on diethyl azodicarboxylate (DEAD) to form a zwitterion intermediate that generates the anionic nucleophile through deprotonation. The triphenylphosphine is also activated as a better electrophile to be attacked by the alcohol.

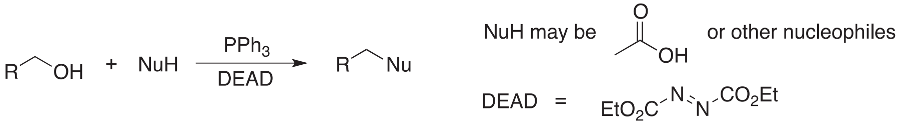


Figure 4.7.13. General scheme for Mitsunobu reaction.

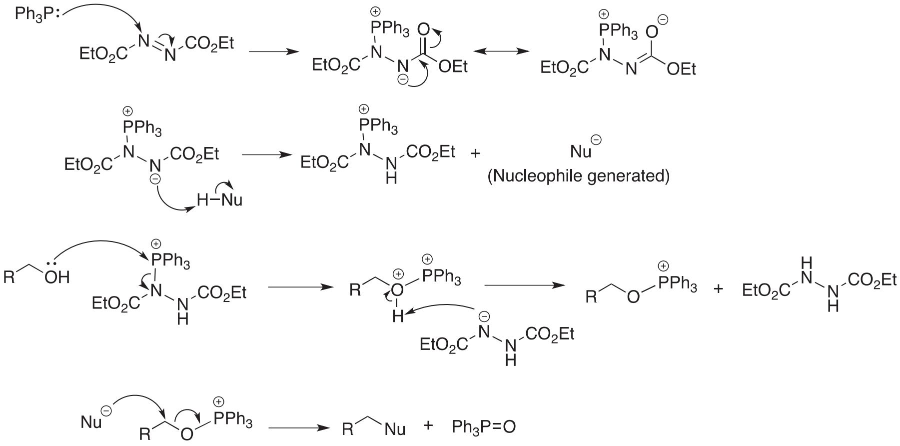


Figure 4.7.14. Mechanism for Mitsunobu reaction.

Now that the alcohol oxygen is a better leaving group, the nucleophile attacks to generate the product and triphenylphosphine oxide, which is very stable due to its strong $P{=}O$ bond.

4. Solvent

Since nucleophilic substitution involves charged intermediates and transition states, the reaction is promoted by **polar solvents**. We will divide polar solvents into 2 categories, **polar protic** and **polar aprotic** solvents.

Protic solvents are solvents that contain a labile proton, which is a hydrogen bonded to an electronegative atom such as oxygen or nitrogen. The labile proton allows protic solvents to form hydrogen bonds with negatively-charged species. At the same time, the electronegative atoms are able to solvate positively-charged species. This makes **protic solvents able to solvate both positive and negative charges**. Common protic solvents are water, methanol, ethanol, isopropanol and acetic acid.

Aprotic solvents are solvents without any labile proton. They usually have electronegative atoms that can solvate positive charges, but lack hydrogen bonding to solvate negative charges. Thus, **aprotic solvents only solvate positive charges**. Common aprotic solvents are acetone, ethyl acetate, acetonitrile, diethylether, tetrahydrofuran (THF) and N,N-dimethylformamide (DMF).

S_N2 reactions are promoted by polar aprotic solvents. This is because nucleophile strength is critical in the rate of S_N2 reactions and we have emphasised previously that it is important to free the nucleophile. Polar aprotic solvent only solvates the cation, thus releasing the free anion as the nucleophile. On the other hand, polar protic solvents will solvate the negatively-charged nucleophile and reduce the rate of S_N2 reaction.

S_N1 reactions are promoted by polar protic solvents. Unlike in S_N2 reactions, nucleophile strength is not important in S_N1 reactions. Instead, the rate-determining step is the decomposition of substrate to form carbocation and leaving group. This step is accelerated by the stabilisation of carbocation and leaving group. Protic solvents are able to solvate both the positively-charged carbocation and negatively-charged leaving group. The solvation of weak nucleophiles such as water and amines by polar protic solvents is also not as significant as solvation of strong nucleophiles that are negatively charged, such as hydroxides.

Table 4.13 shows a summary of the differences between S_N1 and S_N2 reaction mechanisms.

Generally, S_N2 reactions are more useful as they can ensure the formation of only one stereoisomer. We will discuss a few examples of S_N2 reactions.

With oxygen nucleophiles, we can synthesise ethers through an S_N2 reaction. This is known as **Williamson ether synthesis**. It involves the S_N2 reaction of an alkoxide nucleophile attacking an alkyl halide, as shown in Figure 4.7.15.

Table 4.13. Differences between S_N1 and S_N2 reaction mechanisms.

	S_N2	S_N1
Mechanism	One-step, Concerted	Two-steps with carbocation intermediate
Rate Equation	Rate = k_r[R-X][Nu]	Rate = k_r[R-X]
Stereochemistry	Inversion	Racemisation
Substrate	Less sterically hindered (Methyl > Primary > Secondary) Not possible with tertiary substrates	Carbocation stability (Tertiary, Benzylic, Allylic) Not possible with primary or methyl substrates
Nucleophile	Strong nucleophile required	Nucleophile strength is not important
Leaving Group	Moderately important	Very important (-OTf > -OTs > -OMs > -I > -Br)
Solvent	Polar aprotic	Polar protic

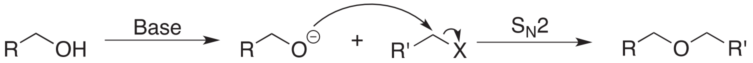


Figure 4.7.15. General scheme and mechanism for Williamson ether synthesis.

With nitrogen nucleophiles, synthesis of amines is a bit trickier. Amines are good nucleophiles, and they become even better nucleophiles after reaction since alkyl groups are electron-donating. This leads to over-reaction and many unwanted products may be generated, as shown in Figure 4.7.16.

Usually such reactions stop at the tertiary amine product, but with excess alkyl halide, the quaternary ammonium salt may also be formed. There are multiple methods developed to synthesise amines without the problem of over-reaction. We will examine 3 of them here:

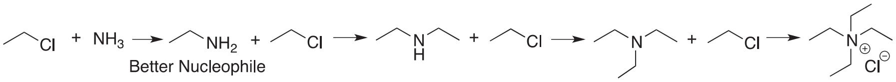


Figure 4.7.16. Reaction of ammonia with chloroethane.

1. Gabriel synthesis of primary amines

This method uses potassium phthalimide as the amine reagent. The phthalimide is a lot less nucleophilic than a normal amine due to the electron-withdrawing effects of the carbonyl groups. On top of that, the nitrogen already has 2 substituents, so it only forms one new bond with alkyl halide. After the nucleophilic substitution,

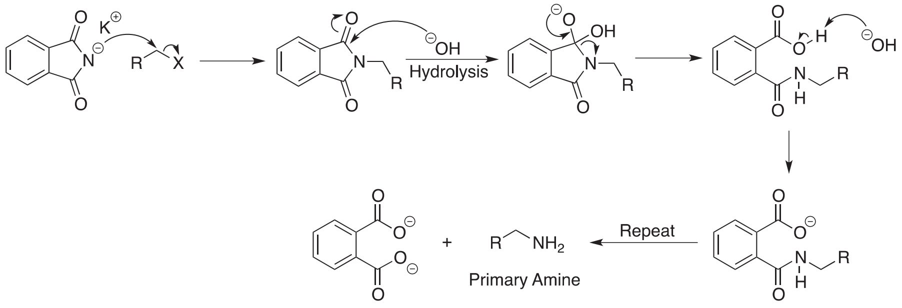


Figure 4.7.17. Reaction scheme and mechanism for Gabriel synthesis of primary amines.

the phthalimide group can be removed by hydrolysis. The mechanism is shown below, but details into the hydrolysis will be explained further in part 4.7.3. For now, the driving force of hydrolysis is the deprotonation of the carboxylic acid to form carboxylate anion, which is no longer electrophilic. The full mechanism for Gabriel synthesis of primary amines is shown in Figure 4.7.17.

2. Using azides and hydroxylamines as nitrogen nucleophiles

Azides are nitrogen nucleophiles that do not undergo multiple substitution reactions as they can only undergo nucleophilic substitution once. Azides can be converted to amines by many reductive methods, for example catalytic hydrogenation and **Staudinger reaction**. The general scheme is shown in Figure 4.7.18. In Figure 4.7.19, we will show the mechanism using azide for nucleophilic substitution followed by reduction to amine using the Staudinger reaction.

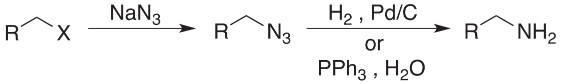


Figure 4.7.18. General scheme for synthesis of primary amines from azides.

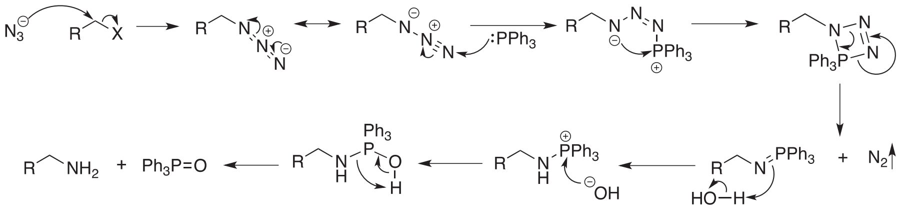


Figure 4.7.19. Mechanism for nucleophilic substitution by azide and Staudinger reaction.

Hydroxylamines can react with carbonyl compounds to form oximes, as shown in part 4.6.1. Oximes can be reduced to form primary amines using catalytic hydrogenation or hydride reducing agents, such as $LiAlH_4$. The general scheme is shown in Figure 4.7.20.

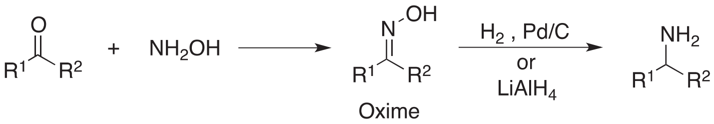


Figure 4.7.20. General scheme for using hydroxylamines to prepare primary amines.

3. Reductive amination

The most general method to make amines is reductive amination, shown in Figure 4.7.21. It is used to add an alkyl group to any existing amine. From ammonia, we will get a primary amine; from a primary amine, we will get a secondary amine and from a secondary amine we will get a tertiary amine. The mechanism for formation of iminium has been shown in part 4.6.1. In reductive amination, a reducing agent is added to the reaction mixture, reducing the iminium ion upon its formation. The reducing agent of choice here is **sodium cyanoborohydride**, $Na(CN)BH_3$. The cyano group is highly electron-withdrawing, making the cyanoborohydride group a much weaker reducing agent than borohydride. Thus, when added in the same reaction mixture, only the charged iminium ion will be reduced instead of the starting carbonyl compound.

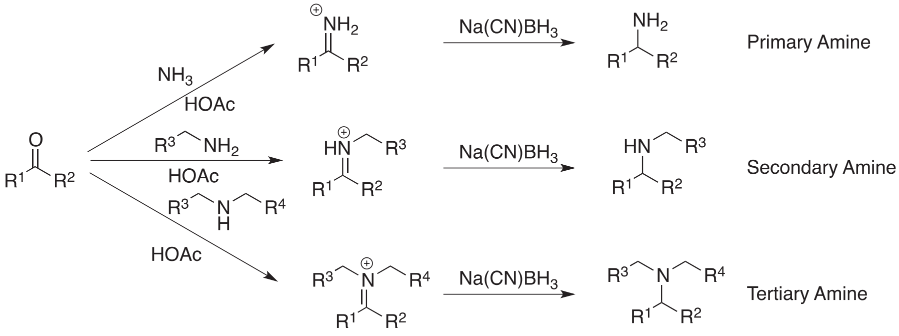


Figure 4.7.21. Reaction scheme for reductive amination.

Other than the commonly encountered S_N2 and S_N1 reactions, there is a less common mechanism to take note of, the **S_N2' reaction**. This mechanism is only encountered for compounds with leaving groups at the allylic position. We will look at some sample substrates and consider the differences between S_N2 and S_N2' reactions.

In the example in Figure 4.7.22, there are 2 different substrates that undergo nucleophilic substitution. Both substrates are allylic chlorides that can undergo S_N2' reaction and S_N2 reaction. Through different pathways, they form the same major product. We will consider the 2 main factors that affects whether a reaction proceed through the S_N2 or S_N2' mechanism:

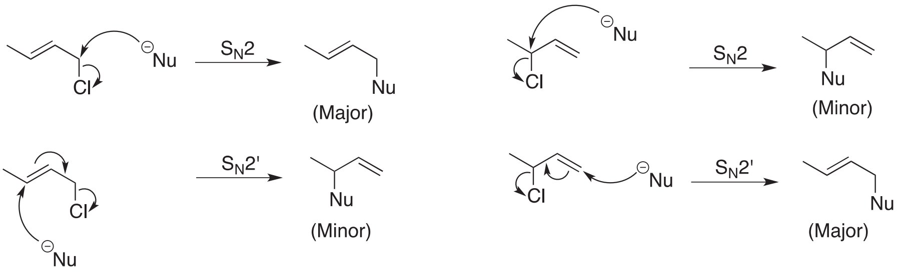


Figure 4.7.22. Diagram showing 2 different substrates producing the same major product.

1. Steric effect

The nucleophile in all S_N2/S_N2'-type reactions prefer to attack the less hindered carbon centre, comparing the sp^2 and sp^3-carbon centres. This is the kinetic factor that determines the selectivity of nucleophilic attack.

2. Stability of C=C double bond

The product formed have 2 different double bond positions, depending on which mechanism is followed. The more stable double bond will be favoured thermodynamically. This means that the more substituted double bond will be favoured for simple alkene compounds.

The synthesis of allylic halides is challenging due to the stabilised allyl cation that forms if the halogen leaves. This makes allylic bromides and allylic iodides too reactive and they easily equilibrate between their 2 forms through the loss and regain of halide. The useful variant that we may prepare without fear of equilibration is allylic chloride. This is because chloride is a much poorer leaving group than bromide and iodide.

Thus, we will consider 2 methods to prepare allylic chlorides without equilibration:

1. Mesylation of corresponding allylic alcohol followed by substitution

This method is simple and requires only a S_N2 reaction. The alcohol is converted into a good leaving group and is substituted by chloride, as shown in Figure 4.7.23.

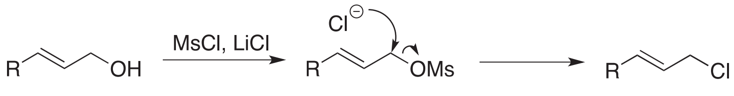


Figure 4.7.23. Reaction scheme for preparation of allylic chloride via mesylation.

2. Mitsunobu reaction

We have previously seen the Mitsunobu reaction used for nucleophilic substitution of alcohols. To produce allylic chlorides, we need a suitable reagent to provide the chloride nucleophile. In this case, it is hexachloroacetone. The general reaction scheme is shown in Figure 4.7.24.

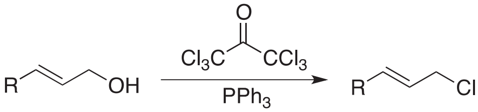


Figure 4.7.24. Reaction scheme for preparation of allylic alcohols via Mitsunobu reaction.

Now that we are able to effectively synthesise allylic alcohols, we must consider how to carry out S_N2' reactions selectively. While most nucleophiles will follow the selectivity rules described above to decide whether to follow the S_N2 or S_N2' pathway, we may favour the S_N2' pathway by using organocopper reagents. As mentioned in part 4.6.2, organocopper reagents are selective for conjugate addition as copper can coordinate to $C{=}C$ double bonds. This ability to coordinate to double bonds allows organocopper reagents to favour S_N2' reactions. For example, the minor product in Figure 4.7.22 could be formed with the use of an organocopper nucleophile, as shown in Figure 4.7.25.

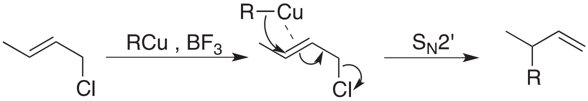


Figure 4.7.25. Reaction scheme showing the selectivity of organocopper reagents.

The last important thing to discuss about S_N2' reactions is their stereochemistry. While the S_N2 reaction causes an inversion, the **S_N2' reaction has an overall syn stereochemistry**. This means that the **attacking nucleophile will approach on the same face as the leaving group**. It is incorrect to say that there is a retention of chirality as the nucleophile will attack a different carbon from the original chiral centre.

The reason for the syn stereochemistry is that S_N2' reactions can be broken down into 2 nucleophilic attacks, the attack of the nucleophile on the double bond and the attack of the double bond on the leaving group. Since these 2 steps follow S_N2 stereochemistry that there must be a backside attack, the reaction is made up of 2 anti attacks, giving the final product an overall syn stereochemistry. Figure 4.7.26 shows an example of the syn stereochemistry.

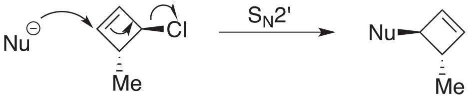


Figure 4.7.26. Stereochemistry example for S_N2' reaction on chiral substrate.

4.7.2 *Nucleophilic conjugate substitution*

We have previously discussed nucleophilic conjugate addition in part 4.6.2, and discussed the factors that determine whether it is a 1,4 or 1,2-attack. In this chapter about substitution, we have learnt that the difference between addition and substitution is the presence of a leaving group. In this part, we will look at the general reaction of nucleophilic conjugate substitution (Figure 4.7.27), its mechanism, and some characteristic reactions.

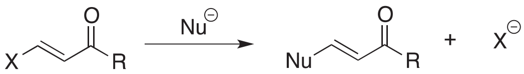


Figure 4.7.27. General reaction for nucleophilic conjugate substitution.

Similar to nucleophilic conjugate addition, carbonyl groups are not the only electron-withdrawing groups that can conjugate with alkenes to give them electrophilic character. While α,β-unsaturated carbonyl compounds will be used as the examples, do not forget that α,β-unsaturated nitriles and nitro compounds can also undergo similar reactions. The main difference between substitution and addition is the saturation of the product. The product of conjugate addition reactions is the saturated compound with the electron-withdrawing group while the product of conjugate substitution reactions retains the unsaturation in the starting material. This is due to the addition-elimination mechanism shown in Figure 4.7.28.

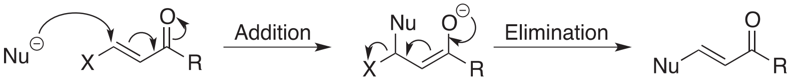


Figure 4.7.28. Mechanism for nucleophilic conjugate substitution.

The product is usually the trans-alkene due to its higher thermodynamic stability. The first step (addition) is also accelerated as most leaving groups are electron-withdrawing, increasing the electrophilicity at the β-carbon. In such nucleophilic conjugate substitution reactions, it is important to control the reactivity as the product may still undergo addition from the nucleophile. The control is possible by using only one equivalent of nucleophile. We will examine an example of nucleophilic conjugate substitution reaction used in the synthesis of a drug, Tagamet, shown in Figure 4.7.29.

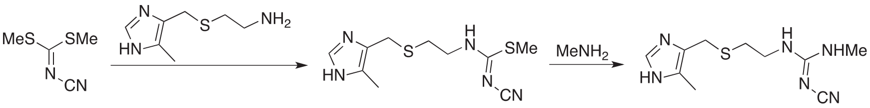


Figure 4.7.29. Selected section from synthesis of Tagamet.

This synthesis makes use of 2 consecutive nucleophilic conjugate substitution reactions. It is worthy to note that the double bond in this reaction is a $C{=}N$ double bond instead of $C{=}C$ double bond, which increases the electrophilicity at the carbon. Despite this change, the mechanism of the reaction is identical. It is important to identify such patterns in organic chemistry as organic reactions are often varied.

4.7.3 *Nucleophilic substitution of carboxylic acid derivatives*

Carboxylic acid derivatives include acyl chlorides, acid anhydrides, esters and amides. They can easily convert between each other through nucleophilic substitution reactions. The general mechanism for the **nucleophilic substitution at carbonyl oxygen** is shown in Figure 4.7.30.

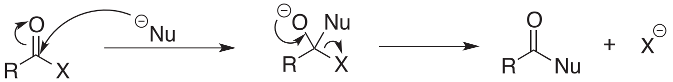


Figure 4.7.30. General mechanism for nucleophilic substitution at carbonyl oxygen.

The first step of the reaction mechanism is the same as in nucleophilic addition, except that one substituent on the carbonyl carbon is a leaving group. The second step is the elimination of the leaving group. We must take note that the elimination step may eliminate the nucleophile as well, regenerating the starting material. Thus, we must compare the electrophilicities and leaving group abilities of the various carboxylic acid derivatives to determine which reactions can proceed. Figure 4.7.31 shows the series of carbonyl compounds with decreasing electrophilicity and increasing stability.

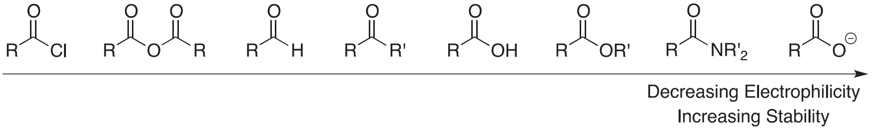


Figure 4.7.31. Reactivity series for carbonyl compounds.

Other than aldehydes and ketones, all other carbonyl compounds shown in the reactivity series have leaving groups. These carbonyl compounds can interconvert between each other through reactions. Thermodynamically, it is favourable to form compounds with increasing stability. Thus, acyl chlorides may be used to form any of the other carboxylic acid derivatives, as shown in Figure 4.7.32.

The reactivity of acid anhydride is similar, just that it is unable to react with chloride to generate acyl chloride. We will move on to look at how to prepare esters and amides from carboxylic acid. Carboxylic acid is only weakly electrophilic due to

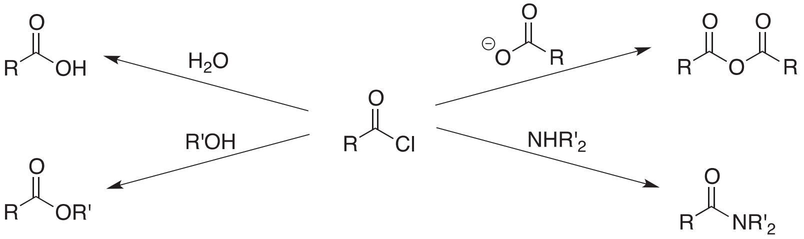


Figure 4.7.32. Reactions of acyl chlorides to form other carboxylic acid derivatives.

the presence of 2 oxygen groups. We will discuss the methods used to prepare other carboxylic acid derivatives from carboxylic acid.

1. Acid catalysis

To activate the carbonyl group, we may use acid to protonate the oxygen and increase its electrophilicity. In other nucleophilic reactions, base catalysis often works equally well by activating the nucleophile. However, in the current reaction, carboxylic acids are also deprotonated by base to form carboxylate salt, which is not electrophilic enough to undergo nucleophilic attack. Thus, base catalysis cannot be used to form carboxylic acid derivatives from carboxylic acid. Acid catalysis is useful in the synthesis of esters by reacting carboxylic acid with alcohols, known as **Fischer esterification**, as shown in Figure 4.7.33.

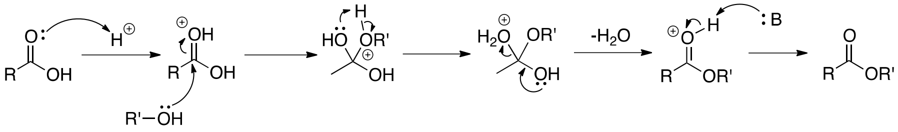


Figure 4.7.33. Mechanism of Fischer esterification.

Note that every step in the esterification process is reversible, and the product will most likely be a mixture of carboxylic acid and ester. To improve the yield of ester, we can remove the water from the reaction mixture during the reaction, shifting the equilibrium towards the formation of ester. The reaction usually takes many hours with reflux under strong acidic conditions. Acid catalysis may be used in such ester synthesis, but it cannot be used for amide synthesis. Strong acid capable of protonating the carboxylic acid will definitely protonate the amine nucleophile, rendering it no longer nucleophilic. Direct reaction between amine and carboxylic

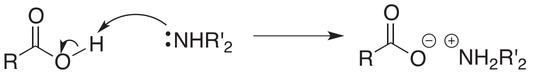


Figure 4.7.34. Formation of salt from reaction of carboxylic acid with amine.

acid will also be a simple acid-base reaction, which is much faster than a nucleophilic attack. Upon formation of ammonium and carboxylate salt, both nucleophile and electrophile are deactivated and the reaction will stop, as shown in Figure 4.7.34.

2. Converting carboxylic acids to better electrophiles

The second method is to convert carboxylic acids to a better electrophile before the nucleophilic substitution takes place. This can be done in many ways, such as converting carboxylic acids to acyl chlorides or acid anhydrides, and using coupling agents. Carboxylic acids may be converted to acyl chlorides with the use of chlorinating agents, most commonly thionyl chloride, $SOCl_2$. We have previously mentioned this reagent as a reagent to convert hydroxyl groups into chloro groups, and its reaction with carboxylic acids to generate acyl chlorides is shown in Figure 4.7.35.

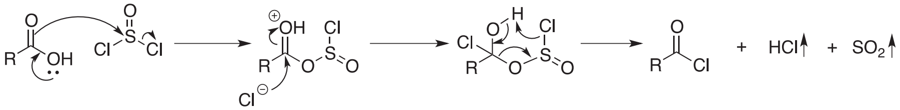


Figure 4.7.35. Mechanism of conversion of carboxylic acids to acyl chlorides using $SOCl_2$.

Other chlorinating reagents such as PCl_5 may also be used to convert carboxylic acids to acyl chloride through a similar mechanism, though their use is less common than $SOCl_2$. Thermodynamically, this reaction generates the highly reactive and unstable acyl chloride, but it is compensated by the entropy of the 2 stable gases evolved. This makes the reaction extremely useful, as acyl chlorides are the most reactive carboxylic acid derivatives. As we have seen above, they may be converted into any other carboxylic acid derivative easily. Thus, a possible synthetic route to prepare amides from carboxylic acids would be to first convert the carboxylic acid to an acyl chloride before the addition of amine, as shown in Figure 4.7.36.

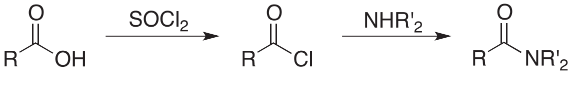


Figure 4.7.36. Possible synthetic route for amides through acyl chlorides.

Other than acyl chloride, another reactive electrophile intermediate is acid anhydride. Acid anhydrides may be prepared from carboxylic acids by reaction with acyl chlorides or other more electrophilic acid anhydrides. One example is in **Yamaguchi esterification**, where trichlorobenzoyl chloride is used to form an acid anhydride before addition of alcohol to form the ester, as shown in Figure 4.7.37.

Other than trichlorobenzoyl chloride, trifluoroacetic anhydride (TFAA) is also commonly used to convert carboxylic acids to acid anhydrides. Acid anhydrides will also react with amines to form amides.

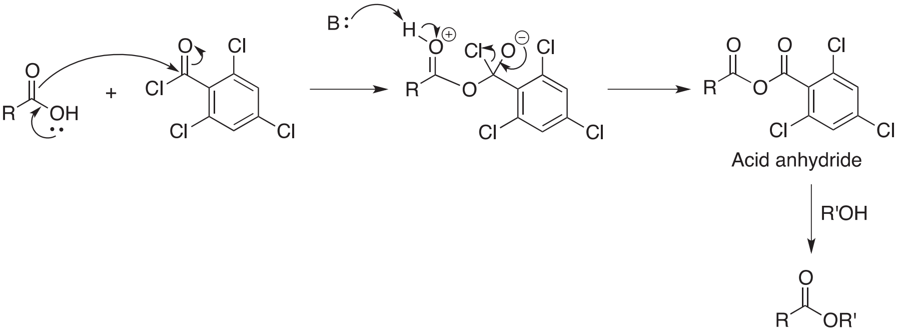


Figure 4.7.37. Reaction scheme for Yamaguchi esterification through acid anhydride intermediate.

3. Using coupling agents

Due to the extensive synthetic use of nucleophilic substitution reactions at the carbonyl carbon, the yield and rate of such reactions must be improved. The use of coupling agents achieves both of these objectives in a one-pot reaction. They work by reacting with the carboxylic acid first to form a more electrophilic intermediate that reacts with the nucleophile. This is similar to first converting the carboxylic acid to acyl chloride or acid anhydride, but the yield is improved as this reaction is carried out in one-pot without work-up and purification to isolate the intermediate. The most commonly employed coupling agent is ***N*,*N′*-dicyclohexylcarbodiimide (DCC)**, and the mechanism it follows is shown in Figure 4.7.38.

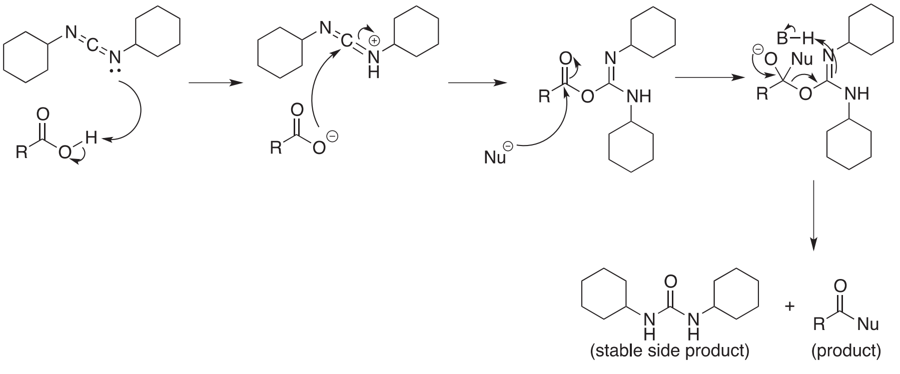


Figure 4.7.38. Mechanism for DCC coupling of carboxylic acid and nucleophile.

As can be seen from the mechanism, the active functionality in the coupling agent is the carbodiimide functionality. Thus, other carbodiimides with different substituents may also act as coupling agents with slightly different properties, such as 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC). Coupling agents are often employed even in reactions that may proceed in acid, such as esterification, as they provide more reliable and higher yielding pathways. For example, the esterification reaction using DCC and DMAP (nucleophilic catalyst) is known as **Steglich esterification**.

Background 4e. Nucleophilic catalysis

Nucleophilic substitution reactions may be accelerated through the use of nucleophilic catalysts. Nucleophilic catalysts are efficient nucleophiles that can quickly perform nucleophilic substitution at carbonyl carbon to generate a more electrophilic intermediate, then act as good leaving groups to be substituted by the actual nucleophile. Thus, nucleophilic catalysts must fulfil 3 general conditions:

1. Good nucleophile
2. Forms a more electrophilic intermediate (usually electron withdrawing)
3. Good leaving group

One of the best nucleophilic catalysts is **4-(dimethylamino)pyridine, abbreviated as DMAP**. The catalysed reaction pathway using DMAP is shown in Figure 4.7.39.

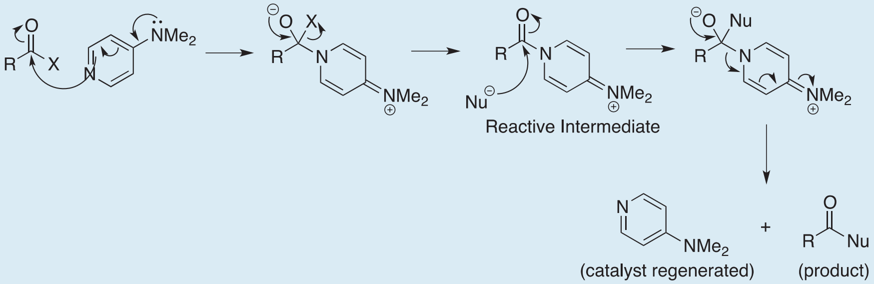


Figure 4.7.39. Reaction mechanism of catalysed nucleophilic substitution by DMAP.

The first step involves the nucleophilic attack by DMAP on the carbonyl carbon. DMAP has strongly electron-donating dimethylamino group that increases the nucleophilicity of the pyridine nitrogen. Thus, it is a good nucleophile. The reactive intermediate has the cationic DMAP substituent that withdraws electron density from the carbonyl carbon, making it more electrophilic for the nucleophile to attack. Finally, as a cationic species, it is a good leaving group and is regenerated at the end of the reaction.

Esters have similar reactivity to carboxylic acids and may be used to prepare amides. They can react directly with amines in a nucleophilic substitution reaction as they do not have any highly acidic protons. Amides are the most thermodynamically stable carboxylic acid derivatives and do not react to generate other carboxylic acid derivatives, other than hydrolysis to carboxylic acids. While esters and amides are more stable than carboxylic acids (in the carboxylate form), they can be hydrolysed to generate carboxylic acids.

The hydrolysis of esters and amides may be carried out in both acid and base. Acid catalysis gives us a reversible pathway, and the yield can be improved by adding a large excess of water and distilling away the alcohol or amine side product. The mechanism is the exact reverse of acid-catalysed Fischer esterification shown in Figure 4.7.33. More noteworthy is the basic hydrolysis of esters and amides. While we specifically mentioned that base catalysis may not be used for preparation of esters and amides as the carboxylate salt is deactivated due to low electrophilicity, this property is useful to drive hydrolysis reactions as it makes the hydrolysis reaction irreversible. Thus, a stoichiometric amount of base is used to deprotonate the carboxylic acid product and form the stable carboxylate salt. Since hydrolysis of esters and amides to carboxylic acid is not thermodynamically favourable, the driving force from the irreversibility of the deprotonation reaction is able to improve the overall reaction yield. To illustrate this, the mechanism for basic hydrolysis of esters is shown in Figure 4.7.40.

Other than carboxylic acid derivatives, another electrophilic functional group that is at the same oxidation level as carboxylic acid is nitrile. Nitriles may be prepared via aliphatic nucleophilic substitution of alkyl halides by cyanide ion, and it can easily interconvert with carboxylic acid derivatives. Nitriles may be converted into carboxylic acids by hydrolysis through an amide intermediate, both with acid and base catalysis. Acidic hydrolysis of nitriles is more common synthetically, and its mechanism is shown in Figure 4.7.41.

The reverse reaction to generate nitriles from carboxylic acid derivatives is the dehydration of amides. A commonly used dehydrating agent is $POCl_3$ and its mechanism for converting amides to nitriles is shown in Figure 4.7.42.

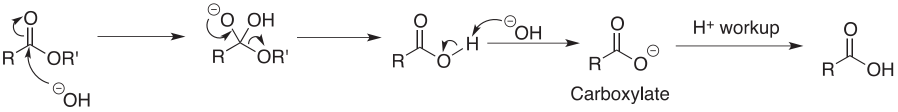


Figure 4.7.40. Mechanism for basic hydrolysis of esters.

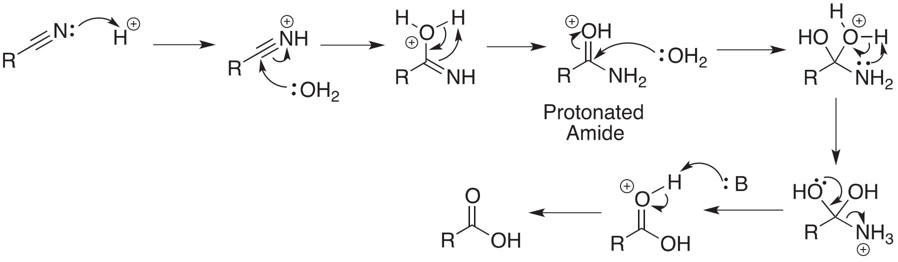


Figure 4.7.41. Mechanism for acidic hydrolysis of nitriles.

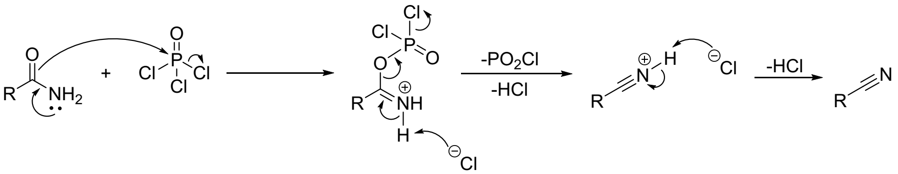


Figure 4.7.42. Mechanism for dehydration of amide to nitrile with $POCl_3$.

It seems easy to prepare ketones from carboxylic acid derivatives through nucleophilic substitution using carbon nucleophiles. In reality, due to the high nucleophilicity of carbon nucleophiles such as Grignard reagents, the reaction does not stop at the ketone stage and the reagent will perform nucleophilic addition on the ketone to generate a tertiary alcohol, as shown in Figure 4.7.43.

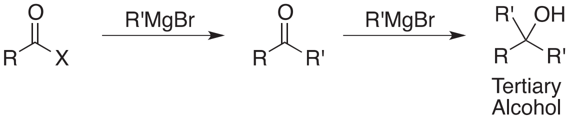


Figure 4.7.43. Reaction of a carboxylic acid derivative with Grignard reagent.

This reaction is difficult to control, especially if the carboxylic acid derivative is less electrophilic than ketone. Thus, there are many methods developed to achieve a clean conversion to ketone.

1. Increasing electrophilicity and decreasing nucleophilicity

We have previously learnt about Gilman reagents as soft organocopper reagents. Not only are they soft, they are also much weaker carbon nucleophiles than the common organolithium or Grignard reagents. They only perform nucleophilic attack at very electrophilic centres such as acyl chlorides, and do not react with ketones. Thus, we are able to obtain the ketone product by performing a nucleophilic substitution using Gilman reagents on acyl chlorides, as shown in Figure 4.7.44.

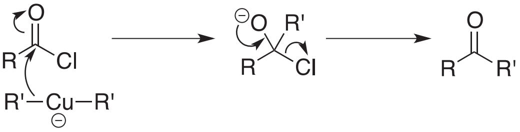


Figure 4.7.44. Mechanism for reaction of Gilman reagent with acyl chloride to form ketones.

2. Forming stable tetrahedral intermediates

Stable tetrahedral intermediates may be formed in certain special conditions. This means that the leaving group does not leave until the workup when the reaction is quenched. The tetrahedral intermediate is unable to undergo further nucleophilic

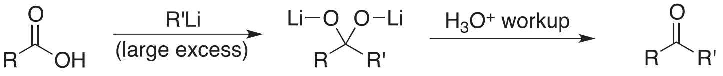


Figure 4.7.45. Stable tetrahedral intermediate formed from carboxylic acid with excess organolithium.

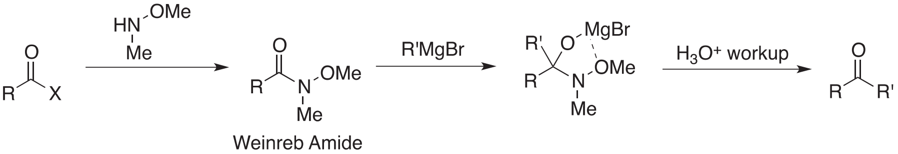


Figure 4.7.46. The preparation of Weinreb amide from carboxylic acid derivatives and its reaction with Grignard reagent.

attack by the carbon nucleophile and the strong carbon nucleophile is destroyed in the workup step. One method to make use of stable tetrahedral intermediates is to use a large excess (>2 equivalents) of organolithium reagent when reacting with a carboxylic acid. The organolithium reagent will deprotonate the carboxylic acid, forming double oxoanions in the tetrahedral intermediate that are unable to act as leaving groups. This tetrahedral intermediate decomposes only upon workup, and all remaining organolithium reagent is destroyed. This is shown in Figure 4.7.45.

A more reliable method to generate a stable tetrahedral intermediate is through the use of **Weinreb amides**. Weinreb amides are specially designed amides with a methoxy group bonded to the amide nitrogen. This allows the metal to coordinate to both the methoxy group and the carbonyl oxygen in the tetrahedral intermediate, stabilising it through chelation. Since there are 2 ligands that may bind to the metal, a divalent metal will stabilise the intermediate best, and Grignard reagents with magnesium (2+) may be used as the nucleophile. The reaction pathway is shown in Figure 4.7.46.

It is worthy to note that amides may be easily prepared from the carboxylic acid derivatives as they are most thermodynamically stable, which also explains why the tetrahedral intermediate is stable. The amine can only leave after the acid workup protonates it, in the process destroying any excess Grignard reagent that may cause an over-addition.

3. Using nitriles

Nitriles are also electrophiles that can be prepared from dehydration of amides. They do not have a leaving group, thus they are unable to undergo nucleophilic substitution. Instead, with Grignard reagents, they undergo nucleophilic addition to form a deprotonated imine, which is no longer electrophilic due to the negative charge present on the nitrogen. Upon workup, the imine may be hydrolysed to ketone. This method prepares ketones without any risk of over-addition due to the reaction pathway following a nucleophilic addition mechanism, shown in Figure 4.7.47.

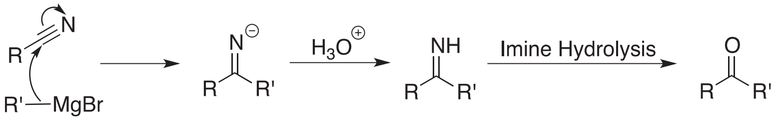


Figure 4.7.47. Preparation of ketones from nucleophilic addition to nitriles.

4.7.4 *Nucleophilic aromatic substitution on benzene*

Aromatic rings are exceptionally stable and react very differently from aliphatic compounds. Generally, both the S_N1 and S_N2 mechanisms for nucleophilic substitution do not work on aromatic rings, as shown in Figure 4.7.48. S_N1 reactions require the formation of stable carbocation, but a phenyl cation is highly unstable as the positive charge resides in a vacant sp^2-orbital not conjugated with the p-orbitals of the phenyl ring. S_N2 reactions require the nucleophile to attack the σ^*-orbital of the $C{-}X$ bond, which means approaching the carbon from directly behind. Since aromatic compounds are planar, this means that the nucleophile must approach from within the aromatic ring, which is impossible. The inversion of the sp^2-carbon will also cause the benzene ring to distort and bend, which is energetically unfavourable.

Figure 4.7.48. Both S_N1 and S_N2 reactions cannot happen on aromatic rings.

However, **nucleophilic aromatic substitution (S_NAr)** may happen through a mechanism similar to nucleophilic conjugate substitution (refer to part 4.7.2). This means that the nucleophile first adds to the benzene ring before the leaving group is expelled. The nucleophilic addition step requires a good electron-withdrawing group on the aromatic ring to stabilise the anion formed in the intermediate. The subsequent elimination of leaving group is fast. The general S_NAr mechanism is shown in Figure 4.7.49.

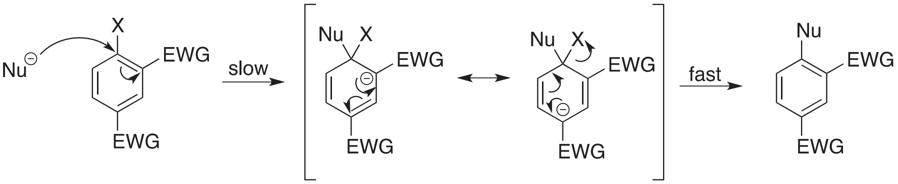


Figure 4.7.49. General mechanism of S_NAr reaction.

The rate determining step is the addition of nucleophile to the aromatic ring. The rate of addition of nucleophile to the aromatic ring is determined by a few factors:

1. Strength of nucleophile

Since the nucleophilic addition to the aromatic ring follows a bimolecular rate law, the strength of nucleophile will definitely affect the rate of reaction. However, we will not elaborate here as the nucleophilic strength follows exactly that of a $\mathrm{S_N2}$ reaction.

2. Leaving group

At first glance, it may be confusing why the leaving group will affect the rate of the addition step. Indeed, the leaving group ability will only affect the rate of the fast second step, which will not affect the overall rate. However, the leaving group plays another role in this reaction, which is to withdraw electrons from the aromatic carbon, making it more electrophilic. Thus, the reactivity order of leaving groups for nucleophilic aromatic substitution is $\mathrm{F} \gg \mathrm{Cl} \approx \mathrm{Br} > \mathrm{I}$. The highly electronegative fluorine withdraws electrons from the adjacent carbon through the inductive effect, making it more electrophilic and accelerating the nucleophilic addition step. Even though fluoride is the most basic leaving group, the overall rate is unaffected as the second step is much faster than the first step.

3. Presence of electron-withdrawing groups at ortho/para positions

As we can see from the mechanism shown in Figure 4.7.49, the attack of the nucleophile generates an anion that is delocalised in the ring. Electron-withdrawing groups are able to stabilise the anion by allowing the negative charge to delocalise over them. From the resonance structures, we note that the negative charge is able to delocalise to the ortho and para positions in the ring. This means that electron withdrawing groups placed at these positions are able to withdraw electron density and stabilise the negative charge. The best electron-withdrawing groups are those that can withdraw electron density through conjugation, such as carbonyl compounds, nitriles and nitro compounds. However, groups may also accelerate the reaction through inductive electron-withdrawing effect such as F or $\mathrm{CF_3}$.

Nucleophilic substitution can be performed on benzene through another mechanism, much higher in energy. This is through the **benzyne** intermediate, which is a benzene ring where one double bond becomes a triple bond. The additional π-bond is formed by the overlap of 2 sp^2-orbitals on the plane of the molecule. This overlap is weak and unstable, making benzyne a highly reactive intermediate. The additional π-bond does not delocalise into the benzene π-system as it is perpendicular to all the p-orbitals. This special characteristic makes benzyne electrophilic at the triple bond, and sometimes even nucleophilic when there is a strong electrophile.

The benzyne mechanism is an elimination-addition reaction, opposite to the $\mathrm{S_NAr}$ mechanism we have just learnt. Elimination reactions will only be covered in detail in the next chapter, but they are essentially the removal of an adjacent proton and leaving group together to form a new bond. The deprotonation step usually requires the use of strong base, and this is especially so for benzyne as the new bond formed is weak. Upon formation of benzyne, it reacts immediately with any available nucleophile to form the product.

We will look at a sample reaction in Figure 4.7.50 using sodium amide as both the base and nucleophile.

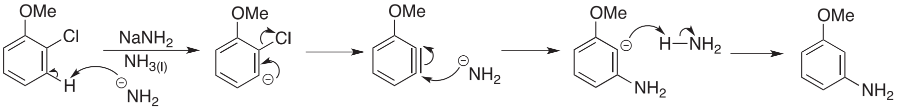


Figure 4.7.50. Mechanism of nucleophilic attack with benzyne intermediate.

The interesting part of this reaction is that the entering and leaving groups are at different positions. After the elimination of HCl to form benzyne, the nucleophile may approach from both positions (ortho and meta to OMe). This is when we have to consider the regioselectivity of the reaction based on steric and electronic effects.

1. Steric effect:

In all other aromatic reactions, the reagents attack the p-orbitals that are perpendicular to the plane of the molecule. Since the p-orbitals are far from any substituents on benzene, the size of such substituents has little effect on the rate of reaction. However, benzyne is attacked at the sp^2-orbital on the plane of the other substituents. Thus, the steric effect will favour the attack of the nucleophile on the position further from the substituent.

2. Electronic effect:

The substituent may be electron-donating or electron-withdrawing. In this case electron-withdrawing substituents is preferred as it will be able to stabilise the negative charge in the intermediate. While oxygen is usually considered an electron-donating group due to π-effects from the lone pair donation to the benzene ring, it is electron-withdrawing through inductive σ-effect. The inductive effect is more significant in this case as the anion is in the sp^2-orbital instead of p-orbital. Thus, the anion formed closer to the oxygen substituent would be stabilised better through inductive electron-withdrawing effect.

4.7.5 *Nucleophilic substitution on aromatic heterocycles*

Aromatic heterocycles are varied in structure and property. They are usually more reactive than benzene due to the inclusion of a heteroatom that may change the electrophilic and nucleophilic properties of the aromatic system. Due to the polarity introduced by the heteroatom, different aromatic heterocycles with different structures will have different properties and undergo different reactions. The aromatic heterocycle that is most suited to nucleophilic substitution is **pyridine**.

Until now, we have mainly seen the use of pyridine as a base, or sometimes as a nucleophilic catalyst (DMAP). Here, pyridine may also act as a reagent for nucleophilic aromatic substitution. Remember that for nucleophilic aromatic substitution, an electron-withdrawing substituent is usually required to stabilise the negative charge. In this case, the nitrogen in the pyridine acts as the electron-withdrawing group to stabilise the negative charge, as the negative charge may be delocalised onto the nitrogen. The mechanism for the nucleophilic aromatic substitution on 2-chloropyridine is shown in Figure 4.7.51.

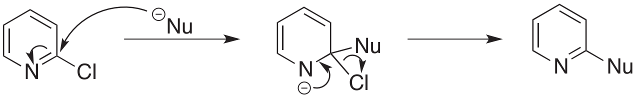


Figure 4.7.51. Mechanism for nucleophilic aromatic substitution on pyridine.

The nucleophilic substitution follows a S_NAr mechanism, which means that the negative charge may only be stabilised if the leaving group is in the 2, 4 or 6 position. The rest of the conditions follow that of S_NAr on benzene. The starting material may be prepared from pyridine through electrophilic substitution, which will be covered in chapter 4.10.

4.8 Elimination Reactions

Elimination reactions are reactions where a group is lost from a molecule, the opposite of addition reactions. The molecule usually becomes unsaturated, forming $C{=}C$ double bonds. In this chapter, we will discuss the different mechanisms for elimination and discuss the selectivity of such reactions. We will also learn about the different methods of preparing alkenes, mostly through elimination reactions.

4.8.1 *E1 and E2 mechanisms*

Elimination reactions are generally reactions that remove 2 groups on adjacent carbons to form an alkene, as shown in Figure 4.8.1.

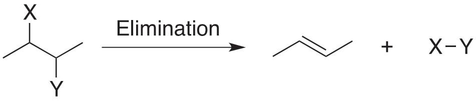


Figure 4.8.1. General scheme for elimination reaction.

Most of the time in elimination, one of the groups being eliminated is a proton, meaning that either X or Y is H. This is the most common elimination substrate as the elimination reaction can be easily driven by using a strong base that can deprotonate the proton. As the proton is removed as H^+, the other group must be removed as X^- to keep both products neutral in charge. Even in carbonyl chemistry, we commonly see elimination occurring in tetrahedral intermediates. Examples of elimination reactions are shown in Figure 4.8.2.

Similar to S_N1 and S_N2 mechanisms for nucleophilic substitution, elimination reactions also have first-order $(E1)$ and second-order $(E2)$ rate laws. The $E1$ and $E2$ mechanisms are shown in Figure 4.8.3.

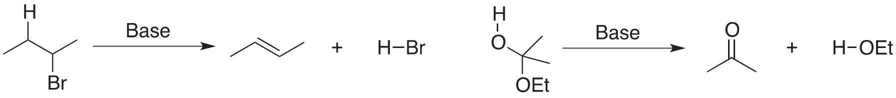


Figure 4.8.2. Examples of elimination reactions.

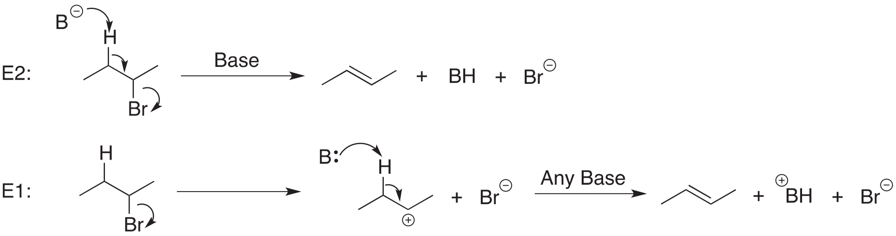


Figure 4.8.3. E2 and E1 reaction mechanisms.

It is easy to spot the similarities between $E1/E2$ and S_N1/S_N2. $E1$ follows a first-order rate law depending only on the concentration of the substrate while $E2$ follows a second-order rate law that also depends on the concentration of the base. Thus, the factors that apply to S_N1 and S_N2 reactions also apply to $E1$ and $E2$ reactions. However, base is used rather than nucleophile in elimination reactions. Table 4.14 lists the summarised results from the comparison of $E1$ and $E2$ reaction mechanisms, while the details may be found in part 4.7.1 where we compared the effects on S_N1 and S_N2 reactions.

We will explain the selectivity in elimination reactions. We will first discuss the regioselectivity, followed by the stereoselectivity.

Regioselectivity refers to the preferred position for the reaction to take place. In nucleophilic substitution, the only possible reaction site is at the carbon bonded to heteroatom, so there was no regioselectivity consideration. In the case of elimination, it is common to find multiple protons at the right position and orientation to undergo elimination. The regioselectivity issue is shown in Figure 4.8.4.

Table 4.14. Comparison between E1 and E2 reaction mechanisms.

	E2	**E1**
Mechanism	One-step, Concerted	Two-steps with carbocation intermediate
Rate Equation	Rate = k_r[Substrate][Base]	Rate = k_r[Substrate]
Stereochemistry	Stereospecific	Stereoselective
Substrate	Requires proton to be anti-periplanar to the leaving group	Carbocation stability (Tertiary, Benzylic, Allylic) Not possible with primary or methyl substrates
Base	Strong base required	Base strength is not important
Leaving Group	Moderately important	Very important (-OTf > -OTs > -OMs > -I > -Br)
Solvent	Polar aprotic	Polar protic

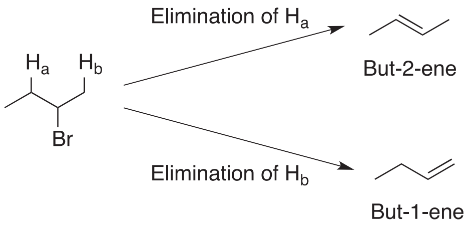


Figure 4.8.4 Regioselectivity issue in elimination reactions.

This is a simple example where there is more than 1 hydrogen available for elimination. To determine which reaction pathway is predominant, we need to consider the thermodynamic and steric factors:

1. The thermodynamic product, but-2-ene, is known as the **Zaitsev product**. The stability of an alkene increases with the number of electron-donating substituents on it. This is because electron-donating substituents increase the electron density in the π-bond of the alkene, strengthening the $C{=}C$ double bond. The $sp^3\,C{-}sp^2\,C$ bond is also stronger than a normal $sp^3\,C{-}sp^3\,C$ bond due to conjugation between the HOMO of the $C{-}H$ on the alkyl group and the LUMO of the alkene.
2. The kinetic product, but-1-ene, is known as the **Hoffman product**. It is a kinetic product formed mainly using bulky and strong bases. The steric hindrance at less substituted carbon centres is smaller, allowing bases to access them faster and form the kinetic product. There are also 3 terminal H_b compared with $2\ H_a$, which means that there is a higher probability to form the Hoffman product.

The thermodynamic and kinetic products are formed depending on the reaction conditions. The thermodynamic product is usually formed when the reaction is carried out under high temperature and for a long time, allowing equilibrium to be established. The kinetic product is formed quickly in reactions that happen at low temperature and for a short time.

Note that the kinetic Hoffman product is only formed through E2 mechanism. The strength of base does not affect the E1 mechanism and the elimination step is the fast step. Thus, the thermodynamic Zaitsev product will always be formed in preference to the kinetic Hoffman product in an E1 reaction.

Stereoselectivity in elimination reactions no longer refers to the chirality at tetrahedral carbon centres. It refers to the alkene stereochemistry as the C=C double bond has a high energy barrier for rotation. The stereoselectivity issue is shown in Figure 4.8.5.

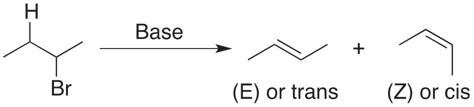


Figure 4.8.5. Stereoselectivity consideration for elimination to form alkenes.

For stereoselectivity, we have to treat E2 and E1 reactions separately. E2 reactions are stereospecific while E1 reactions are stereoselective. For E1 reactions, the stereoselectivity is based entirely on steric hindrance. Upon the formation of the cation, the single bond may freely rotate such that the large groups point away from each other. Thus, the trans product is favoured as shown in Figure 4.8.6.

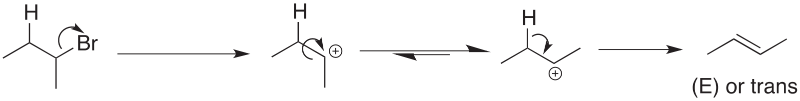


Figure 4.8.6. Stereoselective elimination through E1 mechanism.

E2 reactions require the orbitals in the substrate to be lined up and in the correct orientation for the elimination to occur. The new π-bond is formed from the overlap of the C–H σ-orbital with the C–X σ*-orbital, thus the C–H bond and C–X bond must be aligned. There are 2 such arrangements, known as syn-periplanar and anti-periplanar, as shown in Figure 4.8.7.

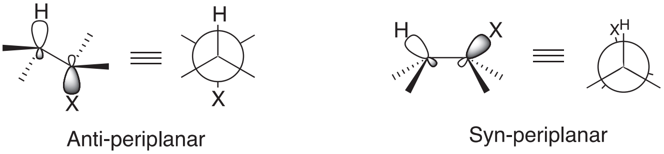


Figure 4.8.7. Anti-periplanar and syn-periplanar arrangement of H and X.

Background 4f. Newman projection

Newman projections are commonly used to show relative stereochemistry across single bonds. It allows a chemist to see across a single bond and understand the stability of different conformations of the single bond.

Newman projections are drawn by viewing a molecule across a C–C bond. The front carbon is shown in front while the back carbon is represented by a circle and the bonds coming out of the circle. We will look at Newman projections of butane as an example in Figure 4.8.8.

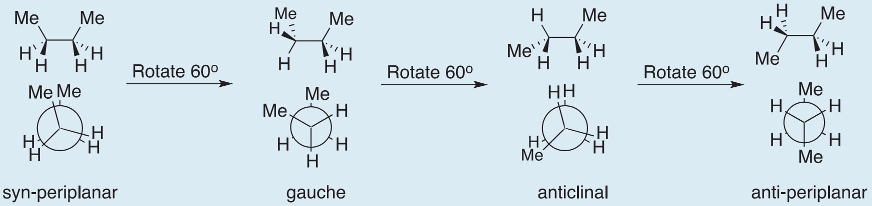


Figure 4.8.8. Conformations of butane shown by Newman projection.

The conformations are in general classified as eclipsed or staggered. **Eclipsed** conformations have the bonds directly overlapping each other, as in syn-periplanar and anticlinal conformations. When drawing the Newman projections for eclipsed conformation, we slightly displace the bonds to show both the front and back atoms even though the atoms at the back are directly behind those in front. **Staggered** conformations have the bonds 60° away from each other. Usually, eclipsed conformations are higher in energy and less stable than staggered conformations due to the repulsion between the filled bonding orbitals. In the staggered conformation, there is also hyperconjugation from the σ-orbital to the σ*-orbital that further stabilises it.

It is important to be able to interpret Newman projections quickly, especially those for staggered conformations, which are much more common. In such Newman projections, the groups opposite to each other are anti while the groups next to each other are syn. The relationships are shown in Figure 4.8.9. From this Newman projection, A is anti to C but syn to B.

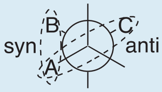


Figure 4.8.9. Relationship between groups represented on the Newman projection.

Syn-periplanar conformation is the highest energy conformation and is rarely observed. While the 2 orbitals are aligned, they are not fully parallel in the syn-periplanar conformation. Thus, E2 reactions rarely happen on syn-periplanar substrates.

Instead, the molecule usually adopts the anti-periplanar conformation before elimination via E2 mechanism. As the molecule will rotate to the anti-periplanar conformation, the stereochemistry of the product is determined by the chirality of the chiral centres and the E2 reaction is stereospecific.

In Figure 4.8.10, the substrate is originally not in the anti-periplanar conformation. Before E2 elimination can take place, the substrate must rotate about the single bond to the anti-periplanar conformation. After the E2 elimination, the groups syn to each other remain syn, while the groups anti to each other remain anti. Note that the product formed is the (Z)-product despite the (E)-product being more thermodynamically favourable sterically. When there are multiple choices for the anti-periplanar transition state, the steric argument (similar to E1) applies and the least hindered product is formed selectively. As the E2 reaction can only take place when the substrate is aligned in the anti-periplanar conformation, it is a stereospecific reaction where the stereochemistry of the product is determined by the stereochemistry of the reagents.

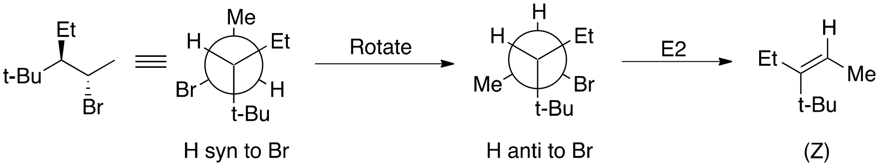


Figure 4.8.10. Stereospecific E2 reaction.

Now that we have learnt about the E1 and E2 reactions, we will have to compare elimination to nucleophilic substitution reactions as they act on the same substrates. Overall, elimination reactions are more thermodynamically favourable as there is a significant increase in entropy due to the formation of 2 products from one substrate. Also, the activation energies of elimination reactions are higher due to more bonding changes occurring in elimination reactions. Thus, at higher temperatures, elimination is favoured over substitution reactions. We must also look at other factors, and we will first compare S_N1 and E1 reactions.

Both S_N1 and E1 reactions happen on substrates with a good leaving group that is capable of forming a stable carbocation. There are certain special substrates that only allow for nucleophilic substitution where there is no adjacent hydrogen for elimination. When a substrate is able to undergo both S_N1 and E1 reactions, **a mixture of both products** is usually obtained. This is due to the high reactivity of the carbocation intermediate that any weak base or nucleophile is able to perform both E1 and S_N1 reactions. However, it is possible to tune the selectivity such that one reaction pathway may be more favoured. Generally, the carbocation centre is highly charged and reactive, but more sterically hindered. Thus, small nucleophiles, such as water, will prefer to directly attack the carbocation centre and perform S_N1 reaction predominantly. On the other hand, large bases, such as triethylamine, will find it easier to deprotonate the highly accessible proton and favour the E1 reaction.

In the end, it is still difficult to get a clean E1 or S_N1 reaction. Thus, the E2 and S_N2 reactions are more synthetically useful.

E2 and S_N2 reactions are both one-step reactions driven by a strong base or a strong nucleophile. The key to selectivity between the two is in the base or nucleophile used. As we have mentioned in chapter 4.4, nucleophilicity and basicity are similar in many aspects. However, there are some differences between bases and nucleophiles that we mentioned in part 4.4.3. In most substrates, the proton is much less sterically hindered than the electrophilic carbon centre. Thus, we can easily force a E2 reaction using a strong, hindered base. The common bases employed for this are 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), which are heterocyclic amine bases that are strong and bulky. On the other hand, better nucleophiles are usually more polarisable as the efficacy of the nucleophilic attack depends on the orbital overlap between the nucleophile and electrophile. Small nucleophiles such as hydroxide ion will tend to undergo nucleophilic substitution as the electrophilic carbon centre carries a partial positive charge that makes it more reactive than the adjacent proton.

When forming alkenes, we use E2 reactions as far as possible, as there are a variety of strong and bulky bases that we can choose from. Even in tertiary substrates that can undergo E1 reaction, we may use a strong base to avoid the selectivity issue between S_N1 and E1 reactions.

4.8.2 *E1cB mechanism*

Other than E1 and E2 mechanisms, there is another highly specific mechanism for elimination reactions, the E1cB mechanism. It stands for “E1 conjugate base”, an E1 reaction where the intermediate is a conjugate base. This mechanism only happens on substrates with an adjacent anion-stabilising electron-withdrawing group. The conjugate base is first formed via deprotonation before the leaving group is eliminated. It is considered an E1 reaction because the elimination step is unimolecular. However, the rate law for the E1cB reaction actually depends on the concentration of base, as it directly influences the concentration of conjugate base. This mechanism happens frequently in enolate reactions that we will discuss in chapter 4.11. For now, the overall E1cB mechanism is shown in Figure 4.8.11.

The surprising thing about E1cB is that the leaving group X can be hydroxide. Hydroxide is a poor leaving group that does not leave readily in nucleophilic substi-

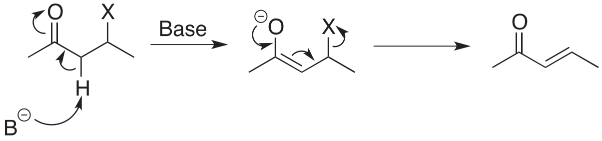


Figure 4.8.11. E1cB mechanism with ketone as electron-withdrawing group.

tution or elimination. This reaction is actually rather tricky. The most acidic proton in the molecule is the hydroxide proton, so it should be deprotonated first. There will still be an equilibrium established between the alkoxide and the enolate. Since the elimination is irreversible, after a long reaction time at elevated temperatures, the stable elimination product is formed. This is shown in Figure 4.8.12.

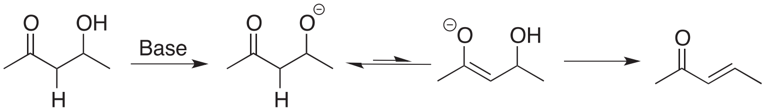


Figure 4.8.12. Elimination of OH through E1cB mechanism.

4.8.3 *Alkene synthesis*

Alkenes are one of the most basic and fundamental functional groups in organic chemistry. They can participate in many reactions to form a variety of other functional groups. However, their preparation is often challenging because of the underlying regioselectivity and stereoselectivity issues that we have discussed previously. Here we will describe a few commonly used methods for alkene preparation.

Julia olefination is a stereoselective elimination reaction where only the (E)-alkene is formed. Depending on how the starting material is prepared, it is also regiospecific. The general reaction scheme for Julia olefination is shown in Figure 4.8.13.

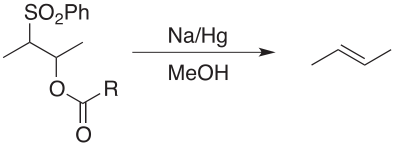


Figure 4.8.13. General reaction scheme for Julia olefination.

The starting material for Julia olefination is a sulfone. Sulfones are useful in organic chemistry as they are good anion-stabilising groups. Substituted sulfones may be prepared from sulfonyl chlorides, as shown in Figure 4.8.14.

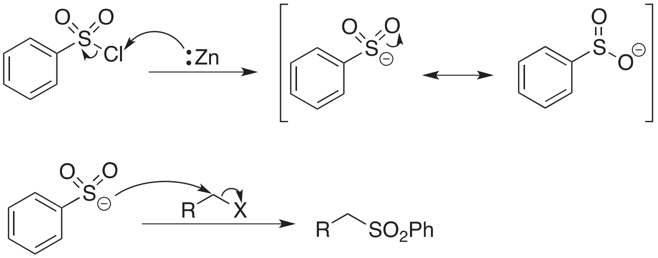


Figure 4.8.14. Preparation of substituted sulfones.

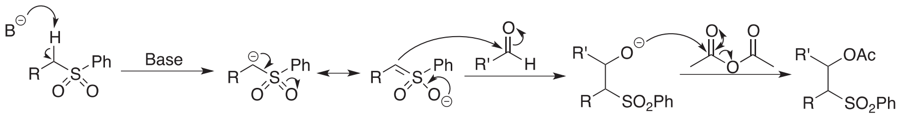


Figure 4.8.15. Preparation of the starting material for Julia olefination.

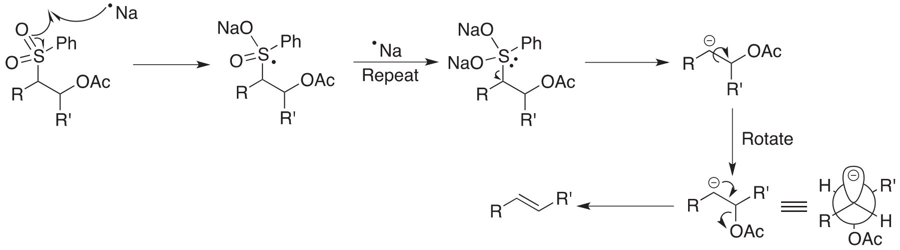


Figure 4.8.16. Reaction mechanism for Julia olefination.

This preparation involves the formation of a sulfone nucleophile using zinc followed by an S_N2 reaction to generate the substituted sulfone. As sulfone is an anion-stabilising group, the adjacent α-proton is acidic and can be deprotonated by a base. This allows for a nucleophilic addition to an aldehyde, followed by acetylation with acetic anhydride. This reaction sequence is shown in Figure 4.8.15.

Now that we have figured out how to prepare the starting material, we need to consider the stereoselectivity of the reaction. The product of Julia olefination is always a (E)-alkene regardless of the original stereochemistry in the starting material. To understand why, we need to analyse the reaction mechanism, which is shown in Figure 4.8.16.

Sodium metal reacts as a radical, donating electrons to the sulfone. The electron-rich sulfone leaves to form a carboanion, which is able to rotate freely such that the alkyl groups are anti to each other. This is the most stable conformation and leads to the formation of the (E)-alkene.

Tip 4d. Abbreviations in mechanism drawing

Reaction mechanisms are important in allowing us to understand how organic reactions proceed. However, they are usually long and tedious to draw. Thus, there are certain abbreviations commonly used when drawing mechanisms which may help to condense long mechanisms.

1. Substitutions at carbonyl group may be abbreviated by using a bidirectional arrow. This can be seen from the last step in Figure 4.8.15. This allows us to show that the carbonyl group is involved while the substitution occurs. Without the arrow, it will be incorrect to draw the mechanism as S_N2. The different mechanistic drawings are compared in Figure 4.8.17.

(*Continued*)

Tip 4d. (*Continued*)

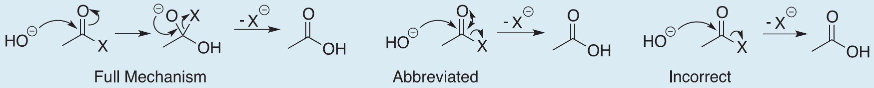


Figure 4.8.17. Comparison between the different mechanistic drawings.

2. The arrows in proton transfer may often be neglected. We may just include $+H^+$, $-H^+$ or $\pm H^+$ above the reaction arrow to describe the movement of protons. This is because in most reaction systems, there are solvent molecules that can facilitate the movement of protons. An example of the abbreviation is shown in Figure 4.8.18.

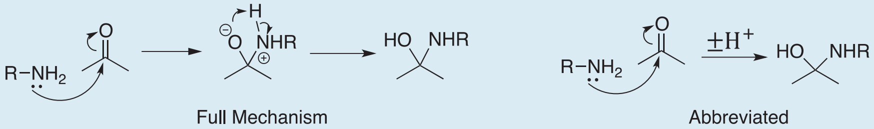


Figure 4.8.18. Abbreviation of the commonly encountered proton transfer step.

A more general method to prepare alkenes is **Peterson elimination**. Unlike Julia's olefination, Peterson elimination is able to form both (E) and (Z) alkenes, based on the substrate stereochemistry reaction conditions used. The general scheme for Peterson elimination is shown in Figure 4.8.19.

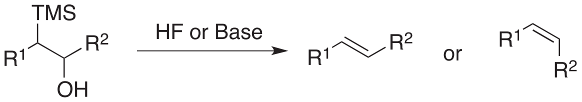


Figure 4.8.19. General reaction scheme for Peterson elimination.

Peterson elimination is a **stereospecific** reaction, where the product stereochemistry depends entirely on the stereochemistry of the starting material and the reaction conditions. The preparation of starting material usually involves the nucleophilic addition of a silylcarbanion to a carbonyl compound as shown in Figure 4.8.20.

The starting material is usually prepared with good diastereoselectivity depending on the electronic and steric effects of the substituents. The elimination may then be carried out using either acidic or basic conditions. Let us first look at the mechanism for Peterson elimination in acid using HF in Figure 4.8.21.

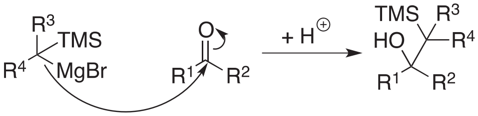


Figure 4.8.20. Peterson elimination staring material preparation.

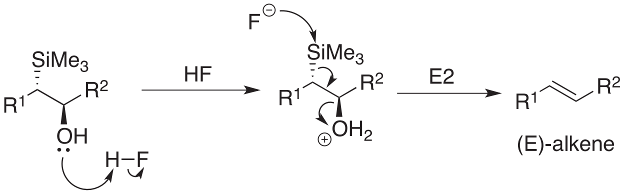


Figure 4.8.21. Mechanism of Peterson elimination in HF.

Note that under acidic conditions, Peterson elimination follows the E2 mechanism. The only difference is that the proton in E2 elimination is replaced by a trimethylsilyl group in Peterson elimination. In substrates where there are multiple protons on the same carbon, they can undergo E2 elimination to give alkenes of both configurations. Since trimethylsilyl is a specific proton equivalent, we can use fluorides to carry out elimination of trimethylsilyl group as fluorides have high affinity for silicon. Using this method, the alkene may be prepared regiospecifically and stereospecifically.

The opposite alkene configuration may be obtained in basic condition with the same substrate, and the mechanism is shown in Figure 4.8.22.

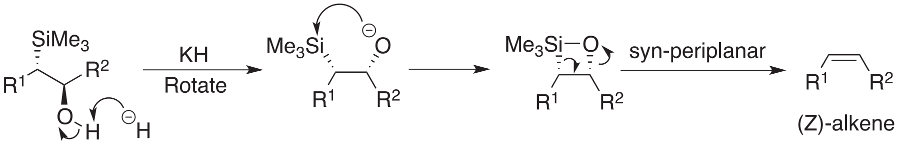


Figure 4.8.22. Mechanism of Peterson elimination in base.

In basic condition, the 4-membered ring key intermediate is formed, which allows a syn-periplanar elimination to occur. This elimination forms the alkene of an opposite configuration compared to the anti-periplanar elimination in HF. The final configuration of the alkene depends on the original stereochemistry of the reagent and the reaction condition employed. Thus, the Peterson elimination is a very good stereospecific reaction to control the alkene configuration.

Other than forming alkenes through elimination, we may form alkenes from carbonyl compounds. The most characteristic reaction to convert C=O double bonds to C=C double bonds is the **Wittig reaction**. The Wittig reaction is a reaction between a carbonyl compound and a phosphonium ylid. A ylid is a special type of zwitterion, with positive and negative charges on adjacent atoms. We will first look at how to prepare phosphonium ylids in Figure 4.8.23.

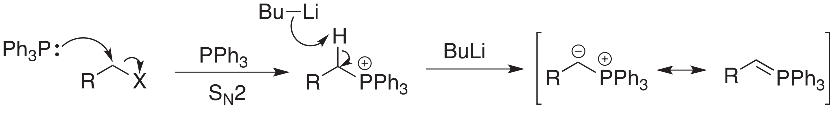


Figure 4.8.23. Preparation of phosphonium ylids from alkyl halides.

Phosphonium ylids may be prepared from alkyl halides through nucleophilic substitution by triphenylphosphine, followed by deprotonation using a strong base. The proton on the carbon directly adjacent to the phosphorous is slightly acidic due to the anion-stabilising effect of phosphorous. The ylid itself may be represented by a double bond resonance structure to show that the electron density is delocalised, however it is still important to note that the carbon is the most nucleophilic part of the ylid.

The Wittig reaction converts carbonyl compounds to alkenes, and its general scheme is given in Figure 4.8.24.

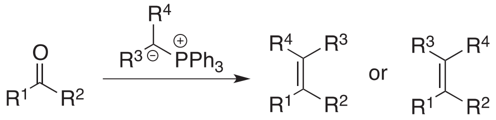


Figure 4.8.24. General scheme for Wittig reaction.

The Wittig reaction is stereoselective and the configuration of the alkene depends on the type of phosphonium ylid used. An unstabilised ylid gives a (Z)-alkene product while a stabilised ylid gives a (E)-alkene product. The stability of the ylid generally depends on the stability of the carbanion. If the carbanion is conjugated to an electron-withdrawing group, the ylid is stabilised. Other ylids, such as alkyl phosphonium ylids, are considered unstabilised. To understand the unique selectivity of the Wittig reaction, we must first look at the mechanism of the reaction, as shown in Figure 4.8.25.

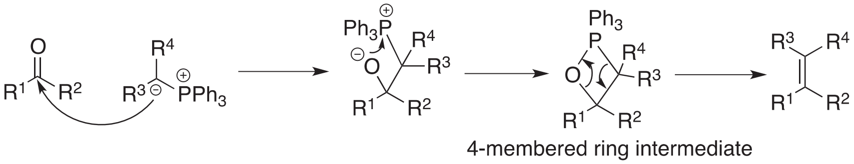


Figure 4.8.25. Mechanism for the Wittig reaction.

The Wittig reaction starts with a nucleophilic attack on the carbonyl compound by the phosphonium ylid, followed by the formation of a 4-membered ring key intermediate. The overall driving force of the reaction comes from the final step, where the strong P=O double bond is formed.

The Wittig reaction ends with a stereospecific syn-periplanar ring-opening mechanism, similar to the base-catalysed Peterson elimination. Thus, the configuration of the product depends on the approach of the ylid to the carbonyl group. The ylid would approach the carbonyl at right angles for optimal orbital overlap, keeping the large substituents apart, leading to the (Z)-alkene product. However, the electronegative groups in the stabilised ylids electrostatically repel the carbonyl group, keeping away from each other, leading to the (E)-alkene product. Thus, unstabilised ylids will form (Z)-alkenes while stabilised ylids will favour the (E)-alkene.

A modification on the Wittig reaction allows for the stereoselective formation of (E)-alkene. The **Horner-Wadsworth-Emmons reaction (HWE reaction)** uses phosphonate ester enolates instead of phosphonium ylids to react with carbonyl compounds. The general scheme for HWE reaction is shown in Figure 4.8.26.

The reaction mechanism is similar to Wittig reaction, with the same stereochemical considerations. The phosphonate ester enolate is similar to a stabilised ylid, thus it reacts with the carbonyl compound keeping the electronegative groups apart. The 4-membered ring intermediate collapses in the same syn-periplanar manner, leading to the stereoselective formation of (E)-alkene.

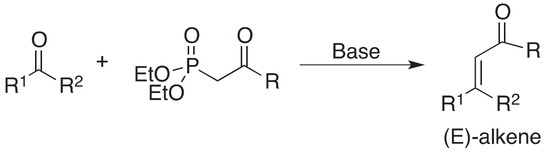


Figure 4.8.26. General reaction scheme for HWE reaction.

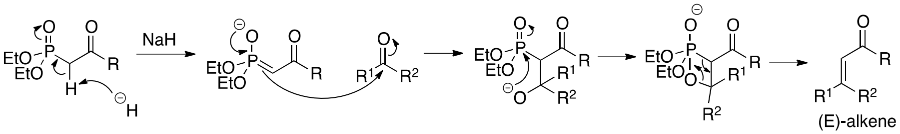


Figure 4.8.27. Mechanism for HWE reaction.

4.9 Electrophilic Addition

We have learnt many methods to prepare alkenes in the previous chapter. In this chapter, we will cover the reactivity of alkenes. C=C double bonds have high electron density, thus they usually react as nucleophiles, rarely as electrophiles in the case of conjugate nucleophilic attack. This series of reactions are called electrophilic addition as we introduce electrophiles to the alkene for them to react. C≡C triple bonds have similar properties to double bonds, and their reactions will also be covered shortly in the second part of this chapter.

4.9.1 *Electrophilic addition to alkenes*

We will start with the simplest reaction of alkenes, the electrophilic addition of halogens. One of the most basic chemical tests for unsaturation is to test if the compound decolourises bromine water. This test is based on the reaction between the alkene and bromine water, as shown in Figure 4.9.1.

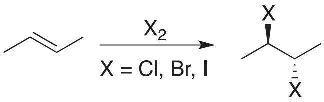


Figure 4.9.1. Overall reaction for electrophilic addition of halogen to alkene.

The mechanism involves a 3-membered ring intermediate, known as the chloronium ion, bromonium ion or iodonium ion for Cl, Br and I respectively. The mechanism is shown in Figure 4.9.2.

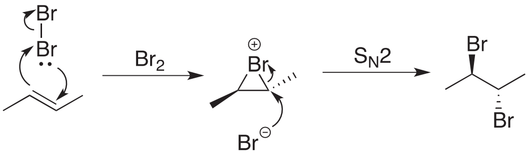


Figure 4.9.2. Mechanism for the electrophilic addition of halogen to alkene.

The first step is interesting as it involves the formation of a 3-membered bromonium ion. The main interaction is the nucleophilic attack of the alkene on bromine, where the π-orbital of the alkene attacks the σ*-orbital of bromine. The bromonium ion may be attacked and opened from either carbon, leading to a racemic mixture. In this case, the product is a meso compound, thus the enantiomers are identical.

Due to the formation of a 3-membered ring followed by ring opening through an S_N2 reaction, **the 2 halogens will always be anti to each other** in the product. This is known as diastereoselectivity, as only one diastereomer is formed. To be more exact, the electrophilic addition of bromine to alkenes should be considered **diastereospecific** as the product stereochemistry depends on the reactant stereochemistry. In this case, if we started with a (Z)-but-2-ene instead, we will instead have the reaction shown in Figure 4.9.3.

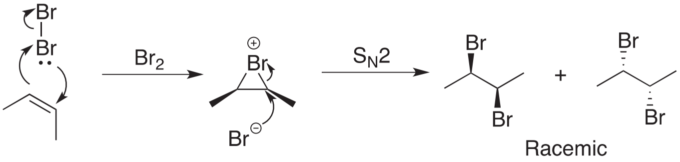


Figure 4.9.3. Mechanism for electrophilic addition of bromine to a (Z)-alkene.

Note that the other diastereomer is formed when the (Z)-alkene is used instead of the (E)-alkene. The diastereomer formed is entirely dependent on the stereochemical configuration of the alkene.

The electrophilic addition of halogen to alkene must be carried out in organic solvent such as CCl_4. In aqueous media, water acts as a nucleophile to open the

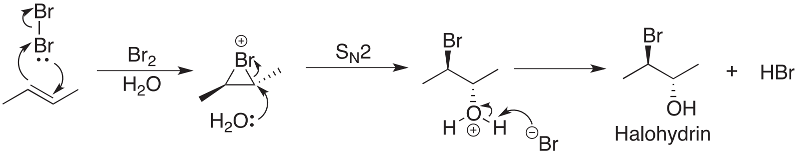


Figure 4.9.4. Mechanism for halohydrin formation.

3-membered ring intermediate and a halohydrin is formed instead. The scheme and mechanism for halohydrin formation is shown in Figure 4.9.4.

With the electrophilic addition of halogens to alkene, we did not face any regioselectivity issue as the same halogen is added to both carbons. In the formation of halohydrin, and in many other reactions to come in this chapter, the electrophilic addition to alkene is unsymmetric. To determine the regioselectivity of such reactions, we will need to employ the **Markovnikov's rule**. In the case of halohydrin formation, Markovnikov's rule states that the water will be added to the side with less hydrogens. Markovnikov's rule may be used for many electrophilic addition reactions and it is much more important to understand its chemical basis rather than remembering the result for each individual reaction.

Markovnikov's rule is based on carbocation stability. In the series of electrophilic addition reactions, we will be exposed to many cationic intermediates. The stability of the cationic intermediates will determine their ratios in the reaction mixture. In this case of halohydrin formation, we have to examine the halonium ion intermediate. Let us look at an example of electrophilic addition to an unsymmetrical alkene in Figure 4.9.5.

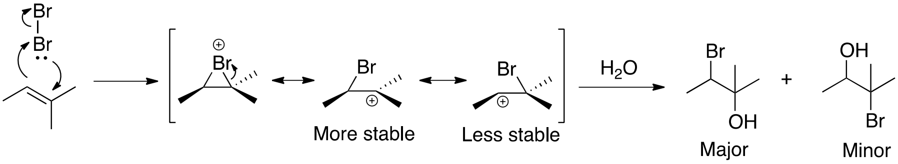


Figure 4.9.5. Halohydrin formation from unsymmetric alkene.

To determine which carbon the water nucleophile will attack, we have to determine which carbon is better able to stabilise the positive charge. In this case, the carbon with more substituents is able to form a more stable carbocation due to the electron-donating effect of alkyl groups. Since this carbon would carry greater positive character, the nucleophile will preferentially attack it to form the major regioisomer. In all cases where Markovnikov's rule can be applied, we should use the cation stability argument to justify the regioselectivity.

Another common electrophilic addition reaction involves the addition of HX across a double bond. This reaction proceeds through a carbocation intermediate, and its regioselectivity is determined by Markovnikov's rule.

As shown in Figure 4.9.6, the major product formed has the halogen attached to the more substituted side of the alkene. We will show the mechanism in Figure 4.9.7 and use the carbocation stability argument to explain why.

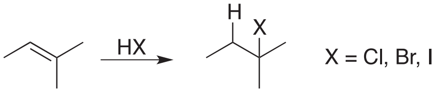


Figure 4.9.6. Overall reaction scheme for addition of HX across double bond.

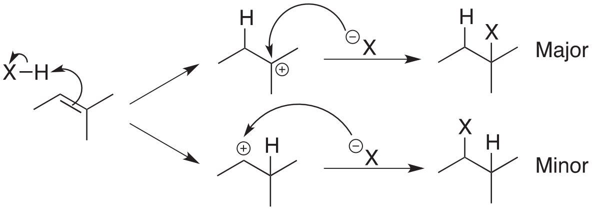


Figure 4.9.7. The 2 different reaction pathways for the HX addition to alkene.

The regioselectivity depends on the first step where the proton is added to the alkene and the carbocation is formed. The tertiary carbocation is preferentially formed due to the stabilising effect of electron-donating alkyl groups, forming the major regioisomer. This reaction is not stereoselective as the carbocation is planar and there is an equal probability for the halogen anion to approach from either side.

It is of synthetic importance to provide methods to add water across an alkene. The simplest method is to use dilute sulfuric acid, since hydrogen sulfate is a poorer nucleophile than water. The reaction follows the same pathway as addition of HX, just that water acts as the nucleophile to add to the carbocation intermediate. The general reaction scheme is shown in Figure 4.9.8.

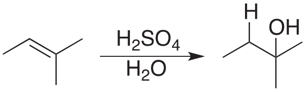


Figure 4.9.8. Hydration of alkene using dilute sulfuric acid.

However, this method is rather inconsistent as the hydration reaction is reversible. A better method for hydration of alkene is known as **oxymercuration**. The general reaction scheme is shown in Figure 4.9.9.

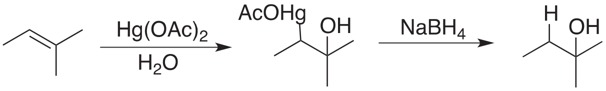


Figure 4.9.9. General scheme for oxymercuration hydration of alkene.

As can be seen, the regioselectivity of products formed from oxymercuration follow Markovnikov's rule. This is due to the 3-membered ring cation intermediate that is formed similar to the halonium ion. After the 3-membered ring is opened by water, the carbon-mercury bond is cleaved using $\mathrm{NaBH_4}$. The mechanism for oxymercuration is shown in Figure 4.9.10.

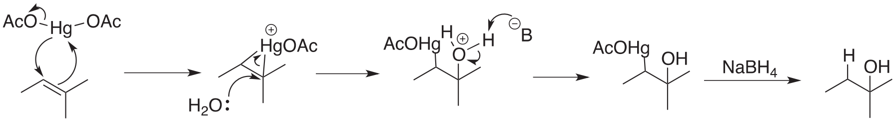


Figure 4.9.10. Mechanism for oxymercuration hydration of alkenes.

All the reactions we have discussed up to this point produce the regioisomer favoured by Markovnikov's rule. However, we need options to produce the other regioisomer, also known as the anti-Markovnikov product. **Hydroboration** is a hydration reaction that produces the anti-Markovnikov product. The overall reaction scheme for hydroboration is shown in Figure 4.9.11.

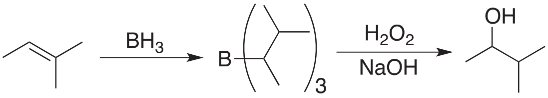


Figure 4.9.11. Overall reaction scheme for hydroboration oxidation.

The special regioselectivity may be attributed to both electronic and steric effects. Electronically, the π-electrons are donated to boron, thus the more substituted side with hydrogen should carry greater positive character. Sterically, a fully substituted Boron with 3 alkyl groups is sterically hindered, thus the boron would prefer to be attached to the less substituted side. The mechanism is shown in Figure 4.9.12.

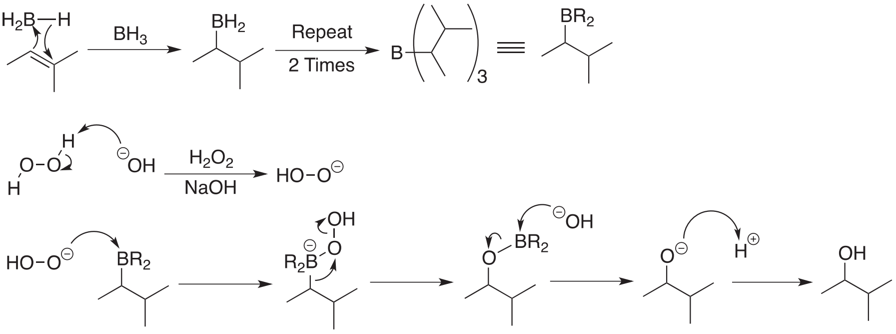


Figure 4.9.12. Mechanism for hydroboration oxidation.

An interesting reaction to form 3-membered oxygen containing rings is **epoxidation**. By now we should already be familiar with epoxides, and know a few methods to prepare them. We will now introduce the most general and popular method to synthesise epoxides using peroxyacids. The reaction scheme is shown in Figure 4.9.13.

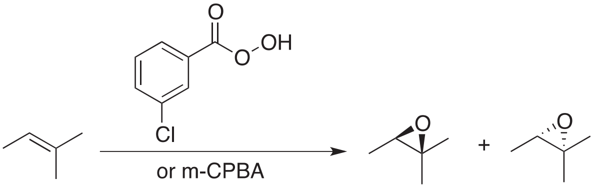


Figure 4.9.13. Reaction scheme for epoxidation using peroxyacid.

The mechanism for epoxidation by peroxyacid is one concerted step, as shown in Figure 4.9.14.

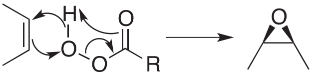


Figure 4.9.14. Mechanism for epoxidation of alkene by peroxyacid.

Due to the concerted one-step reaction pathway, the epoxidation reaction is stereospecific, and the product stereochemistry is dependent on the reagent stereochemistry. A cis-alkene will form a syn-epoxide while a trans-alkene will form an anti-epoxide.

Peroxide epoxidation may be directed by hydroxyl groups as hydroxyl groups will form hydrogen bonding interactions with the peroxyacid such that the epoxide is formed on the same side as the hydroxyl group. For better selectivity and rate-acceleration, we may employ metal catalysts together with alkyl peroxides, as shown in Figure 4.9.15.

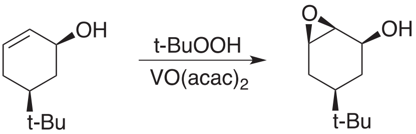


Figure 4.9.15. Stereoselective metal-catalysed epoxidation.

For epoxidation of acid-sensitive substrates, we may use nitriles with hydrogen peroxide to generate peroxyimidic acid in-situ, as shown in Figure 4.9.16.

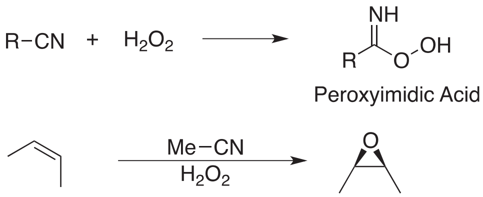


Figure 4.9.16. Epoxidation using peroxyimidic acid generated in-situ.

Another common epoxidation reagent is dioxiranes. Dioxiranes are unstable and must be prepared in-situ. The most common dioxirane, dimethyldioxirane (DMDO) may be generated from acetone and peroxymonosulfate. It may then be reacted with alkenes through a concerted mechanism to form epoxides, as shown in Figure 4.9.17.

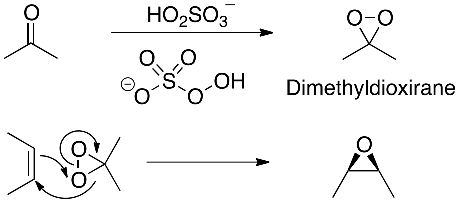


Figure 4.9.17. Epoxidation using DMDO generated in-situ.

Unlike the opening of other 3-membered cationic rings, the regioselectivity for epoxide ring-opening is rather complicated. Since the epoxide is actually a neutral species, the influence of the electronic factors and steric factors need to be weighed against each other. It is also significantly less reactive than the other 3-membered ring intermediates. Thus, epoxide ring opening requires either a strong acidic catalyst or a basic nucleophile, 2 reaction conditions that give different regioselectivities.

Let us start by considering the acid-catalysed ring-opening of epoxides. In acidic conditions, the ring-opening reaction of epoxides follows a similar reaction mechanism as ring opening of bromonium ions that we mentioned in the start of the chapter. The epoxide is first protonated to an oxonium ion. The opening of the oxonium ion usually follows Markovnikov rule that we mentioned before with the more substituted side opening.

The base-catalysed ring-opening of epoxides follow a purely S_N2 mechanism, thus the regioselectivity is opposite to the acid-catalysed reaction. The main factor to consider is the steric hindrance at the reacting carbon centre. Thus, the less substituted carbon centres with less steric hindrance will react faster with the nucleophile.

However, there is an exception for acid-catalysed ring-opening reactions when one side has no substituents while the other has one substituent. This was experimentally studied and the opening occurred mostly on the less hindered side. The regioselectivities of epoxide ring-opening are summarised in Figure 4.9.18.

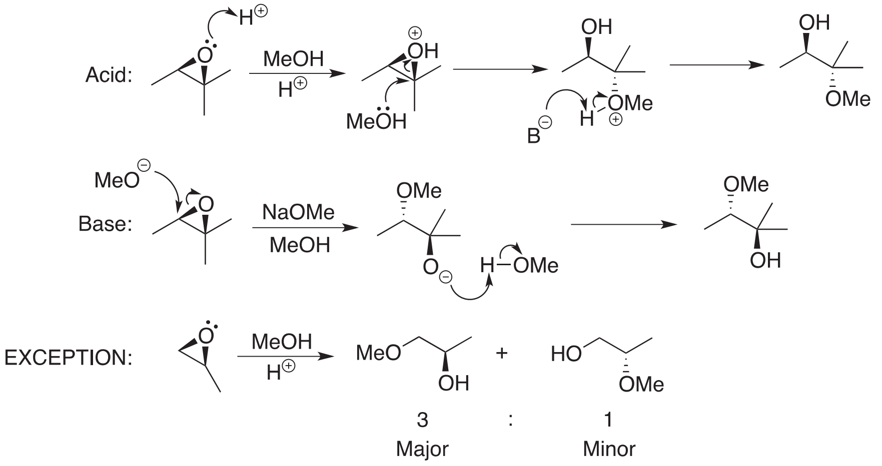


Figure 4.9.18. Regioselectivities of the ring-opening of epoxides.

Next, we will look at the **dihydroxylation** of alkenes. This reaction uses a metal oxidant (OsO_4) that allows the addition of 2 hydroxyl groups in a concerted one-step pathway. However, the metal oxidant is expensive and usually not used in stoichiometric amounts. Instead, another oxidant such as *N*-methylmorpholine-*N*-oxide (NMO) is used in stoichiometric amount to regenerate the metal oxidant. The overall reaction is shown in Figure 4.9.19.

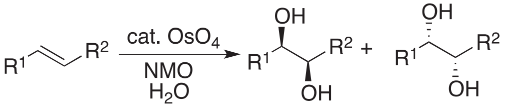


Figure 4.9.19. General scheme for dihydroxylation of alkenes.

The 2 hydroxyl groups will be added syn to one another due to the concerted reaction mechanism, as shown in Figure 4.9.20.

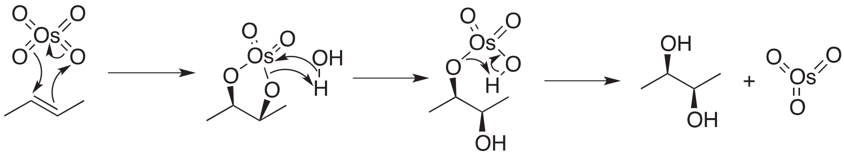


Figure 4.9.20. Mechanism for dihydroxylation of alkenes.

The 1,2-dihydroxyl compound produced through dihydroxylation can undergo oxidative cleavage with $NaIO_4$, known as the **Malaprade oxidation**. The single bond between the 2 hydroxyl groups will be cleaved and the hydroxyl groups will be oxidised to aldehydes or ketones. The general reaction is shown in Figure 4.9.21.

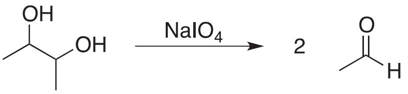


Figure 4.9.21. General scheme for Malaprade oxidation.

The mechanism for such cleavage again follows a concerted cyclic pathway, as shown in Figure 4.9.22.

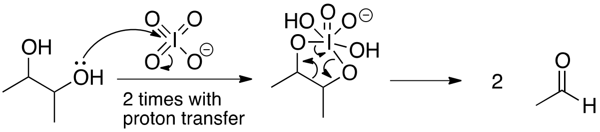


Figure 4.9.22. Mechanism for Malaprade oxidation.

A milder version of the Malaprade oxidation is the **Criegee oxidation**. For Criegee oxidation, the conformation of the diol is highly important and there is a high selectivity for cis-diols to be reacted rather than trans-diol. For acyclic molecules, conformation usually can be changed for an energy penalty, but in cyclic molecules, it is usually difficult to twist the rings, especially when the rings are smaller than 6-membered. Criegee oxidation uses lead(IV) acetate as the oxidant, and follows a similar mechanism with Malaprade oxidation, as shown in Figure 4.9.23.

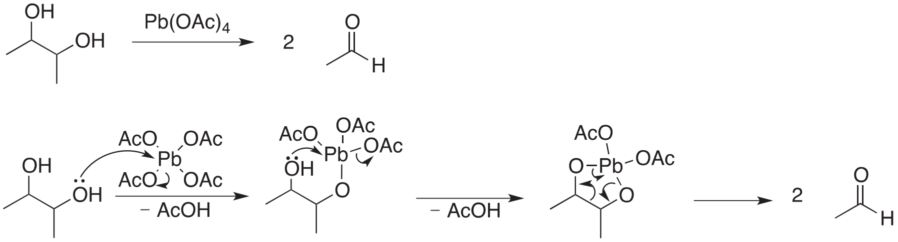


Figure 4.9.23. Reaction scheme and mechanism for Criegee oxidation.

A procedure that is able to perform oxidative cleavage on the C=C double bond in one step is known as **ozonolysis**. This procedure starts with the addition of ozone to the double bond, while the conditions for the second step may be chosen depending on the oxidation state of the desired product. The different conditions and products are shown in Figure 4.9.24.

Ozonolysis proceeds through a cyclic mechanism that we will discuss in chapter 4.14. The ring forming reactions are all 1,3-dipolar cycloadditions, which happen due to the special nature of ozone with adjacent positive and negative charges. The mechanism for the most common reaction with dimethylsulfide in the second step in shown in Figure 4.9.25.

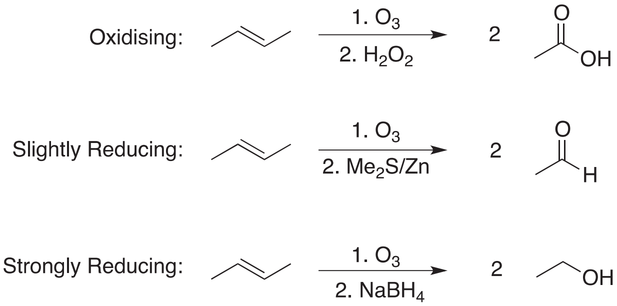


Figure 4.9.24. The different conditions for ozonolysis and their products.

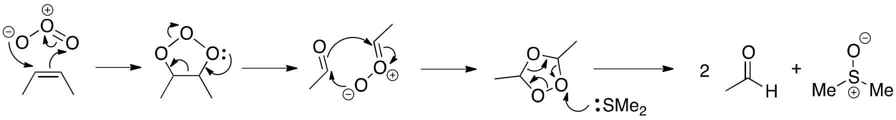


Figure 4.9.25. The mechanism for ozonolysis using dimethylsulfide in the second step.

4.9.2 *Electrophilic addition to alkynes*

Electronically, alkynes are fundamentally similar to alkenes. Thus, they participate in many of the electrophilic addition reactions that are stated previously. The most synthetically useful electrophilic addition reactions of alkynes are the hydration reactions: oxymercuration and hydroboration. However, the oxidation level of the product is one higher than that of alkene hydration as there is a remaining double bond. This product with a hydroxyl group attached to one end of the alkene is known as an **enol**, which we will discuss in chapter 4.11. Enols can convert to carbonyl compounds through a simple **tautomerisation**. **Tautomers** are molecules with the same molecular formula but different connectivity, and can easily interconvert, usually through the migration of a proton.

Owing to this fact, the oxymercuration of alkynes produce ketones, as shown in Figure 4.9.26. For terminal alkynes, the reaction produces methyl ketones. The regioselectivity depends on the stability of the carbocation intermediate, following the same rule as alkenes.

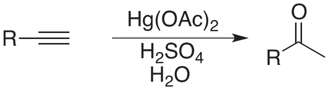


Figure 4.9.26. Reaction scheme for oxymercuration of alkynes.

The mechanism, shown in Figure 4.9.27, follows the same route as that of alkene oxymercuration, except that the enol product is able to **tautomerise** to a ketone.

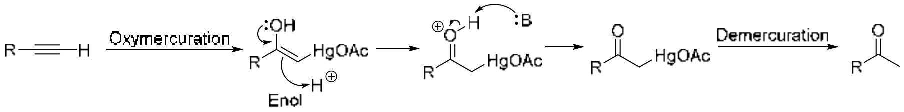


Figure 4.9.27. Brief mechanism for oxymercuration of alkynes.

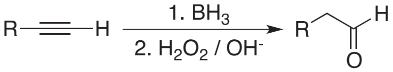


Figure 4.9.28. General scheme for hydroboration of alkynes.

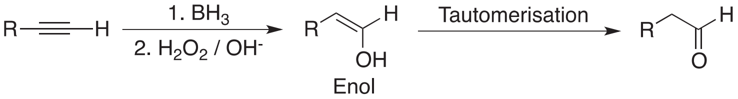


Figure 4.9.29. Brief mechanism for hydroboration of alkynes.

Hydroboration of alkynes will form the anti-Markovnikov product, where the oxygen is added to the less substituted side of the alkyne. For a terminal alkyne, an aldehyde may be prepared through hydroboration. The overall reaction is shown in Figure 4.9.28.

The reaction mechanism follows that of alkene hydroboration, except that an enol product would be formed. The enol will proceed to tautomerise to an aldehyde, as shown in Figure 4.9.29.

4.10 Electrophilic Substitution

In the previous chapter, we have looked at electrophilic addition reactions to alkenes and alkynes. The attack on electrophiles usually start with an electron pair from a π-bond, and this remains the same for electrophilic substitution. However, in the case of electrophilic substitution, an electrophile must be substituted. This is most commonly a proton, and the driving force for the loss of the proton is the regeneration of aromaticity. Thus, electrophilic substitution only happens on aromatic compounds.

4.10.1 *Electrophilic aromatic substitution on benzene*

The most common aromatic structure we encounter is benzene. Due to its aromaticity, it is highly unreactive and we have yet to explore its reactions other than the nucleophilic aromatic substitution reactions we discussed in chapter 4.7. The most common reaction pathway for benzene is through electrophilic aromatic substitution. First, we will look at the general reaction scheme as shown in Figure 4.10.1.

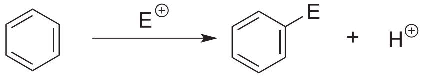


Figure 4.10.1. General reaction scheme for electrophilic aromatic substitution.

Tip 4e. Representing benzene

The true electron distribution and structure of benzene was discussed in chapter 4.3. However, we will often see 2 different representations of benzene, shown in Figure 4.10.2. One has the 3 double bonds shown while the other has a circle in the centre to represent the electrons being fully delocalised. While the circle of electrons may be a better representation of the delocalisation, it is inconvenient when drawing mechanisms, especially when the different resonant structures of intermediates must be shown. Thus, it is recommended to represent benzene with 3 double bonds, and its other resonance structure will be implied.

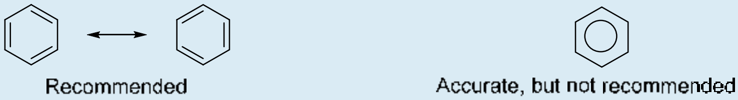


Figure 4.10.2. Different representations of benzene.

The mechanism for electrophilic aromatic substitution comprises of 2 steps. The first step is electrophilic addition, forming a carbocation. Unlike in electrophilic addition, the carbocation is not attacked by a nucleophile. Instead, the second step is similar to an E1 reaction, where deprotonation occurs at the carbon adjacent to the carbocation. The general mechanism is shown in Figure 4.10.3.

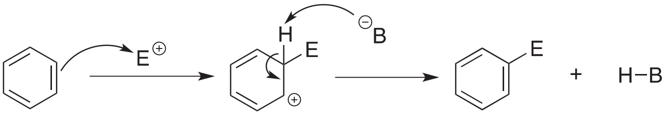


Figure 4.10.3. General mechanism for electrophilic aromatic substitution.

The main challenge in electrophilic aromatic substitutions is to have a good enough electrophile to initiate the reaction. Unlike electrophilic addition mentioned in the previous chapter, benzene is a much less reactive nucleophile than alkenes due to the high energy penalty required to destroy aromaticity. In the next part, we will discuss methods to generate common electrophiles for electrophilic aromatic substitution.

Firstly, for halogenation reactions, the halogen is no longer a good enough electrophile for reaction. We need to generate a halogen cation by adding a Lewis acid to the halogen, as shown in Figure 4.10.4.

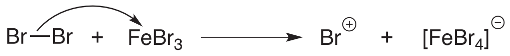


Figure 4.10.4. Mechanism for generation of halogen cation.

Common Lewis acids employed for this purpose are $AlCl_3$ and $FeBr_3$. The halogen cation can proceed to react with benzene in an electrophilic aromatic substitution reaction as shown in Figure 4.10.5. Note that this method of halogenation is only possible for chlorides and bromides.

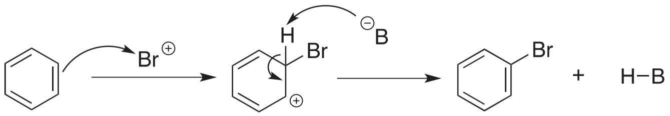


Figure 4.10.5. Mechanism for halogenation of benzene with halogen cation.

Next, we will look at nitration of benzene rings. Nitration requires harsh conditions, as the nitronium cation NO_2^+ must be formed as the electrophile. This is achieved by using a mixture of concentrated nitric acid and concentrated sulfuric acid as shown in Figure 4.10.6.

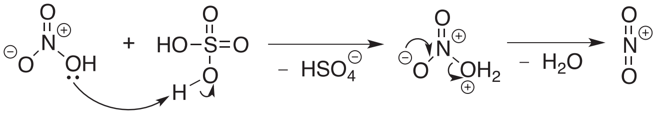


Figure 4.10.6. Mechanism for formation of nitronium ion.

The nitronium ion may proceed to react with benzene through the same electrophilic aromatic substitution mechanism, as shown in Figure 4.10.7.

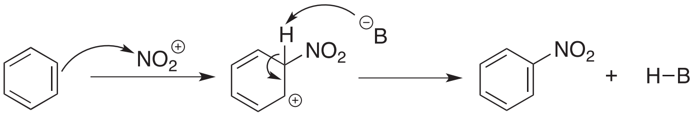


Figure 4.10.7. Mechanism for nitration of benzene with nitronium ion.

Nitration of benzene is a highly useful reaction as this forms a $C–N$ bond. The nitro group may be reduced to an amino group, with many possible reaction conditions developed for this reduction. The classic method is using tin in hydrochloric acid, however, other methods, such as catalytic hydrogenation and reduction with $LiAlH_4$, have been reported. The amine may further react to form a diazonium salt, which is a reactive intermediate that undergo further substitution reactions, such as the Sandmeyer reaction (refer to chapter 4.5). The full reaction scheme is shown in Figure 4.10.8.

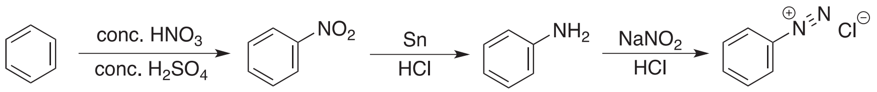


Figure 4.10.8. Full reaction scheme for formation of diazonium ion.

Diazonium arene is an extremely versatile intermediate. It allows us to add many substituents to the benzene ring that are difficult to add directly. In Figure 4.10.9, we show the various reactions that diazonium arenes can participate in.

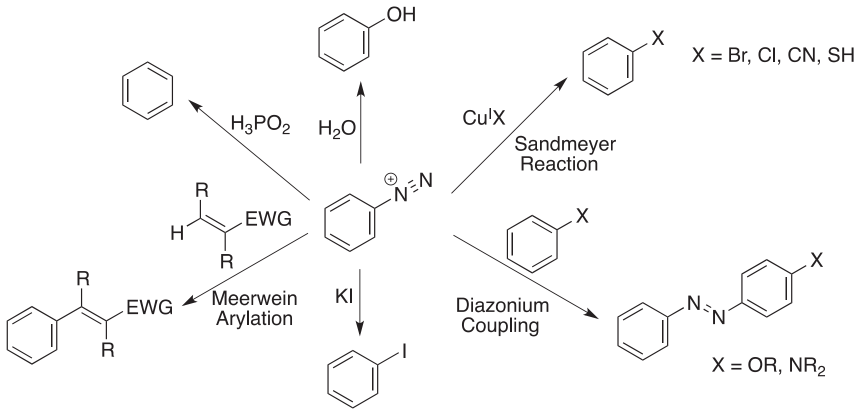


Figure 4.10.9. Reactions of diazonium arene.

The mechanisms of these reactions are varied, and some are the subject of scientific debate. As we move along in the book, we will look at the common mechanisms and it is good to explore the possible mechanisms or understand them logically. As can be seen, the hydroxyl, cyano and iodo groups may be attached to benzene through this reaction. These groups are difficult to be added onto benzene through other methods. Another group that is difficult to attach to benzene is the fluoro group, and this can also be achieved through a diazonium arene intermediate, through the use of tetrafluoroboric acid as shown in Figure 4.10.10.

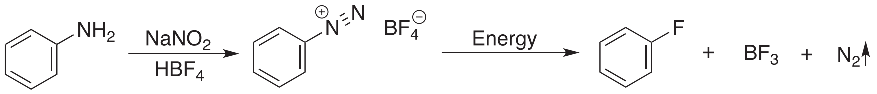


Figure 4.10.10. Preparation of fluorobenzene through diazonium intermediate.

We would like to further explore the formation of the reactive diazonium intermediate. Its high reactivity can be mainly attributed to the leaving group, nitrogen gas, which is a highly stable gas, favouring the reaction both thermodynamically and kinetically. The mechanism for the formation of diazonium arene from aniline is shown in Figure 4.10.11.

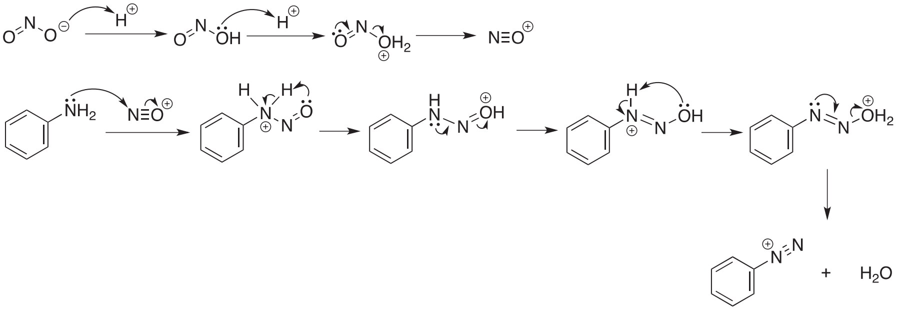


Figure 4.10.11. Mechanism for the formation of diazonium salt from aniline.

Sodium nitrite first reacts with acid to form the reactive electrophile NO^+ that adds to aniline. The further dehydration leads to the diazonium salt, which is unstable and prone to spontaneous decomposition. Thus, the reaction is usually carried out at lower temperatures, such as 0°C. The diazonium intermediate is then quickly reacted to form the product.

While diazonium reactions are versatile, it is a multi-step reaction that may cause some loss of yield. We will continue to look at some direct substitutions at the benzene ring. **Sulfonation** is similar to nitration, just that concentrated nitric acid is not added. The sulfonyl group may be directly substituted onto the benzene ring through the reactive HSO_3^+ intermediate. The intermediate is generated from concentrated sulfuric acid as shown in Figure 4.10.12.

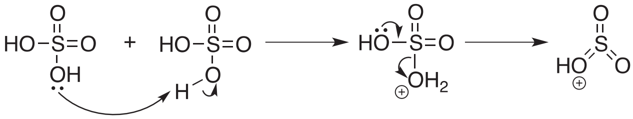


Figure 4.10.12. Formation of reactive HSO_3^+ electrophile from concentrated sulfuric acid.

The electrophile further reacts with benzene through the classic electrophilic aromatic substitution mechanism and the sulfonyl group is attached to benzene, as shown in Figure 4.10.13.

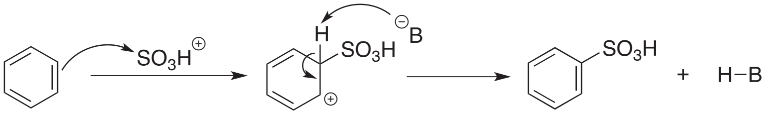


Figure 4.10.13. Mechanism for sulfonation of benzene.

Up to now, we have discussed many reactions that provide us with many paths to aromatic $C-X$ bonds, where X are heteroatoms, especially through diazonium arene intermediate. However, we have yet to discuss formation of $C-C$ bonds, the backbone of organic chemistry. This can be done through **Friedal-Crafts reactions**. This consists of **Friedal-Crafts alkylation** and **Friedal-Crafts acylation**. We will first look at Friedal-Crafts alkylation. In this reaction, the cation is a carbocation, as a C–C bond must be formed. The carbocation may be generated using acids, and a range of possibilities are shown in Figure 4.10.14.

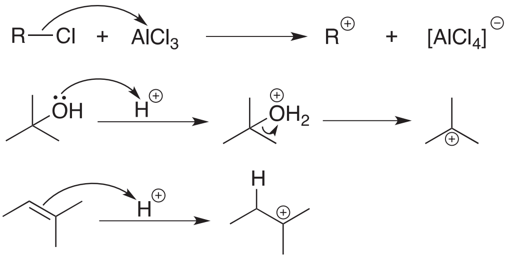


Figure 4.10.14. Different methods to generate carbocations for Friedal-Crafts alkylation.

Theoretically, we would expect these cations to react with benzene through the same electrophilic aromatic substitution mechanism as we have seen for many reactions above. The general reaction is shown in Figure 4.10.15.

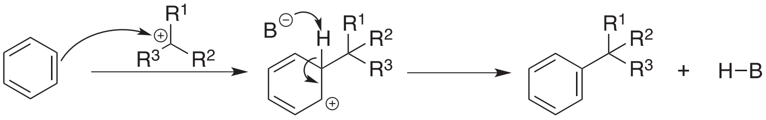


Figure 4.10.15. General mechanism for the Friedal-Crafts alkylation of benzene.

Ideally, the reaction may be carried out with large scope of R^1, R^2 and R^3. However, in reality, there are many concerns for the Friedal-Crafts alkylation, and we will discuss the 2 main concerns here:

1. Unstable carbocations rearrange readily

Note that in the examples, we generally use tertiary carbocations as they are more stable. It is possible to form any carbocation by adding Lewis acids to alkyl halides, and this seems to be a general method of generating alkylbenzenes. However, unstable carbocations will undergo **rearrangement** to shift the positive charge to a more substituted carbon centre that increases the stability of the carbocation. We will look at the most common carbocation rearrangements, which involves hydride shift and methyl shift. For such mechanisms, we would usually draw it with an arrow that follows the bond, to show the electrons and the atom moving as a group, or using an arrow with a loop. In Figure 4.10.16, the secondary carbocations undergo rearrangements to tertiary carbocations. Due to the rate of such rearrangements, they will likely occur before the electrophilic aromatic substitution, leading to a less expected product.

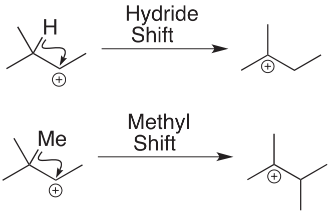


Figure 4.10.16. Examples of hydride and methyl shift.

2. Friedal-Crafts alkylation usually leads to over-substitution

As alkyl groups activate and make the benzene ring more reactive, the benzene ring is likely to undergo further substitution to form both mono-substituted and multi-substituted products, as shown in Figure 4.10.17. The next section will discuss in detail the substituent effects on the benzene ring.

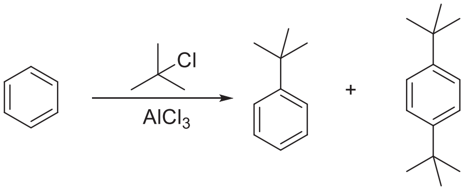


Figure 4.10.17. Friedal-Crafts alkylation will often lead to over-substitution.

Due to the limitations of Friedal-Crafts alkylation, Friedal-Crafts acylation is the preferred method for preparation of aromatic C–C bonds. Friedal-Crafts acylation allows the carbocation to be stabilised by the adjacent oxygen, forming the acylium ion intermediate. The acylium ion intermediate is more stable and does not rearrange readily. The formation of acylium ion is shown in Figure 4.10.18.

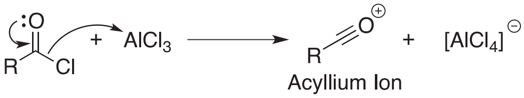


Figure 4.10.18. Formation of acylium ion from acyl chloride and Lewis acid.

The acylium ion then proceeds to react with benzene through electrophilic aromatic substitution as shown in Figure 4.10.19.

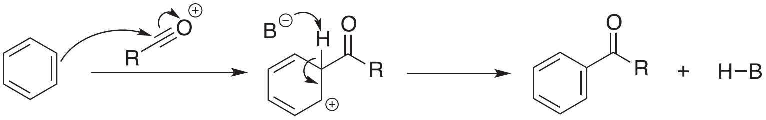


Figure 4.10.19. Mechanism for Friedal-Crafts acylation of benzene.

Since the acyl group deactivates the benzene ring, making it less prone to further reaction, there is no over-substitution observed for Friedal-Crafts acylation. The carbonyl group is also easily removed through Clemmensen or Wolff-Kishner reduction, or converted into other functional groups. The reduction reactions will be covered in part 4.12.2.

The only limitation for the Friedal-Crafts acylation is that methanoyl chloride, $HCOCl$, is unstable and may not be used as a reagent in Friedal-Crafts acylation. Thus, it is difficult to formylate benzenes. To do that, we may employ the **Gattermann** or **Gattermann-Koch** reaction.

The Gattermann-Koch reaction is essentially a Friedal-Crafts acylation using $HCOCl$, however, the $HCOCl$ is formed in-situ from CO and HCl. The Gattermann reaction avoids $HCOCl$ completely, using a nitrogen derivative by adding HCN and HCl to the reaction mixture. These reactions for formylation of benzene are shown in Figure 4.10.20.

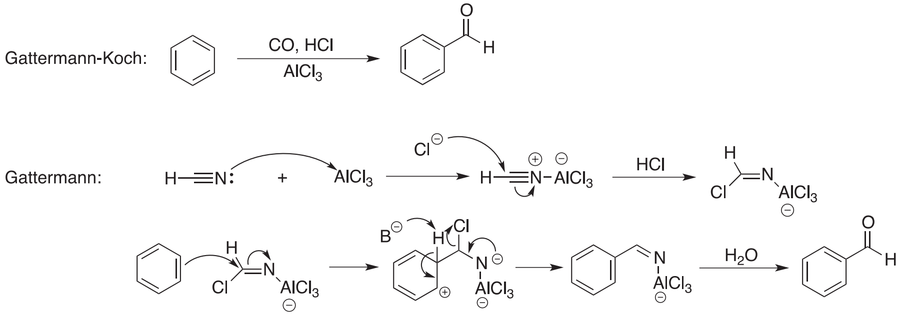


Figure 4.10.20. Formylation reactions of benzene.

Now that we have discussed the main electrophilic aromatic substitution reactions on benzene, we will move on to consider substituent effects. In electrophilic aromatic substitution reactions, benzene acts as a nucleophile by attacking with electrons from its aromatic system. Thus, it is a better nucleophile if the ring is more electron-rich. This can be achieved by attaching electron-donating substituents to the ring, activating the ring. On the other hand, addition of electron-withdrawing substituents to the ring will decrease the electron density in the ring, deactivating the ring. Thus, electron-donating groups are able to significantly speed up the electrophilic aromatic substitution while electron-withdrawing groups slow down the reaction.

Other than affecting the rate of reaction, the position of the substitution is also dependant on the substituents on benzene before reaction. Generally, **electron-donating substituents direct new substitution to occur ortho, para to them while electron-withdrawing substituents direct new substitution meta to them**. These electronic effects must be explained by the resonance structures of the carbocation intermediate, as shown in Figure 4.10.21.

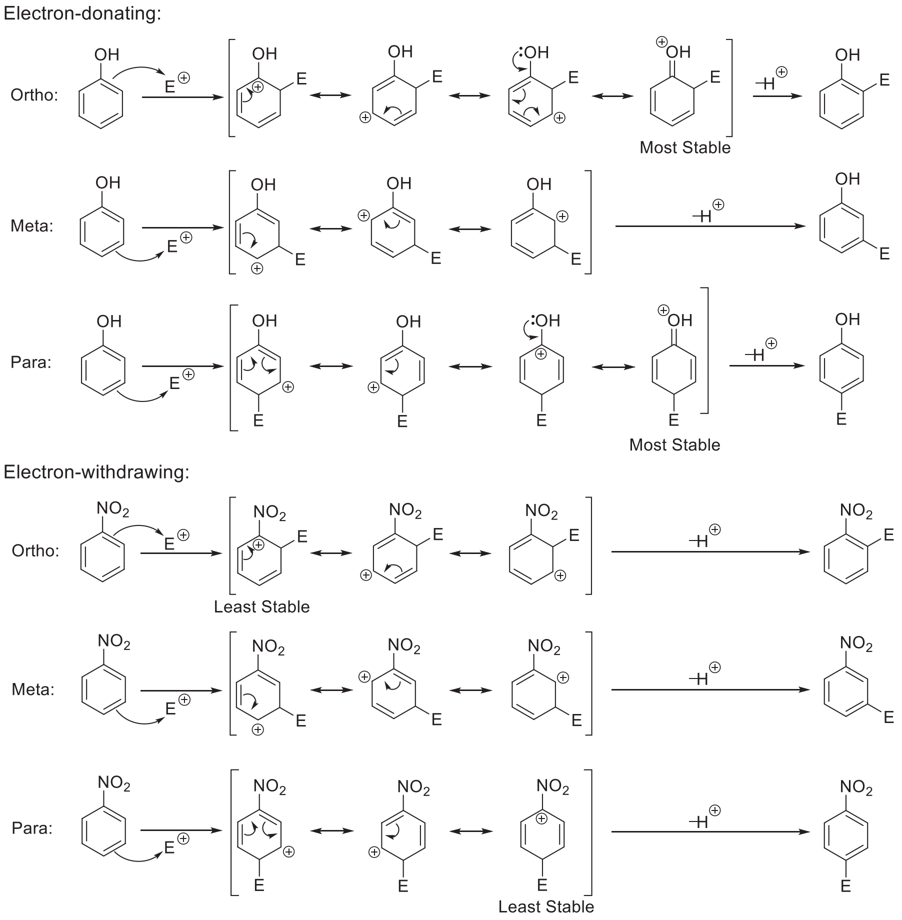


Figure 4.10.21. Resonance structures of aromatic carbocation intermediates.

Let us first rationalise the ortho, para-directing effects of electron-donating substituents. In this example, phenol is used as the starting material as the hydroxyl group is a strongly electron-donating substituent. If we look at the resonance structures for the intermediate carbocation, we see that there are 4 resonance structures for reactions at the ortho or para positions versus 3 resonance structures for reactions at meta positions. The key difference is whether the carbocation can be placed adjacent to the electron-donating group such that the cation may be stabilised by the lone pair of electrons from the heteroatom. This is possible only when the substituent is added to the ortho or para positions.

When the substituent is electron-withdrawing, the effect is opposite. The carbocation adjacent to an electron-withdrawing substituent is the least stable as the electron density is further withdrawn from the carbocation. Thus, the 3 resonance structures that result from substitution at the meta position are more stable than the resonance structures that result from substitution at the ortho and para positions.

The case for electron-withdrawing substituents is simpler, as only the meta product may be formed. When it comes to electron-donating substituents, both ortho and para products may be formed. How do we tell which product is formed as the major product? This is a difficult question that is dependent on the electron-donating group and the electrophile. Since the consideration of resonance structures is based on electronic effects, we could consider the steric differences between ortho and para substitutions. The steric effect may be significant for bulky groups as the benzene ring is fully planar, making it quite difficult for adjacent groups to avoid each other. Thus, based on the steric consideration, the para-substituted product would be preferred. However, in the case of a mono-substituted aromatic ring, there is only one para position while there are 2 ortho positions. Thus, statistically speaking, in the event that the likelihood of ortho substitution and para substitution are equal, there should be a 2:1 ratio of ortho to para products. However, certain ortho-directing substituents may have electron-withdrawing inductive effects, such as oxygen and nitrogen functional groups. These groups would slightly deactivate the ortho-position by withdrawing electron density form the ortho positions. The inductive effect gets progressively weaker further from the electronegative atom, thus the para-position is less deactivated. In conclusion, it is difficult to determine which product is preferred and mixtures with significant amounts of both products are usually obtained.

The next question is for more complex aromatic systems with multiple substituents. With multiple substituents, it is possible for the substituents to direct for the same substitution position or different substitution positions. When different substituents direct for different substitution positions, we need to **follow the directing effects of the most activating substituent, which is the strongest electron donor**. This is because activating groups are able to kinetically accelerate the reaction by increasing the nucleophilicity of the benzene ring, and the reaction is most likely to take place through the path in which the most stable resonance structure may be formed. A simple example is shown in Figure 4.10.22.

In the example, the hydroxyl group is the most electron-donating group, thus it activates the benzene ring the most and the substitution pattern would follow the

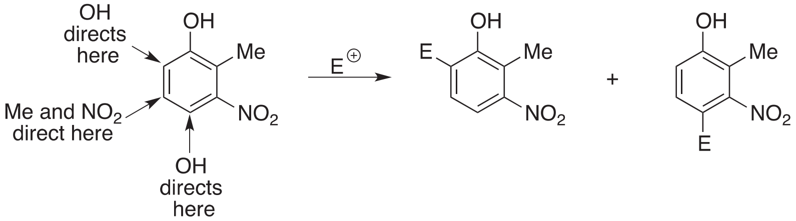


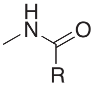
Figure 4.10.22. Example of electrophilic aromatic substitution on multi-substituted benzene.

directing effects of OH. It does not matter how many other substituents direct for other positions.

Since the substitution pattern is mainly determined by the strongest electron-donating group, we would look at different substituents and rank their electronic characteristics from most electron-donating to most electron-withdrawing. To do so, we must understand the basis for the electron-donating and electron-withdrawing effects of substituents. This involves both the inductive and resonance effects of the substituent. Let's look at the hydroxyl group for example. Oxygen is more electronegative than carbon, so by inductive effect, it withdraws electrons away from carbon, and should be considered an electron-withdrawing group. However, the resonance effect is more significant, as there are lone pairs on the oxygen atom that may be donated into the aromatic ring. Recall that benzene has a ring of delocalised electrons that come from the orthogonal p-orbitals of the sp^2-carbon atoms. In this case, the oxygen has a p-orbital that is aligned parallel to the benzene p-orbitals, allowing the lone pair of electrons from the p-orbital to delocalise into the benzene ring. This increases the electron density in benzene, activating it by increasing its nucleophilicity.

Electron-withdrawing substituents are similarly conjugated to the π-system of benzene. However, it is electron-deficient and pulls electrons away from the benzene ring. This deactivates the benzene ring. Table 4.15 ranks the electronic effects of substituents from the most activating to the most deactivating.

Table 4.15. Activating and directing effects of substituent groups.

Activating effect	**Substituent group**	**Directing effect**
Strongly Activating	$—O^{\ominus}$	ortho, para
Strongly Activating	$—NR_2$, $—NH_2$	ortho, para
Strongly Activating	$—OR$, $—OH$	ortho, para
Activating		ortho, para
Activating	—R (Alkyl)	ortho, para
Deactivating	Halogens: $F > I > Cl \approx Br$	ortho, para
Deactivating	$—CN$	meta
Deactivating	$—SO_3R$	meta
Deactivating	$—CO_2R$, $—CO_2H$	meta
Deactivating	$—COR$, $—CHO$	meta
Strongly Deactivating	$—CF_3$	meta
Strongly Deactivating	$—NO_2$	meta

The rankings on the table follow the electron-donating and electron-withdrawing effects of the substituent groups. The only interesting fact to draw our attention to is the halogens. Halogens are electron-withdrawing through the inductive effect due to their high electronegativity, but electron-donating through the resonance effect. We would expect fluorine to be the most deactivating as it has the highest electronegativity, and for the electron-withdrawing inductive effect to decrease with electronegativity down the group. In fact, fluorine is the least deactivating because the resonance effect, where the 2p lone pair is donated into the benzene ring, is the most significant. The extent of the resonance effect depends on the overlap between benzene orbitals and the halogen orbitals, and the orbital overlap is more effective when the orbitals are of similar size, in the case of 2p-2p overlap for fluorine.

The other irregularity for halogens is that they are electron-withdrawing substituents that deactivate the benzene ring, but they direct further substitution at the ortho and para positions. This is again due to the resonance effect where the halogen is able to donate electrons from its lone pair to stabilise the cation adjacent to it.

Highly activated benzene rings, such as phenol, can react with weaker electrophiles. One famous method of preparing salicylic acid, the **Kolbe-Schmitt process** (Figure 4.10.23), utilises the high reactivity of phenol to efficiently synthesise salicylic acid.

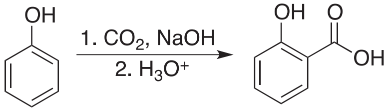


Figure 4.10.23. General scheme for the Kolbe-Schmitt process.

The mechanism of the Kolbe-Schmitt process follows electrophilic aromatic substitution with carbon dioxide as the electrophile, as shown in Figure 4.10.24.

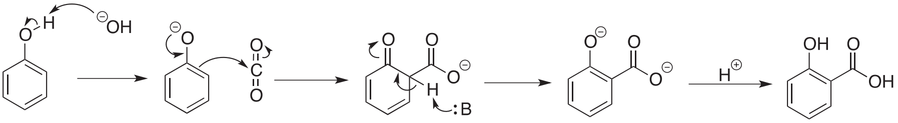


Figure 4.10.24. Mechanism for the Kolbe-Schmitt process.

While high reactivity due to activating substituents may allow more reaction pathways, it may also lead to unwanted reactions. This happens when electrophilic aromatic substitution reactions are carried out on aniline, as the amino group is strongly activating. To prevent over-substitution, we may protect the amine by using acetic anhydride to make it less activating. The full reaction scheme is shown in Figure 4.10.25.

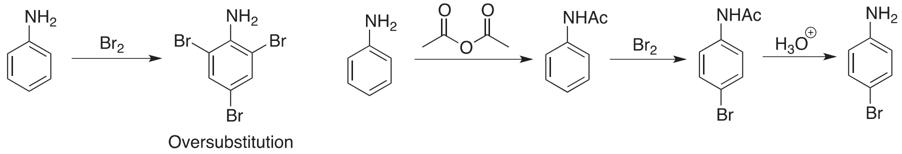


Figure 4.10.25. Scheme to protect amine on aniline to avoid oversubstitution.

4.10.2 *Electrophilic aromatic substitution on aromatic heterocycles*

In chapter 4.7, we saw that pyridine is electron-poor and good at nucleophilic aromatic substitutions. For electrophilic aromatic substitutions, we require electron-rich aromatic rings such as the 5-membered aromatic heterocycles.

Generally, pyridine is too electron-deficient to undergo the electrophilic aromatic substitution reactions mentioned in this chapter. To perform electrophilic aromatic substitution on pyridine, we need to activate it by oxidising it to **pyridine *N*-oxide**. The oxidation is usually carried out by a peroxyacid. The pyridine N-oxide is more electron-rich due to the strongly electron-donating oxide substituent. It is able to undergo the electrophilic aromatic substitution reactions stated in this chapter. To reduce the pyridine N-oxide back to pyridine, we may use a phosphine such as $\mathrm{PCl_3}$ due to the strong $\mathrm{P{=}O}$ bond that can be formed. A sample reaction scheme for nitration is shown in Figure 4.10.26.

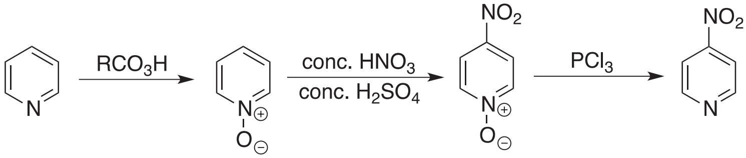


Figure 4.10.26. Reaction scheme for nitration of pyridine through pyridine N-oxide.

It is much easier to carry out electrophilic aromatic substitution on electron-rich heterocycles. These are 5-membered ring heterocycles with one heteroatom. The most reactive in this group is pyrrole, as nitrogen is the most strongly electron-donating. Furan is less reactive than pyrrole, while thiophene is the least reactive in the group, having similar reactivity to benzene. The general scheme for the electrophilic aromatic substitution of such heterocycles is shown in Figure 4.10.27.

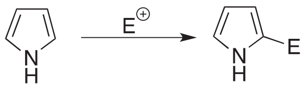


Figure 4.10.27. General scheme for electrophilic aromatic substitution on pyrrole.

Notice that the electrophile is regioselectively added to the 2nd or 5th carbon of pyrrole, not the 3rd or 4th. To understand the regioselectivity of the reaction, we must examine the mechanism carefully as shown in Figure 4.10.28.

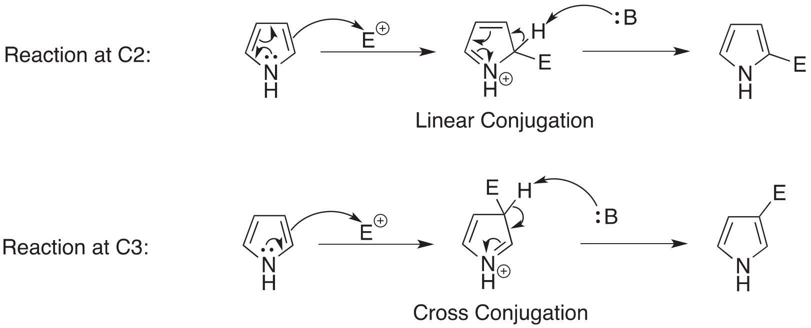


Figure 4.10.28. Mechanisms for electrophilic aromatic substitution at different positions.

Reaction at the 2nd carbon gives a linearly conjugated intermediate cation, which is more stable than the cross-conjugated cation intermediate for a reaction at the 3rd carbon. We will look at the formylation of such heterocycles, through the **Vilsmeier reaction**. This reaction may be applied to benzene as well, but it is more commonly used on pyrrole. Figure 4.10.29 shows the general reaction scheme for the Vilsmeier reaction.

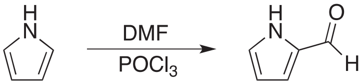


Figure 4.10.29. General reaction scheme for Vilsmeier reaction on pyrrole.

The first reaction happens between *N*,*N*-dimethylformamide (DMF) and $POCl_3$ to generate the electrophile that reacts with pyrrole through electrophilic aromatic substitution. The full mechanism is shown in Figure 4.10.30.

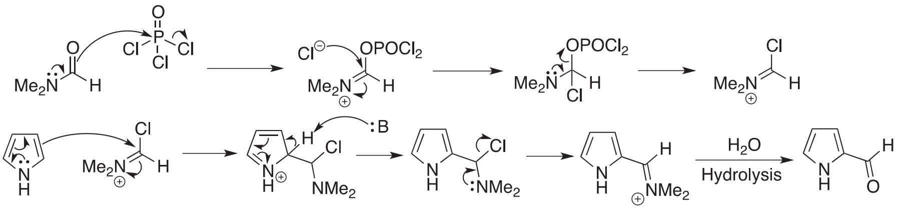


Figure 4.10.30. Mechanism for Vilsmeier reaction on pyrrole.

4.11 Enolate Chemistry

In the previous chapters, we have completed our discussion on the key reaction pathways of organic compounds. From this chapter onwards, we will start looking at more complicated reactions that are built up from the different mechanisms. In this chapter, we will look at one of the most useful intermediates in organic chemistry, the enolate ion. Enolate chemistry is a classical and powerful technique used by organic chemists mainly for the preparation of C–C bonds, which is difficult given the current set of reactions we have learnt so far. Modern chemistry has developed new methods for this purpose, which include various coupling and pericyclic reactions, some involving the use of metal catalysts. However, enolate chemistry is still relevant as a well-developed method for formation of C–C bonds.

4.11.1 *Enols and enolates*

Enols are just tautomers of carbonyl compounds, and enolate is just the anion of enol. In a solution of carbonyl compound, there is usually an equilibrium between the keto and enol forms, as shown in Figure 4.11.1.

The equilibrium constant for keto-enol tautomerisation is usually very small. This is because the C=O double bond is much stronger than the C=C double bond, making the keto form a lot more stable than the enol form. Despite the small amount of enol, it presents a key reactivity for carbonyl compounds. As we have seen in chapter 4.6, carbonyl compounds usually act as electrophiles as the carbonyl carbon may be attacked by nucleophiles. Enols, on the other hand, are good nucleophiles. They may react with electrophiles at either the oxygen or the alkene carbon. This makes carbonyl reactivity highly diverse as the keto and enol forms present opposite reactivity.

It is clear that with the small equilibrium constant, it is not possible to react carbonyl compounds directly as nucleophiles, as the concentration of enol will be too small. Instead, we may use acid or base to form enols or enolates, as shown in Figure 4.11.2.

It is important to note that formation of enol is catalysed by acid while the formation of enolate by base requires a stoichiometric amount of base. The enolate anion, carrying a negative charge, is also a much better nucleophile than the enol. To understand the reactivity of the enolate ion, we need to visualise the molecular orbitals of enolate as shown in Figure 4.11.3.

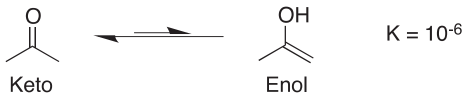


Figure 4.11.1. Keto-Enol tautomerisation of acetone.

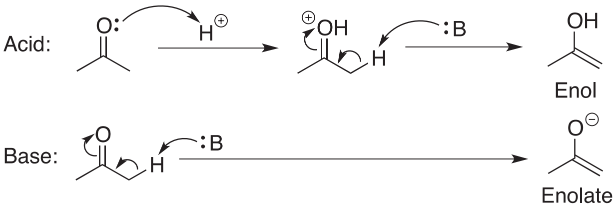


Figure 4.11.2. Formation of enol and enolate using acid and base respectively.

Figure 4.11.3. Highest Occupied Molecular Orbital (HOMO) of the enolate ion.

The negative charge lies mainly on oxygen, but the carbon has the larger HOMO coefficient. In this case, both the oxygen and the carbon may act as nucleophiles. The oxygen is a hard nucleophile that reacts mainly through charge interactions. Carbon, on the other hand, is a soft nucleophile that tends to react through orbital overlap with the electrophile. In the case of enolates, we usually want to promote reaction at the carbon as it is much easier to form an oxygen nucleophile than carbon nucleophile.

We will now compare the conditions that promote reactions at oxygen and carbon. Firstly, the choice of electrophile is important. A hard electrophile is likely to react at oxygen while a soft electrophile would preferentially react at carbon. For example, the methylation of enolate at oxygen would be favoured by hard electrophiles such as the trimethyloxonium ion $(\mathrm{Me_3O^+})$ while the methylation at carbon would be favoured by soft electrophiles such as methyl halides.

Other than the choice of electrophile, we can tune the intrinsic reactivity of the enolate ion through solvent effects and the base used to generate the enolate ion. Polar aprotic solvents are able to solvate cations well but not anions. This allows for the cation from the base to be solvated and unable to chelate to the oxyanion in the enolate. This leaves the oxyanion open and more reactive, promoting reaction at oxygen. On the other hand, less polar solvents such as ether do not solvate both cation and anion well, allowing the cation from the base to chelate to oxygen, reducing the nucleophilicity of the oxygen and promoting reaction at carbon. The solvent effects mainly focus on whether the metal cation is free to chelate to oxygen. The identity of the metal cation is also highly important in its ability to chelate to oxygen. Generally metal cations in the same period with similar orbital size would chelate better to oxygen, especially lithium, which chelates very well to oxygen, allowing reaction at carbon. To promote reaction at oxygen, a larger non-chelating metal may be used in the base, such as potassium. These effects are summarised in Table 4.16.

Table 4.16. Effects of reaction conditions on the reactivity of enolate.

	Reaction at oxygen	**Reaction at carbon**
Solvent effects	Polar aprotic solvents (DMSO, DMF)	Ethereal solvents (THF, DME)
Choice of metal in base	Larger, non-chelating metals (Na, K)	Smaller, chelating metals (Li, Mg)

We will now take a look at common enolates and how to prepare them. The most common enolates are formed from ketones in the presence of base, as we have seen previously. Since we would usually like the enolate to react at carbon, the standard base to use for formation of enolate is **lithium diisopropylamide** (LDA). It is able to form lithium enolates effectively through a 6-membered ring transition state, as shown in Figure 4.11.4.

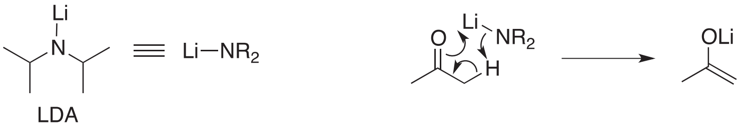


Figure 4.11.4. Structure of LDA and mechanism for enolisation.

LDA is a strong and bulky base, thus it avoids the problem of direct nucleophilic attack at the electrophilic carbonyl carbon centre. It reacts with the most accessible proton in the molecule and quickly deprotonates it. It increases the acidity of the α-protons on the molecule by chelating with the carbonyl oxygen. This makes it an excellent base for the formation of enolate ions.

To form enolates of asymmetric ketones, there is usually a regioselectivity problem, as the enolate may be formed on either side of the ketone. The problem is illustrated in Figure 4.11.5.

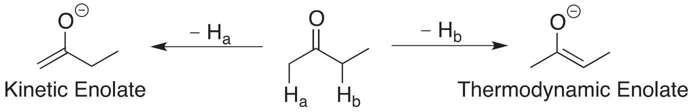


Figure 4.11.5. Regioselectivity in asymmetric enolates.

The kinetic enolate is formed at the less substituted side while the thermodynamic enolate is formed at the more substituted side. The thermodynamic enolate is more stable as the alkene is more substituted, while the kinetic enolate is formed faster as the terminal protons are less sterically hindered. It is important to control the reaction to form the desired enolate. This can be done by choosing the appropriate base. Strong, bulky bases used at low temperatures favour the kinetic enolate while weaker bases left to react over longer time at higher temperatures favour the thermodynamic enolate. Thus, LDA is useful in preparing kinetic enolates, while thermodynamic enolates are commonly prepared by using alkoxide bases in alcoholic solvents.

Other than ketones, enolates may also be formed from carboxylic acid derivatives and some other functional groups. Within carboxylic acid derivatives, ester is the most common functional group to form enolates as they are relatively stable and the α-proton is the most acidic proton in the molecule. Figure 4.11.6 shows different methods of preparing ester enolates.

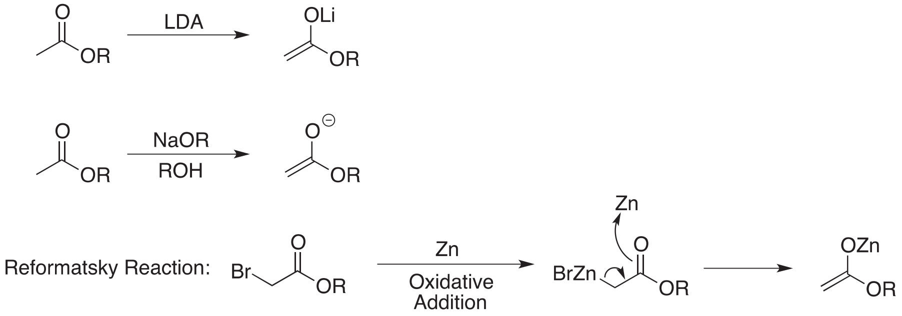


Figure 4.11.6. Methods for preparation of ester enolates.

Ester enolates may be prepared by both strong and weak bases. When using alkoxides, there is a possible side reaction of nucleophilic acyl substitution that may occur at the carbonyl carbon. Thus, the alkoxide and alcohol chosen to prepare ester enolates should be the same as the ester. In this case, any nucleophilic acyl substitution reactions will result in the same original ester. A special reaction for formation of ester enolates is the **Reformatsky reaction**. The Reformatsky reaction allows the formation of zinc enolates by reacting zinc with α-bromoesters. This reaction is useful as a selective way to prepare ester enolates.

Acyl halides are highly reactive and it is extremely difficult to prepare enolates from acid halides. Such enolates are also short-lived, as they can collapse with the loss of halide to form ketenes. Ketenes are important reagents useful in pericyclic reactions, and they may be prepared through such a method, as shown in Figure 4.11.7. Thus, do not attempt to prepare enolates from acyl halides.

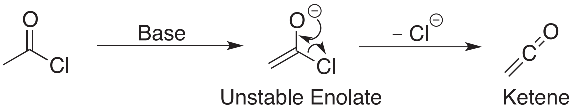


Figure 4.11.7. Reaction of acyl halides with base.

Carboxylic acids are able to form enolates provided 2 equivalents of base is added. The first equivalent of base is used to neutralise the acid, leaving the carboxylate anion, which requires a strong base to be further deprotonated. The carboxylate anion is already anionic and much more difficult to deprotonate. It is generally easier to form the enol of carboxylic with acidic catalysis. The reactions to prepare enols and enolates of carboxylic acids are shown in Figure 4.11.8.

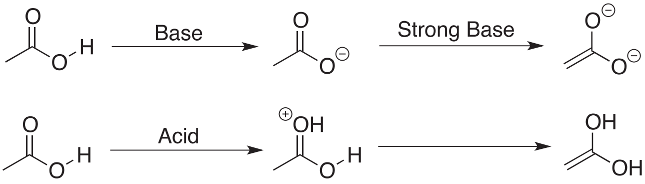


Figure 4.11.8. Reactions to prepare enolates and enols of carboxylic acids.

Enolates of amides are also difficult to prepare. In amides, the proton attached to the nitrogen is the most acidic. Reactions of amides in base usually result in a good nucleophile that attacks from the amide nitrogen. With excess strong base, it is still possible for an amide enolate to be prepared, but such reactions are rare. It is more common to use the nucleophilicity of the amide nitrogen for reactions.

Other anion stabilising functional groups are also able to form enolates. Examples include the nitro and nitrile groups, and their enolates are shown in Figure 4.11.9.

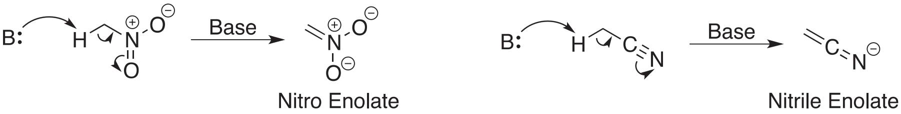


Figure 4.11.9. Preparation of nitro and nitrile enolates.

You may be wondering why we have not mentioned the preparation of aldehyde enolates yet, or might be thinking that aldehyde enolates are just like ketone enolates. In fact, aldehyde enolates are extremely difficult to prepare due to the high reactivity of aldehyde. It is not possible to prepare lithium enolates of aldehydes using LDA due to 2 chief reasons:

1. The highly electrophilic carbon of aldehyde is able to react with LDA through a nucleophilic addition reaction, which is irreversible once the alcohol is further deprotonated by LDA. This is possible as the aldehyde hydrogen is a very small substituent that does not sterically hinder the approach of LDA to the electrophilic carbon centre.
2. During the short time for the enolisation to occur, there is a mixture of aldehyde and enolate in the solution. Aldehydes are wonderful electrophiles while enolates

are good nucleophiles and they can react with each other through aldol reaction, which we will be exploring in detail soon. Due to its ability to react with itself (in two different forms), it is likely for the aldehyde to react during the formation of the enolate.

As such, direct preparation of aldehyde enolates is challenging. However, aldehydes are important and useful in enolate reactions and many reactions require their enolates as the reagent. Thus, multiple methods have been developed, known as **specific enol equivalents**, that allow for aldehyde enolate equivalents to be prepared. These enol equivalents allow us better controls in enolate formation, and may be used for any reactive carbonyl compounds.

The first enol equivalent that we will discuss is **Stork's enamine**. Enamines have the same general structure as enols, but they have higher nucleophilicity due to the stronger electron-pushing nitrogen. However, they are still weaker in nucleophilicity than negatively charged enolates. For asymmetric ketones, enamine formation favours the less substituted end, giving rise to the kinetic product. This is due to the unfavourable steric hindrance that arises from the double bond, forcing the amine and side group to be planar, as shown in Figure 4.11.10.

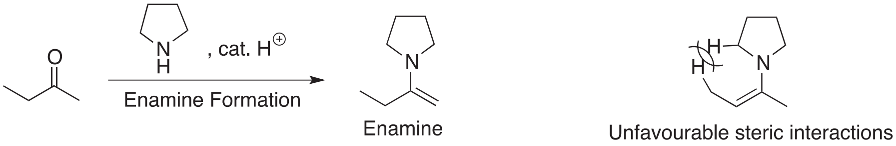


Figure 4.11.10. Enamine formation and its regioselectivity.

Note that enamine formation can only be achieved with a secondary amine, and we would usually pick a cyclic or bulky amine to increase the stability of the enamine product. However, enamines are not without their drawbacks. The tertiary nitrogen may still be nucleophilic and react with electrophiles to form quaternary ammonium salts. To prevent such side reactions, we need highly S_N2-reactive electrophiles to react with the enamine, such as benzylic halides or α-halocarbonyls. Thus, enamines are best reacted with good S_N2 electrophiles.

If enamines are enol equivalents, then **aza-enolates** are enolate equivalents. Our second enol equivalent is aza-enolates, which are essentially enolates formed from imines. Their preparation route is shown in Figure 4.11.11.

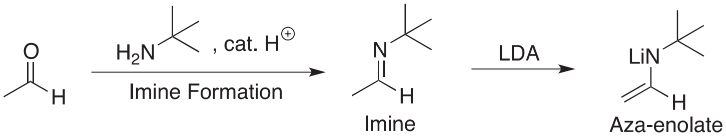


Figure 4.11.11. Preparation of aza-enolates.

The preparation of aza-enolates avoids the problems faced while preparing aldehyde enolates, as imines are less electrophilic than aldehydes. This avoids both the problems of self-reaction and direct nucleophilic attack of base, such as LDA. Aza-enolates are also much more reactive than enamines, able to react with a wider variety of electrophiles. For asymmetric imines, the regioselectivity follows the same trend as enolates from asymmetric ketones, depending on the reaction conditions. Similar to enamines, the nitrogen in aza-enolate is also nucleophilic and may react with electrophiles, thus we have to choose primary amines with a large bulky substituent, such as the tert-butyl group.

Both enamines and aza-enolates are generally employed with S_N2 reactive electrophiles. The third enol equivalent that we will introduce is the **silyl enol ether**, which may be used with S_N1 reactive electrophiles. The preparation of silyl enol ethers is shown in Figure 4.11.12.

Note that silyl enol ethers must be prepared through reaction at oxygen. In this case, the affinity of silicon with oxygen is very high, thus the reaction mechanism starts with the formation of the strong silicon-oxygen bond. This further polarises the carbonyl $C{=}O$ double bond, making it much easier to deprotonate the α-proton. The full mechanism is shown in Figure 4.11.13.

For asymmetric ketones, the silyl enol ether forms as the thermodynamic product, because preparation of silyl enol ethers is under conditions that encourage equilibration to form the most stable product, with weak bases and long reaction times. Silyl enol ethers allow us to conveniently react S_N1 reactive electrophiles such as tert-butyl chloride in the presence of Lewis acid catalysts.

These 3 specific enol equivalents are often used to provide additional control over the enolate reactions we run, as we will soon see that enolate reactions may often form multiple products.

Control may be afforded to enolate formation by employing stable enolates. The most common stable enolates are enolates of 1,3-dicarbonyl compounds. These enolates are further stabilised by another carbonyl group and it allows the "centre

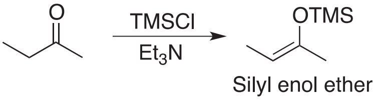


Figure 4.11.12. Preparation of silyl enol ethers.

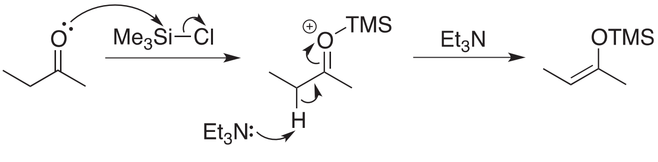


Figure 4.11.13. Mechanism for the formation of silyl enol ether.

carbon" between the carbonyl groups to be preferentially deprotonated, leaving no room for regioselectivity problems. Common 1,3-dicarbonyl compounds are shown in Figure 4.11.14.

These esters are commonly used to perform enolate reactions due to the ease of forming enolates with them. It is also not a concern when only one carbonyl group is required in the final product. Due to the structural feature of a 1,3-dicarbonyl functionality, these compounds readily undergo **decarboxylation**. The most common decarboxylation procedure is a 2-step sequence of base hydrolysis followed by heating in acid, as shown in Figure 4.11.15.

The first step is just a simple ester hydrolysis to carboxylic acid. The second step is mainly driven by the positive entropy from the loss of carbon dioxide gas, which is most favourable at higher temperatures as $\Delta G = \Delta H - T\Delta S$. Decarboxylation follows a 6-membered ring cyclic transition state. The mechanism for decarboxylation is shown in Figure 4.11.16.

The drawback of this decarboxylation is that both ester groups are hydrolysed and the final product is a carboxylic acid. To preserve the other ester, it is possible for an alternative decarboxylation that utilises the S_N2 mechanism. **Krapcho decarboxylation** employs milder conditions that tolerate a large range of functional groups. The general scheme and mechanism of Krapcho decarboxylation is shown in Figure 4.11.17.

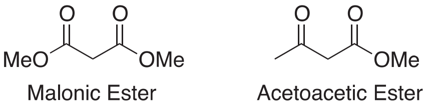


Figure 4.11.14. Common 1,3-dicarbonyl compounds.

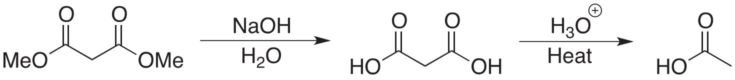


Figure 4.11.15. Reaction scheme for decarboxylation.

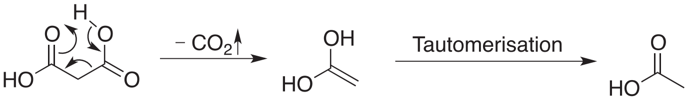


Figure 4.11.16. Mechanism for decarboxylation.

Figure 4.11.17. Reaction scheme and mechanism of Krapcho decarboxylation.

As can be seen from the mechanism, Krapcho decarboxylation follows an S_N2 mechanism with the chloride ion serving as a nucleophile. The driving force is the same, from the release of carbon dioxide gas. Since it is an S_N2 reaction, the key factor is the steric hindrance at the carbon centre. Thus, Krapcho decarboxylation works best for methyl esters, and is inefficient with most other esters. The limited scope is the main drawback of this reaction.

4.11.2 *Enolate reactions*

In the previous section, we have extensively discussed the formation of various enolates. Now we will start looking at how enolates react, and why they are so useful. The first reaction we will look at is **halogenation**.

Halogenation may be carried out in acidic or basic conditions, leading to vastly different products, as shown in Figure 4.11.18.

In the acid-promoted halogenation reaction, the enol formed reacts with the halogen once to form the product. Under basic conditions, the enolate formed reacts with multiple equivalents of halogen. If there is a methyl ketone moiety, the CX_3^- ion will be a leaving group, as it has 3 electron-withdrawing halogen atoms to stabilise the negative charge. If the halogen used is iodine, iodoform will be formed. It will be observed as a pale yellow solid precipitate, and is commonly used as an organic test for methyl ketones.

The main difference is that in acid promoted halogenation, only one halogen is added, while in base promoted halogenation, multiple halogens are added and it is not possible to stop the reaction at monohalogenation stage. This means that for acid promoted halogenation, further reaction with halogen is slower while for base promoted halogenation, further reaction with halogen is faster. This can be understood if we consider the intermediates in each reaction. In the acid promoted reaction, the reaction intermediates are all positively-charged, destabilised by electron-withdrawing groups such as the added halogen. On the other hand, the

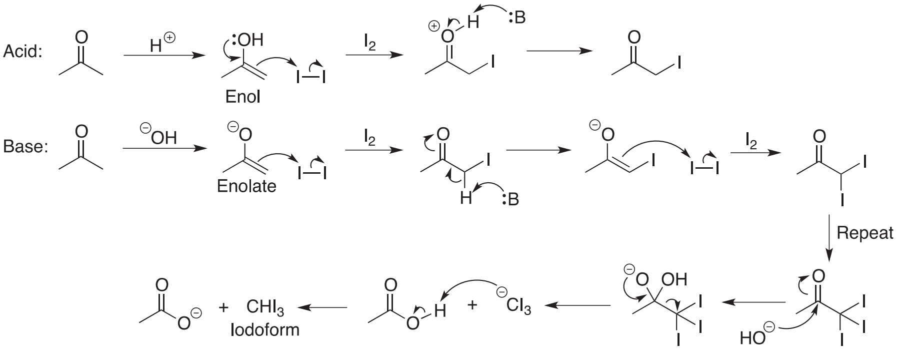


Figure 4.11.18. Acid and base promoted halogenation at α-carbon.

intermediates of the base promoted reaction are all negatively-charged, stabilised by the electron-withdrawing halogen. Thus, the base promoted reaction speeds up with more substitution, and it is common to get multi-substituted products. To prevent oversubstitution, we would utilise the acid promoted reaction, adding 1 equivalent of halogen together with acetic acid (which acts as both a solvent and an acid catalyst) under thermodynamic conditions.

Regarding regioselectivity, the acid promoted halogenation reaction is under thermodynamic control while the base promoted halogenation reaction is under kinetic control.

The next reaction we will look at is **nitrosation** at the α-carbon. Nitrosation is an important reaction as it allows us to synthesise 1,2-dicarbonyl compounds, which is challenging by conventional methods. The reaction scheme for nitrosation is shown in Figure 4.11.19.

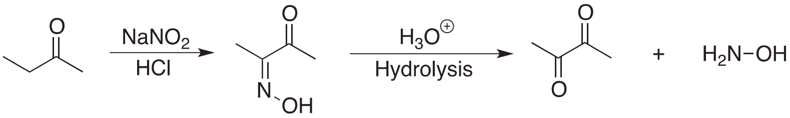


Figure 4.11.19. Reaction scheme for nitrosation.

The immediate product from nitrosation is an oxime, which can be hydrolysed to a ketone and hydroxylamine, as we have seen in chapter 4.6. The mechanism for nitrosation is shown in Figure 4.11.20.

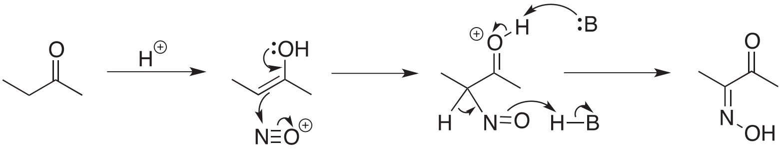


Figure 4.11.20. Mechanism for nitrosation to form oxime.

The reagents $NaNO_2$ in HCl is used to form the NO^+ cation, which reacts with enol to form an oxime. The formation of NO^+ cation has been discussed in part 4.10.1 as it was a key intermediate for the synthesis of diazonium ions.

We will now move to the key $C–C$ bond formation reactions of enolates, which are the main reason for their utility. The simplest reaction is **enolate alkylation**. Theoretically, enolate alkylation is a simple reaction that just requires the addition of an alkylating agent to an enolate, as shown in Figure 4.11.21.

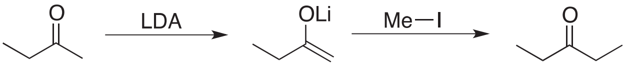


Figure 4.11.21. A simple enolate alkylation reaction scheme.

For simple alkylations, the above scheme is sufficient. However, we have to always consider three main factors:

1. Stability of the enolate and the possibility for self-reaction
2. Regioselectivity
3. Stereoselectivity

For stereoselectivity, we have to choose special enolates such as Boron enolates to achieve a good diastereoselectivity. Stereoselectivity for enolate reactions may be determined using stereochemical models, such as Felkin-Anh, Houk and Zimmerman-Traxler models. These models are beyond the scope of this book, but it is encouraged for you to read up and have a basic understanding of the models.

In this book, we will focus more on the first 2 factors of enolate stability and regioselectivity. While lithium enolates are the most common and straightforward, their high reactivity may lead to self-reaction. Thus, as mentioned previously, lithium enolates should never be prepared for aldehydes. When preparing lithium enolates of other carbonyl compounds such as ketones and esters, it is advised to add the carbonyl compound slowly to a large amount of LDA at low temperatures, such that all carbonyl compounds added will react immediately and completely to form enolates and there is never a mixture of enolates and carbonyl compounds to react. In certain cases, where the carbonyl compounds are too reactive, we may apply the 3 specific enol equivalents that we learnt previously, as shown in Figure 4.11.22.

It is important to note the electrophiles used for each enol equivalent. Stork's enamine is reacted under milder conditions than aza-enolate, and requires a more reactive S_N2 reactive electrophile. On the other hand, silyl enol ethers react with S_N1 reactive electrophiles under Lewis acid catalysis.

We will now move on to reactions between carbonyl compounds, starting with the **aldol reaction**. The general scheme is shown in Figure 4.11.23 for an aldol reaction between 2 acetone molecules.

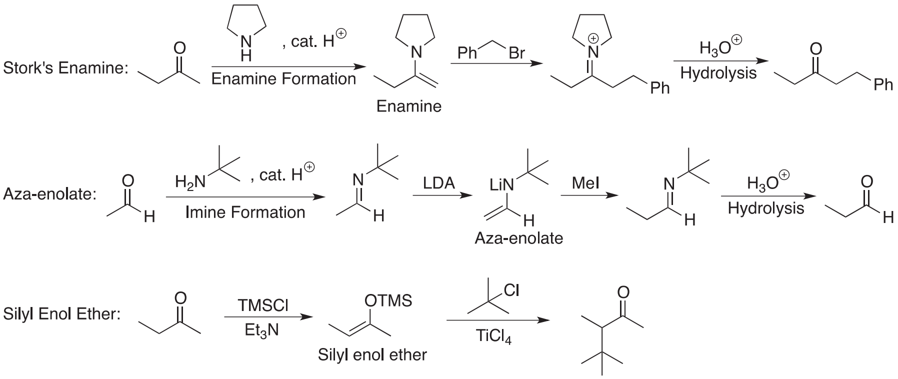


Figure 4.11.22. Using specific enol equivalents for alkylation.

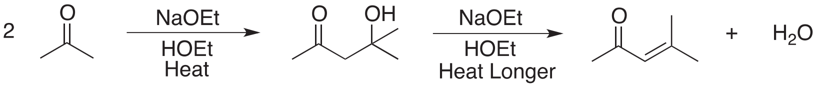


Figure 4.11.23. General scheme for an aldol reaction and condensation.

When heated with base, the first product that will be formed is the β-hydroxyketone, known as the aldol addition product. Upon prolonged heating in base, the aldol addition product loses water though E1cb mechanism, forming the aldol condensation product, an α,β-unsaturated ketone. The mechanism for the aldol reaction is shown in Figure 4.11.24.

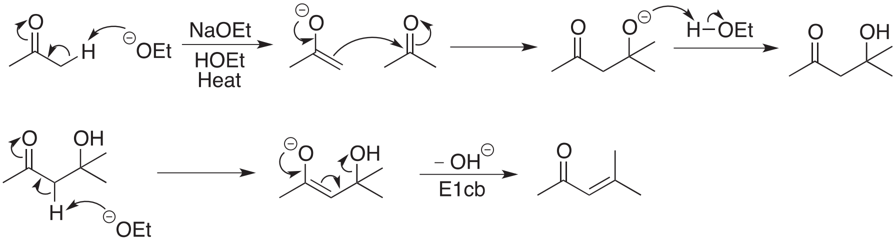


Figure 4.11.24. Mechanism for aldol reaction and condensation.

This example is simple because it is a self-reaction. Cross-reactions, involving 2 different carbonyl compounds, pose a greater challenge. The main challenge is controlling which carbonyl acts as the nucleophile and which as the electrophile. In such cases, mixing the 2 carbonyl compounds together with base will result in a mixture of 4 products as shown in Figure 4.11.25, which is highly undesirable.

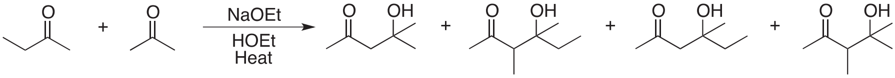


Figure 4.11.25. Possible products from an aldol cross-reaction.

The 4 products consist of the 2 self-reaction products and 2 cross-reaction products. Thus, chemists have developed different methods to improve the selectivity of the reaction. One method involves the use of 1,3-dicarbonyl compounds as the enolate for aldol reaction. This is known as the **Knoevenagel condensation**. In such reactions, the 1,3-dicarbonyl compound would definitely serve as the nucleophile as the α-proton of a 1,3-dicarbonyl compound is much more acidic than normal carbonyl compounds. With stoichiometric amount of base, all of the 1,3-dicarbonyl compound would be converted into enolate form, and there should be no concern for the 1,3-dicarbonyl compound reacting with itself. The base selected should be relatively weak and only deprotonates the 1,3-dicarbonyl compound, preventing the other carbonyl compound from becoming an enolate.

Thus, the reaction would proceed with high selectivity for the desired product. After the reaction, the additional carbonyl group may be removed by decarboxylation. In certain cases, the decarboxylation may be performed in one step together with the condensation. This is known as the **Doebner modification of Knoevenagel condensation**. The reaction scheme is shown in Figure 4.11.26.

Another way is to perform the reaction stepwise, employing enol equivalents. The first method involves making a lithium enolate first before adding the other carbonyl compound as an electrophile, as shown in Figure 4.11.27.

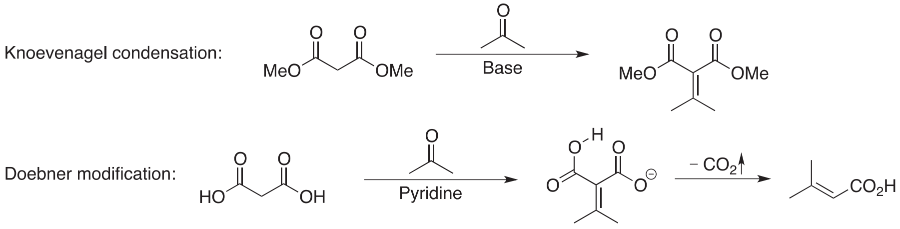


Figure 4.11.26. Reaction scheme for Knoevenagel condensation and the Doebner modification.

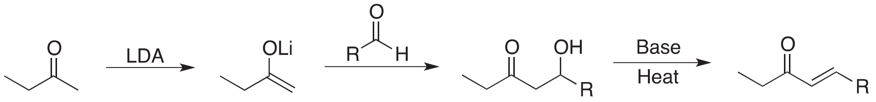


Figure 4.11.27. Aldol cross-reaction between a lithium enolate and aldehyde.

By performing the reaction stepwise, we are able to choose the desired carbonyl compounds as the enolate and the electrophile, respectively. The electrophile is usually strongly electrophilic, such as aldehydes. The regioselectivity of enolate formation follows the reaction conditions, and LDA forms the kinetic enolate. The same regioselectivity may be obtained using enamines and aza-enolates.

To form a thermodynamic enolate, we may use silyl enol ether as the enol equivalent. The aldol reaction using silyl enol ether is known as **Mukaiyama aldol reaction**. The reaction scheme is shown in Figure 4.11.28.

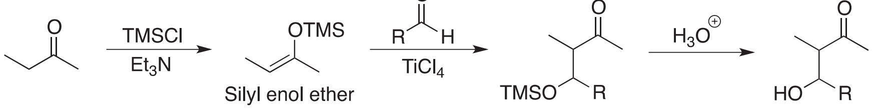


Figure 4.11.28. General reaction scheme for Mukaiyama aldol reaction.

Note that just as the case of alkylation of silyl enol ether, the aldol reaction of silyl enol ethers also requires a Lewis acid catalyst. The Lewis acid is able to increase the electrophilicity of the aldehyde by coordinating to the carbonyl oxygen. It is important to note that the main difference between using lithium enolate and silyl enol ether is the regioselectivity of the enolate, with silyl enol ether being the thermodynamic enolate.

It is important to note that reactive electrophiles generally give higher yield and less side products. To prevent side reactions, it is strategic to choose electrophiles that do not have α-protons. These electrophiles are unable to form enolates, cutting down on the possible side reactions. A few examples of such non-enolisable electrophiles are shown in Figure 4.11.29.

It may seem that formaldehyde is the perfect electrophile being highly reactive and unable to form enolates. The problem is that formaldehyde is just too reactive. If an enolate is reacted directly with formaldehyde, there will be over-reaction and multiple products would be formed. Not only so, formaldehyde becomes a good reducing agent in base through the **Cannizzaro reaction**. The reaction scheme for an aldol reaction with formaldehyde and the mechanism for Cannizzaro reaction is shown in Figure 4.11.30.

It should be clear by now that it is not possible to directly react formaldehyde in an aldol reaction with good control. Instead, we have to use the **Mannich reaction**, which first converts the formaldehyde to an iminium ion. The aldol reaction proceeds with the iminium ion to first form a tertiary amine, which can be removed by elimination. The general scheme for Mannich reaction is shown in Figure 4.11.31.

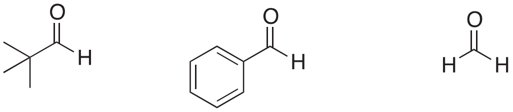


Figure 4.11.29. Examples of carbonyl compounds that are unable to form enolates.

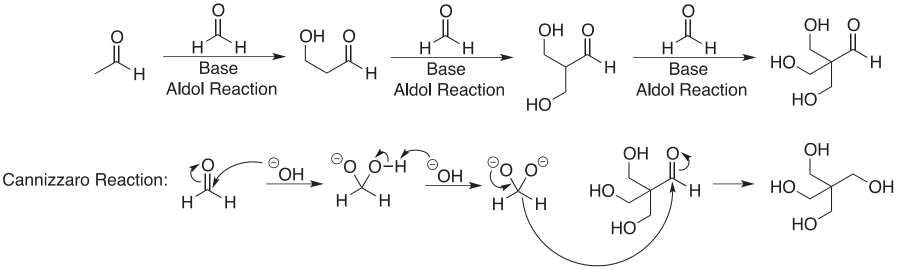


Figure 4.11.30. Reaction scheme and mechanism for aldol reaction with formaldehyde.

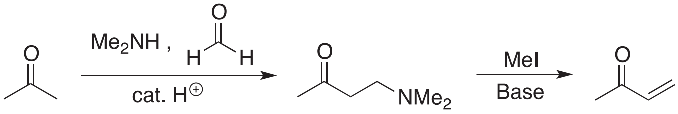


Figure 4.11.31. General reaction scheme for Mannich reaction.

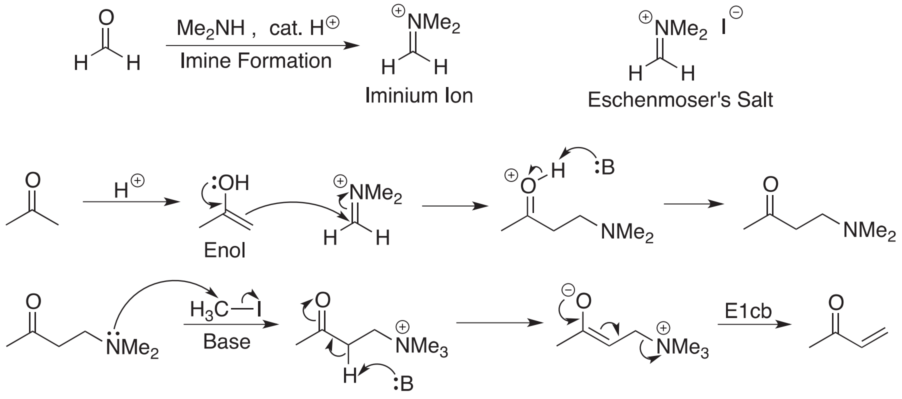


Figure 4.11.32. Full mechanism for Mannich reaction.

The mechanism involves the formation of iminium ion by reaction of formaldehyde with the secondary amine, which is then attacked by the enol. The tertiary amine can be removed by further alkylation to a quaternary ammonium salt, followed by E1cb elimination. The full mechanism is shown in Figure 4.11.32.

The iminium ion is commercially available as a reagent, Eschenmoser's salt, and may be directly added to the enolate. The Mannich reaction provides an indirect pathway for aldol reactions involving formaldehyde. As we are able to react and condense any carbonyl compounds together through aldol reaction, the aldol reaction is one of the most versatile and widely used reactions in classic organic chemistry.

Just to provide an example of what aldol reaction can accomplish, we will take a look at **Robinson annulation**, a one-pot cyclisation reaction to form 6-membered rings. The reaction scheme is shown in Figure 4.11.33.

The driving force for Robinson annulation is the high stability of 6-membered rings. It is a reliable method to prepare 6-membered rings. The full mechanism is shown in Figure 4.11.34.

The mechanism for Robinson annulation is just a series of enolate reactions, starting with a conjugate addition. The formed enolate does not immediately react with the other carbonyl group in an aldol reaction as that would form an unstable 4-membered ring. Instead, there is a proton transfer to form the enolate on the other side of the ketone, which attacks to form the 6-membered ring. The aldol reaction is followed by E1cb elimination to form the final aldol condensation product.

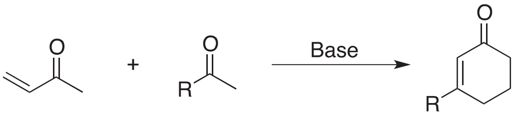


Figure 4.11.33. Reaction scheme for Robinson annulation.

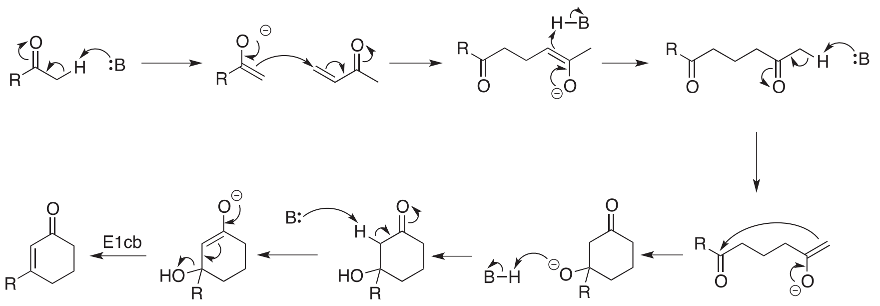


Figure 4.11.34. Full mechanism for Robinson annulation.

Tip 4f. Forming rings of different sizes

In organic chemistry, we often encounter rings of different sizes. For many organic reactions, the stability of the ring formed is an important driving force for the reaction. There are 2 main factors for the favourability of different ring sizes:

1. Enthalpy: Thermodynamic stability

The stability of a ring depends mainly on the ring strain it experiences. Ring strain arises from angle strain and torsional strain. Angle strain is when the ring angle deviates significantly from the ideal 109.5° tetrahedral angle, while torsional strain arises from steric repulsions between eclipsing atoms on rings. These strains are the greatest for small rings.

2. Entropy

When straight-chain molecules form rings, there is a decrease in entropy as straight chain molecules are much more flexible and have more microstates, while the ring constricts the atoms together. The entropy effect makes it difficult to form large rings as long chains usually have high entropy and the ends are unable to come together to form the ring.

While enthalpy favours large rings, entropy favours small rings. Thus, medium-sized rings are the most favourable. While small 3 and 4-membered rings are highly strained, 5 and 6-membered rings are generally free from the ring strain. Large rings with more than 7 atoms usually take much longer to form due to the entropy effect. Experimentally, it is found that the rate of ring formation follows the general trend:

$$5 > 6 > 3 > 7 > 4 > \text{Larger Rings}$$

For all intramolecular aldol reactions, the selectivity is mostly determined by the ring size of the product. Reactions favour 5 and 6-membered ring products, while other ring sizes are less likely to be formed.

In the previous part, we have discussed enolates formed from different carboxylic acid derivatives, but acid anhydride was left out. This is because the enolate reaction of acid anhydrides is different from the rest. This reaction, known as **Perkin reaction**, returns an α,β-unsaturated carboxylic acid, similar to the Doebner modification of Knoevenagel reaction, but uses an acid anhydride as the reagent instead. The reaction scheme is shown in Figure 4.11.35.

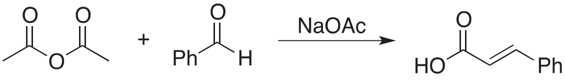


Figure 4.11.35. Reaction scheme for Perkin reaction.

The mechanism of this reaction is very special, as anhydrides contain an acyl group that can be easily transferred or eliminated as a leaving group. After the enolate attack, the acyl group is first transferred and then eliminated, as shown in Figure 4.11.36.

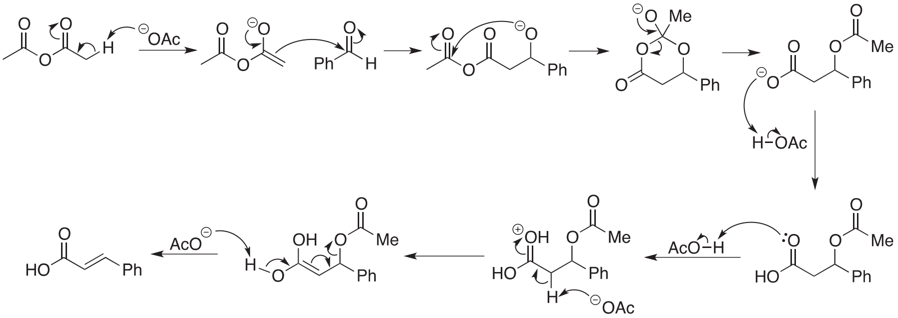


Figure 4.11.36. Full reaction mechanism for Perkin reaction.

The final reaction we will look at in this chapter is the **Claisen condensation**. Claisen condensation is the reaction of an enolate with an ester, which is at a higher oxidation state than all the ketone and aldehyde electrophiles we have been previously looking at. Thus, instead of forming an alcohol at the β-carbon, a carbonyl group is added to the β-carbon instead. The general scheme for Claisen condensation is shown in Figure 4.11.37.

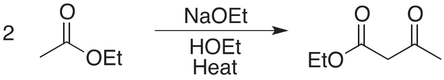


Figure 4.11.37. General scheme for Claisen condensation.

The mechanism for Claisen condensation is similar to aldol condensation, just that the ester has a good leaving group that is eliminated after the enolate attack. The mechanism for Claisen condensation is shown in Figure 4.11.38.

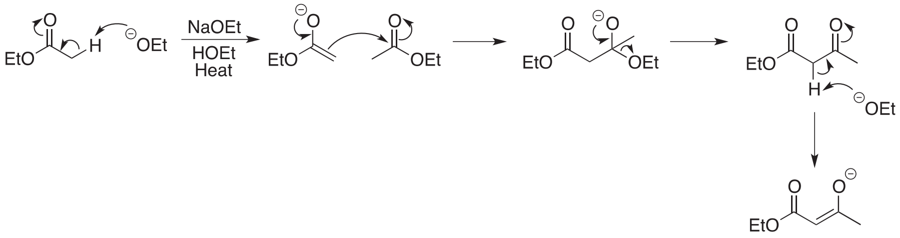


Figure 4.11.38. Mechanism for Claisen condensation.

One key step to take note is the final deprotonation, which is relatively easy for the 1,3-dicarbonyl product. Every step in Claisen condensation is reversible (and favours the reactants) other than the final deprotonation, thus this final deprotonation step provides the necessary driving force for the entire reaction to reach completion.

Similar to aldol reactions, Claisen condensations also face many selectivity issues. Cross Claisen condensations may be carried out between 2 esters or carried out between an ester and a ketone. When Claisen condensation is carried out between 2 esters, we may first prepare the lithium enolate of one ester to react with the other ester, as shown in Figure 4.11.39.

Similar to aldol reactions, we would like to choose an electrophile that is non-enolisable. Some common non-enolisable esters are shown in Figure 4.11.40.

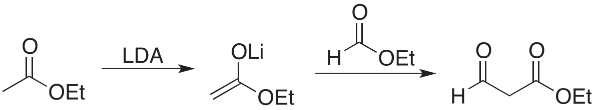


Figure 4.11.39. Cross Claisen condensation using lithium enolate.

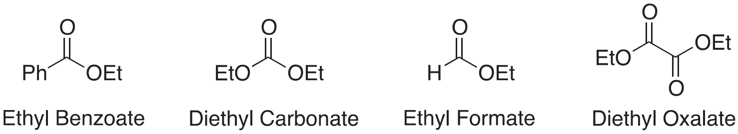


Figure 4.11.40. Common non-enolisable esters.

Of the non-enolisable esters, diethyl oxalate and diethyl carbonate are the most noteworthy. Diethyl carbonate is a stable compound with 2 leaving groups on the same carbonyl group, allowing it to undergo nucleophilic substitution twice. Diethyl oxalate is highly electrophilic due to the adjacent carbonyl groups which increase the electrophilicity of each other.

It is possible to acylate ketones by performing Claisen condensation between a ketone (as the nucleophile) and an ester (as the electrophile). In this case, we could employ the 3 enol equivalents discussed previously. With esters as nucleophiles, it is also possible to use zinc enolates, made from the Reformatsky reaction. With weaker nucleophiles, it is possible to use a better electrophile such as acyl chloride.

4.12 Oxidation and Reduction

We have discussed redox reactions in chapter 2.5, and here we will look at organic redox reactions. In organic chemistry, oxidation is usually the addition of oxygen or formation of additional bonds to oxygen, while reduction is usually the addition of hydrogen. In this chapter, we will look at the myriad of reagents dedicated to oxidation and reduction, and explore the different selectivities they offer.

4.12.1 *Oxidation*

Over the past few chapters, we have explored in detail carbonyl chemistry, from nucleophilic substitution to enolate reactions. Carbonyl compounds have a large variety of reactions at their different oxidation states, from alcohol to carboxylic acid. It is important to have selective oxidants to increase the oxidation state of the functional group.

Strong oxidants oxidise primary alcohols all the way to carboxylic acids, secondary alcohols to ketones, while tertiary alcohols cannot be oxidised. The most commonly used strong oxidant is **Jones reagent**, a mixture of chromium trioxide and sulfuric acid. A similar oxidant would be hot acidified potassium permanganate. The reaction scheme for Jones oxidation is shown in Figure 4.12.1.

The reaction mechanism involves the oxidation of alcohol first to aldehyde, followed by the hydration of aldehyde to a geminal diol, in which one alcohol is oxidised through the same process. The full mechanism is shown in Figure 4.12.2.

Strong oxidants are commonly used on less sensitive substrates as the reaction conditions are harsh and side oxidations may occur. To achieve higher selectivity, weaker oxidising agents were developed extensively, and we will discuss some of them here.

Firstly, we will look at the **Oppenauer oxidation**. The Oppenauer oxidation is a gentle method to oxidise secondary alcohols to ketones without affecting other functional groups such as amines and sulfides. It is able to oxidise primary alcohols, but it is not recommended as there will be side reactions such as aldol reaction of the aldehydes. The scheme for Oppenauer oxidation is shown in Figure 4.12.3.

Oppenauer oxidation is fully reversible and the direction of the reaction depends on the amount of reactants and products. The reverse reduction reaction is known as Meerwein-Ponndorf-Verley (MPV) reduction. This is a redox reaction between the alcohol and ketone with a Lewis acid catalyst $Al(Oi\text{-}Pr)_3$. As the oxidant used is acetone, there is no risk of overoxidation. The reaction goes through a 6-membered ring transition state, as shown in the mechanism in Figure 4.12.4.

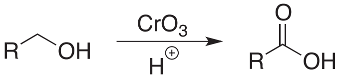


Figure 4.12.1. Reaction scheme for Jones oxidation.

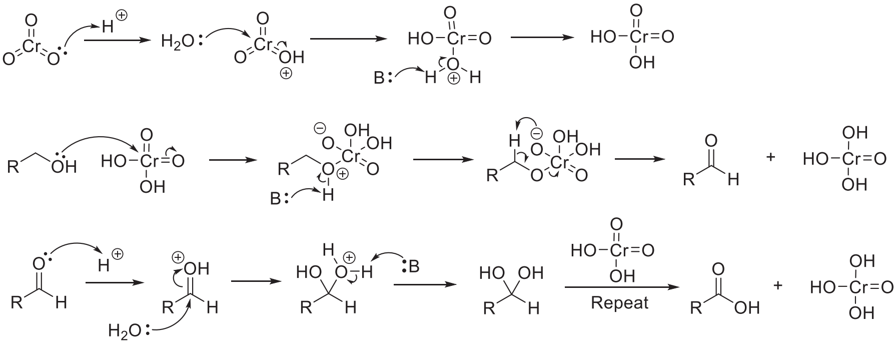


Figure 4.12.2. Full reaction mechanism for Jones oxidation.

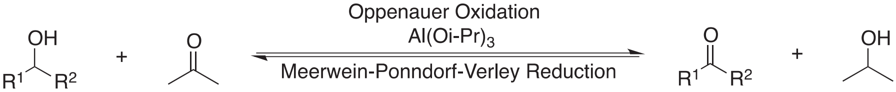


Figure 4.12.3. Reaction scheme for Oppenauer oxidation and MPV reduction.

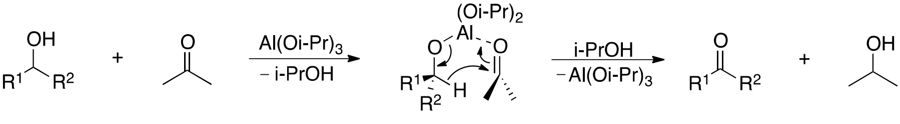


Figure 4.12.4. 6-membered ring mechanism of Oppenauer oxidation.

Next, we will discuss **N-oxoammonium mediated oxidation**. Unlike the Oppenauer oxidation, N-oxoammonium ion favours the oxidation of the primary alcohol to aldehyde. The aldehyde may be further oxidised to carboxylic acid by adding sodium hypochlorite. It is important to appreciate the selectivity of this reaction as the primary alcohol may be oxidised all the way to carboxylic acid without touching the secondary alcohol. The general scheme for the reaction is shown in Figure 4.12.5.

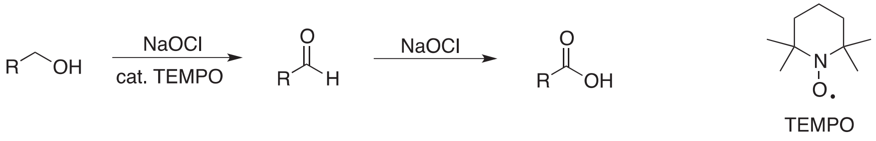


Figure 4.12.5. Reaction scheme of N-oxoammonium mediated oxidation.

We have previously met TEMPO in chapter 4.5, as a stable radical species. Its stability comes from the steric shielding provided by the 4 methyl groups. Thus, it is difficult for it to be attacked by more hindered secondary alcohols, making it highly selective for primary alcohols. This can be seen from the mechanism as shown in Figure 4.12.6.

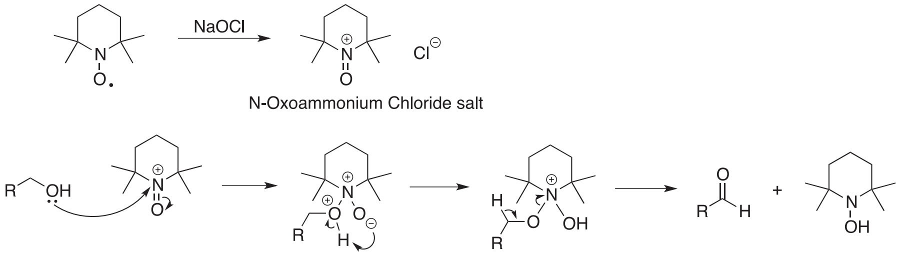


Figure 4.12.6. Mechanism for N-oxoammonium mediated oxidation.

Another common group of mild oxidants stem from chromates. **Pyridinium Chlorochromate (PCC)**, **Pyridinium Dichromate (PDC)**, also known as **Cornforth reagent**, and **Collins reagent** are all weak oxidising agents used to oxidise alcohols to the aldehyde and ketone oxidation level. The structures of the oxidants are shown in Figure 4.12.7.

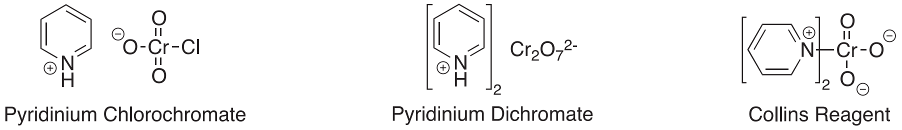

Pyridinium Chlorochromate
Pyridinium Dichromate
Collins Reagent

Figure 4.12.7. Structures of weak chromate based oxidants.

While PCC and PDC are easily available, Collins reagent is usually prepared in-situ from a mixture of chromium trioxide and pyridine in dichloromethane. Due to the higher stability and ease of use, PCC is the most commonly used in this group.

Other mild oxidising agents include **Dess-Martin Periodinane (DMP)** and **Tetrapropylammonium Perruthenate (TPAP)**, which have structures as shown in Figure 4.12.8. These oxidising agents are also able to oxidise alcohols to the aldehyde oxidation level. TPAP is a ruthenium complex which is very expensive, thus

Figure 4.12.8. Structures of other mild oxidants.

it is common to use TPAP catalytically while using N-methylmorpholine-N-oxide (NMO) as the stoichiometric oxidant.

A milder and more interesting oxidation reaction is the **Swern oxidation**, which utilises dimethyl sulfoxide (DMSO) as the oxidising agent. It is widely applied as it is able to tolerate many functional groups. The general reaction scheme is shown in Figure 4.12.9 below.

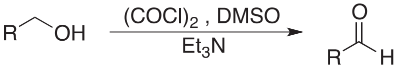


Figure 4.12.9. General scheme of Swern oxidation.

The mechanism involves the reaction of DMSO with $(\mathrm{COCl})_2$ to form the reactive intermediate $\mathrm{SMe_2Cl^+}$ which further reacts with the alcohol to form the aldehyde. The oxidation is favoured due to the large amount of gaseous products produced. The mechanism is shown in Figure 4.12.10.

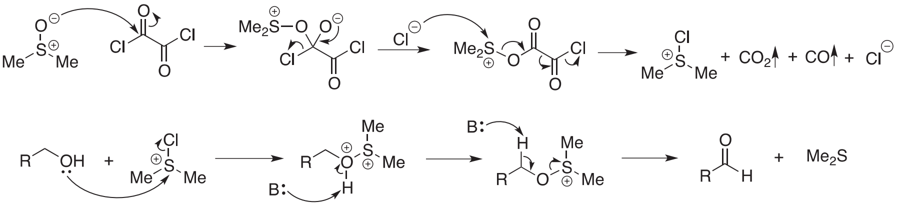


Figure 4.12.10. Full mechanism for Swern oxidation.

Next, we will look at oxidising agents that oxidises aldehydes to carboxylic acid. For such reactions, strong oxidants such as Jones reagent would definitely work. However, there are some other noteworthy reagents that may be used for this purpose.

The **Tollens' reagent** is a famous organic qualitative analysis test used to detect aldehydes and α-hydroxyketones, with the positive result forming a silver mirror on the wall of the glassware. Tollens' reagent is the silver(I) diammine complex which can be prepared by adding aqueous sodium hydroxide to silver nitrate solution, followed by dissolving the silver(I) oxide precipitate with aqueous ammonia. It oxidises aldehydes to carboxylic acid while the silver(I) is reduced to metallic silver on the surface of the glassware. The general reaction scheme is shown in Figure 4.12.11.

If we would like an aldehyde to be directly oxidised to an ester, we may use **MnO_2-mediated oxidation**. This method employs cyanide as a nucleophilic catalyst, which is first added to the aldehyde and then substituted by an alcohol after the oxidation. The general reaction scheme is shown in Figure 4.12.12.

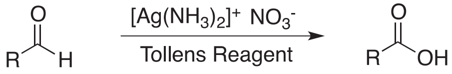


Figure 4.12.11. General reaction scheme for oxidation by Tollens' reagent.

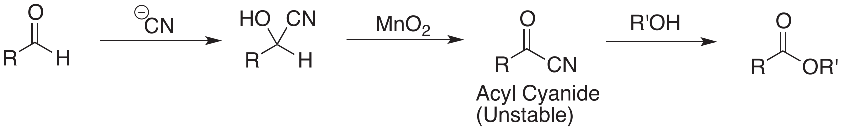


Figure 4.12.12. Reaction scheme for MnO_2-mediated oxidation from aldehyde to ester.

While a ketone is unable to be directly oxidised, it may be oxidised to an ester through a rearrangement reaction known as **Baeyer-Villiger oxidation**. This is a rearrangement oxidation reaction driven by peroxy compounds, most commonly meta-chloroperoxybenzoic acid (m-CPBA). The general reaction scheme is shown in Figure 4.12.13.

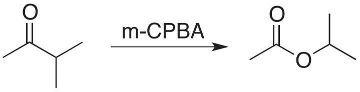


Figure 4.12.13. Reaction scheme for Baeyer-Villiger oxidation.

The Baeyer-Villiger oxidation involves a migratory rearrangement that breaks the weak peroxide $O–O$ bond. The full mechanism is shown in Figure 4.12.14.

Baeyer-Villiger oxidation is commonly used to increase the ring size of cyclic ketones by 1. Upon the addition of peroxyacid, both groups attached to the $C=O$ carbon may migrate and result in different ester products. As a rule of thumb, the migrating group is the group that is able to stabilise a carbocation better. In this case, the migrating isopropyl group forms a more stable carbocation than the methyl group, leading to only 1 ester product.

Other oxidising agents target the carbons adjacent to a carbonyl group. We will look at 4 such reactions useful to introduce different functionalities near to carbonyl groups, as shown in Figure 4.12.15.

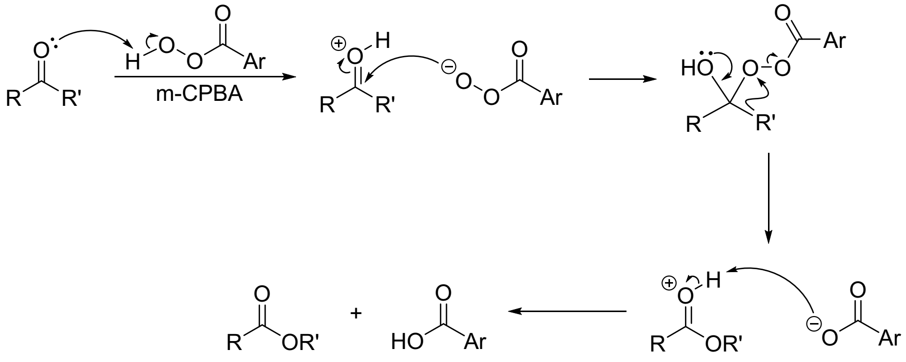


Figure 4.12.14. Mechanism for Baeyer-Villiger oxidation.

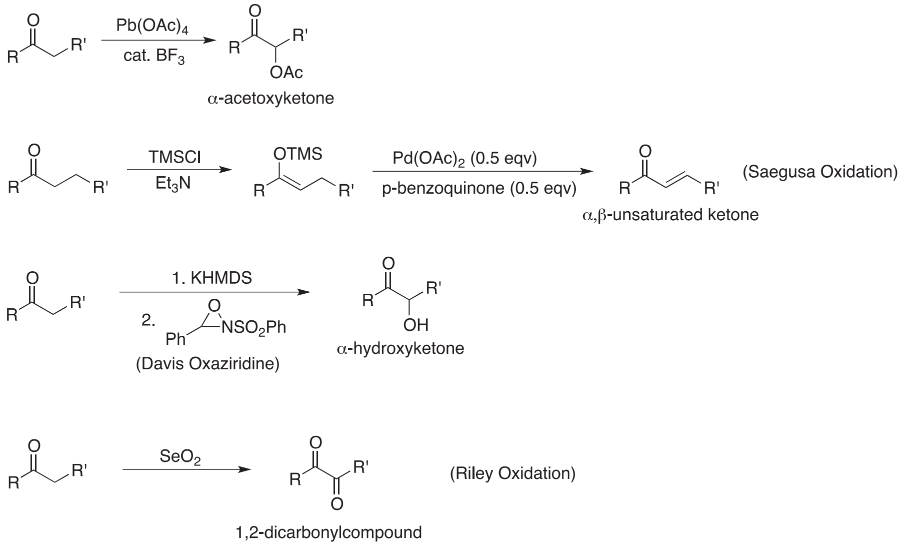


Figure 4.12.15. Reactions to add functionalities adjacent to carbonyl groups.

4.12.2 *Reduction*

Reduction may be performed with an even larger variety of methods which are selective for different functionalities. Reduction may be classified into 4 large groups: catalytic hydrogenation, hydride-donor reagents, radical hydrogen donors and dissolving metal reductants. We will now look at these 4 groups of reductants in greater detail.

Catalytic hydrogenation is the addition of hydrogen gas to a functional group with a heterogeneous metal catalyst. It is generally used to reduce C–C multiple bonds in alkenes and alkynes. The general scheme is shown in Figure 4.12.16.

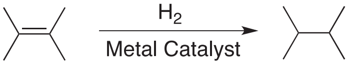


Figure 4.12.16. General scheme for catalytic hydrogenation.

The 4 most common metal catalysts for hydrogenation are as follows:

1. Palladium on carbon (Pd/C):

This catalyst is a mixture of around 5–10% palladium with 90–95% carbon. The palladium is used in the form of a fine powder on charcoal support to maximise the active surface area while saving the amount of palladium. Pd/C is insoluble and can be easily removed by filtration and reused.

2. Adam’s catalyst (PtO_2):

Platinum metal itself is an active catalyst but notoriously difficult to use and prepare. Adam’s catalyst, PtO_2, is not an active hydrogenation catalyst by itself. However, in hydrogen gas environment, it can be reduced to platinum metal in-situ to participate in catalytic hydrogenation.

3. Raney nickel ($RaNi$):

Raney nickel is prepared from a nickel-aluminium alloy. While it appears to a finely divided grey powder, each particle of the powder is a three-dimensional mesh. During the preparation process, hydrogen gas is absorbed within the pores of the catalyst, thus freshly prepared Raney nickel may be used for hydrogenation without adding hydrogen gas.

4. Lindlar catalyst ($Pd/BaSO_4$ or $Pd/CaCO_3$ poisoned with $Pb(OAc)_2$ and quinoline):

Compared to carbon, barium sulfate and calcium carbonate allow product to escape from the catalyst faster, preventing over-reduction of sensitive substrates. The addition of lead and quinoline further reduces the activity of the catalyst, allowing the catalyst to selectively reduce alkynes to cis-alkenes.

In Figure 4.12.17, we show a list of common catalytic hydrogenation reactions, ranging from substrates that are easiest to hydrogenate to substrates that are hardest to hydrogenate.

The mechanism for catalytic hydrogenation involves surface chemistry, which we will not discuss extensively in this book. A general overview of the mechanism involves the hydrogen first being adsorbed onto the metal surface, forming $M–H$ bonds. After that, the functional group to be reduced is also adsorbed onto the metal surface. In the example of alkenes, they may be adsorbed onto the metal surface through formation of π-complexes, σ-bonds or π-allyl complexes. This may be followed by the insertion of hydrogen to complete the reduction. Catalytic hydrogenation may also be performed with homogenous metal catalysts. Detailed discussion about organometallic complexes will be covered in chapter 4.15.

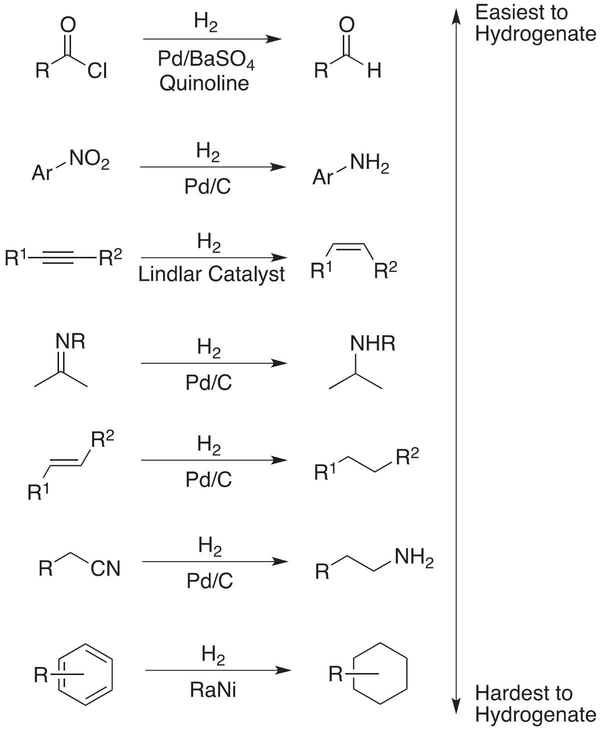


Figure 4.12.17. List of common catalytic hydrogenation reactions.

From the mechanism, we observe that the functional group is attached to the metal surface on one side for reaction. Thus, all catalytic hydrogenation reactions have **syn-products**, where both hydrogens are added to the same side of the substrate.

Other than reduction of multiple bonds, catalytic hydrogenation may also be used for **hydrogenolysis**, the cleavage of single bonds through addition of hydrogen. This is most commonly used for the removal of functional groups at allylic and benzylic positions. It is easier to cleave allylic and benzylic bonds as the intermediate may be stabilised by conjugation. An example is given in Figure 4.12.18.

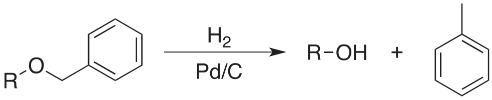


Figure 4.12.18. Example of hydrogenolysis at benzylic position.

Hydrogen-transfer may be carried out by non-metal organic compounds as well. **Diimide** (H–N=N–H) is a highly unstable hydrogen-transfer reagent that is generated in-situ by mixing $NH_2OSO_3^-$ and NH_2OH. It is highly selective for alkenes

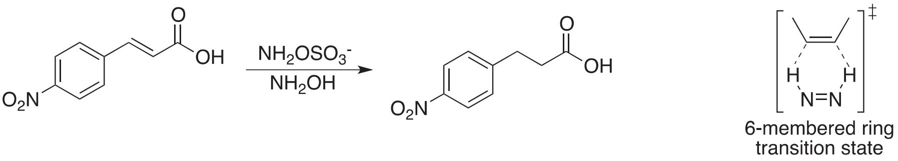


Figure 4.12.19. Sample reaction and transition state for diimide reduction.

and does not hydrogenate other functional groups such as nitro and cyano. As the reaction proceeds through a concerted 6-membered ring transition state, hydrogens are added syn to each other, similar to metal-catalysed hydrogenation. A sample reaction and the transition state is shown in Figure 4.12.19.

The second large group of reductants are the **hydride-donor reagents**. These reagents most commonly contain a group 13 element, but there are group 14 hydride-donor reagents as well, although less commonly used. Unlike catalytic hydrogenation which is selective for $C{-}C$ multiple bonds, hydride-donor reagents selectively reduce carbonyl groups. The mechanism for such reductions involves the activation of carbonyl group by metal cation coordination with carbonyl oxygen followed by nucleophilic attack of hydride. The general mechanism is demonstrated with $LiAlH_4$ and shown in Figure 4.12.20.

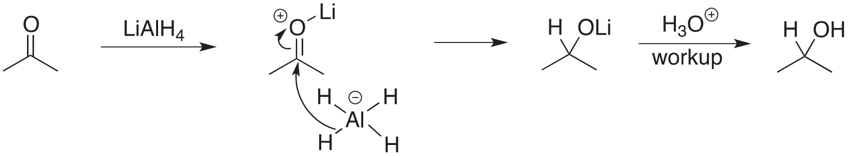


Figure 4.12.20. General mechanism for reduction with hydride-donor reagents.

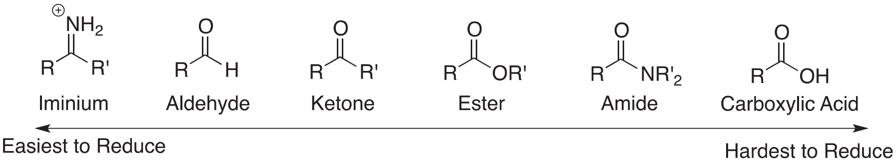


Figure 4.12.21. Reactivity level of carbonyl compounds.

Similar to oxidising agents, reducing agents for carbonyl groups also vary in strength. Depending on the species to be reduced, different reducing agents should be selected. Figure 4.12.21 shows carbonyl compounds from the easiest to reduce to most difficult to reduce.

The 2 most common hydride-donor reagents are $LiAlH_4$ and $NaBH_4$. $LiAlH_4$ is a strong reducing agent that must be used in dry ether while $NaBH_4$ is a mild reducing agent used in alcoholic solvent. $LiAlH_4$ reduces the full range of carbonyl compounds to alcohols and amides to amines, while $\mathrm{NaBH_4}$ only reduces iminium ions, aldehydes and ketones.

The reactivity of hydride-donor reagents depends on various factors. The greater the Lewis acidity and hardness of the cation, the better the cation chelates to the carbonyl oxygen and activates the carbonyl group for nucleophilic attack. The ligands on the anion will affect the nucleophilicity of the hydride.

Thus, we are able to control the reactivity by tuning the cation and anion we choose. For example, $\mathrm{LiBH_4}$ would be a stronger reducing agent than $\mathrm{NaBH_4}$ as Li chelates better to oxygen. In fact, $\mathrm{LiBH_4}$ is able to reduce esters as well as iminium ions, aldehydes and ketones. In reductive amination, we require a weaker reducing agent to reduce only the iminium ion intermediate without affecting the carbonyl group. Therefore, we substituted a hydride in $\mathrm{NaBH_4}$ for the electron-withdrawing cyano ligand, creating the milder $\mathrm{Na(CN)BH_3}$ reducing agent.

There are multiple selectivity issues we need to consider when performing reduction at a carbonyl functionality. Firstly, we need to choose the best reducing agent to selectively reduce the carbonyl functionality as required. Secondly, we need to consider if we require full reduction or partial reduction.

As we have previously mentioned, $\mathrm{Na(CN)BH_3}$, $\mathrm{NaBH_4}$, $\mathrm{LiBH_4}$ and $\mathrm{LiAlH_4}$ are reducing agents of increasing reducing power, allowing us to selectively reduce more electrophilic carbonyl groups in the presence of less electrophilic ones. A problem arises when we want to selectively reduce the less electrophilic carbonyl group in the presence of a more electrophilic one. To achieve this selectivity, we have to make use of **borane** $(\mathrm{BH_3})$ as a reducing agent.

Unlike the reducing agents we have been discussing previously, borane is a very poor reducing agent on its own. It has neither a chelating cation nor a negatively-charged boron. Applying the arguments from above, it is unable to increase the electrophilicity of the carbonyl group. Also, its hydrides are low in nucleophilicity. However, we must not forget that borane is a good Lewis acid (just like $\mathrm{BF_3}$) that is able to chelate to an electron-rich carbonyl group. Through chelation, the carbonyl group is activated and the boron becomes negatively charged, allowing the nucleophilic attack of hydride at the carbonyl carbon. This is the general idea for reduction by borane and the main requirement is an electron-rich carbonyl group that borane can chelate to. Thus, borane is only able to reduce carboxylic acids and amides, the most electron-rich carbonyl groups.

The actual mechanism for reduction is more complicated due to the labile proton of carboxylic acid. A triacylborate intermediate is formed that is even more electrophilic than esters as the lone pair on oxygen delocalises partially into the empty p-orbital of boron. The detailed reaction mechanism is given in Figure 4.12.22.

To summarise the various reducing agents discussed, Table 4.17 shows the reducing agents and which carbonyl functional groups they can be used to reduce.

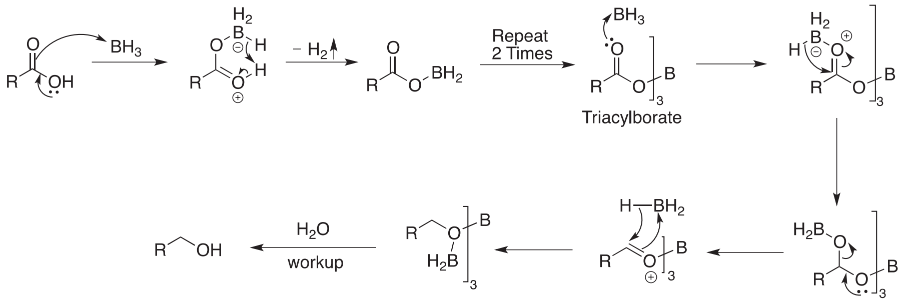
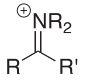
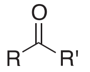
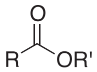
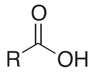


Figure 4.12.22. Detailed mechanism for reduction of carboxylic acid by borane.

Table 4.17. Reducing agents and carbonyl functional groups they reduce (Y = Yes, N = No).

	 Iminium Ion	 Aldehyde/Ketone	 Ester	 Carboxylic Acid
$Na(CN)BH_3$	Y	N	N	N
$NaBH_4$	Y	Y	N	N
$LiBH_4$	Y	Y	Y	N
$LiAlH_4$	Y	Y	Y	Y
BH_3	N	N	N	Y

Back in part 4.6.2, we have discussed conjugated nucleophilic attack. In the case of hydride-donor reagents, they are also able to perform conjugated nucleophilic attack on α,β-unsaturated carbonyl compounds. This leads to a selectivity problem, depending on whether we are targeting to reduce the alkene or the carbonyl. If we use a standard reducing agent, such as $NaBH_4$, we will likely end up with a mixture of products, some with the alkene reduced, some with the carbonyl reduced and some with both alkene and carbonyl reduced. Thus, we have developed methods to selectively reduce either the alkene or the carbonyl.

To reduce only the alkene, we may utilise **selectride reducing agents**. Selectrides have bulky sec-butyl groups attached to the boron, thus the hydride is only able to reduce the less-hindered alkene. A sample reaction is shown in Figure 4.12.23.

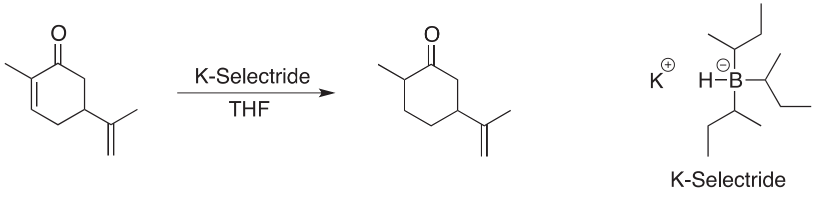


Figure 4.12.23. Sample reaction and structure of K-selectride.

To reduce only the carbonyl group, we may use **Luche reduction**. Luche reduction is carried out with $NaBH_4$ and a hard, Lewis acidic metal salt $CeCl_3$. $CeCl_3$ is able to chelate to the carbonyl oxygen and strongly activate the carbonyl group for reduction. A sample reaction is shown in Figure 4.12.24.

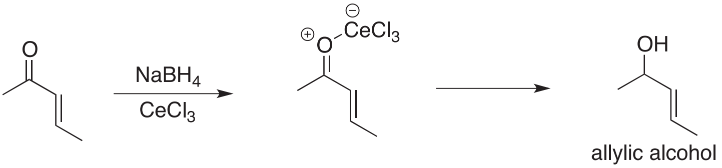


Figure 4.12.24. Sample Luche reduction of an α,β-unsaturated carbonyl compound.

Another selectivity aspect that we have to take note of is preventing over-reduction. Just like how Lindlar catalyst allows catalytic hydrogenation of alkynes to stop at the alkene stage, **diisobutylaluminium hydride (DIBAL)** is able to reduce esters and nitriles to aldehydes. DIBAL is an alane and works in a similar fashion as borane, first chelating to the ester before hydride transfer. The tetrahedral intermediate is stable at –70°C and not further reduced. The aldehyde is obtained upon workup, during which any excess DIBAL is quenched by water. The general mechanism for DIBAL reduction is shown in Figure 4.12.25.

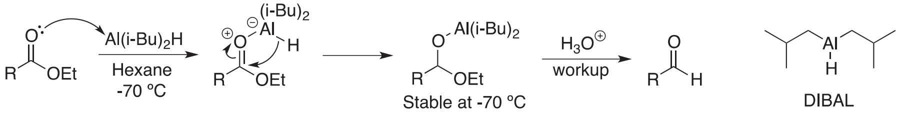


Figure 4.12.25. General mechanism for reduction with DIBAL.

More recently, **Group 14 hydride donors** have been gaining popularity as weaker alternatives to group 13 hydride donors. They usually have a silicon central atom as the silicon-hydrogen bond is capable of transferring a hydride to carbocations. They can be used in acidic conditions to reduce alcohols to alkanes, as shown in Figure 4.12.26.

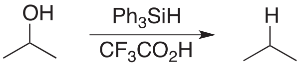


Figure 4.12.26. Reduction of alcohol to alkane by silane.

In the presence of a strong Lewis acid such as BF_3 or $TiCl_4$, aldehydes and ketones can be sufficiently activated for reduction by silanes. The alcohol intermediate will be further reduced to alkane. The full reaction is shown in Figure 4.12.27.

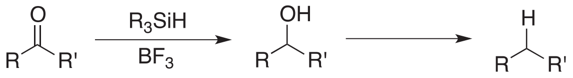


Figure 4.12.27. Reduction of aldehydes and ketones to alkanes by silane.

Reduction occurs through electron gain, thus, we are able to carry out **dissolving metal reductions**, as dissolving metal in liquid ammonia is able to generate a solution of electrons. We have previously seen an example in part 4.5.4, where we discussed the Birch reduction. When a ketone is attacked by free electrons, it will form a ketyl intermediate. Depending on reaction conditions, the ketyl intermediate may proceed to react in different ways, as shown in Figure 4.12.28.

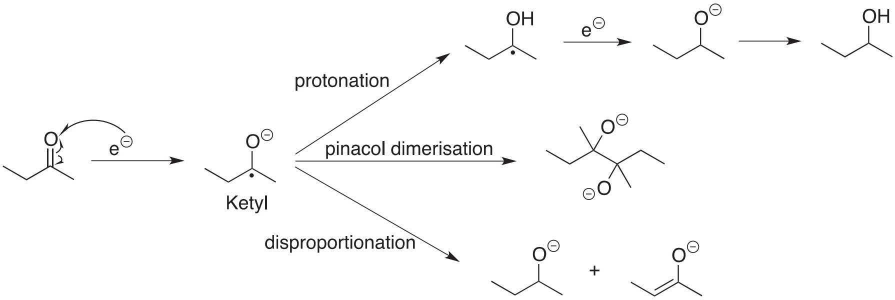


Figure 4.12.28. Dissolving metal reduction of ketones.

The most versatile one-electron reductant is **samarium(II) iodide** (SmI_2). It is able to reduce a large variety of functional groups through radical pathways. Its unique application is removing functional groups at the α-position of carbonyl compounds. A list of possible reduction reactions by SmI_2 is shown in Figure 4.12.29.

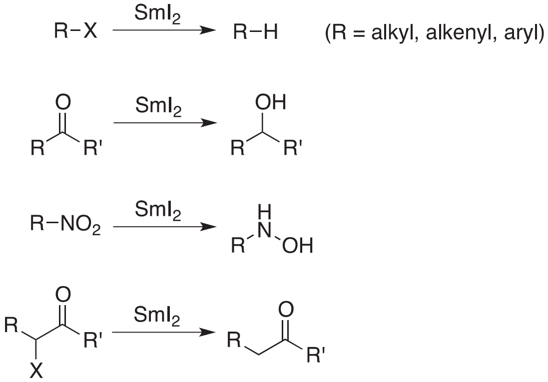


Figure 4.12.29. List of reduction reactions by SmI_2.

The final category of reduction reactions that we will discuss is the **reductive deoxygenation of carbonyl group**. In classic organic synthesis, the carbonyl group is a versatile functionality that is able to act as both nucleophile and electrophile. Thus, they are often introduced to form bonds and have to be removed at the end of the synthesis. We have already discussed one such method for reductive deoxygenation: using silane with a strong Lewis acid. Now we will look at three other methods for carbonyl deoxygenation.

1. Clemmensen reduction

Clemmensen reduction uses zinc amalgam and hydrochloric acid to reduce aldehydes and ketones to alkanes. It is particularly effective at reducing aryl-alkyl ketones, the products of Friedal-Crafts acylation. Clemmensen reduction is carried out under strongly acidic conditions, thus it cannot be used on acid-sensitive substrates. The reaction scheme for Clemmensen reaction is shown in Figure 4.12.30.

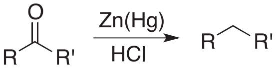


Figure 4.12.30. General scheme for Clemmensen reduction.

2. Wolff-Kishner reduction

While Clemmensen reduction is carried out under strongly acidic conditions, Wolff-Kishner reduction is carried out in base. Wolff-Kishner reduction employs hydrazine as the reducing agent, generating nitrogen gas as a driving force for the reaction. The reaction has been previously discussed in chapter 4.6, and the mechanism can be found in Figure 4.6.19.

3. Mozingo reduction

When the substrate is sensitive to both acid and base, we may employ the milder Mozingo reduction. Mozingo reduction involves the formation of thioketal followed by desulfuration using catalytic hydrogenolysis. The reaction scheme for Mozingo reduction is shown in Figure 4.12.31.

Figure 4.12.31. Reaction scheme for Mozingo reduction.

4.13 Protecting Groups in Organic Chemistry

Protecting groups is a useful strategy in organic synthesis to achieve desired chemoselectivity. Protecting groups are usually able to defend against certain reaction conditions where the functional group would have been otherwise affected. Protecting groups must be easily added and removed without causing significant loss of yield. In this chapter, we will discuss some common protecting groups. For each protecting group, it is important to note the conditions for protection and deprotection and what the protecting group protects against.

4.13.1 *Protecting groups for aldehydes and ketones*

As we have learnt, aldehydes and ketones have a large variety of reactivities as both electrophiles and nucleophiles. To protect aldehydes and ketones, we usually react the carbonyl group with diols or dithiols to form a cyclic acetal or dithiane. The most common protecting group is **ethane-1,2-diol (ethylene glycol)**, which is able to form a stable cyclic acetal that is inert in base. The reaction scheme for protection and deprotection is shown in Figure 4.13.1.

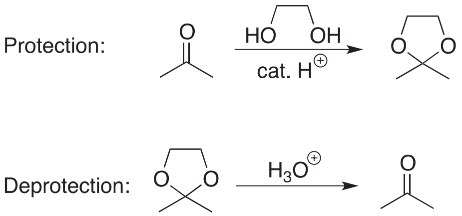


Figure 4.13.1. Protection and deprotection using ethylene glycol.

Ethylene glycol acetal is stable in base but labile in acid. An alternative that is tolerant to both acid and base is 1,3-dithiolane. The reaction scheme for protection and deprotection is shown in Figure 4.13.2.

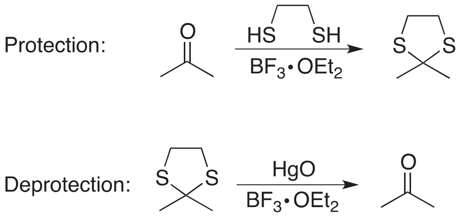


Figure 4.13.2. Protection and deprotection with 1,3-dithiolane.

For **1,3-dithiolane**, protection and deprotection is more challenging, requiring the use of strong Lewis acid. It is also important to note that when used to protect aldehydes, the aldehyde hydrogen becomes acidic and may be deprotonated with strong base. This provides us with interesting synthetic routes which we will discuss in chapter 4.16.

4.13.2 *Protecting groups for alcohols*

Alcohols are good nucleophiles that must be protected against electrophiles and oxidising agents in the case where the alcohol is not to be reacted. There is a large list of protecting groups that can be used for alcohol, but we will only discuss the 5 most common protecting groups in this chapter.

First, we will look at **silyl protecting groups**. We have previously encountered trimethylsilyl in silyl enol ethers, and indeed, this is the most fundamental silyl protecting group for alcohols. Of course, there are many other silyl protecting groups that can better protect the alcohol. These protecting groups are generally bulkier and prevent reactive species from getting near the alcohol. Figure 4.13.3 shows a series of silyl protecting groups from least to most inert.

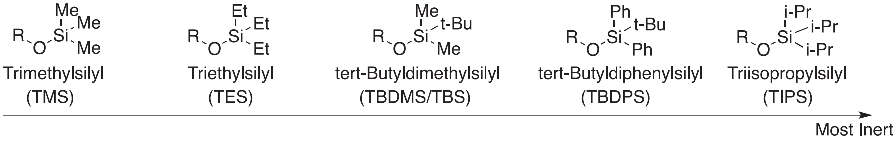


Figure 4.13.3. Common silyl protecting groups from least to most inert.

To protect an alcohol with a silyl protecting group, just react the alcohol with a chloride of the silyl protecting group. For deprotection, tetrabutylammonium fluoride (TBAF) is the most common reagent used, as it provides a fluoride anion to attack the silicon, removing the protecting group. Fluorine has a high affinity for silicon, allowing it to displace the alkoxide as a leaving group. The reaction scheme for protection and deprotection is shown in Figure 4.13.4.

The second protecting group is **benzyl ether**, an extremely inert protecting group that protects the alcohol against both acidic and basic conditions. The reaction scheme for protection and deprotection is shown in Figure 4.13.5.

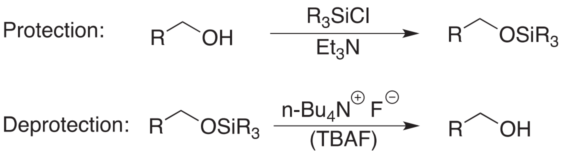


Figure 4.13.4. Protection and deprotection of silyl protecting groups.

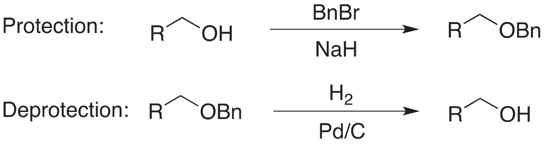


Figure 4.13.5. Protection and deprotection with benzyl ether.

As benzyl ether is stable in both acidic and basic conditions, the best way to remove it is through hydrogenolysis. It is thus not suitable in substrates with functional groups sensitive to catalytic hydrogenation, such as alkenes and alkynes.

While the first 2 protecting groups form inert ethers, the next 2 protecting groups that we will discuss form stable acetals. Just like the ethylene glycol acetal used to protect aldehydes and ketones, acetals are excellent protecting groups against base but labile in acid. The 2 common acetal protecting groups that we will look at here are the **tetrahydropyranyl (THP) acetal** and the **methoxymethyl (MOM) acetal**. The conditions for protection and deprotection of both acetal protecting groups are shown in Figure 4.13.6.

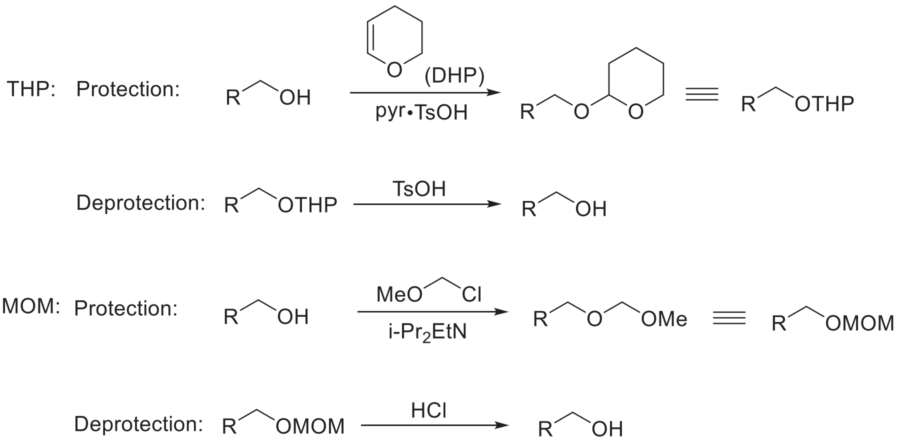


Figure 4.13.6. Protection and deprotection of acetal protecting groups for alcohol.

The last alcohol protecting group that we will discuss is the **2,2,2-trichloroethyl carbonate (Troc)** protecting group, a carbonate protecting group. The Troc protecting group is generally stable in both acid and mild base, and deprotection is usually done with zinc dust in acetic acid. The methods for protection and deprotection are shown in Figure 4.13.7.

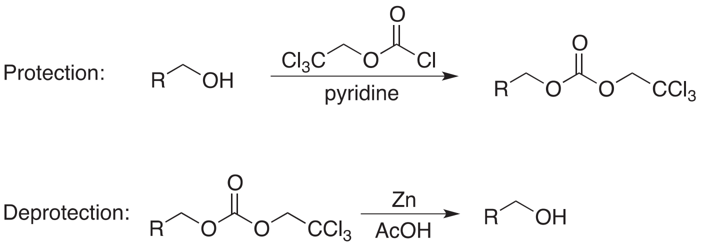


Figure 4.13.7. Protection and deprotection of Troc protecting group.

4.13.3 *Protecting groups for amines*

Since alcohols and amines are of similar chemical reactivity, many protecting groups can be used to protect both alcohols and amines. For example, the benzyl and Troc protecting groups that we discussed previously may also be used to protect amines. The classification provided here in this book is not absolute, however, we try to classify the protecting groups based on the functional group that they are most commonly used to protect.

The first protecting group we will look at for amines is the **tert-butoxycarbamate (Boc)** protecting group. Boc protecting group may be used to protect amines against base, and it is labile in acid. Deprotection of Boc is easy as the reaction is driven by the release of carbon dioxide gas. The conditions for protection and deprotection are shown in Figure 4.13.8.

Another common carbamate protecting group is the **carboxybenzyl (Cbz)** protecting group. The Cbz protecting group is useful in protecting amines against electrophiles. It is labile under strong Lewis acids, but deprotection is usually carried out by hydrogenolysis, as the benzylic C–O bond can be easily cleaved. The methods for protection and deprotection are shown in Figure 4.13.9.

The last protecting group that we are going to discuss is the **fluorenylmethyloxycarbonyl (Fmoc)** protecting group. The Fmoc protecting group is stable in acids but base-labile. Its lability stems from the proton on the 5-membered ring that can be easily removed to create an aromatic system. The conditions for protection and deprotection are shown in Figure 4.13.10.

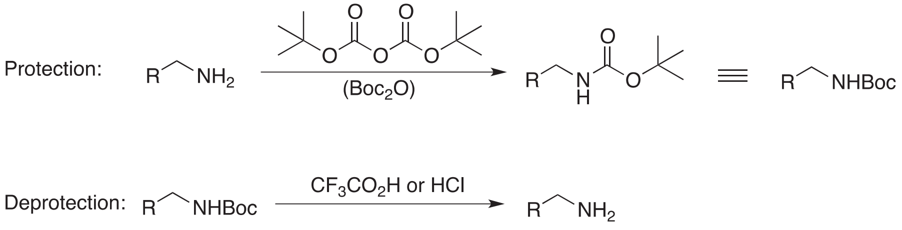


Figure 4.13.8. Protection and deprotection of Boc protecting group.

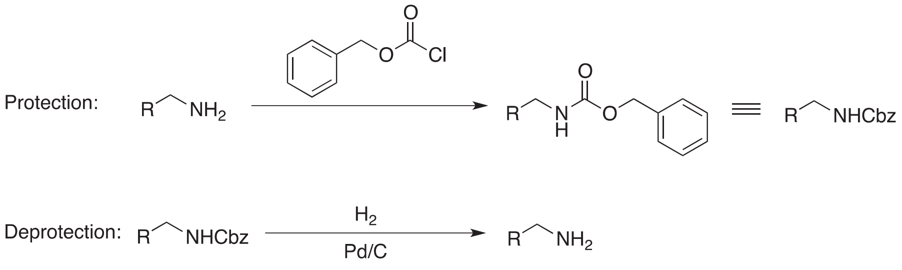


Figure 4.13.9. Protection and deprotection of Cbz protecting group.

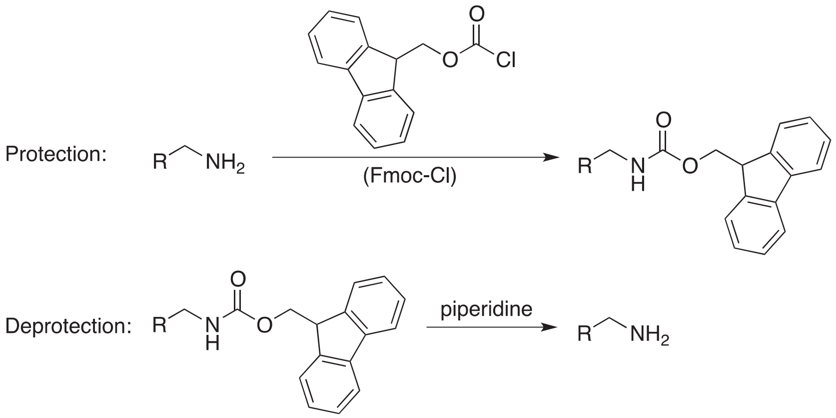


Figure 4.13.10. Protection and deprotection of Fmoc protecting group.

4.14 Pericyclic Reactions

In this chapter, we will explore a new type of organic reaction, the pericyclic reaction. Pericyclic reactions have been gaining popularity as they are extremely useful for the synthesis of cyclic products.

4.14.1 *The nature of pericyclic reactions*

Pericyclic reactions are different from ionic and radical reactions, which we may consider as linear reactions. The key feature of pericyclic reactions is a cyclic transition state where all bond-forming and bond-breaking take place in concert, and the orbitals involved overlap in a continuous cycle, without the formation of an intermediate. When showing the mechanism for a pericyclic reaction, the curly arrows indicating electron flow should form a circle. Since the electron flow follows a circle where the electron density is delocalised, it is acceptable to draw the curly arrows in either clockwise or anti-clockwise direction. Pericyclic reactions are also highly stereospecific, and the configuration of the product depends entirely on the configuration of the reactant. In general, pericyclic reactions are not affected by catalysts or by changes in solvent.

There are 3 types of pericyclic reactions, which we will discuss in detail in the next few parts of this chapter. The 3 types of pericyclic reactions are classified by the number and type of bonds broken and formed. The 3 types are:

1. Sigmatropic rearrangement

No change in total number of σ and π bonds.

2. Electrocyclic

The total number of σ-bonds is increased by 1 while the total number of π-bonds is decreased by 1.

3. Cycloaddition

The total number of σ-bonds is increased by 2 while the total number of π-bonds is decreased by 2.

Since pericyclic reactions are essentially elementary reactions that do not have intermediates, they are all reversible reactions that follow Le Chatelier's principle. Depending on the relative stability of the reactants and products, pericyclic reactions may proceed in either direction. Reactions that proceed in the opposite direction are known as retro-reactions, and cause an opposite change in number and type of bonds.

To understand the mechanism of pericyclic reactions, we must explore the frontier orbital theory, which was first proposed in 1950s by Fukui. In pericyclic reactions, the reactive orbitals are the π-orbitals of a conjugated system. To find the frontier orbitals, we must first look at the MO diagram of conjugated π-systems. As an example, we will look at a 6-electron conjugated π-system, with its MO diagram shown in Figure 4.14.1.

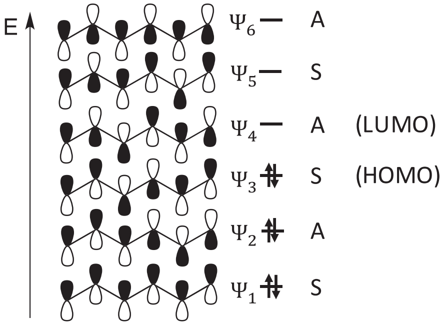


Figure 4.14.1. MO-diagram for a 6-electron conjugated π-system.

In the context of pericyclic reactions, it is important to consider the symmetry of the orbitals, especially the frontier orbitals. When considering the symmetry of the molecular orbital, we just look at the first and last p-orbital in the π-system. If the first and last p-orbital have the same orientation, the molecular orbital is said to be symmetric. If the first and last p-orbital have opposite orientations, the molecular orbital is said to be antisymmetric. In the MO diagram, the symmetric MOs are labelled as S and the antisymmetric MOs are labelled as A. There is a clear pattern that Ψ_1 is symmetric and the symmetry alternates as we move to the higher energy MOs. The HOMO of the π-system is the same as the number of electron pairs in the π-system, for example, the HOMO for the 6-electron π-system is Ψ_3, as there are 3 electron pairs. In all π-systems, Ψ_3 is symmetric, thus we can conclude that in a 6-electron π-system, the HOMO is symmetric. As a general rule, the HOMO for all π-systems with odd number of electron pairs (i.e. 2 electrons, 6 electrons, 10 electrons etc.) is symmetric while the HOMO for all π-systems with even number of electron pairs (i.e. 4 electrons, 8 electrons etc.) is antisymmetric.

All that has been explained above is true when the reaction is carried out under thermal conditions, where the π-system is in ground state. Under photochemical conditions, where light is shone to provide energy to the reaction mixture, 1 electron from the HOMO will be excited to the LUMO. The new MO diagram is shown in Figure 4.14.2.

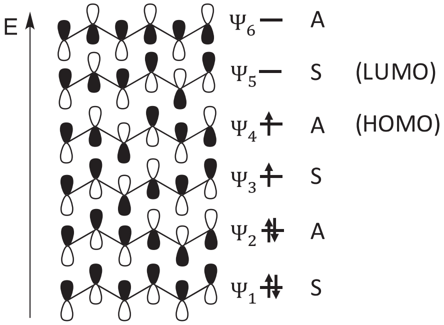


Figure 4.14.2. MO-diagram for 6-electron conjugated π-system excited by light.

As we can see from the MO diagram, the new HOMO is Ψ_4 and the new LUMO is Ψ_5. Most importantly, the symmetries of the HOMO and LUMO are reversed. Thus, as a general conclusion, under photochemical conditions, the HOMO for all π-systems with odd number of electron pairs is antisymmetric while the HOMO for all π-systems with even number of electron pairs is symmetric.

It is important to realise that the photochemical condition is complementary to the thermal condition. The frontier orbitals, reaction conditions and their symmetry will form the basis for the Woodward-Hoffmann rules that we will discuss in the next few parts.

4.14.2 *Sigmatropic rearrangement*

As we have stated previously, there is no change in total number of σ and π-bonds in a sigmatropic rearrangement. It is a reaction where an allylic σ-bond shifts. To better understand sigmatropic rearrangements, let us look at the most classic example of Cope rearrangement, as shown in Figure 4.14.3.

Cope rearrangement occurs on 1,5-dienes. It is an example of a [3,3]-sigmatropic rearrangement. We will first learn the nomenclature for sigmatropic rearrangements. In every sigmatropic rearrangement, there will be an existing

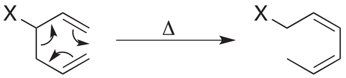


Figure 4.14.3. General reaction scheme and mechanism of Cope rearrangement.

σ-bond broken and a new σ-bond formed. The steps to number the sigmatropic rearrangement are as follows:

1. Identify the σ-bond that will be broken.
2. Starting from the σ-bond to be broken, number the atoms along the conjugated π-system starting from 1.
3. Identify the 2 atoms that will be connected by the new σ-bond. The sigmatropic rearrangement will be numbered by the numbers of these 2 atoms.

As an example, Figure 4.14.4 shows how to classify Cope rearrangement as a [3,3]-sigmatropic rearrangement.

Another key sigmatropic rearrangement that we will discuss is the Claisen rearrangement. The general scheme and mechanism is shown in Figure 4.14.5.

Claisen rearrangement occurs on allyl vinyl ethers or allyl phenyl ethers. While the sigmatropic rearrangement step is reversible, the tautomerisation to regenerate aromaticity is irreversible, acting as the driving force for the reaction. You should practice classifying the Claisen rearrangement and observe that it is another [3,3]-sigmatropic rearrangement. It is synthetically useful to introduce functionalities ortho to a hydroxyl group on a benzene ring. It is easy to prepare the starting material for Claisen rearrangement from phenol through an S_N2 reaction, as shown in Figure 4.14.6.

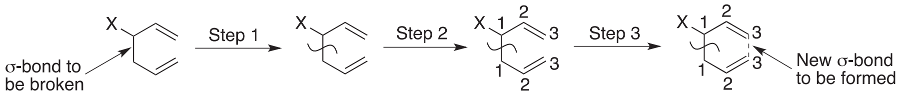


Figure 4.14.4. Example of classifying sigmatropic rearrangements.

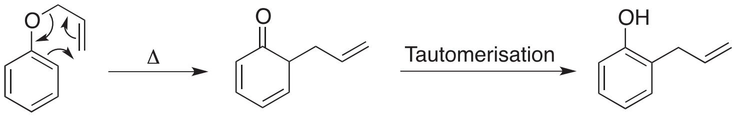


Figure 4.14.5. General scheme and mechanism for ortho-Claisen rearrangement.

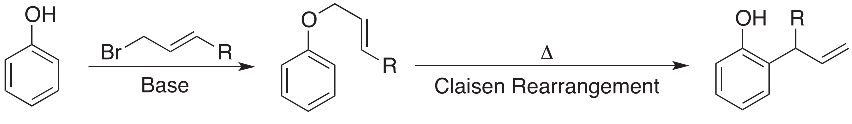


Figure 4.14.6. Synthetic application of Claisen rearrangement.

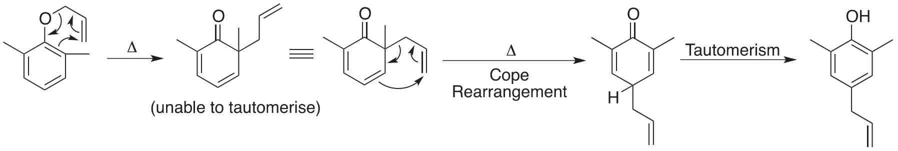


Figure 4.14.7. Reaction scheme and mechanism for para-Claisen rearrangement.

The current variation of Claisen rearrangement that we are discussing is also known as the ortho-Claisen rearrangement, and it is the most common variation of Claisen rearrangement. In some special cases when the ortho-positions are blocked, it is possible for para-Claisen rearrangement to occur. The reaction scheme and mechanism for para-Claisen rearrangement is shown in Figure 4.14.7.

Note that the para-Claisen rearrangement is just an ortho-Claisen rearrangement followed by a Cope rearrangement. It is important to identify the requirements for common rearrangements such as the 1,5-diene relationship for Cope rearrangement. This is because there are many cases where pericyclic reactions can occur consecutively, until a stable end-product is obtained.

The last variation of Claisen rearrangement is the Ireland-Claisen rearrangement, which occurs on the allyl ester of a carboxylic acid. The reaction scheme and mechanism for Ireland-Claisen rearrangement is shown in Figure 4.14.8.

The Ireland-Claisen rearrangement is useful to synthesise γ,δ-unsaturated carboxylic acids, which is challenging through conventional synthetic routes.

Finally, we will look at hydrogen and carbon shifts. Hydrogen shift is the most common type of sigmatropic rearrangement. We will look at a few examples of hydrogen shifts, as shown in Figure 4.14.9.

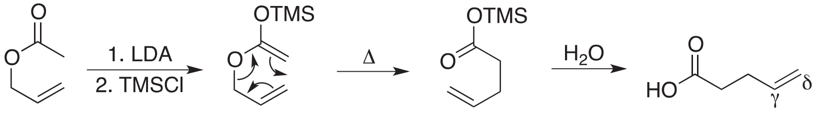


Figure 4.14.8. Reaction scheme and mechanism for Ireland-Claisen rearrangement.

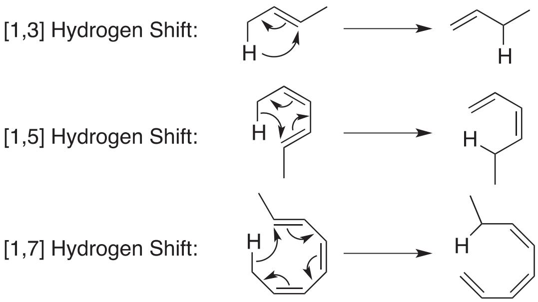


Figure 4.14.9. Examples of hydrogen shifts.

For hydrogen and carbon shift, we can classify the shift as suprafacial or antarafacial. Since the conjugated π-system is made up of sp^2-hybridised carbon atoms, it is a fully planar system. A suprafacial shift occurs when the migrating group moves across the same face of the π-system. An antarafacial shift occurs when the migrating group moves to the opposite face of the π-system. Figure 4.14.10 shows examples of suprafacial and antarafacial hydrogen shifts.

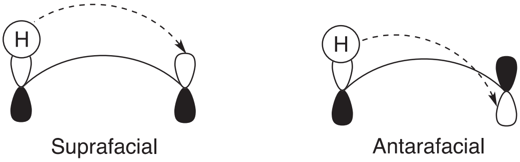


Figure 4.14.10. Examples of suprafacial and antarafacial hydrogen shifts.

Suprafacial shift is easy as there is no need to move to the opposite face of the π-system. Thus, there are no geometric limitations on suprafacial shift. On the other hand, antarafacial shift is challenging as the migrating group needs to cross to the opposite face of the π-system. Thus, antarafacial shift is only possible when the cyclic transition state has 7 or more atoms in the ring.

To determine if a shift is suprafacial or antarafacial, we must refer to the Woodward-Hoffmann table for sigmatropic rearrangements (Table 4.18).

Table 4.18. Woodward-Hoffmann rules for sigmatropic rearrangement.

No. of electron pairs in the reacting system	**Reaction conditions**	**Allowed mode of ring closure**
Even number	Thermal	Antarafacial
	Photochemical	Suprafacial
Odd number	Thermal	Suprafacial
	Photochemical	Antarafacial

Let us analyse the reactions we have learnt in this part according to the Woodward-Hoffmann rules. For the [3,3]-sigmatropic rearrangements, there are 3 electrons pairs in the reacting system. Under thermal condition, the shift is suprafacial, which is allowed. As the cyclic transition state only has 6 atoms, antarafacial shift is impossible. To understand the Woodward-Hoffmann rules, we must go back to frontier orbital theory. If we look at Cope rearrangement as an example, we may envision the reaction occurring as if the σ-bond is being homolytically cleaved, leaving 2 radical fragments. When we look at the symmetry of the HOMO of the 2 radical fragments, we see that they overlap in-phase. This is shown in Figure 4.14.11.

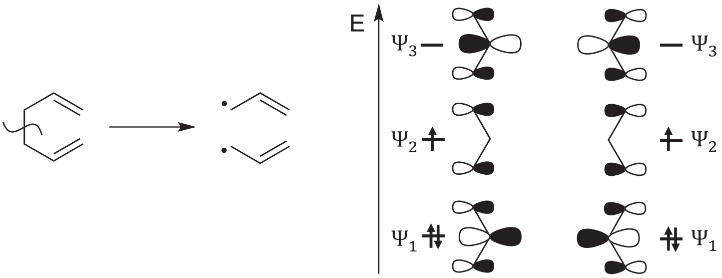
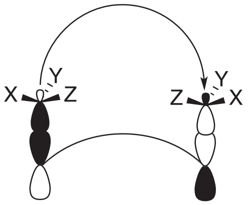


Figure 4.14.11. Frontier orbital theory applied to Cope rearrangement.

For hydrogen shift, the H shifts along the HOMO of the π-system. To determine if the shift is suprafacial or antarafacial, we just have to consider the symmetry of the HOMO of the reacting system. For example, the [1,3] hydrogen shift has 2 electron pairs in the reacting system. Under thermal conditions, the HOMO is Ψ_2, which is antisymmetric. This indicates that the hydrogen must perform an antarafacial shift, which corresponds to the result from Woodward-Hoffmann table. Under photochemical conditions, the HOMO becomes Ψ_3, which is symmetric, allowing suprafacial hydrogen shift. Since the cyclic transition state only has 4 atoms, antarafacial hydrogen shift is impossible. Thus, [1,3] hydrogen shift is only possible under photochemical conditions. Similarly, [1,5] hydrogen shift is only allowed under thermal conditions. From [1,7] hydrogen shift onwards, the cyclic transition state is large enough to allow antarafacial hydrogen shift, so both thermal and photochemical condition may be used.

Hydrogen shift is easy to analyse as hydrogen only has a 1s orbital, with a single sign. For carbon shift, the same rules apply, but it is possible for the migrating carbon to invert, changing the sign of the bonding orbital. Figure 4.14.12 shows an example of a suprafacial carbon shift involving the inversion at the migrating carbon centre.



Antisymmetric HOMO

Figure 4.14.12. Suprafacial carbon shift involving inversion at migrating carbon centre.

Thus, [1,3] carbon shift is possible under thermal conditions as the carbon centre is able to invert. In such cases, it is important to note the change in stereochemical configuration of the migrating carbon centre.

4.14.3 *Electrocyclic reactions*

Electrocyclic reactions are unimolecular ring-closing reactions that exchange an existing π-bond with a newly formed σ-bond. As per all pericyclic reactions, electrocyclic reactions are reversible and the reaction direction depends on the stability of the reactants and products. Since electrocyclic reactions are ring-closing reactions, the main factor to consider is the stability of the ring that is formed. As we have seen from Tip 4f in part 4.11.2, 5 and 6-membered rings are the most favourable. Thus, electrocyclic reactions forming 6-membered rings are the most common. We will look at such an example in Figure 4.14.13.

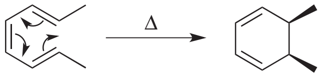


Figure 4.14.13. Example of an electrocyclic reaction that forms a 6-membered ring.

From the example, observe that 1 π-bond is exchanged for the ring-closing σ-bond. This is the key feature of electrocyclic reactions. The main question left to answer is how to determine the stereochemistry of the product. Pericyclic reactions are highly stereospecific and the configuration of the product depends entirely on the configuration of the reactant. To determine the stereochemistry, we must first look at the Woodward-Hoffmann rules for electrocyclic reactions, shown in Table 4.19.

Table 4.19. Woodward-Hoffmann rules for electrocyclic reactions.

No. of conjugated π-bonds	**Reaction conditions**	**Allowed mode of ring closure**
Even number	Thermal	Conrotatory
	Photochemical	Disrotatory
Odd number	Thermal	Disrotatory
	Photochemical	Conrotatory

Let us understand the 2 modes of ring closure, conrotatory and disrotatory. To form the new σ-bond, the two p-orbitals at the ends of the π-system rotate 90° and overlap head-on. For the σ-bond to be formed, the lobes of the p-orbitals that overlap must be of the same sign. When the two p-orbitals rotate in the same direction to form the new σ-bond, it is known as **conrotatory**. When the two p-orbitals rotate in opposite directions to form the new σ-bond, it is known as **disrotatory**.

To understand the results of the Woodward-Hoffmann table, we must go back to frontier orbital theory. Notice that the mode of ring closure depends entirely on the symmetry of the HOMO, as demonstrated in Figure 4.14.14.

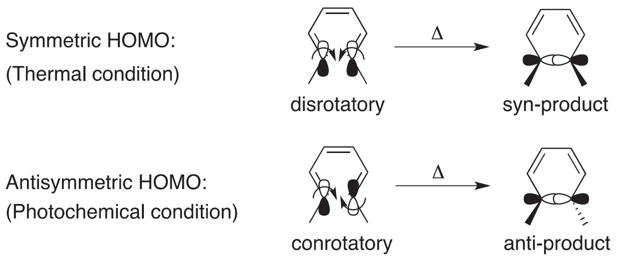


Figure 4.14.14. Determining mode of ring closure and product configuration from HOMO symmetry.

As the HOMO symmetry is reversed under photochemical conditions, the opposite mode of ring closure would be observed.

4.14.4 *Cycloaddition reactions*

Cycloaddition is a ring-forming bimolecular reaction, where 2 molecules combine to form a ring. In this reaction type, 2 π-bonds are lost in exchange for 2 new σ-bonds. Cycloaddition reactions are classified by the number of p-orbitals in each component of the reaction. Figure 4.14.15 shows common examples of cycloaddition reactions.

To determine if a cycloaddition reaction is allowed, we must refer to the Woodward-Hoffmann table for cycloaddition reactions, shown in Table 4.20.

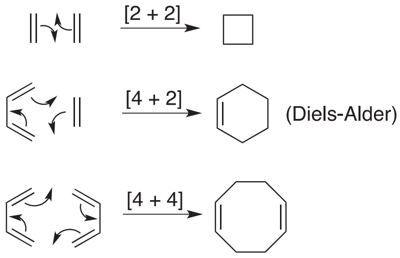
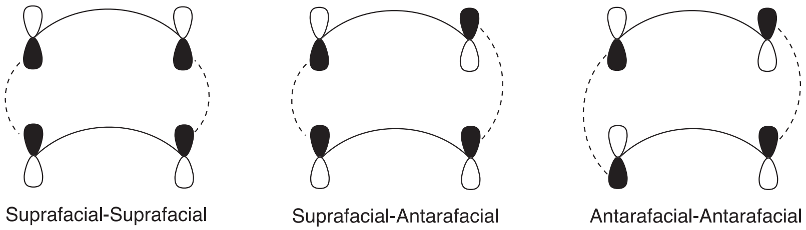


Figure 4.14.15. Common examples of cycloaddition reactions.

Table 4.20. Woodward-Hoffmann rules for cycloaddition reactions.

Total number of π-bonds in reacting system	**Reaction conditions**	**Allowed mode of ring closure**
Even number	Thermal	Antarafacial
	Photochemical	Suprafacial
Odd number	Thermal	Suprafacial
	Photochemical	Antarafacial



Suprafacial-Suprafacial

Suprafacial-Antarafacial

Antarafacial-Antarafacial

Figure 4.14.16. 3 theoretical modes of ring closure.

According to the table, [2 + 2] cycloaddition is only possible under photochemical conditions while [4 + 2] cycloaddition is possible under thermal conditions. Using these reactions as example, we will explain the Woodward-Hoffmann rules by frontier orbital theory, and the result may be generalised to all cycloadditions. Since there are 2 different molecules undergoing cycloaddition, there are theoretically 3 different modes of ring closure, as shown in Figure 4.14.16.

Here, suprafacial and antarafacial must be applied to each individual molecule. When both molecules interact in a suprafacial manner, we have the most favourable suprafacial-suprafacial mode of ring closure. When 1 molecule interacts in a suprafacial manner and the other in an antarafacial manner, we have the suprafacial-antarafacial mode of ring closure, which has geometrical limitations. 2 molecules that can interact antarafacial-antarafacial will also certainly be able to interact suprafacial-suprafacial, and since suprafacial interaction is much easier than antarafacial interaction, the antarafacial-antarafacial interaction mode is not observed in reality. Thus, in the Woodward-Hoffmann table, one molecule is treated as always interacting in a suprafacial manner and the mode of ring closure shows the interaction of the other molecule.

Let us look at [2 + 2] cycloaddition. In cycloaddition reactions, one molecule will use its HOMO to react with the LUMO of the other molecule. In a 2-electron π-system, the HOMO is Ψ_1 and the LUMO is Ψ_2. Ψ_1 is symmetric while Ψ_2 is antisymmetric. Under thermal conditions, the mode of ring closure would be suprafacial-antarafacial, consistent with the Woodward-Hoffmann table. This is impossible as the transition state is a 4-membered ring, which is too small for antarafacial interaction. Thus, [2 + 2] cycloaddition is only allowed under photochemical conditions. Under photochemical conditions, the HOMO (of the excited molecule) will also become Ψ_2, which is antisymmetric, allowing for a suprafacial-suprafacial mode of ring closure.

It is more interesting with [4 + 2] cycloaddition, also known as **Diels-Alder reaction**. In Diels-Alder reaction, the 4-electron component is known as the diene while the 2-electron component is known as the dienophile. For Diels-Alder reaction, we must consider the MO energies of the 2 molecules to determine which molecule reacts with the HOMO and which with LUMO, as shown in Figure 4.14.17.

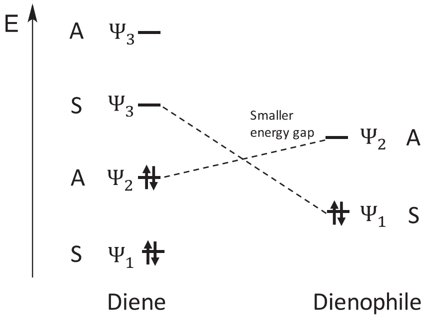


Figure 4.14.17. MO energy levels of diene and dienephile.

From the MO diagram, it is clear that the HOMO of the diene should interact with the LUMO of the dienophile for best overlap. This is known as normal electron demand Diels-Alder reaction. There are special cases where the LUMO of the diene reacts with the HOMO of the dienophile as the orbital energies are affected by the substituents on the diene and dienophile. Such reactions are rare and known as inverse electron demand Diels-Alder reactions. In normal electron demand Diels-Alder reactions, we could further close up the HOMO-LUMO energy gap by adding electron-donating groups to the diene and electron-withdrawing groups to the dienophiles. In both cases, we can see that the symmetries of the HOMO and LUMO are the same, and the mode of ring closure is suprafacial-suprafacial under thermal conditions. This is a highly favourable reaction as it forms 6-membered rings, and has been widely applied in organic syntheses.

As Diels-Alder reactions are very useful, we will proceed to discuss the stereoselectivity and regioselectivity in detail. Diels-Alder reactions is stereospecific, meaning that the stereochemistry in the reagents is faithfully reproduced in the

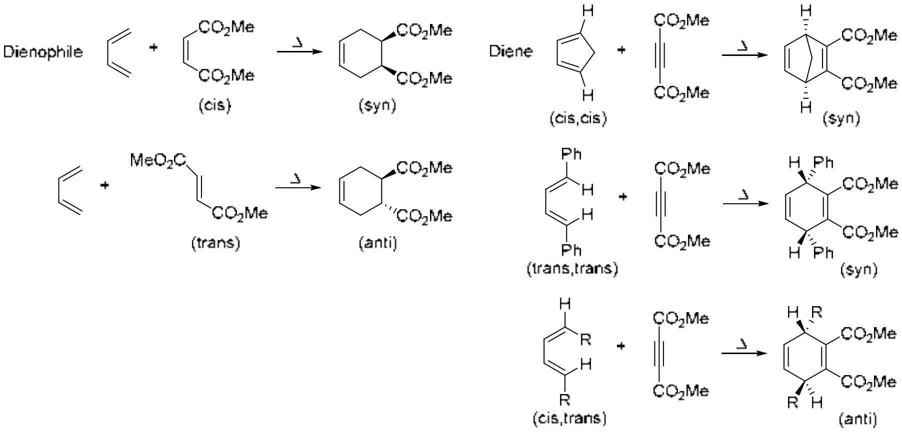


Figure 4.14.18. Stereochemistry of reagents faithfully reproduced in products.

products. The cis/trans configuration of the dienophile corresponds to the syn/anti configuration in the product, and the cis-cis/cis-trans/trans-trans configuration of the diene determines the stereochemistry at the ring junctions. This is illustrated in Figure 4.14.18.

The question arises when both diene and dienophile have stereochemical configurations. In such cases, 2 possible products may be formed that retains the stereochemical information of the reagents. An example is shown in Figure 4.14.19.

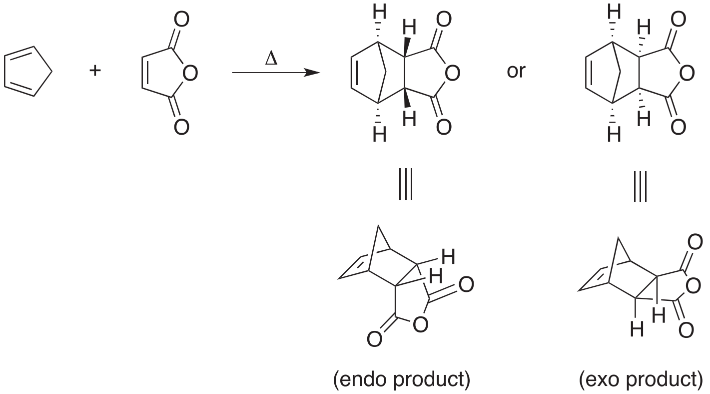


Figure 4.14.19. Example of 2 possible products when both diene and dienophile have stereochemical configurations.

Based on a plane defined by the 2 newly formed bonds, the endo-product is the molecule with electron-withdrawing group and alkene on the same side of the plane. In such cases, the endo-product is kinetically favoured while the exo-product is thermodynamically favoured. The endo-product is kinetically favoured due to secondary orbital interactions between the electron-withdrawing groups on the dienophile and the developing π-bond at the back of the diene, which lowers the energy of the transition state. The exo-product is thermodynamically favoured due to the lower steric strain in the product. Thus, it is possible to control which product is formed by varying the reaction conditions. Under standard conditions, the endo-product is usually formed. Given any diene and dienophile, the following steps will allow us to easily draw the endo-product:

1. Stack diene on top of dienophile with the electron-withdrawing group under the diene.
2. Show all the hydrogens at the carbons going to become chiral centres.
3. The directions in which the hydrogens point will indicate their stereochemical relationship.

Figure 4.14.20 shows how to apply the rules to draw the endo-product.

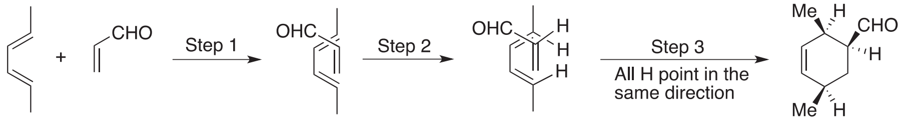


Figure 4.14.20. Drawing the endo-product of a Diels-Alder reaction.

The Diels-Alder reaction is not only stereoselective, but also regioselective. To determine the regioselectivity, we may treat the cycloaddition as a polar reaction, where the most nucleophilic site attacks the most electrophilic site. Figure 4.14.21 shows an example where we face a regioselectivity concern.

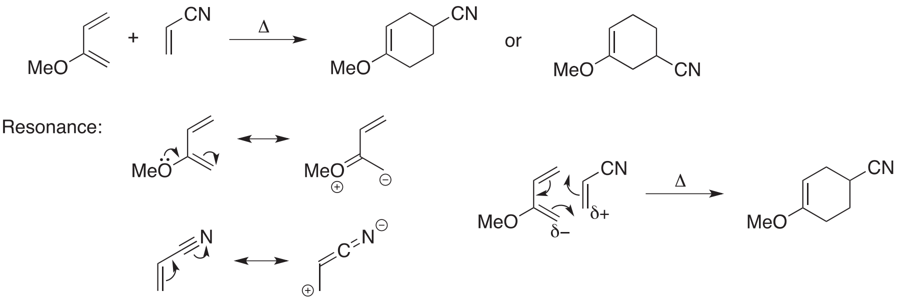


Figure 4.14.21. Determining the regioselectivity of a Diels-Alder reaction.

A special diene may be used to prepare 6-membered ring enones, known as the **Danishefsky's diene**. The structure of Danishefsky diene and its reaction scheme is shown in Figure 4.14.22.

A variation of the Diels-Alder reaction is the **Alder-ene reaction**, a group transfer pericyclic reaction. The general scheme for Alder-ene reaction is shown in Figure 4.14.23.

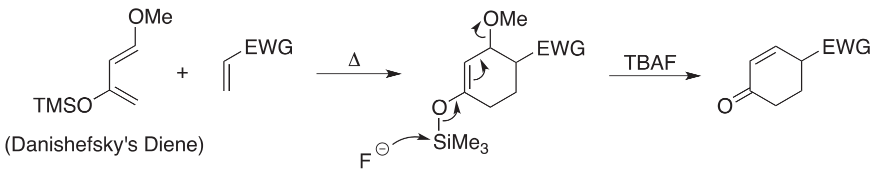


Figure 4.14.22. Reaction scheme for Diels-Alder reaction using Danishefsky's diene. EWG refers to electron-withdrawing group.

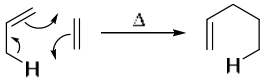


Figure 4.14.23. General scheme for Alder-ene reaction.

The alkene with allylic hydrogen is known as the ene. Similar to the Diels-Alder reaction, the LUMO of the enophile reacts with the HOMO of the ene. However, the activation energy for Alder-ene reaction is significantly higher since a σ-bond needs to be cleaved. To lower the activation energy, it is common to utilise Lewis acid catalysts. The regioselectivity may be determined by applying the same considerations as applied in Diels-Alder reactions.

Cycloaddition reactions may also occur on charged species, most commonly the 1,3-dipolar cycloadditions, which are formally [3 + 2] cycloadditions. As the name suggests, such cycloadditions are highly useful to prepare 5-membered rings. We will look at an example in Figure 4.14.24.

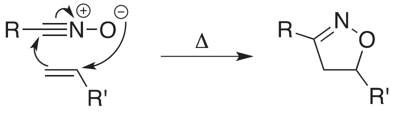


Figure 4.14.24. 1,3-dipolar cycloaddition with a nitrile oxide.

Firstly, the 1,3-dipole does not have the positive and the negative charges in a 1,3-relationship. Instead, it is the electrophilic and nucleophilic centres that are in a 1,3-relationship. The other component is known as dipolarophile. In such reactions, the dipole provides 4 π-electrons while the dipolarophile provides 2, so it has an odd number of electron pairs and favours the suprafacial mode of ring closure under thermal conditions. Depending on whether the dipolarophile is electron-rich or electron-poor, the dipole may react with either LUMO or HOMO, thus both types of electron-demand is observed for 1,3-dipolar cycloaddition.

Secondly, 1,3-dipolar cycloadditions are highly stereospecific and regioselective, similar to Diels-Alder reactions. The regioselectivity may be determined by the same method, while the stereochemistry depends on the stereochemistry of the starting material. A simple example is shown in Figure 4.14.25.

Figure 4.14.25. Stereospecificity in 1,3-dipolar cycloadditions.

1,3-Dipolar cycloadditions are popular methods to prepare interesting 5-membered rings, such as isoxazoles, which may be prepared with nitrile oxides reacting with alkynes. We have also encountered 1,3-dipolar cycloaddition in ozonolysis, a useful reaction to cleave alkene double bonds.

4.15 Organometallic Chemistry

At this point, we are nearing the end of the theory section of this book. The reactions that we will discuss in this chapter will require the knowledge from both coordination chemistry and organic chemistry. Organometallic chemistry is a relatively new field that has provided us with many synthetic routes that we were unable to access directly with classical organic chemistry. As organometallic chemistry is a large field, we will only discuss some common reactions. There are many specialised textbooks on organometallic chemistry that you may like to refer to for more information on this field.

4.15.1 *Organometallic reaction pathways*

Based on electronegativity, a metal-carbon bond is polarised with the partial negative charge on the carbon atom, leading to unique reactivity. The stability of organometallic complexes stems from the metal's ability to have π-backbonding with certain organic species. Figure 4.15.1 shows the common examples of π-backbonding in organometallic complexes.

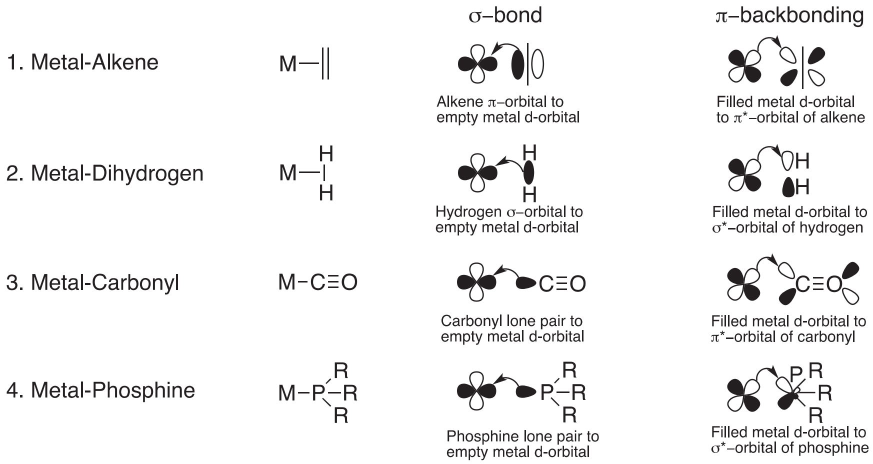


Figure 4.15.1. Important organometallic structures with π-backbonding.

There are 4 major organometallic reaction pathways that constitute most organometallic reactions.

1. Ligand substitution reactions

We have previously discussed ligand substitution reactions in detail in coordination chemistry. As a recap, Figure 4.15.2 shows the general scheme for a ligand substitution reaction.

$$L_nM{-}L + L' \xrightarrow[\text{Substitution}]{\text{Ligand}} L_nM{-}L' + L$$

Figure 4.15.2. General scheme for ligand substitution reaction.

Ligand substitution reactions may go through associative, dissociative or interchange mechanisms, depending on the electron count and geometry of the intermediate.

2. Oxidative addition and reductive elimination

Oxidative addition and reductive elimination are opposites of each other. They are very important in organometallic chemistry as they allow us to prepare organometallic complexes. Figure 4.15.3 shows the general scheme for oxidative addition and reductive elimination.

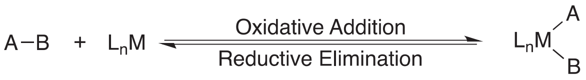


Figure 4.15.3. General scheme for oxidative addition and reductive elimination.

For the metal to undergo oxidative addition, it must have a low electron count (≤16), a low oxidation state and an unsaturated coordination number. This is because oxidative addition increases the electron count, oxidation state and coordination number of the metal by 2. This is the opposite for reductive elimination, where the metal must start with a high electron count, oxidation state and coordination number as they will all decrease by 2 in reductive elimination.

3. Insertion and elimination

Similar to oxidative addition and reductive elimination, insertion and elimination is a complementary pair of reactions. There are 2 main categories of insertion reactions, 1,1-insertion and 1,2-insertion. The general scheme is shown in Figure 4.15.4.

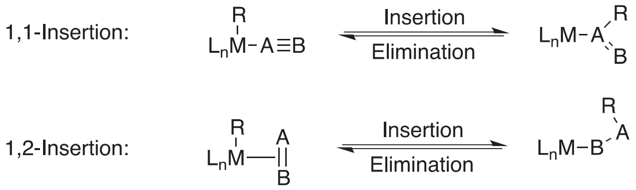


Figure 4.15.4. General scheme for insertion and elimination.

The most common migratory insertion reaction is the 1,1-insertion of C≡O into a metal-alkyl bond to generate an acyl group. The starting material must have both the alkyl group and CO as ligands on the metal centre. The generally accepted route of CO insertion is through the migration of the alkyl group, although CO migration may be observed in rare cases.

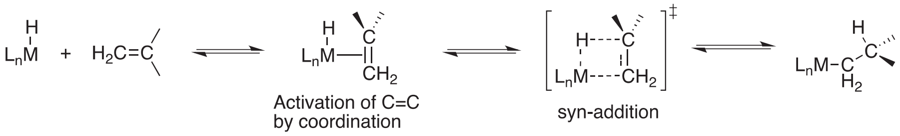


Figure 4.15.5. Mechanism of 1,2-insertion of olefin.

For 1,2-insertion, the most common group that inserts is an olefin. The mechanism for 1,2-insertion of olefins goes through a 4-membered ring transition state where the less-substituted carbon is placed with the metal. The reverse reaction is known as β-hydride elimination, following the reverse of the insertion pathway. The mechanism for olefin 1,2-insertion is shown in Figure 4.15.5.

4. Reactions of coordinated ligands

When a ligand is coordinated to the metal, it is activated and able to react in special ways. The most common reaction that can occur on coordinated ligands is nucleophilic addition. Figure 4.15.6 shows nucleophilic addition on CO, alkene and π-allylpalladium.

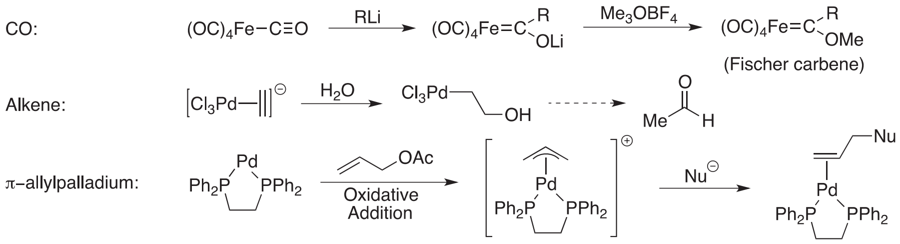


Figure 4.15.6. Common nucleophilic additions on coordinated ligands.

4.15.2 *Palladium-catalysed reactions*

Palladium metal has been widely used in homogenous catalysis and the 2010 Nobel Prize in Chemistry was awarded to palladium-catalysed cross-couplings in organic synthesis. The 3 most important types of palladium-catalysed reactions are:

1. Cross-coupling of organometallics with organic halides.
2. Coupling of olefins with organic halides.
3. Catalytic reactions via π-allylpalladium intermediates.

The cross-coupling of organometallics with organic halides is a common reaction used to synthesise new C–C bonds. There is a large variety of palladium coupling reactions discovered over the years by different scientists. The general reaction and various variations are shown in Table 4.21.

Table 4.21. Named cross-coupling reactions.

$$\text{R−m} \quad + \quad \text{R'−X} \xrightarrow{\text{[M] cat.}} \text{R−R'} \quad + \quad \text{mX}$$

Cross-coupling reactions	**[M] cat.**	**m**	**R**	**R'**	**X**
Kumada-Corriu (1972)	Ni/Pd	Mg	Aryl, alkyl, vinyl	Aryl, alkyl, vinyl	Cl, Br, I, OTs
Sonogashira (1975)	Pd/CuI	Cu	Aryl, alkyl, vinyl	Aryl, alkyl	Br, I
Negishi (1977)	Ni/Pd	Zn	Aryl, alkyl, vinyl, alkynyl, benzyl, allyl	Aryl, allyl, benzyl, propargyl	Cl, Br, I, OTs
Stille (1978)	Pd	Sn	Aryl, alkyl, vinyl, benzyl, allyl, acyl	Aryl, vinyl, benzyl, alkynyl	Cl, Br, I, OTs
Suzuki (1979)	Pd	B	Aryl, alkyl, alkynyl	Aryl, alkyl	Cl, Br, I, OTs
Hiyama (1988)	Ni/Pd	Si	Aryl, alkyl, vinyl	Aryl	Br, I, OTs

As can be seen, the cross-coupling of organometallics with organic halides is a very well-research area, as it allows us to easily form new $\mathrm{C{-}C}$ bonds. The limitation lies in the scope, as it is much easier to prepare $\mathrm{sp^2C{-}sp^2C}$ bonds through cross-coupling than $\mathrm{sp^3C{-}sp^3C}$ bonds. The catalytic cycle for such cross-coupling is shown in Figure 4.15.7.

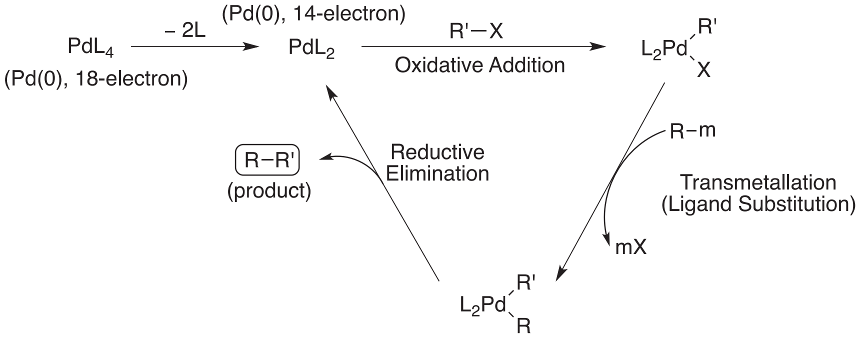


Figure 4.15.7. Catalytic cycle for cross-coupling of organometallics with organic halides.

The steps involved in the catalytic cycle are oxidative addition, transmetallation and reductive elimination, which we have discussed in the previous part. The key point to note is that the active catalyst is a 14-electron $\mathrm{PdL_2}$ species, which must be generated in-situ. In this case, we started with $\mathrm{PdL_4}$, which is most commonly

$Pd(PPh_3)_4$, and 2 ligands must dissociate before the catalytic reaction begins. This is because PdL_4 is an electron-rich stable 18-electron complex that does not readily undergo oxidative addition.

An extra step for such reactions is to prepare the organometallics for cross-coupling, during which the selectivity can by controlled by choosing the metal used. As each metal has slightly differing reactivity, extensive research has been conducted in this area.

Other than organometallics, olefins also can couple with organic halides in the **Heck reaction**. This reaction was first reported by Mizoroki in 1971 and subsequently extensively developed by Heck. The general reaction scheme is shown in Figure 4.15.8.

The full catalytic cycle for Heck reaction is shown in Figure 4.15.9.

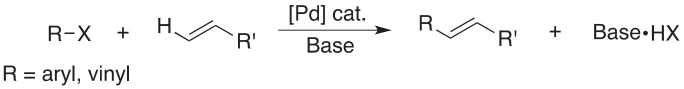


Figure 4.15.8. General scheme for Heck reaction.

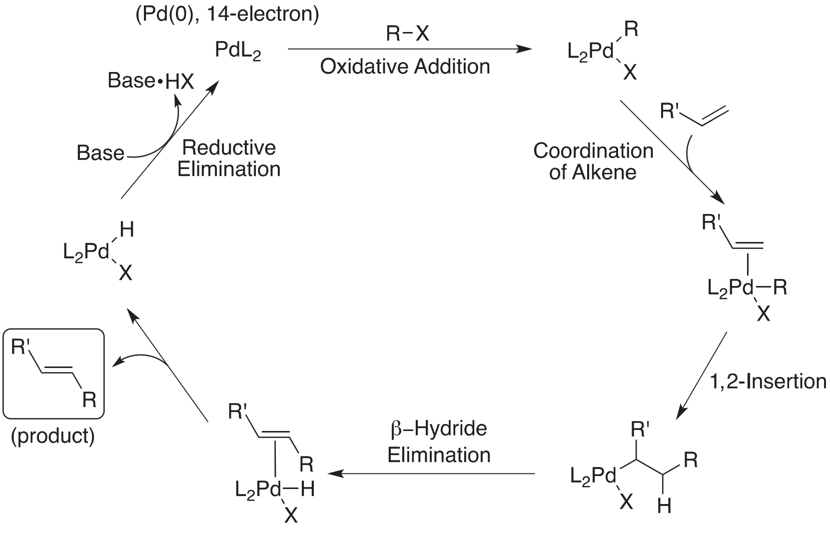


Figure 4.15.9. Catalytic cycle for Heck reaction.

The catalytic cycle for Heck reaction is more complex than that of cross-coupling reactions, however, the key points remain the same. The extra insertion and elimination steps have been discussed in the previous part, and the active catalyst is the same, PdL_2.

Not only does the Heck reaction provide an entirely new route to adding substituents, the stereochemistry of the alkene is retained. This is because both the insertion and elimination steps occur in a syn-fashion. Heck reactions have even been applied in preparation of carbonyl compounds when allylic alcohols are used as the alkene component.

The last type of catalytic reactions proceeds through a π-allyl intermediate, known as the **Tsuji-Trost reaction**. The Tsuji-Trost reaction is essentially an allylic substitution reaction that is catalysed by palladium. The general scheme for Tsuji-Trost reaction is shown in Figure 4.15.10.

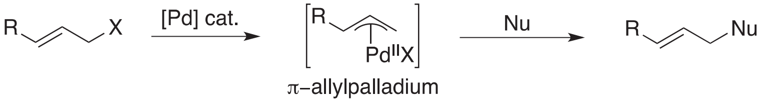


Figure 4.15.10. General scheme for Tsuji-Trost reaction.

The scope of this reaction is very wide, accommodating many different carbon, nitrogen and oxygen nucleophiles. While allylic substitution can be easily carried out without catalysis, the Tsuji-Trost reaction allows us to develop a large range of ligands that can improve the selectivity of the allylic substitution. Many chiral phosphine ligands have been developed for asymmetric allylic substitutions.

4.15.3 *Olefin metathesis*

A metathesis reaction is one where different kinds of molecules exchange parts to form other kinds of molecules. It is a very broad definition, but in this part, we will focus on the metal-catalysed exchange of alkylidene units in alkenes.

There are 6 different types of alkene metathesis reactions, which we will briefly introduce below:

1. Self-metathesis (SM)

Self-metathesis occurs when an alkene undergoes a metathesis reaction with itself, as shown Figure 4.15.11.

Figure 4.15.11. Example of self-metathesis.

2. Cross-metathesis (CM)

Cross-metathesis is the exchange of alkylidene units between alkenes, and is the most general type of metathesis reaction. An example is shown in Figure 4.15.12.

Figure 4.15.12. Example of cross metathesis.

3,4. Ring-closing metathesis (RCM) and Ring-opening metathesis (ROM)
Ring-closing metathesis occurs when a ring is formed through a metathesis reaction, and ring-opening metathesis is the reverse. A general scheme is shown in Figure 4.15.13.

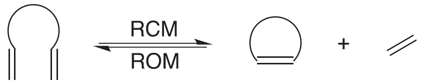


Figure 4.15.13. General scheme for ring-closing and ring-opening metatheses.

5. Ring-opening metathesis polymerisation (ROMP)
Ring-opening metathesis polymerisation is ring-opening metathesis followed by polymerisation of the product, also through metathesis. A general scheme is shown in Figure 4.15.14.

Figure 4.15.14. General scheme for ring-opening metathesis polymerisation.

6. Acyclic diene metathesis polymerisation (ADMET)
As the name suggests, acyclic diene metathesis polymerisation occurs on linear dienes repeatedly to form a polymer, as shown in Figure 4.15.15.

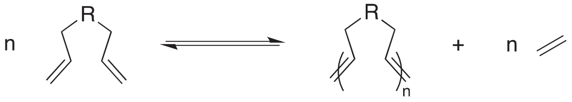


Figure 4.15.15. General scheme for acyclic diene metathesis polymerisation.

Alkene metathesis reactions are mostly equilibria reactions, and the reactions may be driven by removal of products, usually the volatile ethene gas. The catalyst used in olefin metathesis is metal carbene, which is classified into 2 types: Fischer carbene and Schrock carbene.

Fischer carbenes feature strong π-acceptor ligands bonded to the metal, such that the carbene carbon atom is electrophilic. Schrock carbenes are the opposite of Fischer carbene as they do not have π-acceptor ligands attached to the central metal and the carbene carbon is nucleophilic. Figure 4.15.16 shows the distinction between the 2 classes of carbenes.

Fischer and Schrock carbenes may be used for many different reactions, which are discussed extensively in specialised organometallic texts. Here, we will only look at the 2 common catalysts for olefin metathesis, Schrock and Grubbs catalyst. Schrock catalyst is highly reactive with poor tolerance for other functional groups in the substrate. It is able to carry out metathesis of tri and tetra-substituted alkenes.

On the other hand, Grubbs catalyst is tolerant of common functional groups such as carbonyl, hydroxyl and amino groups. It is less reactive, but more selective towards sterically unhindered and strained olefins. Unlike Schrock catalyst, tri and tetra-substituted olefins are unreactive towards Grubbs catalyst. The structures of the 2 catalysts are shown in Figure 4.15.17.

Finally, we will look at the catalytic cycle for olefin metathesis using a metal carbene catalyst. The mechanism has been a point of contention for a long time until the key metallacyclobutane intermediate was isolated and characterised by Schrock in 1989. The full catalytic cycle is shown in Figure 4.15.18.

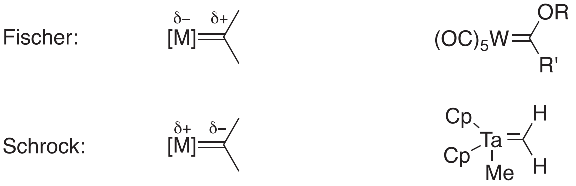


Figure 4.15.16. Fischer and Schrock carbenes.

Schrock Catalyst Grubbs Catalyst

Figure 4.15.17. Structures of Schrock and Grubbs catalysts.

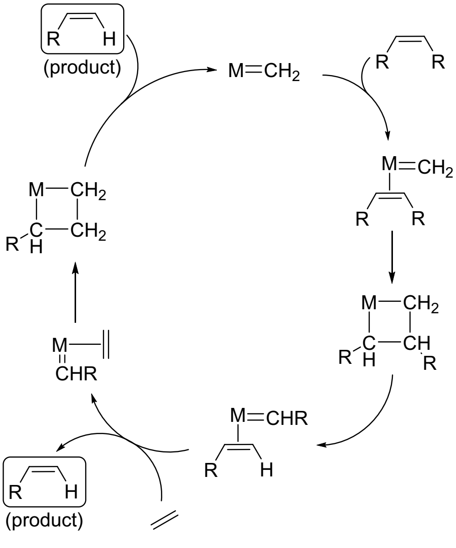


Figure 4.15.18. Catalytic cycle for olefin metathesis.

4.16 Retrosynthetic Analysis

So far, we have only been looking at forward reactions, predicting the reaction products from the reagents. In this last chapter for organic chemistry, a new perspective of looking at organic reactions will be introduced. It will allow us to predict the necessary reagents and starting materials from the products. Through this chapter, you will see that predicting the intermediates will be much easier if we are able to work from both forward and backward directions.

4.16.1 *Introduction to retrosynthetic analysis*

The process of breaking down products into starting materials through reactions is known as retrosynthetic analysis. It is a powerful technique commonly used by research scientists to devise reasonable synthetic routes for natural products.

We will start off with introducing the basic terms and notations used in retrosynthetic analysis. The desired final product is known as the **target molecule**. **Disconnections** may be imagined as the reverse of forward reactions, breaking a bond in the molecule. They are represented by the **retrosynthetic arrow** (⇒).

Synthons are the idealised fragments resulting from a disconnection and must be replaced by a feasible reagent in the actual synthesis. There are usually multiple reagents that correspond to a synthon. Other than disconnections, it is also possible to carry out **Functional Group Interconversion (FGI)** and **Functional Group Addition (FGA)**. FGIs are usually redox reactions, such as interconversions between alcohol, aldehyde and carboxylic acid oxidation levels. It is usually much more difficult to see appropriate FGAs, where we add a functional group to facilitate disconnection. Figure 4.16.1 shows a simple target molecule and how we may apply retrosynthetic analysis to propose a reasonable synthetic route for it.

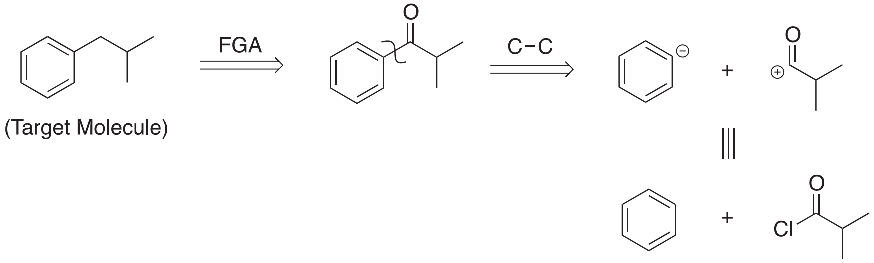


Figure 4.16.1. Sample retrosynthetic analysis of a simple target.

In this example, we see that the side chain may not be disconnected directly as it corresponds to Friedal-Crafts alkylation, which is unreliable. It is important to spot the FGA to allow for Friedal-Crafts acylation.

With the large arsenal of reactions that you have learnt in previous chapters, it is possible to prepare almost any organic compound. However, when a complex target arises, it is difficult to determine where to disconnect first. Here we present 3 strategies that should be applied when performing retrosynthetic analysis.

1. Disconnect next to heteroatom

Unlike $\mathrm{C{-}C}$ bonds, $\mathrm{C{-}X}$ bonds are polar and easier to form as it is usually obvious which species to pick as nucleophile and which as electrophile. This is especially beneficial if the $\mathrm{C{-}X}$ bond is near the middle of the molecule, such that the molecule may be separated into 2 fragments of similar size and complexity.

2. Achieve chemoselectivity by controlling the order of events

A complex target may require many disconnections, so it is important to know which disconnections to perform first. A general rule of thumb is to disconnect the most reactive functional groups first, which corresponds to adding these functional groups last in the actual synthesis. This will help us avoid chemoselectivity challenges as reactive functional groups will often be affected by reagents used in the synthesis. Common reactive functional groups are amines and alcohols. In certain cases when it is difficult to disconnect such functional groups at the start, we may employ protecting groups to keep them inert through the synthesis. The order of events is also critical when performing reactions on the benzene ring, as different functional groups have different activating and directing effects.

3. Two-group disconnections are favoured over one-group disconnections

This concept will become clearer after we discuss the possible disconnections in the next part of this chapter. Essentially, two-group disconnections allow us to use one functional group to disconnect another. For example, let us look at a sample synthon and its possible reagents in Figure 4.16.2.

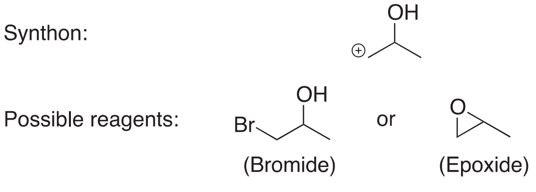


Figure 4.16.2. A sample synthon and its corresponding reagents.

While the bromide seems like the most straightforward choice, there is actually another choice, the epoxide. By using the epoxide, we are making use of the presence of the alcohol to facilitate our synthesis, performing a two-group disconnection. This alkyl bromide is less favoured due to many considerations, such as the low atom efficiency and the reactive free hydroxyl group. In the next part, we will discuss the various one-group and two-group disconnections.

4.16.2 *Disconnections*

Disconnections are undoubtedly the most critical part of retrosynthetic analysis. They are the steps that allow us to break down a complex target into starting materials. As we mentioned previously, disconnections may be classified as one-group or two-group disconnections. We will start by discussing one-group disconnections.

One-group disconnections are often applied in simpler targets where there are less functional groups. They are most commonly C–X disconnections; however, there are also a few one-group C–C disconnections. Figure 4.16.3 shows a general idea for one-group C–X disconnections, which we will discuss first.

One-group C–X disconnections are simple and straightforward, however, they may not be applied to all targets, such as amines. Here we will look at 4 strategies to prepare amines, as shown in Figure 4.16.4.

One-group C–C disconnections require a nucleophilic carbon, which leaves us with the main-group organometallic compounds. These compounds are generally most useful for preparing alcohols but they may also be used to prepare ketones in special reactions. The characteristic one-group C–C disconnections are shown in Figure 4.16.5.

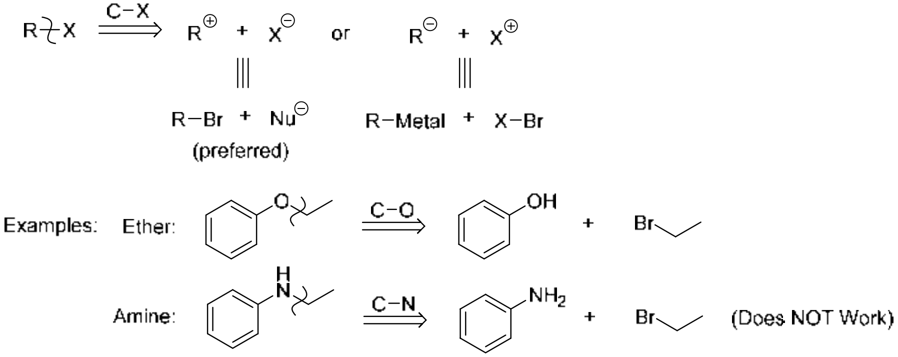


Figure 4.16.3. Scheme and examples of one-group C–X disconnection.

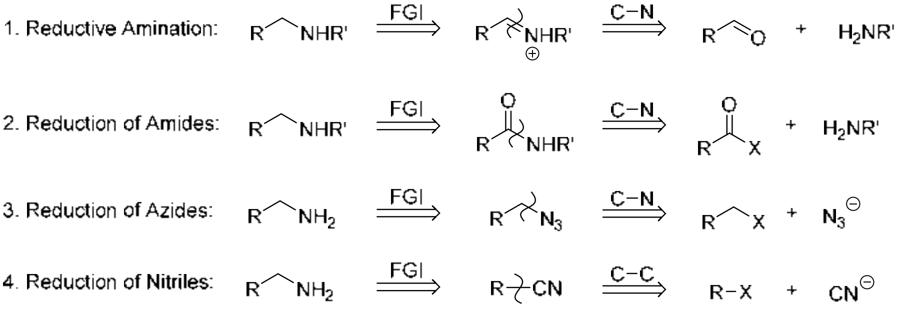


Figure 4.16.4. Four methods to synthesise amines.

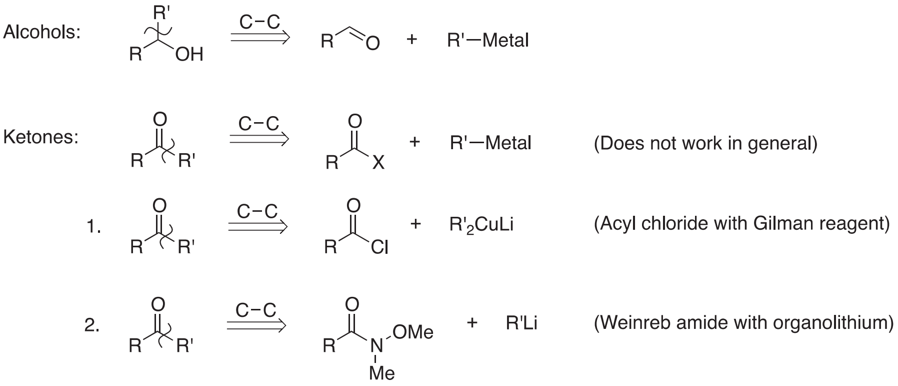


Figure 4.16.5. One-group C–C disconnections.

While one-group C–X disconnections may still be useful in certain cases, one-group C–C disconnections are limited in scope and require very harsh conditions, making their use rather limited. Instead, for C–C disconnections, two-group disconnections are preferred.

When discussing two-group disconnections, it is most important to consider the relationship between the two groups involved. By relationship, we refer to how close or far the two groups involved are from each other, judging by the number of carbons between them. We will consider 1,2-disconnections (adjacent) up to 1,6-disconnections, as it becomes difficult to involve both functional groups when they are too far apart. We will split the two-group C–C disconnections into 2 large categories:

1. Natural polarity: 1,3 and 1,5
2. Umpolung (unnatural polarity): 1,2; 1,4 and 1,6

You must be wondering how this distinction is made. In two-group C–C disconnections, the most useful functional group is the carbonyl group, as it is able to act as both nucleophile and electrophile. However, its polarity alternates as we move away from the carbonyl group, as shown in Figure 4.16.6.

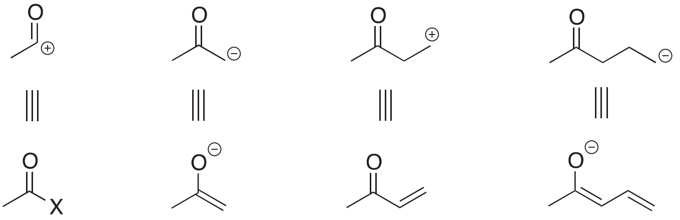


Figure 4.16.6. Alternating polarity of carbon atoms moving away from the carbonyl group.

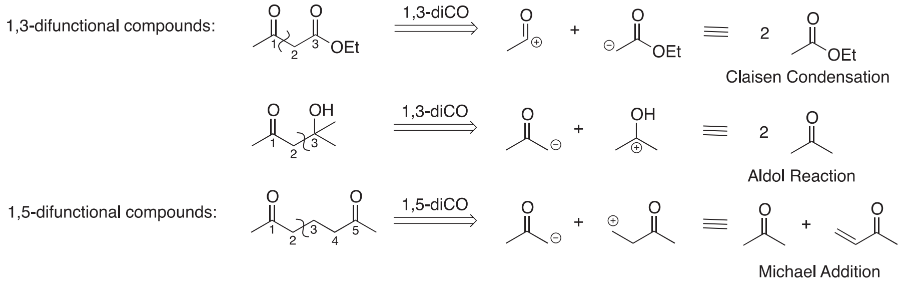


Figure 4.16.7. Preparation of 1,3 and 1,5-difuctional compounds using natural polarity.

The polarities shown above are the natural polarities, which is what we expect each carbon atom to act as. By using synthons with natural polarity, we are able to easily prepare 1,3 and 1,5-difuctional compounds, as shown in Figure 4.16.7.

Preparation of 1,2; 1,4 and 1,6-difuncitonal compounds is significantly more difficult as one synthon must be of unnatural polarity. A synthon with the opposite and unnatural polarity is known as **umpolung**.

4.16.3 *Umpolung synthons*

The most useful umpolung synthon is none other than acyl anions, which is a carbonyl group that is nucleophilic at the carbon. Of course, synthons are idealised and we must find appropriate reagents that are equivalent to acyl anion. There are 4 **acyl anion equivalents** that we introduce below:

1. Cyanide

Cyanide is nucleophilic at carbon, and may be easily converted into carbonyl groups, making them excellent acyl anion equivalents. They are also soft nucleophiles that can participate in conjugate addition. Figure 4.16.8 shows examples of how cyanides may be applied in synthesis.

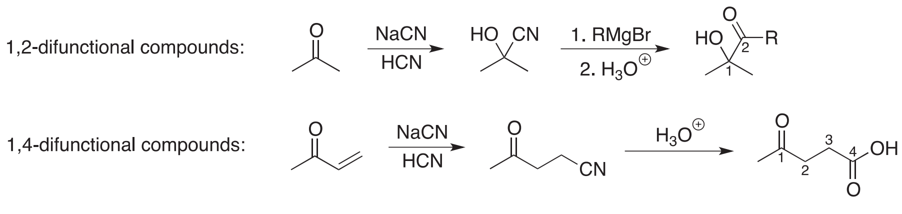


Figure 4.16.8. Use of cyanide as an umpolung synthon.

2. Nitroalkanes

Nitroalkanes are also good nucleophiles at carbon as nitroenolates. They are acyl anion equivalents as the Nef reaction is able to convert the nitro into a carbonyl group.

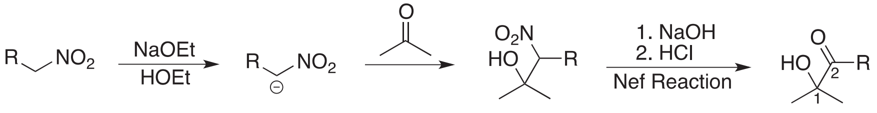


Figure 4.16.9. Use of nitroalkane as an umpolung synthon.

As nitroenolates, they are soft nucleophiles that can react with a large variety of carbon electrophiles. Figure 4.16.9 shows an example of how to apply nitroalkanes as acyl anion equivalents.

3. Dithianes

We have previously encountered dithianes as useful protecting groups for aldehydes and ketones. Dithianes are able to act as acyl anion equivalents as the hydrogen is weakly acidic and may be deprotonated by strong base, such as butyllithium. Of course, this is only possible with dithianes prepared from aldehydes, as there must be a hydrogen present. As a strong base is used for deprotonation, the dithiane anion is a hard nucleophile. Figure 4.16.10 shows an example of a synthetic route that uses dithianes as an acyl anion equivalent.

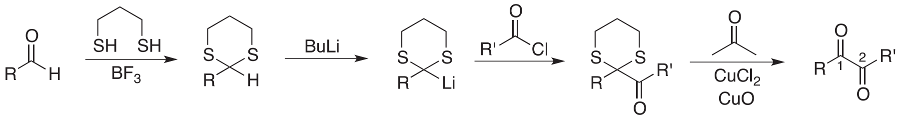


Figure 4.16.10. Use of dithiane as an umpolung synthon.

4. Lithium derivatives of enol ethers

Enol ethers have a vinylic proton that is very weakly acidic. It can only be deprotonated with tert-butyllithium to form an extremely hard nucleophile. Due to the harsh conditions required, this method is rarely used. A scheme showing how it may be applied is given in Figure 4.16.11.

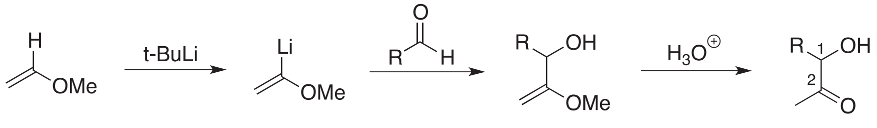


Figure 4.16.11. Use of lithium derivative of enol ether as an umpolung synthon.

These acyl anion equivalents are a good general strategy to achieve unnatural polarity, but there are some other umpolung synthons that are more specific.

For 1,2-difunctional compounds, they may be prepared with alkenes. Epoxides may be prepared from alkenes through oxidation by peroxyacids and can act as umpolung synthons. Alkenes may also undergo dihydroxylation, halogenation or halohydration to form 1,2-difunctional compounds. These reactions are shown in Figure 4.16.12.

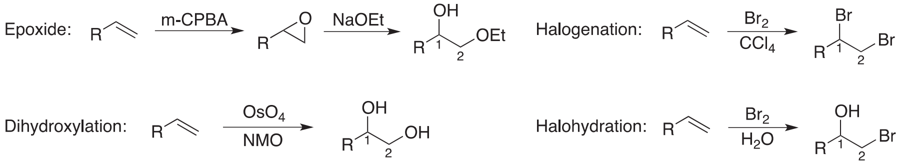


Figure 4.16.12. Reactions to form 1,2-difunctional compounds from alkenes.

Selenium dioxide is a useful oxidant to form 1,2-difunctional compounds. While it may be used to form allylic alcohols, it is also able to perform α-oxidation of methyl ketones, oxidising the methyl group to an aldehyde. The general scheme is shown in Figure 4.16.13.

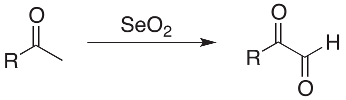


Figure 4.16.13. Reaction scheme for α-oxidation of methyl ketone by SeO_2.

For 1,4-difunctional compounds, they may be prepared through the **Stetter reaction**. This is similar to benzoin condensation, which only forms symmetrical α-hydroxyketones. On the other hand, Stetter reaction allows the preparation of a large scope of 1,4-difunctional compounds using a nucleophilic catalyst. The classical catalyst used is cyanide, and the reaction mechanism is shown in Figure 4.16.14.

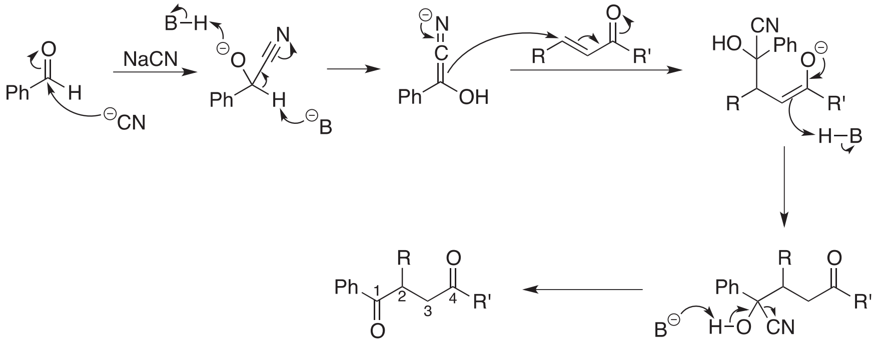


Figure 4.16.14. Full mechanism for preparation of 1,4-difunctional compound with Stetter reaction.

For 1,6-difunctional compounds, they may be prepared using Diels-Alder reaction, which we have discussed in chapter 4.14. The 1,6-difunctional compound may be afforded by ozonolysis of the Diels-Alder product. This is shown in Figure 4.16.15.

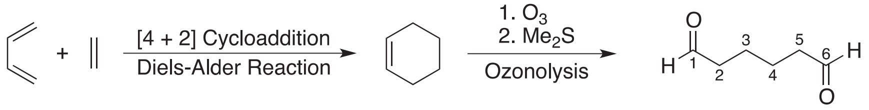


Figure 4.16.15. Preparation of 1,6-difunctional compounds using Diels-Alder reaction.

Another method to prepare 1,6-difunctional compounds is through the Baeyer-Villiger reaction, a rearrangement reaction that forms esters from ketones. Baeyer-Villiger reaction has been previously discussed in part 4.12.1, and the full mechanism can be found in Figure 4.12.14.

When performing Baeyer-Villiger reactions on unsymmetrical ketones, the group that migrates is the group that is able to stabilise a positive charge best. This is generally true for all rearrangements, and comes from empirical evidence. To prepare 1,6-difunctional compounds through Baeyer-Villiger reaction, we just need to start with a cyclohexanone. The full scheme is shown in Figure 4.16.16.

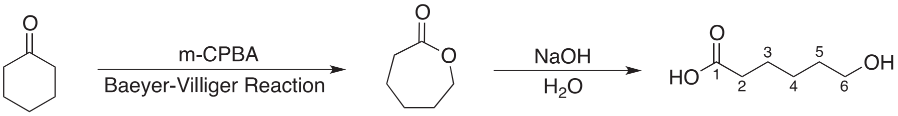


Figure 4.16.16. Reaction scheme to prepare 1,6-difunctional compounds through Baeyer-Villiger reaction.

5. PRACTICAL TECHNIQUES

At IChO, the practical section of the examination has a weightage of 40%, and consists of 3 tasks to be completed in 5 hours. As the name suggests, the practical examination aims to test the students' ability to conduct experiments and attain accurate results. The challenge is to complete all the tasks satisfactorily in 5 hours, which requires good time management and planning. It is advisable to start with the most time-consuming experiment first as there is usually waiting time for the reaction to complete, during which other tasks may be attempted simultaneously. While it is common for lab experiments to yield unexpected results, it is important to not be too affected when an experiment goes awry and to carry on with the other tasks. In this chapter, we will look at titration, organic synthesis and qualitative analysis, the 3 most common experimental tasks.

5.1 Titration

Titration is the most important skill to master for the practical examination, as it appears in the Olympiad every year. Titration is a must-know skill for any aspiring chemist as it is a basic technique that allows us to accurately determine the concentration of unknown solutions. The steps to carry out a titration is simple but require an impeccable degree of accuracy. For a titration task, at least 80–90% of the score is awarded to the **titre value**, which is the value read off the burette. Figure 5.1.1 shows a sample graph of how the titre value may be graded.

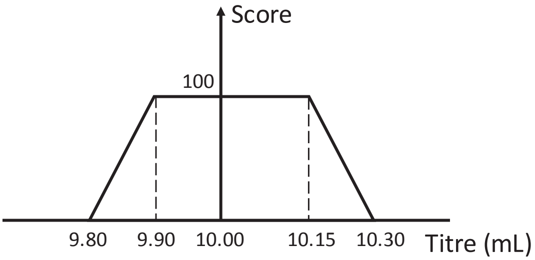


Figure 5.1.1. Sample scoring chart for titration experiments.

In this example, the accurate titre value is 10.00 mL. The full score is awarded over a small range of 9.90 to 10.15 mL. This is followed by a sharp linear decrease in score, and any titre values below 9.80 mL or above 10.30 mL is given zero points. Note that the error margin for overshooting the endpoint is usually slightly larger due to the size of the last drop. As can be seen, the grading of titration results is very strict. Thus, every effort must be made to ensure that the most accurate results are obtained in the most efficient manner.

5.1.1 *Titration skills*

Upon receiving the practical instructions, the first thing to do is to read the question carefully and understand the underlying reactions. This is of paramount importance as you must **identify which reagents are limiting and which are in excess**. For the limiting reagents, they must be prepared and measured very accurately using the most accurate apparatus available. On the other hand, reagents that are in excess should be measured in the most efficient manner.

Titration experiments generally require the preparation of a standard solution, testing the ability to measure mass and volume accurately. We will start by looking at how to measure mass. There are generally 2 types of weighing balances that are commonly available in laboratories, the top pan balance and analytical balance, with different accuracies. The top pan balance is accurate to 2 decimal places while the analytical balance is accurate to 4 decimal places. For limiting reagents, the mass must be measured by using the analytical balance, and recorded accurately to 4 decimal places. This will allow the concentration of the standard solution to be calculated exactly. On the other hand, reagents in excess may be measured with any weighing balance available, and the exact amount need not be recorded down. Nevertheless, it is still a good habit to record it down for any potential checking in the future, especially when the final result goes wrong.

The first step of designing a good titration experiment is choosing the correct **primary standard**. The primary standard must be a molecule that is highly stable and pure, low in hygroscopicity and with a high molar mass. This allows a standard solution to be prepared with a highly accurate concentration. A molecule with high molar mass is good because it minimises the effects of any inaccuracies when weighing the primary standard. Primary standards are usually weighed using weighing paper or weighing boat. Weighing paper is generally cheaper and more common, albeit being more difficult to use. As the weighing paper comes as a square, a crease should be made across the centre diagonal before use. This allows the paper to be easily removed from the balance, and the solid to be easily transferred to a beaker. Weighing boat is a small plastic box that may be placed directly onto the balance. It is also possible to directly place empty small beakers on the weighing balance to measure solid into the beaker. Once the weighing paper, weighing boat or beaker is placed onto the weighing balance, the balance must be zeroed before the addition of solid. To get the most accurate reading, make sure that the sides of the analytical balance is closed tightly to prevent any wind or other external factors to affect the reading. Also, ensure that no solid is spilled onto the pan of the balance.

After the accurate mass of solid is measured, it must be made into a solution of accurate concentration. Standard solutions are always prepared in volumetric flasks, as they have the highest accuracy for an exact volume. However, never directly transfer solid into the volumetric flask. This is because the design of the volumetric flask is not suitable for dissolving the solid, and it is difficult to transfer the solid through the thin neck of the flask. All solids should be first transferred into a beaker and fully dissolved (with careful stirring and heating, if necessary), before the solution is transferred into the volumetric flask. To transfer solution into the volumetric flask, we may either use a glass rod or glass funnel as the opening of the volumetric flask is narrow. A common problem is that solution is stuck on the walls of the neck of the volumetric flask, often above the line marking the exact volume. This solution is difficult to remove, and it is due to the inner walls of the volumetric flask being dirty. Such volumetric flasks should be washed with a dilute acid solution. After the solution is fully transferred into the volumetric flask, the beaker and glass rod or funnel should be rinsed and the rinsing solution must also be transferred into the volumetric flask to prevent any leftover solution from being in the beaker or stuck to the glass rod or funnel. Finally, the solution must be made up to the line on the volumetric flask with a dropper. Nearing the line, the last few drops of water should be added slightly squatting down such that the line is at eye-level to prevent parallax error. The final topping up of liquid in the volumetric flask is especially important, as any overshoot will result in the entire solution being diluted, and the solution must be prepared from the start again.

Once the standard solution has been prepared, we are able to start the titration and determine the concentration of the unknown solution provided. The solution of unknown concentration is known as the **analyte** and is added to the conical flask while the burette is filled with the standard solution, known as **titrant**.

Before starting the titration, we must check for the cleanliness of the apparatus that will be used. If the pipette or burette is washed with water, they must be subsequently conditioned. **Conditioning** is the rinsing of apparatus with the solution that they will be filled with. For example, if the burette is filled with standard solution immediately after washing, the standard solution will be diluted by the leftover water droplets in the burette. Instead of trying to dry the burette, rinsing the burette with the standard solution allows the water droplets to be washed out and only droplets of standard solution to remain.

First, we will discuss the **techniques regarding using the pipette**. There are 2 types of pipettes: bulb pipette and graduated pipette. Bulb pipettes are standardised for one fixed volume and have a characteristic bulb in the centre. Graduated pipettes have many lines to mark different volumes. Bulb pipettes have a higher accuracy than graduated pipettes and are more commonly used in titrations. When handling a pipette, always hold the pipette with 2 fingers above the volume marking. Never hold a pipette with the palm as pipettes are mostly calibrated at 20°C and the additional heat from the palm will cause the glass to expand and the pipette to become inaccurate. Follow the steps below to accurately draw and transfer solution using a bulb pipette:

1. Attach the pipette filler loosely, such that liquid is easily drawn up but the filler is still easily removable.
2. Immerse the pipette tip in the solution and draw the solution until it is above the line.
3. Lift the pipette tip above the solution and check for air bubbles in the pipette. Remove any air bubbles by releasing the solution and drawing it up again.
4. Use the pipette filler to release solution until the line on the pipette. When releasing the solution, the pipette tip must not be immersed in solution and the line should be at eye-level.
5. Once the volume has been adjusted correctly, do not rush to transfer the liquid. Instead, perform a final check on the pipette to ensure that there are no bubbles in the pipette and no excess solution on the tip. Excess solution on the tip may

be removed by tapping the pipette tip on the outside of the conical flask. If there are air bubbles, the solution must be drawn up and adjusted again.

6. Release the solution into the conical flask by removing the filler. While the solution is draining, keep the tip of the pipette in contact with the conical flask side wall by tilting the conical flask.

Draining the pipette has always been a heated topic for discussion. Essentially, the last drop remaining in the pipette has been accounted for during the calibration of the pipette, but how much is the last drop? If we release solution out of the pipette by letting the solution drip naturally, around 1 cm of solution will remain in the pipette tip. By tapping the tip onto the inner walls of the conical flask, we are able to drain out more liquid, and with enough taps, the pipette may be visibly empty. The question remains that how much solution should be left in the pipette to be the most accurate. To answer this, we must understand the physical principle behind the last drop. The last drop remains in the pipette due to the capillary forces between the glass surface and the liquid. Even with repeated tapping and the liquid may seem to be completely drained, it is impossible to drain out the last drop completely. This is the reason for pipettes to be calibrated with the last drop in mind. To accurately drain the pipette, keep the pipette tip touching the conical flask while it is draining. This allows the capillary forces from the glass walls of the conical flask to remove the amount of liquid that is calibrated for, leaving the last drop behind. A similar method would be to gently touch the tip of the pipette to the glass wall of the conical flask after the pipette has been drained by gravity, allowing some liquid to drain onto the wall of the conical flask. For this method, it is important that the pipette is gently put against the glass wall, such that no solution is expelled by force.

For a graduated pipette, the general principles stay the same, just that the volume to be measured may not be a fixed standard number. For example, with a 10 mL graduated pipette, you may be asked to measure 7 mL of solution. It is only in such cases that graduated pipettes come in handy, as the more accurate way of measuring 10 mL of solution would be with a bulb pipette. When using a graduated pipette, it is possible to avoid problems with the last drop by draining a difference: 7 mL of solution may be measured by draining the pipette from 9 mL to 2 mL, for example.

After pipetting, we must prepare the burette of standard solution for titration. Filling the burette is much easier, as we may just use a glass funnel to fill solution in. As a safety precaution, always remove the burette from the stand and fill it up below eye-level such that no solution may get into the eyes. Release some solution to ensure that the tip of the burette is completely filled and ensure that there are no air bubbles. Check that the burette tap is tight (preferably before filling the solution) and no solution is leaking from the tap or tip. Read the initial volume by taking the burette off the stand and holding the burette near the top at eye-level with 2 fingers, allowing gravity to keep the burette straight. For the maximum accuracy, the burette should be read to 4 significant figures, such as 12.38 mL. The last significant figure is usually an estimate, which we can obtain by dividing the burette markings mentally. For example, in the case of 12.38 mL, we should first realise that the meniscus of the solution is between the 2 markings of 12.30 mL and 12.40 mL. Mentally, we are able to divide the space between the marking into 2, and see that the meniscus is below 12.35 mL. By further dividing the space, we are able to read the volume to 4 significant figures.

Before starting the titration, indicators must be added. In some cases, acids or catalysts may be added as well. For these reagents that are added in excess, their volumes do not need to measured exactly. These volumes may be measured quickly with a measuring cylinder, or simply with a dropper. It is important to be efficient in these steps as time is usually tight in a practical examination. The indicator should be added to the solution dropwise, checking for the colour after addition of each drop. Add the least amount of indicator that allows the colour to be clearly seen. This is because the indicator is also able to participate in the reaction and excess indicator may cause the endpoint to become less sharp. Once everything is ready, place a white tile or white piece of paper below the conical flask such that it is easier to see the colour of the solution. The burette should be lowered such that the tip is in the neck of the conical flask.

We are ready to start the titration. Hold the neck of the conical flask with your master hand and keep swirling it while controlling the tap with your non-master hand. At the start, the indicator colour should revert back to the original colour quickly. As the titration progresses, the colour will start taking longer to revert. When the colour starts to stay for a while before reverting, the endpoint is near. At this point, take the conical flask out from under the burette and wash the sides of the flask with water. This flushes any reagents on the walls into the solution. It is important to remove the conical flask from the burette before spraying water in it, as we would not want to spray water at the tip of the burette, diluting the standard solution in it. To get the most accurate endpoint, rather than letting the standard solution drip into the conical flask dropwise, we may use the **half-drop method**. While many students think that the smallest quantity we can dispense with the burette is a full drop, there is a way to dispense only half a drop. This is done by opening the tap slightly and allowing some liquid out of the burette tip before closing the tap. The liquid has not formed a full drop and is still stuck onto the tip of the burette by capillary forces. This half drop of solution may be transferred to the conical flask by tapping the side of the flask against the burette tip. The flask is subsequently removed and the sides rinsed with water to wash the half drop into the flask.

Once there is a large, irreversible change in indicator colour, we may stop the titration to read the final volume. The titre value is the difference between final and initial volumes. This should be recorded on the practical worksheet in tabular form.

The titration should be repeated until 2 titre values of a difference smaller than 0.05 mL are obtained. Thus, it is not necessary to repeat the titration 3 or 4 times if the first 2 values are close to each other. The final titre value that will be scored should be the average of these 2 titre values that are close to each other. If 4 or 5 titrations have been performed to attain 2 values close to each other, do not average the titre values of all these titrations as some may be inaccurate. The reasoning behind obtaining values close to each other is such that these values are not only accurate but reliable.

5.1.2 *Types of titrations*

We will proceed to discuss some common types of titrations, elaborating on the chemical changes that occur during the titrations:

1. Acid-base titration

Acid-base titration is the simplest type of titration, where the concentration of an unknown acid is determined by a standard solution of base, or vice versa. Good primary standards for acid-base titrations include potassium hydrogen phthalate (KHP) and potassium hydrogen iodate. Depending on the strength of the acid and base, the pH at the equivalence point can be predicted, and a suitable indicator must be selected. Acid-base indicators are usually compounds that change colour upon protonation and deprotonation, and the pK_a of the indicator determines its suitability for a titration. For strong acid-strong base titrations, $pH = 7$ at equivalence point, and the common indicators we can use include methyl red, bromothymol blue, thymol blue and phenolphthalein. For strong acid-weak base titrations, the pH at equivalence point falls below 7, and the indicators that should be chosen are methyl orange, bromophenol blue, bromocresol green and congo red. For weak acid-strong base titrations, the pH of the equivalence point is above 7, and indicators such as phenolphthalein, thymolphthalein and alizarine yellow may be used.

2. Complexometric titration

Complexometric titrations are used to determine the concentrations of metal ions. The solution of metal ions is the analyte and a standard solution of ligand is used as the titrant. The indicators used in complexometric titrations are ligands that exhibit different colours depending on whether they are bound to a metal ion or in free form.

The ligand most commonly used in complexometric titrations is ethylenediaminetetraacetic acid (EDTA), which is a hexadentate ligand that binds to most metals in a 1:1 ratio. As it is a chelating ligand, it binds extremely strongly to metals.

Thus, titrations with EDTA involve EDTA binding with all available metal ions, and the indicator colour changes as it goes from being bound to free.

For complexometric titrations, it is important to control the pH of the titration by adding a buffer. This is because the formation constant of complexes is often pH-dependent, and metal ions may precipitate if the pH is too high. The most common acidic buffer is the acetate buffer and the most common basic buffer is the ammonia buffer.

When the analyte contains more than one type of metal ion, we may use masking agents to complex metal ions that we do not want to be titrated. Thus, masking agents are very good ligands that form highly stable complexes with specific metals, preventing EDTA from binding with the metals. The choice of masking agent is highly dependent on the ions that need to be masked, and common masking agents include cyanide, fluoride and triethanolamine.

Other than direct titrations, **back titrations** are also commonly carried out for complexometric titrations. This is useful when the reaction between the metal ion and EDTA is too slow for a successful titration. In a back titration, an excess amount of EDTA is first added and the solution is given time to reach equilibrium. After all the metal ions have been complexed with EDTA, the excess EDTA is titrated with a standard metal ion solution. By determining the amount of EDTA remaining, we are able to calculate the amount of metal ions in the analyte.

3. Redox titration

Redox titrations are based on reactions between oxidising agents and reducing agents. Thus, there are a large variety of redox titrations. In this book, we will focus on the 2 main types: permanganometry and iodometry.

Permanganometry refers to the usage of potassium permanganate as a titrant and indicator. Potassium permanganate solution is a strong oxidising agent with a deep purple colour. During the titration, the analyte is oxidised by potassium permanaganate and permanganate is reduced, losing its purple colour. At the endpoint, the last drop of potassium permanganate will remain in solution and appear pink in colour.

The redox reaction between the analyte and potassium permanganate is usually slow at room temperature. Thus, it is common to heat up the analyte to around 80°C before starting the titration. As the titration progresses, the analyte may cool down and require repeated heating. However, with more Mn^{2+} ions in the solution, the reduction of permanaganate speeds up as Mn^{2+} is able to act as a catalyst. Permanganate reaction is usually carried out in acid such that permanganate may be reduced all the way to Mn^{2+}. In neutral and basic conditions, the brown solid MnO_2 or green complex $[MnO_4^{2-}]$ may be formed.

Iodometry is based on the redox reaction between iodide ions and an oxidising agent. This is an indirect method to determine the concentration of oxidising agents in a sample. An excess of iodide ions, usually in the form of potassium iodide salt, is added to the analyte and iodine is produced. The iodine produced must be immediately titrated with a standard sodium thiosulfate solution, as iodine is poorly soluble in water and can be easily lost from the solution due to its volatility. We may prevent iodine from escaping by stoppering the conical flask or using an excess of iodide ions to form triiodide ions. Iodine reacts with sodium thiosulfate following this reaction:

$$\mathrm{I_2 + 2\ S_2O_3^{2-} \rightarrow S_4O_6^{2-} + 2\ I^-}$$

Iodine may act as the indicator for this reaction as it gradually decolourises. As the final colour change from pale yellow to colourless is rather difficult to see, we may add starch to form a starch-iodine complex that is dark blue. After the addition of starch, the intensity of the dark blue solution does not change until it becomes colourless. Thus, we must titrate quickly until we are close to the endpoint.

The concentration of sodium thiosulfate used in this titration may be determined by using potassium iodate ($\mathrm{KIO_3}$), which is a good primary standard. The reaction equation between $\mathrm{IO_3^-}$ and $\mathrm{S_2O_3^{2-}}$ is shown below:

$$\mathrm{2\ IO_3^- + 12\ H^+ + 10\ S_2O_3^{2-} \rightarrow 5\ S_4O_6^{2-} + I_2 + 6\ H_2O}$$

Iodometry is commonly used to determine the concentration of $\mathrm{Cu^{2+}}$, following the redox reaction:

$$\mathrm{2\ Cu^{2+} + 4\ I^- \rightarrow 2\ CuI_{(s)} + I_2}$$

The white copper(I) iodide precipitate is formed with iodine. As iodine and triiodide tend to adsorb on the surface of copper(I) iodide, thiocyanate ions ($\mathrm{SCN^-}$) may be added to compete with iodine and triiodide to be adsorbed onto the surface. This liberates iodine and triiodide, allowing them to react with thiosulfate and improving the accuracy of the titration.

4. Precipitation titration

The basis of precipitation titrations is that the analyte and titrant form an insoluble precipitate. The most widely used precipitation titration is the determination of chloride ion concentration using silver(I) ions, known as **argentometry**. This may be done with 3 possible methods:

i. Volhard method: A back titration where excess silver nitrate is added to the analyte to precipitate all the chloride ions as silver chloride. The excess $\mathrm{Ag^+}$ ions are titrated with thiocyanate ions using ferric ammonium sulfate as an indicator:

$$\mathrm{Ag^+ + SCN^- \rightarrow AgSCN_{(s)}}$$

At the endpoint, the excess thiocyanate ions form a blood-red iron complex $\mathrm{[Fe(OH_2)_5(SCN)]^{2+}}$.

ii. Mohr method: A direct titration using chromate as an indicator. Upon reaching endpoint, excess silver ions react with chromate to form a red precipitate of silver chromate.

iii. Fajans method: A direct titration using the anionic dye dichlorofluoroscein as an indicator. Prior to the end of the titration, chloride ions that are in excess adsorb on the $AgCl$ surface, imparting a negative surface charge and repelling the anionic dye. At the endpoint, the excess silver(I) ions adsorb on the $AgCl$ surface, imparting a positive surface charge that attracts the anionic dye. The dye changes colour to pink upon adsorption, marking the endpoint.

5.2 Techniques in Organic Synthesis

We have discussed the theory of organic reactions in chapter 4. While the reactions look easy on paper, they are rather challenging to perform in a laboratory. When carrying out an organic synthesis experiment, the most important criteria is the purity. Only when the product is pure will the yield be assessed. In this chapter, we will briefly discuss the common laboratory techniques used in organic synthesis, and provide tips on improving the purity and yield.

5.2.1 *Reflux*

Reflux is the most common technique for organic synthesis when heating is required. Organic solvents are highly volatile and easily lost during heating. We can easily set up a reflux by connecting a Liebig condenser above a round bottom flask. This allows the reaction to be carried out at the boiling point of the solvent without any loss of solvent. During reflux, we should observe the solvent gently boiling and condensing at the side of the condenser, returning to the round bottom flask.

There are a few pointers to note when setting up a reflux:

1. Clamp tightly at the neck of the round bottom flask, and loosely at the condenser. The round bottom flask must be tightly clamped to prevent it from dropping into the oil bath, while the condenser must be loosely clamped to ensure that there is a tight fit between the round bottom flask and condenser.
2. The level of the reaction mixture should be kept slightly above the level of the oil bath at all times to prevent overheating of the reaction mixture, leading to uneven and vigorous boiling.
3. Magnetic stirrers must be placed in both the round bottom flask and oil bath to ensure that the reactants are mixed and that heat is evenly distributed. A flat stirrer should be used for the flat oil bath (paper clip may be used to save cost) while an oval stirrer must be used for the curved round bottom flask.
4. The condenser must be connected to a water pump to supply cool water to aid the solvent condensation. To ensure that the condenser is fully filled, the water inlet should always be below the outlet. Water used to fill the condenser should be room temperature water, instead of ice water. While ice water may allow the

solvent to condense faster, water vapour in the air will also condense on the pipes and glassware. If such water drips into the oil bath, the oil may splash out and become a safety hazard.

5.2.2 *Distillation*

Distillation allows us to separate liquid mixtures based on the different boiling points of the components. For the theory behind distillation, please refer to chapter 2.4. A distillation setup consists of a round bottom flask containing the liquid mixture, distilling head, thermometer, condenser, adapter and collection flask. The points to note for distillation is similar to those of reflux. As it is a larger and more complex setup, it is necessary to use keck clips to secure the joints. Similar to reflux, the clamp for condenser should be kept loose to ensure that the joints are tight.

5.2.3 *Liquid-liquid extraction*

Liquid-liquid extraction is used to separate ionic salts and non-polar organic molecules by using an aqueous phase and an organic phase. The organic product will stay in the organic phase while the ionic salts will move to the aqueous phase. This is a common technique for purification after an organic reaction.

Into a separatory funnel, we pour in the organic reaction mixture and an aqueous layer. The aqueous layer may be water or brine (concentrated salt water), with brine being even more polar. Usually the organic solvent is less dense than water, and will stay as the top layer, unless the organic solvent is chlorinated (dichloromethane, chloroform), then the organic solvent will be at the bottom layer.

It can be mathematically shown that extraction is more efficient with a smaller volume and more extractions. Generally, we recommend to add an amount of aqueous layer similar to the amount of the organic layer, and to perform 3 extractions. When extracting, keep one palm supporting the stopper of the separatory funnel, and use the other hand to vent while shaking. Venting is the action of opening the tap to allow gas/vapour out to prevent pressure build-up in the separatory funnel. This is because organic solvents are highly volatile and vaporise quickly while shaking.

After shaking, the stopper must be removed and the separatory funnel is left on a ring stand for the 2 layers to separate completely. The bottom layer is drawn out through the tap while the top layer is poured out from the top.

5.2.4 *Drying*

After liquid-liquid extraction, we need to dry the organic layer to remove any remaining water, as water is difficult to remove through other methods. This is done by adding anhydrous salt to the organic mixture in a conical flask, as the salt is able to remove water by forming hydrates and by water adsorbing to its surface. The most common salt used for drying is sodium sulfate. Drying usually requires adding a large amount of salt, however, we should try not to add too much salt as the product may adsorb onto the salt as well. Salt that forms hydrates becomes wet, and will clump together at the base of the conical flask. Swirl the conical flask and look for free-floating salt particles. Free-floating salt particles will indicate that the organic layer is dry and no additional salt needs to be added.

The salt may be removed by gravity filtration with a cotton wool plug. While most filtrations are carried out with fluted filter paper, it is faster to remove the large amount of salt with a cotton wool plug. A cotton wool plug is just a small ball of cotton wool placed at the opening of the glass funnel. During filtration, the salt will remain in the glass funnel while the organic solution is obtained dry in the collection flask. As organic product may be adsorbed onto the salt, we may repeatedly wash the salt layer with small amounts of organic solvent. The organic solvent may be easily removed through rotary evaporation or distillation.

5.2.5 *Rotary evaporation*

The rotary evaporator, also known as rotavap, is an elaborate laboratory equipment used to remove organic solvent after a reaction. Rotavap makes use of the principle of boiling point depression at low pressures to remove organic solvents at low temperatures. This is because many organic products are sensitive to high temperature and boiling off the solvent at high temperatures may cause the product to decompose. The solvent that evaporates will flow into the condenser, where it will condense and drip into the solvent collection flask.

The water bath in the rotavap is usually set to a temperature between 40 to 50°C, while the pressure should be set based on the volatility of the solvent. The pressure should be reduced gradually to prevent solvent from boiling violently. The flask should also be rotated at a moderate speed to allow the contents of the round bottom flask to be heated evenly.

Although not entirely necessary, it is recommended to attach the round bottom flask to the rotavap using a keck clip. This is to prevent any accidents of the round bottom flask dropping into the water bath. This is not entirely necessary as the round bottom flask would be tightly held by the vacuum suction of the air pump. Also note that inappropriate position of the keck clip can actually create a gap between the round bottom flask and the rotavap machine, increasing the chance of flask dropping and lowering the evaporation efficiency. It is very important to ensure that the round bottom flask is not more than half-filled before using the rotavap to prevent any product from boiling into the rotavap machine. We can tell that the evaporation is complete when all the solvent has been removed and all that remains in the flask is a small amount of product.

5.2.6 *Suction filtration*

If the product is a solid, it may be isolated from the solvent by suction filtration. Suction filtration makes use of a vacuum pump to efficiently isolate the solid product. The steps to carry out a suction filtration is listed below:

1. Secure the Büchner flask by a clamp and connect the Büchner flask to the vacuum.
2. Place 2 pieces of filter paper on the Büchner funnel. Ensure that the filter papers cover all the holes on the Büchner funnel.
3. Place the Büchner funnel on the Büchner flask. Start the vacuum suction.
4. Seal the filter paper to the Büchner funnel by adding a small amount of poor solvent to wet the filter paper.
5. Once the seal is tight, pour the reaction contents onto the filter paper.
6. To aid with the transfer, we may use a small amount of cold poor solvent to rinse the mixture.
7. When all the solvents are dried by the vacuum suction, break off the vacuum. Add a small amount of cold poor solvent to wash the solid in the funnel. The solid and solvent should be mixed thoroughly for an efficient washing, without breaking the filter paper. The vacuum is then re-applied to remove the washing solvent. The washing can be repeated a few times until the solid is free of impurity.
8. Leave the suction filtration for a while to allow the product to dry by the air being sucked pass the solid.
9. When ready to remove the product, disconnect the vacuum tube from the Büchner flask before switching off the vacuum pump.

It is important to note that while the solubility of the product is low in cold solvent, we should still attempt to minimise the use of cold solvent as excess solvent would still result in loss of yield. In addition, if the amount of solid is small, a Hirsch funnel may be used instead for better recovery of the solid.

5.2.7 *Recrystallisation*

Recrystallisation is a common purification technique that is easily carried out. The most challenging part of recrystallisation is choosing the right solvent, which is usually indicated on the practical manual. The solvent must be able to dissolve the impurities at both high and low temperatures but the product must only be soluble at high temperatures. Recrystallisation works by dissolving the impure product in hot solvent followed by cooling the solution gradually such that only the pure product crystals are formed.

To perform recrystallisation, we must first prepare a small beaker of hot solvent on a hot plate. The impure product should be placed in a small conical flask, with a small amount of solvent. Once we start adding hot solvent, the conical flask should also be kept hot on the hot plate. The conical flask needs to be swirled to dissolve all the impure product with the least amount of hot solvent. Once all the impure product is dissolved, we may remove the conical flask from the hot plate. The whole process of recrystallisation must be carried out quickly as leaving the conical flask on the hot plate for too long may lead to product decomposition or melting. The cooling of the conical flask should be gradual to allow time for the crystals to form. Thus, it is recommended to cool at room temperature until the conical flask is warm before placing the conical flask in an ice bath.

In reality, recrystallisation is rather challenging as it is difficult to get an ideal solvent and the heating must be completed quickly. During cooling, it is also common for the crystals to not form perfectly. Thus, in most laboratory syntheses, flash column chromatography is preferred as a purification method. However, in chemistry Olympiad competitions, recrystallisation is favoured as it can be completed in a much shorter amount of time.

5.2.8 *Chromatography*

Chromatography is an analytical chemistry technique that separates molecules by their polarity. There are many variants of chromatography for different purposes, such as thin-layer chromatography (TLC), column chromatography, high performance liquid chromatography (HPLC) and gas chromatography (GC). We still start by describing the basic principles of chromatography that applies to all the variants.

In chromatography, the sample which contains multiple compounds is first loaded onto the **stationary phase**. The stationary phase is usually in solid phase and does not travel with the sample. On the other hand, there is a **mobile phase** which is usually in the liquid or gaseous phase. The mobile phase moves through the system carrying the sample. The speed and distance the sample travels depends on its interactions with the stationary and mobile phase.

Let’s discuss the theory of chromatography with reference to TLC, the simplest type of chromatography used to analyse reaction mixtures. In TLC, the stationary phase is silica or alumina on glass or aluminium backing. Silica is highly polar due to the hydroxyl groups on its surface. The mobile phase is a less polar solvent, usually a solution consisting of hexane and ethyl acetate. A small amount of sample is loaded onto the start line of the TLC plate with a capillary tube. The start line should be drawn around 1 cm above the base of the TLC plate with a pencil. The TLC plate is then placed into a jar with the mobile phase level below the start line. The jar is then quickly capped to allow the mobile phase to saturate the air in the jar. The mobile phase will slowly creep up the TLC plate, carrying the sample with it. When the mobile phase is nearing the top of the plate, the plate should be removed and a line must be drawn at the solvent front.

Non-polar compounds with polarity similar to the mobile phase will have strong affinity with the mobile phase and move up high on the TLC plate. On the other hand, polar compounds will have strong affinity to the stationary phase and stay closer to the start line. Quantitatively, we are able to define the retention factor (R_f):

$$R_f = \frac{\text{Distance travelled by spot}}{\text{Distance travelled by mobile phase}}$$

The distance travelled by the spot is the distance between the start line and the spot while the distance travelled by the mobile phase is the distance between the start line and solvent front. Thus, the R_f value is always between 0 to 1. A small R_f value indicates a highly polar compound while a large R_f value indicates a non-polar compound. The number of spots on the TLC plate indicates the number of components in the mixture.

Many times, organic compounds might be colourless and visualisation methods would be required to identify the spots. The most common visualisation method is UV light, as conjugated compounds have small π to π^* energy gaps that can be excited by UV light. Other visualisation methods include staining the TLC plate, using stains such as $KMnO_4$ (for compounds that can be oxidised) and ninhydrin (for amines).

It is important to adjust the polarity of the mobile phase for the most optimal separation of components. This often requires a series of trials to find the optimal mobile phase polarity. The most important technique in TLC is spotting the sample onto the plate. We must try to load only a small amount of sample in a small spot. This allows our final developed plate to have small spots for each component for the R_f of each component to be accurately determined. When using the capillary tube to draw sample, there is often too much sample drawn into the capillary tube. We can remove some sample by first spotting the capillary tube on lab tissue until around 1 mm height of sample remains in the capillary tube. This is spotted onto the TLC plate to make a small sample spot. If the sample is too dilute, we can dot multiple times at the same spot, concentrating a small spot. We should never load sample in a large spot.

We must remember that TLC is a technique used to analyse the reaction mixture but not a method for purification as only a little amount of sample is separated during analysis. Purification may be carried out through column chromatography, HPLC or GC, where larger amounts of sample may be loaded and separated. The principles of chromatography remain the same for any type of chromatography.

5.3 Qualitative Analysis

Qualitative analysis is the technique of determining the identity of unknowns. Simple qualitative analysis involves the use of known reagents to determine the identity of unknowns, while more challenging problems involve mixing unknowns to guess their identities.

Qualitative analysis is like problem-solving: organise the results obtained from mixing different unknowns in a table to help in determining their identities. In terms of practical techniques, qualitative analysis only requires mixing solutions in a test tube. However, there are still a few pointers to note:

1. Only a small amount of unknown is required for the reaction to occur. It is usually sufficient to mix 3 drops of each unknown. A small amount of unknown should be mixed first to prevent missing out on any observations. For example, some cations form white precipitates with base that dissolves upon addition of excess base. It is important not to add excess base at first as the white precipitate may not be observed.
2. When drawing unknowns with the dropper, do not bubble air into the solution. While most solutions are relatively stable to air, it is good practice to avoid any unwanted reactions between the unknowns and air. Thus, the proper technique is to remove the dropper from the solution and squeeze the bulb to expel all the air before placing the dropper tip into the solution and drawing the solution.
3. When adding unknown solution to a test tube, never insert the tip of the dropper into the test tube. This is to prevent any other chemicals on the walls of the test tube from contaminating the tip of the dropper, which will be reused for the unknown solution. If the unknown solution is contaminated, the results of all subsequent tests with the unknown will be affected.

A table of observations for reactions between common cations and anions is included (Table 5.1). The observations were obtained by personally carrying out the trials in a laboratory. However, it is still recommended for interested students to carry out their own trials to see the actual colours of the precipitates.

Table 5.1. Table of observations for reactions between common cations and anions.

	NH_4^+	Li^+	Na^+	K^+	Mg^{2+}	Ca^{2+}
Appearance	**Colourless**	**Colourless**			**Colourless**	**Colourless**
SO_4^{2-}	—	—	—	—	—	$CaSO_{4(s)}$ White precipitate on addition of excess SO_4^{2-} (sparingly soluble) soluble in HCl
Cl^-	—	—	—	—	—	—
Br^-	—	—	—	—	—	—
I^-	—	—	—	—	—	—
S^{2-}	—	—	—	—	$Mg(OH)_{2(s)}$ White precipitate and slow production of $H_2S_{(g)}$ gas (rotten egg odour)	$Ca(OH)_{2(s)}$ White precipitate and slow production of $H_2S_{(g)}$ gas (rotten egg odour)
PO_4^{3-}	—	$Li_3PO_{4(s)}$ White precipitate that dissolves in excess HCl	—	—	$Mg_3(PO_4)_{2(s)}$ White precipitate dissolves in HCl	$Ca_3(PO_4)_{2(s)}$ White precipitate
CO_3^{2-}	If heated, $NH_{3(g)}$ gas generated. Basic gas with strong odour	—	—	—	$MgCO_{3(s)}$ White precipitate	$CaCO_{3(s)}$ White precipitate

HCO_3^-	—	—	—	—	—	$CaCO_{3(s)}$ White precipitate
NO_3^-	—	—	—	—	—	—
NO_2^-	—	—	—	—	—	—
NH_3	—	—	—	—	$Mg(OH)_{2(s)}$ White precipitate	—
OH^-	If heated, $NH_{3(g)}$ gas generated. Basic gas and strong odour	—	—	—	$Mg(OH)_{2(s)}$ White precipitate	$Ca(OH)_{2(s)}$ White precipitate
SCN^-	—	—	—	—	—	—
CrO_4^{2-}	—	—	—	—	—	—
OAc^-	—	—	—	—	—	—
$C_2O_4^{2-}$	—	—	—	—	—	$CaC_2O_{4(s)}$ White precipitate

(*Continued*)

Table 5.1. (*Continued*)

	Sr^{2+}	**Ba^{2+}**	**Al^{3+}**	**Sn^{2+}**
Appearance	**Colourless**	**Colourless**	**Colourless**	**Colourless**
SO_4^{2-}	$SrSO_{4(s)}$ White precipitate soluble in HCl	$BaSO_{4(s)}$ White precipitate	—	—
Cl^-	—	—	—	—
Br^-	—	—	—	—
I^-	—	—	—	—
S^{2-}	—	$BaS_{(s)}$ White/Grey precipitate	$Al(OH)_{3(s)}$ White precipitate and slow production of $H_2S_{(g)}$ gas (rotten egg odour)	$SnS_{(s)}$ Dark Brown precipitate
PO_4^{3-}	$Sr_3(PO_4)_{2(s)}$ White precipitate	$Ba_3(PO_4)_{2(s)}$ White precipitate	$AlPO_{4(s)}$ White precipitate	$Sn_3(PO_4)_2$ White precipitate
CO_3^{2-}	$SrCO_{3(s)}$ White precipitate	$BaCO_{3(s)}$ White precipitate	$Al(OH)_{3(s)}$ White precipitate and slow production of $CO_{2(g)}$ gas (acidic)	Hydrated $SnO_{(s)}$ White precipitate
HCO_3^-	$SrCO_{3(s)}$ White precipitate	$BaCO_{3(s)}$ White precipitate	$Al(OH)_{3(s)}$ White precipitate and slow production of $CO_{2(g)}$ gas (acidic)	—

NO_3^-	—	—	—	—
NO_2^-	—	—	$Al(OH)_{3(s)}$ White precipitate with NO_2 Brown gas evolved	Hydrated $SnO_{(s)}$ White precipitate with NO_2 Brown gas evolved
NH_3	—	—	$Al(OH)_{3(s)}$ White precipitate	—
OH^-	$Sr(OH)_{2(s)}$ A little White precipitate	$Ba(OH)_{2(s)}$ Very little White precipitate on excess OH^-	$Al(OH)_{3(s)}$ White precipitate dissolves in excess OH^- to give $[Al(OH)_4]^-$	$SnO_{(s)}$ White precipitate that dissolves in excess OH^- to give $[Sn(OH)_4]^{2-}$
SCN^-	—	—	—	—
CrO_4^{2-}	—	$BaCrO_{4(s)}$ Yellow precipitate soluble in HCl	$Al_2(CrO_4)_{3(s)}$ Yellow precipitate	Solution changes colour from Yellow to Green (Cr^{6+} to Cr^{3+})
OAc^-	—	—	—	—
$C_2O_4^{2-}$	$SrC_2O_{4(s)}$ White precipitate	$BaC_2O_{4(s)}$ White precipitate	$Al_2(C_2O_4)_{3(s)}$ White precipitate	—

(*Continued*)

Table 5.1. (*Continued*)

	Pb^{2+}	Sb^{3+}	Bi^{3+}
Appearance	**Colourless**	**Colourless**	**Colourless**
SO_4^{2-}	$PbSO_{4(s)}$ White precipitate dissolves in excess OH^- to give $[Pb(OH)_4]^{2-}$	—	—
Cl^-	$PbCl_{2(s)}$ White precipitate	—	—
Br^-	$PbBr_{2(s)}$ White precipitate	—	—
I^-	$PbI_{2(s)}$ Bright Yellow precipitate	$SbI_{3(s)}$ Orange-Red precipitate	$BiI_{3(s)}$ Black precipitate dissolves in excess I^- to give Orange solution
S^{2-}	$PbS_{(s)}$ Black precipitate	Sb_2S_3 Orange precipitate that dissolves in excess S^{2-}/OH^- to give a colourless solution	Bi_2S_3 Brown precipitate
PO_4^{3-}	$Pb_3(PO_4)_2$ White precipitate	—	$BiPO_4$ White precipitate
CO_3^{2-}	$PbCO_{3(s)}$ White precipitate	—	$BiO_2(CO_3)_2$ White precipitate disappears with $CO_{2(g)}$ evolved (Bi^{3+} prepared in acid)
HCO_3^-	$PbCO_{3(s)}$ White precipitate	—	$BiO_2(CO_3)_2$ White precipitate disappears with $CO_{2(g)}$ evolved (Bi^{3+} prepared in acid)
NO_3^-	—	—	—

NO_2^-	Solution changes from colourless to Yellow	—	Solution changes from colourless to Green-Yellow with NO_2 Brown gas evolved
NH_3	—	—	—
OH^-	$PbOH_{2(s)}$ White precipitate dissolves in excess OH^- to give $[Pb(OH)_4]^{2-}$	$Sb(OH)_{3(s)}$ White precipitate soluble in excess OH^-	$Bi(OH)_{3(s)}$ White precipitate
SCN^-	—	—	Solution changes from colourless to Yellow
CrO_4^{2-}	$PbCrO_{4(s)}$ Yellow precipitate	Green-Yellow precipitate	$Bi_2(CrO_4)_{3(s)}$ Golden Yellow precipitate
OAc^-	—	—	—
$C_2O_4^{2-}$	$PbC_2O_{4(s)}$ White precipitate soluble in excess oxalate to give $[Pb(C_2O_4)_2]^{2-}$	—	$Bi_2(C_2O_4)_{3(s)}$ White precipitate

(*Continued*)

Table 5.1. (*Continued*)

	Cr^{3+}	**Mn^{2+}**	**Fe^{2+}**
Appearance	**Violet**	**Colourless**	**Very pale Green**
SO_4^{2-}	—	—	—
Cl^-	—	—	—
Br^-	—	—	—
I^-	—	—	—
S^{2-}	$Cr(OH)_{3(s)}$ Grey-Green precipitate	$MnS_{(s)}$ Beige/Peach precipitate	$FeS_{(s)}$ Black precipitate
PO_4^{3-}	$CrPO_4.6H_2O_{(s)}$ Violet precipitate turns into $CrPO_4.4H_2O_{(s)}$ Green precipitate soluble in excess HCl (vigourous gas)/ NaOH	$Mn_3(PO_4)_{2(s)}$ Cream precipitate	$Fe_3(PO_4)_2$ Pale Green precipitate soluble in HCl
CO_3^{2-}	$Cr(OH)_3$ Grey-Green precipitate	$MnCO_{3(s)}$ White precipitate	$FeCO_3$ Green precipitate that dissolves in acid with vigourous gas production
HCO_3^-	$Cr(OH)_3$ Grey-Green precipitate (more Grey than $CO_3{}^{2-}$)	$MnCO_{3(s)}$ Off-White precipitate	$FeCO_3$ Green precipitate that dissolves in acid with vigourous gas production
NO_3^-	Darker Violet (almost Black) solution	—	—

NO_2^-	Violet solution turns Green to dark Green then dark Green precipitate is observed with release of Brown $NO_{2(g)}$ and solution decolourises	—	Solution turns from Green to Brown (Fe^{2+} to Fe^{3+}) with Brown ring $[Fe(H_2O)_5(NO)]^{2+}$
NH_3	$Cr(OH)_3$ Grey-Green precipitate that dissolves in excess OH⁻ to give Violet solution	—	$Fe(OH)_{2(s)}$ Dark Green precipitate
OH^-	$Cr(OH)_3$ Grey-Green precipitate that dissolves in excess OH^- to give Violet solution	$Mn(OH)_{2(s)}$ White precipitate to Brown precipitate (oxidised to MnO_2)	$Fe(OH)_{2(s)}$ Dark Green precipitate turns into Red-Brown precipitate $Fe(OH)_{3(s)}$
SCN^-	Solution changes from Violet to wine Red	—	Solution turns from pale Green to Orange
CrO_4^{2-}	Brown-Black precipitate	Solution turns from colourless to dark Orange (chromate dichromate equilibria)	$Fe(OH)_{3(s)}$ Brown precipitate
OAc^-	Violet precipitate becomes Green precipitate on excess OAc^- soluble in HCl to give Green solution	—	Solution turns from pale Green to Orange
$C_2O_4^{2-}$	Solution changes from Violet to dark Green	MnC_2O_4 White precipitate on heating	$FeC_2O_{4(s)}$ Yellow precipitate

(*Continued*)

Table 5.1. *(Continued)*

	Fe^{3+}	Co^{2+}	Ni^{2+}
Appearance	**Bright Yellow**	**Pink**	**Light Green**
SO_4^{2-}	—	—	—
Cl^-	—	—	—
Br^-	Solution turns from Yellow to Orange ($Br_{2(aq)}$)	—	—
I^-	Solution turns from Yellow to Brown ($I_{2(aq)}$)	—	—
S^{2-}	$Fe_2S_{3(s)}$ Black precipitate dissolves to give a dark Green solution that becomes light Green	$CoS_{(s)}$, $Co_9S_{8(s)}$ Black precipitate	$NiS_{(s)}$ Black precipitate
PO_4^{3-}	$FePO_4$ Yellow precipitate forms on excess $PO_4{}^{3-}$ that is soluble in HCl	$Co_3(PO_4)_{2(s)}$ Violet precipitate dissolves in NH_3 to give straw-coloured solution	$Ni_3(PO_4)_{2(s)}$ Light Green precipitate soluble in NH_3 to give Blue-Violet solution
CO_3^{2-}	$Fe(OH)_{3(s)}$ Brown precipitate that dissolves in acid to give dark Red solution with vigourous gas production	$CoCO_{3(s)}$ Violet precipitate	$NiCO_{3(s)}$ Light Green precipitate

HCO_3^-	$Fe(OH)_{3(s)}$ Brown precipitate that dissolves in acid to give dark Red solution with vigourous gas production	$CoCO_{3(s)}$ Pink-Purple precipitate	$NiCO_{3(s)}$ Light Green precipitate
NO_3^-	—	—	—
NO_2^-	Solution turns from Yellow to Orange-Brown	Pink precipitate formed that turns Brown upon heating	—
NH_3	$Fe(OH)_{3(s)}$ Brown precipitate	Blue precipitate dissolves in excess NH_3 to give straw-coloured solution	Solution turns from Green to Blue and finally to Violet $[Ni(NH_3)_6]^{2+}$ complex
OH^-	$Fe(OH)_{3(s)}$ Brown precipitate	Blue precipitate turns into $Co(OH)_{2(s)}$ Pink precipitate in excess OH^- that is soluble in NH_3 to give straw-coloured solution	$Ni(OH)_{2(s)}$ Bright Green precipitate dissolves in NH_3 to give Blue-Violet solution
SCN^-	Solution turns from Yellow to blood Red	—	—
CrO_4^{2-}	Solution turns Orange due to acidic Fe(III) solution	$CoCrO_{4(s)}$ Brown-Black precipitate	On heating, $NiCrO_4$ Brown precipitate is formed that is soluble in excess NH_3 to give Violet solution
OAc^-	Solution turns from Yellow to Red	—	—
$C_2O_4^{2-}$	Solution becomes a bright Yellow colour	$CoC_2O_{4(s)}$ Pink precipitate	Solution turns Turquoise

(*Continued*)

Table 5.1. (*Continued*)

	Cu^{2+}	**Zn^{2+}**	**Ag^{+}**
Appearance	**Pale Blue**	**Colourless**	**Colourless**
SO_4^{2-}	—	—	$Ag_2SO_{4(s)}$ White precipitate on addition of excess SO_4^{2-} (sparingly soluble)
Cl^-	—	—	$AgCl_{(s)}$ White precipitate dissolves in ammonia to form $[Ag(NH_3)_2]^+$
Br^-	—	—	$AgBr_{(s)}$ Cream precipitate
I^-	$CuI_{(s)}$ White precipitate and $I_{2(aq)}$ Brown solution	—	$AgI_{(s)}$ Yellow precipitate
S^{2-}	$CuS_{(s)}$ Dark Brown precipitate	$ZnS_{(s)}$ White precipitate (UV fluorescent)	$Ag_2S_{(s)}$ Black precipitate
PO_4^{3-}	$Cu_3(PO_4)_{2(s)}$ Pale Blue precipitate	$Zn_3(PO_4)_{2(s)}$ White precipitate soluble in HCl/NH_3	$Ag_3PO_{4(s)}$ Pale Yellow precipitate soluble in NH_3
CO_3^{2-}	$Cu_2(OH)_2CO_3$ Basic Copper Carbonate Light Blue precipitate	$ZnCO_{3(s)}$ White precipitate	$Ag_2CO_{3(s)}$ Yellow precipitate
HCO_3^-	$Cu_2(OH)_2CO_3$ Basic Copper Carbonate Lighter Blue precipitate with evolution of CO_2 gas	$ZnCO_{3(s)}$ White precipitate	$Ag_2CO_{3(s)}$ Yellow precipitate

NO_3^-	—	—	—
NO_2^-	Solution turns from Blue to Green with light Green precipitate that is soluble in NH_3	—	$AgNO_{2(s)}$ White precipitate soluble in excess NH_3
NH_3	$Cu(OH)_{2(s)}$ Blue precipitate soluble in excess NH_3 to give deep Blue-Violet solution $[Cu(NH_3)_4(H_2O)_2]^{2+}$	$Zn(OH)_{2(s)}$ White precipitate dissolves in excess NH_3 to give $[Zn(NH_3)_4]^{2+}$	—
OH^-	$Cu(OH)_{2(s)}$ Blue precipitate soluble in excess NH_3 to give deep Blue-Violet solution $[Cu(NH_3)_4(H_2O)_2]^{2+}$	$Zn(OH)_{2(s)}$ White precipitate dissolves in excess HCl or OH^- to give $[Zn(OH)_4]^{2-}$	$Ag_2O_{(s)}$ Black precipitate soluble in excess NH_3
SCN^-	Solution turns from Blue to Green with Green precipitate on excess SCN^-	—	$AgSCN_{(s)}$ White precipitate
CrO_4^{2-}	$CuCrO_{4(s)}$ Brown precipitate that dissolves in excess NH_3 to give Green solution (deep Blue copper and Yellow chromate)	$ZnCrO_{4(s)}$ Yellow precipitate soluble in HCl, $NaOH$ and NH_3	$Ag_2CrO_{4(s)}$ Red precipitate soluble in excess NH_3
OAc^-	Solution colour deepens from pale Blue to Blue and Blue precipitate forms upon heating	—	$AgOAc(s)$ White precipitate
$C_2O_4^{2-}$	$CuC_2O_{4(s)}$ Sky Blue precipitate	$ZnC_2O_{4(s)}$ White precipitate	$Ag_2C_2O_{4(s)}$ White precipitate dissolves in ammonia to form $[Ag(NH_3)_2]^+$

6. SAMPLE PROBLEMS AND SOLUTIONS

In this chapter, we present 8 practice problems to test your knowledge after reading through the book. These problems were set such that they constitute a sample International Chemistry Olympiad (IChO) competition paper. The questions cover all the major areas of chemistry, from physical to inorganic and finally organic chemistry, following the same question order as the IChO theoretical paper.

Students are given 5 hours to complete a theoretical paper at the IChO, usually with 15 minutes of reading time before starting the paper. The organisers will provide a scientific calculator (the model varies by year), and it is recommended to not be over-reliant on calculator functions (such as equation solver) as the calculator provided may be very different from what you are familiar with.

After completing the problems, there are answers and detailed explanations provided for every question. Feel free to refer back to the main text of the book if you require further clarification on certain topics.

We hope that these problems would provide ample opportunity for self-assessment and give you a taste of competition problems. Please think through the problems carefully before referring to the answers, and enjoy problem solving!

Constants and Formulae

Avogadro constant:	$N_A = 6.022 \times 10^{23}\ \text{mol}^{-1}$	Zero of the Celsius scale:	$273.15\ \text{K}$
Gas constant:	$R = 8.314\ \text{J K}^{-1}\ \text{mol}^{-1}$	Faraday constant:	$F = 96485\ \text{C mol}^{-1}$
Ideal gas equation:	$pV = nRT$	Gibbs energy:	$G = H - TS$
Planck's constant:	$h = 6.6261 \times 10^{-34}\ \text{J} \cdot \text{s}$	Ionic product of water at 298.15 K:	$K_w = 10^{-14}$
$\Delta_r G^0 = -RT \ln K = -nFE^0_{cell}$		Speed of light in vacuum:	$c = 2.9979 \times 10^8\ \text{m} \cdot \text{s}^{-1}$
Nernst equation:	$E = E^0 + \frac{RT}{nF} \ln \frac{c_{ox}}{c_{red}} = E^0 + \frac{0.0591\ \text{V}}{n} \log \frac{c_{ox}}{c_{red}}$ or $E = E^0 - \frac{RT}{nF} \ln Q = E^0 - \frac{0.0591\ \text{V}}{n} \log Q$		
Beer-Lambert law:	$A = \log \frac{I_0}{I} = \varepsilon c l$		
Energy of a light quantum with wavelength λ:	$E = \frac{hc}{\lambda}$		
Volume of a sphere with radius r:	$V = \frac{4}{3} \pi r^3$		
Surface area of a sphere with radius r:	$A = 4 \pi r^2$		
Integrated rate laws:	Zeroth order: $[\text{A}]_t - [\text{A}]_0 = -kt$ First order: $\ln[\text{A}]_t - \ln[\text{A}]_0 = -kt$ Second order: $\frac{1}{[\text{A}]_t} - \frac{1}{[\text{A}]_0} = kt$		

Treat all gases as perfect gases throughout the exam.

Periodic Table of Elements with Relative Atomic Masses

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1 H 1.008																	2 He 4.003
3 Li 6.941	4 Be 9.012											5 B 10.81	6 C 12.01	7 N 14.01	8 O 16.00	9 F 19.00	10 Ne 20.18
11 Na 22.99	12 Mg 24.31											13 Al 26.98	14 Si 28.09	15 P 30.97	16 S 32.07	17 Cl 35.45	18 Ar 39.95
19 K 39.10	20 Ca 40.08	21 Sc 44.96	22 Ti 47.87	23 V 50.94	24 Cr 52.00	25 Mn 54.94	26 Fe 55.85	27 Co 58.93	28 Ni 58.69	29 Cu 63.55	30 Zn 65.38	31 Ga 69.72	32 Ge 72.63	33 As 74.92	34 Se 78.97	35 Br 79.90	36 Kr 83.80
37 Rb 85.47	38 Sr 87.62	39 Y 88.91	40 Zr 91.22	41 Nb 92.91	42 Mo 95.95	43 Tc (98)	44 Ru 101.07	45 Rh 102.91	46 Pd 106.42	47 Ag 107.87	48 Cd 112.41	49 In 114.82	50 Sn 118.71	51 Sb 121.76	52 Te 127.60	53 I 126.90	54 Xe 131.29
55 Cs 132.91	56 Ba 137.33	57 La 138.91	72 Hf 178.49	73 Ta 180.95	74 W 183.84	75 Re 186.21	76 Os 190.23	77 Ir 192.22	78 Pt 195.08	79 Au 196.97	80 Hg 200.59	81 Tl 204.38	82 Pb 207.2	83 Bi 208.98	84 Po (209)	85 At (210)	86 Rn (222)
87 Fr (223)	88 Ra (226)	89 Ac (227)	104 Rf (267)	105 Db (270)	106 Sg (269)	107 Bh (270)	108 Hs (269)	109 Mt (278)	110 Ds (281)	111 Rg (282)	112 Cn (285)	113 Nh (286)	114 Fl (289)	115 Mc (290)	116 Lv (293)	117 Ts (294)	118 Og (294)

58 Ce 140.12	59 Pr 140.91	60 Nd 144.24	61 Pm (145)	62 Sm 150.36	63 Eu 151.96	64 Gd 157.25	65 Tb 158.93	66 Dy 162.50	67 Ho 164.93	68 Er 167.26	69 Tm 168.93	70 Yb 173.05	71 Lu 174.97
90 Th 232.04	91 Pa 231.04	92 U 238.03	93 Np (237)	94 Pu (244)	95 Am (243)	96 Cm (247)	97 Bk (247)	98 Cf (251)	99 Es (252)	100 Fm (257)	101 Md (258)	102 No (259)	103 Lr (266)

6.1 Sample Problem Set

Problem 1. *So Simple, Yet So Unstable*

Halogenated compounds are widely used in the chemical industry and also in our daily life. For example, chlorofluorocarbons were replaced by hydrofluorocarbons as refrigerants due to depletion of the ozone layer. One major concern about some halogenated compounds is their environmental impact, since decomposition produces free radicals, such as $CF_3^\bullet$, $CCl_3^\bullet$, $CF_3O^\bullet$, $CHF_2O^\bullet$ and $CF_3O_2^\bullet$.

One such radical is trifluoromethoxy radical, $CF_3O^\bullet$, which is generated from $CF_3^\bullet$ via $CF_3O_2^\bullet$. It has been postulated that $CF_3O^\bullet$ may react with water in the atmosphere by reaction (1):

$$CF_3O^\bullet + H_2O \rightarrow CF_3OH + OH^\bullet \qquad (1) \qquad \Delta H_1$$

A physical chemistry study has been conducted to determine the spontaneity of reaction (1). The reaction enthalpy and Gibbs free energy of reaction (1) cannot be directly calculated because corresponding values for the radical are not well established. Instead, several related reactions are considered (for simplicity, the unpaired electron of radicals is not shown below):

Acidity of CF_3OH:	$CF_3OH \rightarrow CF_3O^- + H^+$	(2)	ΔH_2
Electron affinity of CF_3O:	$CF_3O + e^- \rightarrow CF_3O^-$	(3)	ΔH_3
Ionization energy of H:	$H \rightarrow H^+ + e^-$	(4)	ΔH_4
Bond energy of $CF_3O{-}H$:	$CF_3OH \rightarrow CF_3O + H$	(5)	ΔH_5

The electronic energies of H atom are given by the expression:

$$E = -\frac{R_H}{n^2}, \qquad n = 1, 2, 3, \ldots$$

where R_H is the Rydberg constant and n is the principal quantum number.

In 1885, Johann Balmer has discovered the Balmer series of hydrogen atom. The Balmer series contain several emission spectral lines from hydrogen atom, corresponding to electronic quantum state transition from $n \geq 3$ to $n = 2$. The first four spectral lines in Balmer series are in the visible light region, with wavelengths of 656.5, 486.1, 434.0 and 410.2 nm, while the other spectral lines in Balmer series are in the ultraviolet region.

1.1. Calculate the Rydberg constant, R_H, in the unit of J. If you are unable to obtain a value of R_H, use 3.000×10^{-18} J for the following calculation(s).

1.2. Calculate the ionization energy of H atom (equation 4), in the unit of $kJ\ mol^{-1}$. If you are unable to obtain a value, use $1500\ kJ\ mol^{-1}$ for the following calculation(s).

Electron affinity of CF_3O (equation 3) is not measured directly but can be calculated indirectly from:

Fluoride affinity of CF_2O: $CF_2O + F^- \rightarrow CF_3O^-$ (6) $\Delta H_6 = -216.7\ \text{kJ mol}^{-1}$

Electron affinity of F: $F + e^- \rightarrow F^-$ (7) $\Delta H_7 = -328.1\ \text{kJ mol}^{-1}$

Bond energy of $F{-}CF_2O$: $CF_3O \rightarrow F + CF_2O$ (8) ΔH_8

The bond energy of $F{-}CF_2O$ can be deduced from the following three reactions:

$$CF_3OOCF_3 \rightarrow 2\ CF_3O \quad (9) \quad \Delta H_9 = 195.8\ \text{kJ mol}^{-1}$$

$$CF_3OOCF_3 \rightarrow CF_3OF + CF_2O \quad (10) \quad \Delta H_{10} = 102.5\ \text{kJ mol}^{-1}$$

$$CF_3OF \rightarrow CF_3O + F \quad (11) \quad \Delta H_{11} = 184.1\ \text{kJ mol}^{-1}$$

1.3. Calculate the bond energy of $F{-}CF_2O$ (equation 8), in the unit of kJ mol^{-1}. If you are unable to obtain a value, use $110.0\ \text{kJ mol}^{-1}$ for the following calculation(s).

1.4. Calculate the electron affinity of CF_3O (equation 3), in the unit of kJ mol^{-1}. If you are unable to obtain a value, use $-100.0\ \text{kJ mol}^{-1}$ for the following calculation(s).

In order to measure the acidity of CF_3OH (equation 2), kinetic studies of the following two acid-base reaction series were conducted at 298 K:

$$X^- + CF_3OH \rightarrow CF_3O^- + HX \quad (12)$$

$$CF_3O^- + HX \rightarrow X^- + CF_3OH \quad (13)$$

where HX and X^- are a series of acids and their respective conjugate bases.

When HX is hydrogen chloride (HCl), the experimental values for the rate constants are:

$$k_{12} > 6.0 \times 10^{-10}\ \text{cm}^3\ \text{molecule}^{-1}\ \text{s}^{-1}$$

$$k_{13} < 1.0 \times 10^{-12}\ \text{cm}^3\ \text{molecule}^{-1}\ \text{s}^{-1}$$

1.5. From these rate constants, estimate the limit (either upper limit or lower limit) of the acidity of CF_3OH (ΔG of equation 2), given that the acidity of HCl is $\Delta G_{\text{acid}}(\text{HCl}) = 1372.35\ \text{kJ mol}^{-1}$. You need to state clearly whether the limit is an upper limit or lower limit by using $\Delta G < \ldots$ or $\Delta G > \ldots$

1.6. With some other experimental results, the ΔG_2 is determined as $1351.43\ \text{kJ mol}^{-1}$. If $\Delta S_2 = 95.81\ \text{J mol}^{-1}\ \text{K}^{-1}$, calculate ΔH_2. If you are unable to obtain a value, use $1200\ \text{kJ mol}^{-1}$ for the following calculation(s).

1.7. Calculate the bond energy of $CF_3O{-}H$ (equation 5), in the unit of kJ mol^{-1}. If you are unable to obtain a value, use $550\ \text{kJ mol}^{-1}$ for the following calculation(s).

1.8. Calculate ΔH_1, given that the bond energy of $HO{-}H$ is $492\ kJ\ mol^{-1}$.

CF_3OH can be prepared in the following synthesis:

Reaction of binary compound **1** (61.7%w/w F) with an equimolar amount of element **2** at 180°C forms compound **3**. Compound **3** has a boiling point of −100°C and is a pale yellow liquid below its boiling point.

Another reaction between a simple and common organic compound **4** (highly toxic, 12.1%w/w C) and a common inorganic salt **5** (45.2%w/w F) forms organic compound **6** and a very common inorganic salt **X**.

Nucleophilic addition of compound **3** to compound **6** in a 1:1 ratio generates compound **7** (47.3%w/w F). Finally, compound **7** is reacted with an equimolar amount of binary compound **8** in an inert solvent at −100°C. Aqueous solution of compound **8** is a common strong acid. Upon cooling to −130°C, long needle crystals of CF_3OH are formed, and element **2** is also formed as the only by-product. CF_3OH is only stable at low temperatures. Upon warming, it decomposes to compound **6** and a binary compound **9** (95.0%w/w F).

1.9. By calculation, deduce the formula of compound **1**. Determine the geometry of compound **1**.

1.10. Deduce the formulae of compound **2**–**9**.

1.11. Write down the balanced reaction equations for all the reactions described above.

Problem 2. *Electrochemistry Puzzles*

Electrochemistry is an area in chemistry with wide applications. For every electrochemical cell, we may determine unknowns (such as concentration or E^0 values) by making appropriate measurements. In this question, we will explore different electrochemical systems through a series of calculations.

We will start by determining the concentration of an unknown solution based on electrochemical measurements.

$$Ag(s), AgCl(s)|KCl(aq, 1.0\ M, 100\ mL)||cell\ solution|Cu(s)$$

An electrochemical cell is constructed as shown above. The cell solution consists of:

$25.0\ mL\ of\ 4.00\ mM\ KCN$
$25.0\ mL\ of\ 4.00\ mM\ KCu(CN)_2$
$25.0\ mL\ of\ 0.400\ M\ acid,\ HX\ with\ pK_a = 9.50$
$25.0\ mL\ of\ KOH\ solution$

2.1. The measured voltage was $-0.440\ V$. Calculate the molarity of KOH solution.

2.2. CN^- is able to form highly stable complexes with Ag^+ and Cu^+ to increase the solubility of their salts. Describe the properties of the CN^- ligand that allow it to bind strongly with Ag^+ and Cu^+ ions.

Given that:

$$K_f([\mathrm{Cu(CN)_2}]^-) = 1.0 \times 10^{16};\ pK_a(\mathrm{HCN}) = 9.21;\ E^0(\mathrm{Cu^+/Cu}) = +0.518\ \mathrm{V};$$

$$E^0(\mathrm{Ag^+/Ag}) = +0.800\ \mathrm{V};\ K_w = 1.0 \times 10^{-14};\ K_{sp}(\mathrm{AgCl}) = 1.8 \times 10^{-10};$$

$$K_{sp}(\mathrm{CuCl}) = 1.72 \times 10^{-7};\ K_f([\mathrm{Ag(CN)_2}]^-) = 1.1 \times 10^{8}$$

Electrochemistry may also be used to analyse the redox properties of a metal. Let us consider a theoretical metal M. A glass membrane $\mathrm{M^{2+}/M}$ selective electrode gives rise to an equilibrium potential of $-0.393\ \mathrm{V}$ against a $\mathrm{Ag/AgCl}$ reference of $0.222\ \mathrm{V}$ when placed in a $1\ \mathrm{L}$ standard solution of $0.100\ \mathrm{mol \cdot dm^{-3}}\ \mathrm{M^{2+}}$ ion prepared by dissolving $\mathrm{MCl_2}$ salt in water. $5.00\ \mathrm{g}$ of $\mathrm{Na_2H_2EDTA}$ ($\mathrm{M_r} = 336$) is then added to the standard solution with a $pH = 12$ buffer (all EDTA exists in $\mathrm{Y^{4-}}$ form). A new cell potential is obtained at equilibrium.

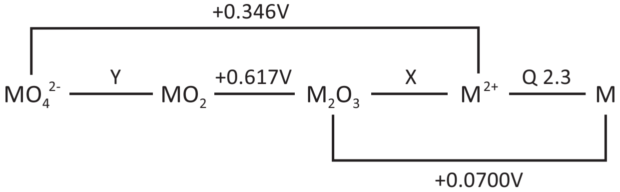
2.3. Calculate the standard reduction potential of $\mathrm{M^{2+}}$. If you are unable to obtain a value, please use $-0.100\ \mathrm{V}$ for the following calculations.

2.4. Calculate the final cell potential obtained.

Given that:

K_f of $[\mathrm{M^{2+}\text{-}EDTA}]$ Complex = 22.3

M follows a theoretical Latimer diagram as shown below:



2.5. Calculate the unknown reduction potentials X and Y.

2.6. Plot a Frost-Ebsworth Diagram for M.

2.7. Using the Frost-Ebsworth Diagram, state the most stable oxidation state of M.

2.8. Using the Frost-Ebsworth Diagram, find out which M-containing species will tend to undergo disproportionation. Write the balanced disproportionation reaction with stoichiometric coefficients. Calculate the equilibrium constant for the disproportionation.

Problem 3. *Sulfur Chemistry*

Sulfur is the 10th most abundant element in the Milky Way Galaxy and the 5th most abundant element on Earth. Sulfur has a long history, from "fire-and-brimstone" in the Bible, to pyrite (fool's gold) in the middle-ages, and black gunpowder in ancient China. In fact, sulfur is one of the major components in the alchemist's reaction vessels. In modern chemistry, approximately 85% of world production (69 million tonnes of sulfur in 2011) is used to produce sulfuric acid in the Contact Process. Sulfur also finds its applications in polymers (e.g. rubber), pesticides and pharmaceuticals.

Fossil fuels contain varying levels of sulfur (0.05–6.0% for crude oil, 0.5–3% for coal and about 10 ppm for natural gas, by mass), which has to be removed before further processing. Despite the removal of sulfur from fossil fuels, the residual sulfur (a maximum of 10 ppm sulfur in gasoline and diesel by the Euro V standard) still poses a problem because its combustion product SO_2 is a major air pollutant.

International Energy Agency has estimated the world total energy consumption to be 3.9×10^{20} J annually, out of which 31.3% is from oil products.

3.1. Calculate the amount of SO_2 (in tonnes) generated by oil products, assuming that the main component of oil products is octane, C_8H_{18}. Also, assume that 80% of the energy by full combustion of octane is utilised and the oil products contain 10 ppm sulfur by mass.

Bond	H–H	C–H	C–C	C=O	O=O	H–O
Bond energy, $kJ\ mol^{-1}$	436	412	348	743 799 in CO_2	497	463

The oxidation of SO_2 in the environment is a subject of interest since it is the main culprit for acid rain and ocean acidification. Research has shown that the aqueous-phase oxidation of SO_2 is a significant pathway for the total transformation of SO_2.

A mechanistic study was conducted for the oxidation of SO_2 in seawater.

For the reaction $2SO_3^{2-} + O_2 \rightarrow 2SO_4^{2-}$, the overall rate equation can be written as:

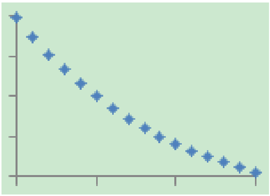
$$-\frac{d[SO_3^{2-}]}{dt} = k[SO_3^{2-}]^a[O_2]^b$$

With an excess of oxygen, the rate equation can be rewritten as:

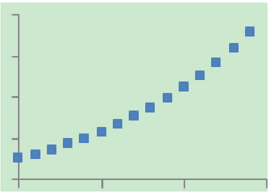
$$-\frac{d[SO_3^{2-}]}{dt} = k'[SO_3^{2-}]^a, \text{ whereas } k' = k[O_2]^b$$

The concentration of sulfite $[SO_3^{2-}]$ is measured against time (t) and three graphs have been plotted, namely $[SO_3^{2-}]$-t, $1/[SO_3^{2-}]$-t and $\ln[SO_3^{2-}]$-t:

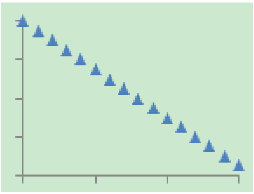
$[SO_3^{2-}]$-t



$1/[SO_3^{2-}]$-t



$\ln[SO_3^{2-}]$-t



3.2. What is the reaction order with respect to sulfite?

k' is measured at different concentrations of oxygen and summarised in the table below (units are not shown):

$[O_2]$	212.0	390.7	652.2	979.2
k'	741.3	955.0	1230.3	1584.9

3.3. Calculate the reaction order (b) with respect to O_2.

A free-radical chain reaction mechanism has been proposed on the oxidation:

Initiation: $Fe^{3+} + SO_3^{2-} \xrightarrow{k_1} Fe^{2+} + SO_3^{\bullet-}$

Propagation: $SO_3^{\bullet-} + O_2 \xrightarrow{k_2} SO_5^{\bullet-}$

$SO_5^{\bullet-} + SO_3^{2-} \xrightarrow{k_3} SO_5^{2-} + SO_3^{\bullet-}$

Comproportionation: $SO_5^{2-} + SO_3^{2-} \xrightarrow{k_4} 2\ SO_4^{2-}$

Termination 1: $2\ SO_3^{\bullet-} \xrightarrow{k_5} S_2O_6^{2-}$

Termination 2: $SO_3^{\bullet-} + SO_5^{\bullet-} \xrightarrow{k_6} S_2O_6^{2-} + O_2$

3.4. By steady-state approximation, deduce the rate law for the oxidation of SO_3^{2-}, assuming that Termination 1 is the major pathway for termination. State the assumption(s) made, if any.

3.5. By steady-state approximation, deduce the rate law for the oxidation of SO_3^{2-} assuming that Termination 2 is the major pathway for termination. State the assumption(s) made, if any.

SO_2 is the major culprit for acid rain and acidification of surface water on earth. In the following questions, you will calculate the acidity of some aqueous solutions related to SO_2.

3.6. An aqueous solution of SO_2 contains $16.75\ \mu g\ cm^{-3}$ of SO_2. What is the pH of this solution? The acid dissociation constants for H_2SO_3 are: $K_1(H_2SO_3) = 1.5 \times 10^{-2}$ and $K_2(H_2SO_3) = 6.8 \times 10^{-8}$. Assume all dissolved SO_2 becomes H_2SO_3.

World Health Organization (WHO) has recommended that the daily average concentration of SO_2 in air should be no more than $20\ mg\ m^{-3}$. At this low concentration (or any similar values), the dissolved H_2SO_3 will be very dilute. In order to measure the pH of this very dilute acidic solution, weak acid H_2SO_3 is oxidised to strong acid H_2SO_4.

3.7. In an experiment, the obtained H_2SO_4 solution has a concentration of $2.0 \times 10^{-8}\ mol\ dm^{-3}$. Calculate the pH of this solution. $K_2(H_2SO_4) = 1.2 \times 10^{-2}$.

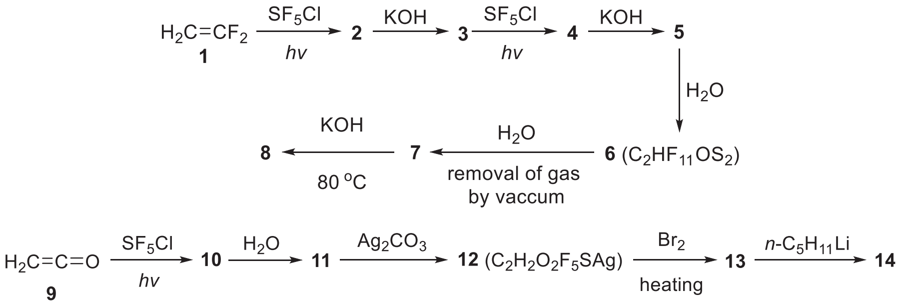
Sulfur is not only an important element in inorganic chemistry, but also a common element in organic chemistry. Chemists have synthesized some interesting sulfur-containing compounds (**8** and **14**) to study their unique properties.

Characterisation has shown that compound **8** has a rare bond with a bond length of 139.2 pm, whereas compound **14** has a more common bond with a bond length of 155.3 pm. NMR spectra of **14** has one hydrogen signal and two fluorine signals.

The bond lengths of some bonds commonly found in organic and inorganic chemistry are tabulated below:

Bond	Length (pm)	Bond	Length (pm)	Bond	Length (pm)	Bond	Length (pm)
C–C	154	O–O	148	S–O	151	H–H	74
C=C	134	C–O	143	S–S	204	H–F	92
C≡C	121	C=O	123	C–S	181	H–O	96
C–H	109	C–F	133	S–F	158	H–S	134

3.8. Draw the structures of **2–8** and **10–14**.



Problem 4. *Safer is Better*

Lithium-ion batteries are widely used in electronic devices in modern society. However, its safety is always a concern. Ternary oxide **A** is potentially a safer electrode material for lithium-ion batteries due to its better thermal stability. During the research of ternary oxide **A**, another ternary oxide **B** with a similar structure was also discovered.

For all the following reactions, assume that the yield is quantitative.

To prepare ternary oxide **A**: 10.00 g of mineral **X** was ground together with 27.02 g of oxide **Y** to a fine uniform powder. This powder was heated at 900°C for 20 hours. A gas with a volume of $13.01\ \mathrm{dm}^3$ was released (the volume was measured at 900°C and 1.013×10^5 Pa) and 31.07 g of white solid **A** was obtained.

4.1. Find the mass of the gas formed in the preparation of **A**.

4.2. Determine the identity of the gas.

4.3. Determine the formula of mineral **X**.

To prepare ternary oxide **B**: 10.00 g of mineral **X** was ground together with 10.81 g of oxide **Y**. Heating of the mixture released the same gas in the same amount, as in the preparation of **A**. The residual solid **Z** has a mass of 14.85 g. **Z** is then quantitatively transferred to a vacuum tube containing 27.02 g of oxide **Y** and 3.24 g of metal **M**. The tube is heated at a rate of $150°\mathrm{C\ h^{-1}}$ to a temperature of 850°C and maintained at this temperature for 16 hours. Finally, 45.11 g of **B** was obtained.

When arranged in a certain order, the number of atoms in **B** are described by geometric progression.

4.4. Determine the formula of oxide **Y**.

4.5. Write the balanced equations for the preparation of **A** and **B**.

Problem 5. *Chromium Complexes*

Transition metals have gained much attention due to their interesting chemical and physical properties and the various applications of transition metal complexes. In particular, this question aims to investigate the properties of chromium, a group 6 transition metal which is commonly used.

Chromium, being in group 6, takes oxidation states from 0 to +6. While compounds of all 7 oxidation states have been reported, chromium(III) is by far the most common oxidation state of chromium. We will start by looking at chromium(III) complexes.

Chromium(III) chloride is a common salt that can be easily obtained in its hydrate form.

5.1. Draw all the possible complexes that can be formed when dissolving chromium(III) chloride hydrate in water. Take note that chromium(III) forms octahedral complexes and assume that all complexes do not have more than 3 chloride ligands in the coordination sphere.

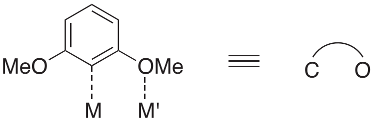
Chromium(III) chloride is a green salt that forms a green solution after dissolving in water. However, upon leaving the solution overnight, the colour changes to violet.

5.2. Explain the colour change, making use of ligand properties and crystal field theory.

5.3. Why is this colour change so slow?

An interesting area in transition metal chemistry is the investigation of metal–metal bonds. Chromium complexes gained considerable attention as supershort

$Cr{-}Cr$ bond distances have been reported for chromium(II) complexes. In 1978, Cotton prepared a chromium complex with a supershort $Cr{-}Cr$ bond of 1.847 Å. This complex is $Cr_2(DMP)_4$, with the structure and coordination mode of DMP ligand shown below.



5.4. Draw the structure of $Cr_2(DMP)_4$, taking into account steric effects. You may simplify the structure of DMP based on the figure above and need not show the $Cr{-}Cr$ interaction.

5.5. Classify the DMP ligand based on its role in $Cr_2(DMP)_4$.

5.6. How does the DMP ligand facilitate the formation of the supershort $Cr{-}Cr$ bond?

We will now use crystal field theory to understand the $Cr{-}Cr$ bonding in $Cr_2(DMP)_4$.

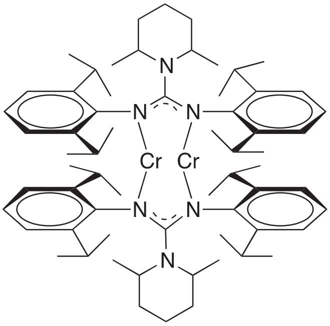
5.7. What is the coordination number and geometry around each Cr centre? Ignore the $Cr{-}Cr$ interaction.

5.8. Draw the crystal field splitting diagram for the Cr atom based on the geometry determined in part 7. Assume that the ligands lie on the xy-plane.

5.9. Construct a molecular orbital diagram to describe the $Cr{-}Cr$ interactions, considering the interactions between the 2 equivalent Cr atoms. There should be 4 (1σ, 2π and 1δ) interactions as the orbital mainly used for bonding with the ligands will not be involved in $Cr{-}Cr$ interactions. Fill in the molecular orbitals with the d-electrons from both chromium centres.

5.10. Calculate the bond order of the supershort $Cr{-}Cr$ bond.

More recently in 2013, Kempe reported the shortest metal-metal bond of 1.706 Å in a chromium(I) complex using guanidinate ligands. The structure of the complex is shown below.

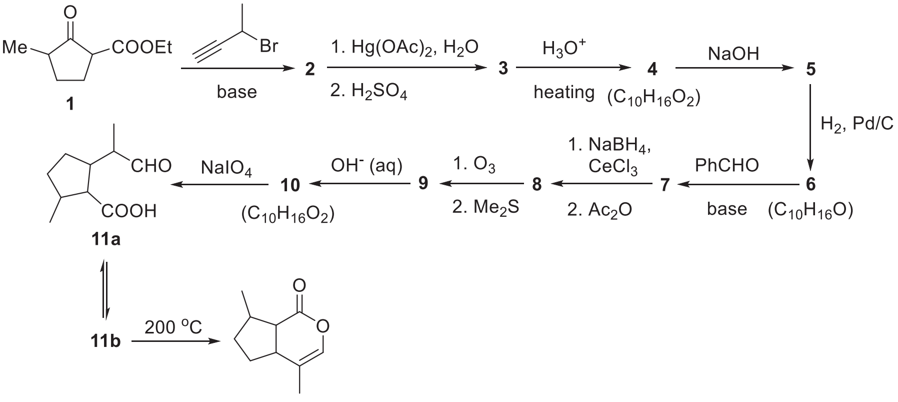


5.11. What is the chief feature of the guanidinate ligand allows for the further shortening of the Cr–Cr bond?

5.12. Based on a similar molecular orbital argument as parts 9 and 10, predict the bond order in this complex. In this case, all five d-orbitals participate in Cr–Cr interactions.

Problem 6. *Cats' Favourite*

Catnip or catmint (*Nepeta cataria* L.) is known to attract the cat family, not only cats, but also lions, tigers and leopards. The active attractant is a monoterpene, nepetalactone, which can be extracted from catnip by steam distillation. The extracted nepetalactone is the (+)-enantiomer. Racemic nepetalactone **12**, as well as the single enantiomer of nepetalactone have been synthesised via various synthetic routes, to study their biological effects on cats.



racemic **12**

Answer the questions about synthesis of racemic **12**, considering the following facts:

- Oxidative cleavage of compound **10** is via its hydrate.
- **11a** is in equilibrium with its bicyclic isomer **11b**.

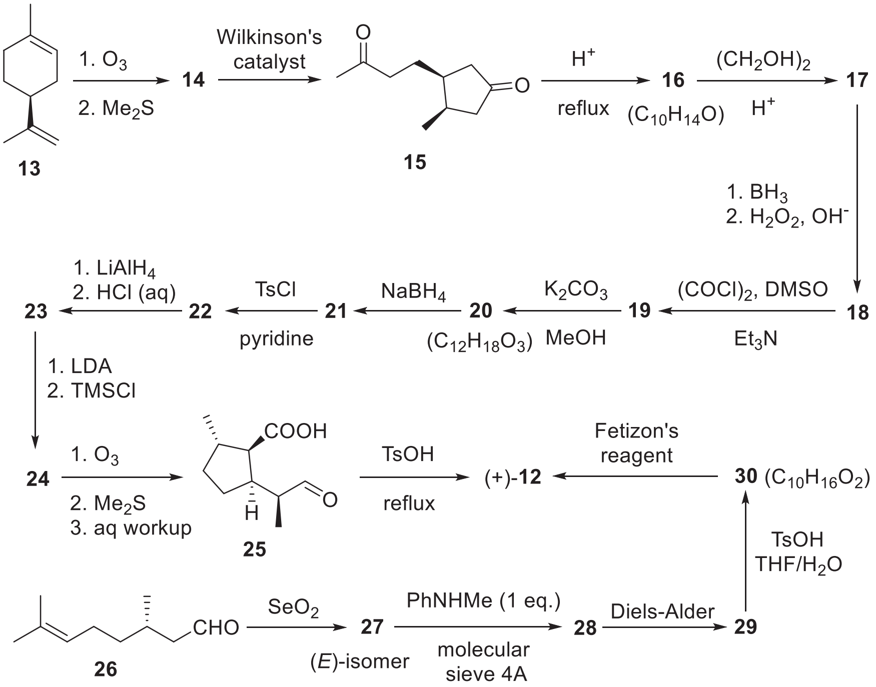
6.1. Compound **1** can be prepared by Claisen condensation of diethyl 2-methylhexanedioate. However, the diester is not symmetric, hence there are two possible condensation products. Explain with mechanism why **1** is the sole product in this Claisen condensation.

6.2. Draw the structure of compounds **2–10** and **11b**.

6.3. How many chiral centres does compound **12** have? How many possible stereoisomers does **12** have?

6.4. In the current synthesis, does the product **12** contain all its possible stereoisomers in equal ratio? If not, draw the major stereoisomers that are in product **12**.

Early studies showed that racemic nepetalactone has weak or no effect on cats. Therefore, scientists have prepared the single enantiomer of nepetalactone to check the bioactivity, using the following two synthetic routes.



Answer the questions about synthesis of (+)-**12**, considering the following facts:

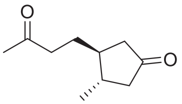
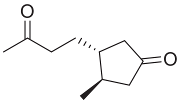
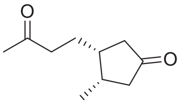
- Wilkinson's catalyst, $RhCl(PPh_3)_3$, catalyses the cyclisation reaction of (substituted) pent-4-enal.
- Compound **16** is not conjugated.
- Compound **30** is a mixture of two stereoisomers.
- Fetizon's reagent (Ag_2CO_3/celite) is a mild oxidiser, which usually oxidises primary alcohol, secondary alcohol or lactol.

6.5. Draw the structures of compounds **14** and **16–24** with proper stereochemistry, where applicable.

6.6. Draw the structure of (+)-**12** with proper stereochemistry. Assign *R*/*S* to all the chiral centres in (+)-**12**.

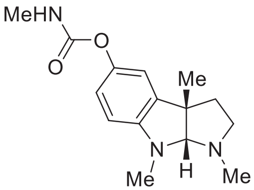
6.7. Draw the structures of compounds **27–30** with proper stereochemistry, where applicable.

6.8. Compound **15** has a total of 4 stereoisomers. If the other stereoisomers of **15** are subjected to the same synthesis route, what will be the product? Write "Y" in the corresponding boxes.

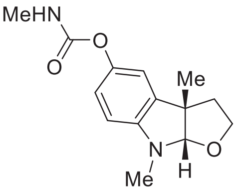
	(+)-**12**	(–)-**12**	neither (+)-**12** nor (–)-**12**
 **15a**			
 **15b**			
 **15c**			

Problem 7. *Alkaloids from Africa*

Calabar bean, the seed of an African herbaceous plant, has been known for its high toxicity to inhibit the neurotransmitter acetylcholine in the central and peripheral nervous system. It has been found that alkaloids (–)-physostigmine (**A**) and (–)-physovenine (**B**), together with other alkaloids, are responsible for the toxicity of Calabar beans.

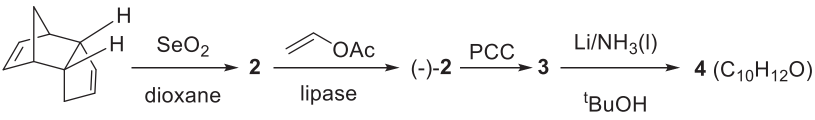


A
(-)-physostigmine



B
(-)-physovenine

Despite their toxicity, scientists utilise the anti-cholinergic (acetylcholine-inhibition) effect of (–)-physostigmine and commercialise it as a drug (Antilirium) to treat glaucoma. (–)-Physovenine is the minor toxic component in Calabar beans. Hence, it needs to be synthesised chemically for scientists to study its potential effectiveness as a drug. The first total synthesis of (–)-physovenine is described below.



racemic endo-**1**

7.1. Draw all possible stereoisomers of dicyclopentadiene **1**.

The synthesis starts from a racemic mixture of endo-**1**. Oxidation of racemic endo-**1** forms a racemic alcohol **2**. Enzyme-catalysed transesterification of racemic **2** with vinyl acetate will convert (+)-**2** to an ester, leaving unreacted (–)-**2** for further synthesis. (–)-**2** is an (*R*)-alcohol.

7.2. Draw the structures of (–)-**2**, **3** and **4**.

The conversion of racemic **2** to (–)-**2** is through a process called enzymatic kinetic resolution (EKR). A kinetic resolution can be either enzyme-catalysed or catalysed by chiral molecules. During a kinetic resolution, partial or complete resolution of a racemate is achieved by virtue of unequal rates of reaction of the enantiomers with a chiral reagent or catalyst. In this case, (+)-**2** reacts faster than (–)-**2**, allowing us to selectively convert (+)-**2** to an ester and obtain enantioenriched (–)-**2**.

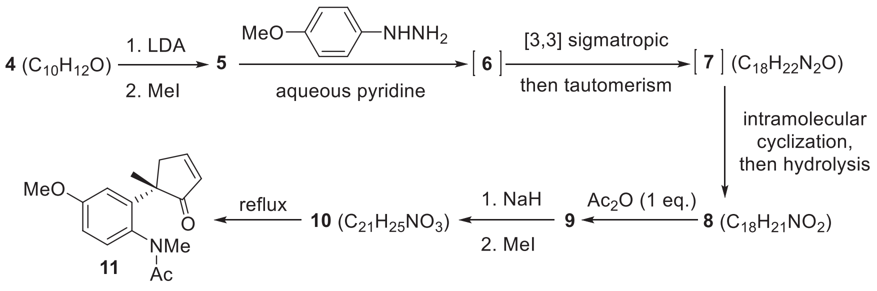
In an experiment, the initial concentration of racemic **2** is c_0(rac-**2**) = $0.01\ \mathrm{mol\ dm^{-3}}$. When the conversion of **2** to ester **C** is 65%, the reaction is quenched. The obtained ester **C** and unreacted alcohol **2** are separated. The enantiomeric excess (*ee*) of the unreacted alcohol **2** is 98%.

7.3. Write the transesterification reaction equation for the formation of ester **C**. Is the reaction reversible?

7.4. Calculate the *ee* of the ester **C**, assuming no side reactions occur and no loss of any materials.

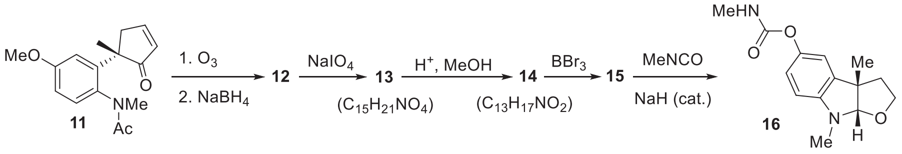
7.5. Compare the rate constants for the esterification of (+)-**2** and (–)-**2**, k_+ and k_- respectively. Which rate constant is larger? Calculate the selectivity (s) of this resolution. By definition, $\mathrm{s} = k_{\mathrm{faster}}/k_{\mathrm{slower}}$. For simplicity of calculation, consider the transesterification reaction as psuedo-first-order with respect to alcohol **2**.

7.6. Calculate the difference in activation energy for the esterification of (+)-**2** and (–)-**2**. $\Delta\mathrm{E_a} = (\mathrm{E_a})_{\mathrm{higher}} - (\mathrm{E_a})_{\mathrm{lower}}$. The reaction is conducted at 25°C.



Methylation of **4** generates a diastereomeric mixture **5**, which reacts with 4-methoxyphenylhydrazine to form a hemiaminal **8** via uncharged intermediates **6** and **7**.

7.7. Draw the structures of **5–10**.



Bicyclic compound **11** is further converted to another bicyclic compound **13**. Refluxing **13** in acidic methanol gives tricyclic compound **14**, which is eventually converted to (–)-physovenine **16**.

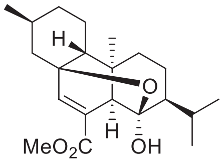
7.8. Draw the structures of **12–15**.

Problem 8. *Treasures from the Ocean*

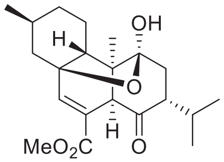
Chatancin **1** is an interesting natural product isolated and identified from a soft coral (*Sarcophyton* sp.) in 1990. It is able to inhibit PAF-induced platelet aggregation, thus it is a potential drug for hypotension and cardiovascular diseases.

Sarcophytin **2** is isolated and identified in 1998 from another soft coral (*Sarcophyton elegans*) of the same family, and has a similar structure compared to chatancin.

Due to their low natural abundance (12 ppm for chatancin and 50 ppm for sarcophytin), synthetic chemists have developed total synthesis routes to obtain sufficient amounts of both for biological study.



1
chatancin

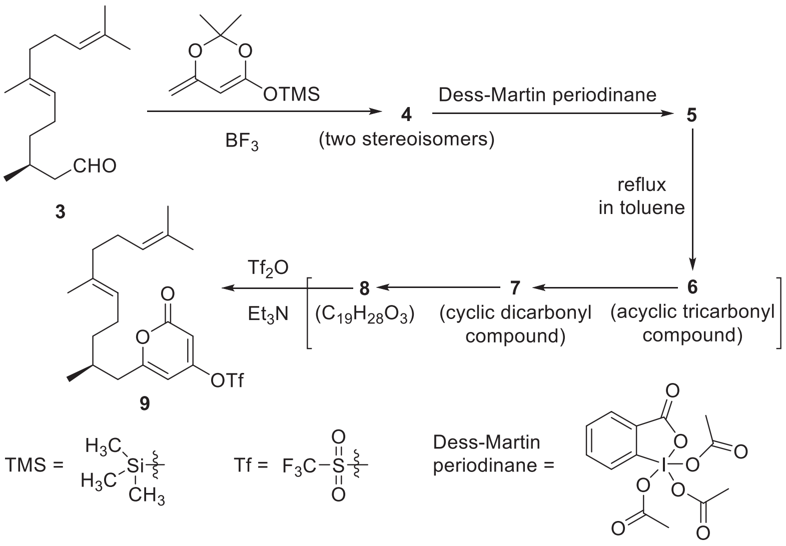


2
sarcophytin

8.1. The naturally occurring chatancin and sarcophytin are (+)-chatancin and (+)-sarcophytin, respectively. What does the symbol (+) mean?

A. Both molecules have more *R* chiral centres than *S* chiral centres.
B. Both molecules have less *R* chiral centres than *S* chiral centres.
C. Both molecules have more *D* chiral centres than *L* chiral centres.
D. Both molecules have less *D* chiral centres than *L* chiral centres.
E. None of the above.

8.2. Chatancin is quite acid sensitive and it is converted to anhydrochatancin ($C_{21}H_{30}O_3$, having 5 chiral centres) under mild acidic condition. Draw the structure of anhydrochatancin.



Scheme 1: Synthesis of key intermediate **9** for chatancin **1**.

The first half of synthesis of chatancin is to prepare a key intermediate **9** (Scheme 1). This synthesis starts from chiral aldehyde **3**, which is converted into a mixture of two stereoisomers of **4**. The two stereoisomers of **4** are not separated, but directly treated with Dess-Martin periodinane to produce compound **5**. Compound **5** is first refluxed in toluene with a trace amount of water and acid, and then treated with trifluoromethanesulfonic anhydride ($\mathrm{Tf_2O}$), finally forming triflate **9**, via a few intermediates: an acyclic tricarbonyl compound **6**, a cyclic dicarbonyl compound **7** and compound **8** with a formula of $\mathrm{C_{19}H_{28}O_3}$.

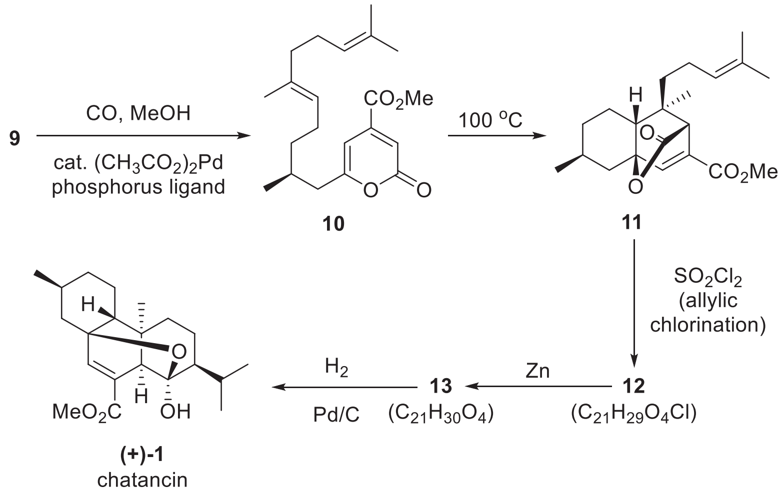
8.3. Draw the structures of compounds **4–8**.

After the synthesis of compound **9**, it is further converted to ester **10** by a Pd-catalyzed methoxycarbonylation using CO and methanol. Heating of ester **10** at 100°C for 4 days affords tricyclic lactone **11**. Compound **11** is then reacted with $\mathrm{SO_2Cl_2}$ to form an allylic chloride **12**, which is transformed into hemiketal **13** and finally chatancin (+)**-1** (Scheme 2).

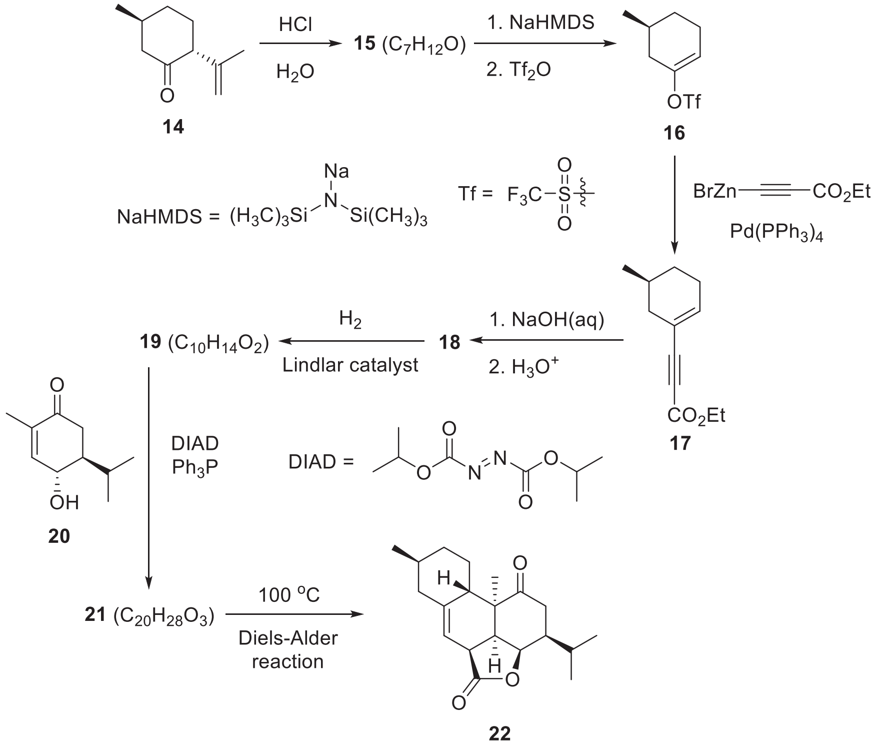
8.4. Draw stepwise mechanism for the conversion from **10** to **11**.

8.5. Draw the structures of compounds **12** and **13**.

Synthesis of sarcophytin **2** starts with chiral ketone **14**. Acid-catalyzed isomerization of **14**, followed by hydrolysis forms **15**. Compound **15** is then converted to **16** (together with a minor regioisomer), which is further converted to **17** via Pd-catalyzed Negishi coupling. **17** is further reacted to form **18**, **19** and **21**, which eventually gives tetracyclic key intermediate **22** by Diels–Alder reaction (Scheme 3).



Scheme 2: Synthesis of chatancin (+)-**1**.

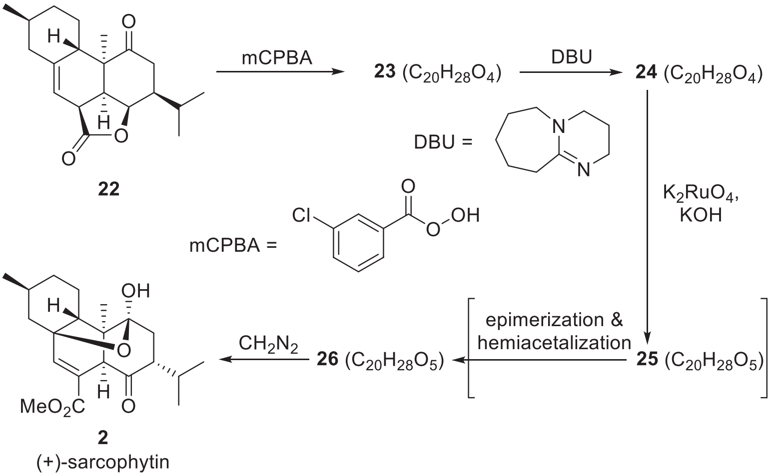


Scheme 3: Synthesis of key intermediate **22** for Sarcophytin **2**.

8.6. Draw the structure of compound **15**. Draw the stepwise mechanism for the formation of **15** from **14**.

8.7. Draw the structures of compound **18**, **19** and **21**.

Tetracyclic compound **22** is then reacted to form **23** and **24** (another tetracyclic compound). Acidic hydrolysis of lactone **24** does not yield a stable product for further reaction; hence the hydrolysis (and subsequent oxidation by K_2RuO_4) is conducted under basic conditions, giving intermediate **25**. Intermediate **25** is not separated but undergoes further epimerization and hemiacetalization under the same condition to form **26**. (+)-Sarcophytin **2** is finally formed when **26** is treated with CH_2N_2.



8.8. Draw the structures of compounds **23–26**.

6.2 Solutions to the Sample Problems

Problem 1. *So Simple, Yet So Unstable*

1.1.

Answer: $R_H = 2.179 \times 10^{-18}$ J

Solution: According to the equation, for quantum numbers $n = 2 \sim 7$, the electronic energies of H atom are:

$$E_2 = -R_H/4 \qquad E_3 = -R_H/9 \qquad E_4 = -R_H/16$$
$$E_5 = -R_H/25 \qquad E_6 = -R_H/36 \qquad E_7 = -R_H/49$$

The smallest energy difference in the Balmer series ($\Delta E_{23} = E_3 - E_2$) has the lowest frequency and hence the longest wavelength (656.5 nm). Accordingly, the other three wavelengths (486.1, 434.0 and 410.2 nm) correspond to ΔE_{24}, ΔE_{25} and ΔE_{26}, respectively. Using any of the values, R_H can be calculated. As a student, you just need to use one value to calculate R_H, but all the calculations will be shown below for your reference:

Transition	Energy gap	Wavelength λ	Energy of light $E = \frac{hc}{\lambda}$	Rydberg constant, R_H
$E_3 \to E_2$	$\Delta E_{23} = E_3 - E_2 = \frac{5}{36} R_H$	656.5 nm	3.027×10^{-19} J	2.179×10^{-18} J
$E_4 \to E_2$	$\Delta E_{24} = E_4 - E_2 = \frac{3}{16} R_H$	486.1 nm	4.086×10^{-19} J	2.179×10^{-18} J
$E_5 \to E_2$	$\Delta E_{25} = E_5 - E_2 = \frac{21}{100} R_H$	434.0 nm	4.577×10^{-19} J	2.180×10^{-18} J
$E_6 \to E_2$	$\Delta E_{26} = E_6 - E_2 = \frac{2}{9} R_H$	410.2 nm	4.843×10^{-19} J	2.179×10^{-18} J
$E_7 \to E_2$	$\Delta E_{27} = E_7 - E_2 = \frac{45}{196} R_H$			

Note that calculated value for the transition $E_5 \to E_2$ is slightly different from the other values. This is due to the round-off errors during calculation. It is quite common in physical chemistry calculations and will not affect following calculations most of the time because the difference is almost always in the last significant figure. The answer has four significant figures following the significant figure rules.

If you use the same method to calculate the wavelength of transition $E_7 \to E_2$, you will get a value of 397.1 nm and it is just beyond the visible light region (400–700 nm). Interestingly, this spectral line (and the $E_8 \to E_2$ line) can actually be seen with the naked eye. This is because the cut-off (400 nm) between visible and ultraviolet light is to a certain extent arbitrary since different people might have slightly different ability to see "into" the ultraviolet region.

1.2.

Answer: $\mathrm{IE(hydrogen)} = \Delta H_4 = 1312\ \mathrm{kJ\ mol^{-1}}$

Solution:

The ionisation of hydrogen atom can be considered as an excitation from ground state $(\mathrm{n} = 1)$ to the highest exited state $(\mathrm{n} = \infty)$. When $\mathrm{n} = \infty$, the electron is so far away from the nucleus that the nucleus has no electron surrounding it and the hydrogen atom is ionised to become $\mathrm{H^+}$.

Thus the ionisation energy $\mathrm{IE} = \Delta H_4 = \mathrm{E}_\infty - \mathrm{E}_1 = 0 - (-R_\mathrm{H}) = R_\mathrm{H} = 2.179 \times 10^{-18}\ \mathrm{J}$

This is the ionisation energy of one hydrogen atom. For 1 mole of hydrogen atoms:

$$\Delta H_4 = 2.179 \times 10^{-18}\ \mathrm{J} \times 6.022 \times 10^{23}\ \mathrm{mol^{-1}} = 1.312 \times 10^{6}\ \mathrm{J\,mol^{-1}} = 1312\ \mathrm{kJ\,mol^{-1}}$$

In case you have not found the value of R_H in question 1, you can use the given "dummy value" $3.000 \times 10^{-18}\ \mathrm{J}$ to solve the current question. The answer of ionisation energy will then be $1807\ \mathrm{kJ\ mol^{-1}}$. You can use this value $(1807\ \mathrm{kJ\ mol^{-1}})$ to continue the further calculations when needed, without a penalty. This is a common practice in IChO to avoid double penalty for students.

1.3.

Answer: Bond Energy $(\mathrm{F{-}CF_2O}) = \Delta H_8 = 90.8\ \mathrm{kJ\ mol^{-1}}$

Solution:

Equation (10) + (11) – (9) gives: $\mathrm{CF_3O} \rightarrow \mathrm{CF_2O} + \mathrm{F}$. This is equation (8).

By Hess's Law (see part 2.1.12), $\Delta H_8 = \Delta H_{10} + \Delta H_{11} - \Delta H_9 = (102.5 + 184.1 - 195.8)\ \mathrm{kJ\ mol^{-1}} = 90.8\ \mathrm{kJ\ mol^{-1}}$

1.4.

Answer: $\mathrm{EA(CF_3O)} = \Delta H_3 = -454.0\ \mathrm{kJ\ mol^{-1}}$

Solution:

Equation (6) + (7) + (8) gives: $\mathrm{CF_3O} + \mathrm{e^-} \rightarrow \mathrm{CF_3O^-}$. This is equation (3).

By Hess's Law, $\Delta H_3 = \Delta H_6 + \Delta H_7 + \Delta H_8 = (-216.7) + (-328.1) + 90.8\ \mathrm{kJ\ mol^{-1}} = -454.0\ \mathrm{kJ\ mol^{-1}}$

1.5.

Answer: $\Delta \mathrm{G}_2 < 1356.50\ \mathrm{kJ\ mol^{-1}}$

Solution:

Equations (12) and (13) are actually reversible reactions: $Cl^- + CF_3OH \overset{K}{\rightleftharpoons} CF_3O^- + HCl$

For equation (12), rate $r_{12} = k_{12}[CF_3OH][Cl^-]$

For equation (13), rate $r_{13} = k_{13}[CF_3O^-][HCl]$

At equilibrium, forward rate and reverse rate should be equal: $r_{12} = r_{13}$

Therefore, $K = \frac{[CF_3O^-][HCl]}{[Cl^-][CF_3OH]} = \frac{k_{12}}{k_{13}} > \frac{6.0 \times 10^{-10}}{1.0 \times 10^{-12}} = 600$

Since $\Delta G^o_{12} = -RT\ln K$, $\Delta G^o_{12} < -8.314 \times 298 \times \ln(600)\ \text{J mol}^{-1} = -15848.8\ \text{J mol}^{-1} = -15.85\ \text{kJ mol}^{-1}$

The Gibbs free energy of this equilibrium $HCl \rightleftharpoons H^+ + Cl^-$ has been given in the question as $\Delta G_{acid}(HCl) = 1372.35\ \text{kJ mol}^{-1}$

By Hess's Law, $\Delta G_2 = \Delta G_{12} + \Delta G_{acid}(HCl) < (-15.85) + 1372.35\ \text{kJ mol}^{-1} = 1356.50\ \text{kJ mol}^{-1}$

Note that this value is only the upper limit of ΔG_2. The researchers have also measured the lower limit of ΔG_2 and used both limits to estimate the value of ΔG_2 (see part 6).

1.6.

Answer: $\Delta H_2 = 1379.98\ \text{kJ mol}^{-1}$

Solution:

Simply apply the thermodynamic relationship $G = H - TS$, we know $\Delta G_2 = \Delta H_2 - T\Delta S_2$ when $\Delta T = 0$. Hence, $\Delta H_2 = \Delta G_2 + T\Delta S_2 = 1351.43 + 298 \times (95.81 \times 10^{-3})\ \text{kJ mol}^{-1} = 1379.98\ \text{kJ mol}^{-1}$

1.7.

Answer: $\Delta H_5 = 522\ \text{kJ mol}^{-1}$

Solution:

Equation (2) – (3) – (4) gives: $CF_3OH \rightarrow CF_3O + H$. This is equation (5).

By Hess's Law, $\Delta H_5 = \Delta H_2 - \Delta H_3 - \Delta H_4 = 1379.98 - (-454.0) - 1312\ \text{kJ mol}^{-1} = 522\ \text{kJ mol}^{-1}$

1.8.

Answer: $\Delta H_1 = -30\ \text{kJ mol}^{-1}$

Solution:

Consider the following two reactions:

Bond energy of $CF_3O{-}H$: $CF_3OH \rightarrow CF_3O + H$ (5) $\Delta H_5 = 522\ \text{kJ mol}^{-1}$

Bond energy of $HO{-}H$: $H_2O \rightarrow OH + H$ (14) $\Delta H_{14} = 492\ \text{kJ mol}^{-1}$

(14) – (5) gives: $H_2O + CF_3O \rightarrow OH + CF_3OH$. This is equation (1).

By Hess's Law, $\Delta H_1 = \Delta H_{14} - \Delta H_5 = 492–522\ \text{kJ mol}^{-1} = -30\ \text{kJ mol}^{-1}$

1.9.

Answer: ClF_3. T-shaped.

Solution:

Since **1** is a binary compound containing fluorine, we can assume compound **1** has the formula of AF_n, then:

$$\frac{19.00 \times n}{A + 19.00 \times n} = 61.7\%$$

(For simplicity, we use A to resemble the atomic mass of element A in this calculation, and the same applies to all other calculations.)

Solving this equation is quite simple, but we can still write an even simpler equation:

$$\frac{19.00 \times n}{A} = \frac{61.7\%}{100\% - 61.7\%}$$

This second equation is equivalent to the first (try to prove by yourself, either by chemistry or mathematics).

Solving the second equation gives us:

$A = 11.79n$ (If you prefer to use the first equation, you will get the same result here.)

We know that n must be an integer, hence:

n	Atomic mass of A	Possible element A (atomic mass)	Absolute error of atomic mass	Relative error of atomic mass
1	11.79	C (12.01)	−0.22	−1.8%
2	23.58	Mg (24.31)	−0.73	−3.0%
3	35.37	Cl (35.45)	−0.08	−0.23%
4	47.16	Ti (47.87)	−0.71	−1.5%
5	58.95	Ni (58.69)	0.26	0.44%
6	70.74	Ga (69.72)	1.02	1.5%

We usually prefer to write down the complete list for $n = 1 \sim 6$, since these are the most common stoichiometry numbers encountered (although 5 and 6 are less common than 1–4). Higher stoichiometry numbers (7 and 8) are very uncommon, if any. As far as we know, 7 and 8 never appeared in any IChO questions for the past 10 years, while 5 and 6 appeared rarely.

Let us now analyse the six possible compounds:

1. CF: Obviously the molecule cannot have only 1 carbon atom and 1 fluorine atom. Nevertheless, it could be C_xF_x, such as C_2F_2 (difluoroethyne, although its stability is questionable) or C_6F_6 (hexafluorobenzene). We can keep this in mind, although the error in atomic mass (–1.8%) is a bit too large.
2. MgF_2: This is a reasonable formula, but the error in atomic mass is too large (–3.0%).
3. ClF_3: This is an uncommon formula, which is probably quite exotic to many students. However, considering the smallest error (–0.23%) in atomic mass, we should give it a try. Since F is more electronegative than Cl, Cl should have a +3 oxidation state. This is not the common oxidation state of Cl (–1), but at the same time a +3 Cl is also not impossible. Recall some common Cl-containing compounds: $HClO$, $NaClO$ and $Ca(ClO)_2$ have a Cl in +1 oxidation state, and they are used in bleach and related products. $KClO_3$ has a Cl in +5 oxidation state, and it is used to prepare oxygen gas in high school laboratories in some countries. $HClO_4$ has a Cl in +7 oxidation state and is a very strong mineral acid, used in synthesis when an ultra-strong acid is needed. Since Cl can have +1, +5 and +7 oxidation states, it should also have a +3 oxidation state. In fact, $NaClO_2$ (with a Cl in +3 oxidation state) is the oxidising reagent in Pinnick oxidation (oxidation of aldehyde to carboxylic acid). After such a long analysis, the final conclusion is that ClF_3 is a very likely candidate for compound **1**, despite it being unfamiliar to many.
4. TiF_4: This is a cousin of our old friend $TiCl_4$ (a common Lewis acid used in many organic reactions), but the atomic mass is a bit off (–1.5% error).
5. NiF_5: The most common oxidation states of nickel are 0 and +2. Less common oxidation states are +1, +3 and +4, but +5 does not exist up to now. So we can safely rule out NiF_5.
6. GaF_6: Similarly, gallium has only 0, +1, +2, +3 and some negative oxidation states, but never +6.

This is a rather long analysis, because we want to show the students how to analyse such questions systematically, rather than trying your luck to "hit" the correct answer. When you are more experienced, you may choose to skip some steps but always bear in mind that the systematical way is the safest way to give the correct answer with the highest confidence level.

Now, we have three more familiar formulae (C_6F_6, MgF_2 and TiF_4) and one less familiar formula (ClF_3). Which one should be the correct answer? Shall we:

a) Choose a more familiar formula, but with a larger error in atomic mass?
b) Choose a less familiar formula, but with a smaller error in atomic mass?
c) Try to find any additional information to help us to decide?

We will leave this part here and see whether we can get some clue from the other parts of the question, then we can still come back.

1.10. and *1.11.*

Answer:

1: ClF_3	**2**: Cl_2	**3**: ClF
4: $COCl_2$	**5**: NaF	**6**: COF_2
7: $CF_3{-}O{-}Cl$	**8**: HCl	**9**: HF

Balanced equations:

a) $ClF_3 + Cl_2 \rightarrow 3ClF$

b) $COCl_2 + 2NaF \rightarrow COF_2 + 2NaCl$

c) $ClF + CF_2O \rightarrow CF_3{-}O{-}Cl$

d) $CF_3{-}O{-}Cl + HCl \rightarrow CF_3OH + Cl_2$

e) $CF_3OH \rightarrow CF_2O + HF$

Solution:

We shall rewrite the paragraph into reaction equations in a standard "chemistry language". This will facilitate our analysis:

a) **1** (61.7%w/w F) + **2** (element) [1:1 ratio] → **3** (b.p. = −100°C, pale yellow liquid)

b) **4** (12.1%w/w C) + **5** (45.2%w/w F, common inorganic salt) → **6** + **X** (very common inorganic salt)

c) **3** + **6** [1:1 ratio, nucleophilic addition] → **7** (47.3%w/w F)

d) **7** + **8** (binary compound, strong acid) [1:1 ratio] → CF_3OH + **2** (element)

e) CF_3OH → **6** + **9** (binary, 95.0%w/w F)

Which reaction shall we start from? Of course, there are different ways to solve the problem, depending on how much prior knowledge the students have. The authors prefer to choose a standard method so that all students can follow with minimum prior knowledge.

The elemental analysis data are given for certain compounds and they provide useful hints to the identities of the compounds. Among the values, one value is particularly large: 95.0%w/w F for binary compound **9**! Why do we choose this value? Because a particularly large value (roughly > 80%) or a particularly small value (roughly < 20%) for a binary compound means that there won't be too many choices, hence deduction is much easier. So let's try to deduce compound **9**:

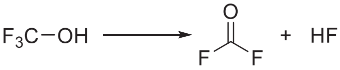
Assume binary compound **9** is BF_n (B is not necessarily boron, but just a symbol for the unknown element):

$$\frac{19.00 \times n}{B} = \frac{95.0\%}{100\% - 95.0\%}$$

Hence, $B = 1.00n$. It could be fairly easy to decide element B should be hydrogen and compound **9** is HF. HeF_4 or LiF_7 may also satisfy the numerical value but neither formula makes sense chemically. Note that the fluorine mass percentage in HF is indeed 94.96% rather than 95.00%, so we shall bear in mind that 95.0% actually means any value between 94.95% and 95.04% (due to rounding) and we shall look at a small range (rather than a single value) in atomic mass calculations. This applies to all mass percentage or atomic mass calculations.

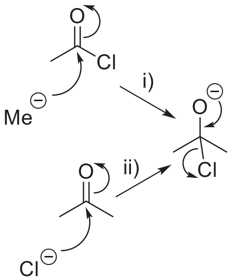
Now that we are pretty confident that compound **9** is HF, we can do a simple "subtraction" in equation (e): compound **6** $= CF_3OH - HF = CF_2O$. Although the stoichiometry of equation (e) is not specified in the paragraph, we can still reasonably <u>assume</u> that CF_3OH and HF is in a 1:1 ratio, since there is only one hydrogen atom in each molecule. So what is CF_2O? It seems like an organic compound since there is a carbon, but there are no hydrogens in the molecule. Organic molecules having halogen atoms are usually organohalides (alkyl halides or aryl halides), in which some hydrogen atoms are replaced by halogen atoms. Here we will do the reverse: replacing the fluorine atoms in CF_2O by hydrogen atoms, and we get CH_2O. Aha, this is familiar and it is formaldehyde! Thus,

Equation (e) is then:



It all makes sense now, since a tetrahedral carbon bonded to both oxygen and halogen is not stable and an elimination reaction will occur to kick out the halogen as a leaving group (although fluoride is a poorer leaving group than chloride, bromide or iodide). Here is a more familiar organic example:

The common tetrahedral intermediate might be formed by either i) addition of a methyl anion (from Grignard or Gilman reagent) towards the acid chloride; or ii) addition of a chloride anion towards the ketone. The obtained tetrahedron intermediate is unstable: carbon-oxygen π-bond will form preferably and chloride will be eliminated, generating the ketone and chloride. That is the reason why aldol condensation (using aldehydes or ketones as electrophiles) can be acid-catalysed (using HCl) without any worries that chloride will add onto the aldehyde or ketone.



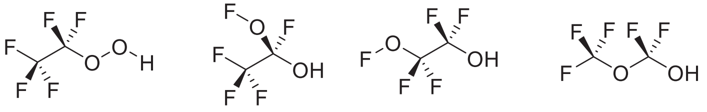
The identity of compound **6** is CF_2O, a cousin of CCl_2O (phosgene, a notorious chemical weapon used in World War I, causing 85,000 deaths and also in World War II by Japanese against Chinese army). The reactivity of CF_2O should also be similar to CCl_2O (more often written as $COCl_2$) — nucleophilic acyl substitution reaction, just like an acid chloride ($RCOCl$).

At this point, you may still have a minor query. All these conclusions up to now are based on an assumption that CF_3OH and HF is in 1:1 ratio in equation (e). How do we know that in the first place? Is there a way to prove the assumption? Indeed, there is at least one way:

CF_3OH has only one hydrogen atom, so to produce 1 equivalent of HF, at least 1 equivalent of CF_3OH is needed. There might be 2, 3 or even more equivalents of CF_3OH (molar ratio of 2:1 or 3:1), but a molar ratio of 1:2 or 1:3 is definitely impossible. Let's examine a few ratios:

Molar ratio	Equation	Degree of unsaturation of organic product
2:1	$2CF_3OH \rightarrow HF + C_2HF_5O_2$	$(2\times2+2-1-5)/2 = 0$
3:1	$3CF_3OH \rightarrow HF + C_3H_2F_8O_3$	$(3\times2+2-2-8)/2 = -1$
3:2	$3CF_3OH \rightarrow 2HF + C_3HF_7O_3$	$(3\times2+2-1-7)/2 = 0$
4:1	$4CF_3OH \rightarrow HF + C_4H_3F_{11}O_4$	$(4\times2+2-3-11)/2 = -2$
4:3	$4CF_3OH \rightarrow 3HF + C_4HF_9O_4$	$(4\times2+2-1-9)/2 = 0$
…	…	…

The degree of unsaturation is also called double bond equivalents (DBEs). It is calculated as: $(C\times2+2-H-X+N)/2$ and it must be a non-negative integer (0, 1, 2, 3, …) You can try other ratios, but the only reasonable degree of unsaturation is 0. As an example, we have shown a few possible structures of $C_2HF_5O_2$ below:



They all either contain unstable bonds, such as the $O–O$ bond (1st structure) and $O–F$ bond (2nd and 3rd structures), or have an unstable hemiacetal structure (4th structure). Therefore, $C_2HF_5O_2$ is very unlikely to be compound **6**. Likewise, the other structures are also unlikely (try to draw them by yourself as a practice).

Finally, we have confirmed the identities of compounds **6** and **9**. We shall rewrite equations (a)–(e) to include the information deduced so far:

a) **1** (61.7%w/w F) + **2** (element) [1:1 ratio] → **3** (b.p. = −100°C, pale yellow liquid)

b) **4** (12.1%w/w C) + **5** (45.2%w/w F, common inorganic salt) → **6**: $CF_2O + X$ (very common inorganic salt)

c) **3** + **6**: CF_2O [1:1 ratio, nucleophilic addition] → **7** (47.3%w/w F)

d) **7** + **8** (binary compound, strong acid) [1:1 ratio] → CF_3OH + **2** (element)

e) CF_3OH → **6**: CF_2O + **9**: HF (binary, 95.0%w/w F)

Since the formula and structure of compound **6** is known now, we have some additional information about equations (b) and (c). Equation (b) is probably easier, since more information is provided in equation (b).

Compound **5** is a common inorganic salt with 45.2%w/w F, hence we can write compound **5** as ZF_n. Z may contain single or multiple elements, and we may consider Z as a whole entity (with $+n$ oxidation state) for the moment:

$$\frac{19.00 \times n}{Z} = \frac{45.2\%}{100\% - 45.2\%}$$

Therefore, $Z = 23.04n$. When $n = 1$, Z is just sodium and compound **5** is NaF (45.25%w/w F). Of course, you may try larger values of n and find other formulae like $LiKF_2$ (45.22%w/w F) or GaF_3 (44.98%w/w F), but NaF is obviously more common than the others. Note that the %w/w F in $LiKF_2$ (45.22%w/w F) is indeed closer to the given value (45.2%w/w F) than NaF (45.25%w/w F). However, this does not mean $LiKF_2$ should be a better answer than NaF. After all, we are having a chemistry competition rather than a mathematics competition, so we shall always consider chemistry first.

Equation (b) is rewritten again as:

b) **4** (12.1%w/w C) + NaF (45.2%w/w F, common inorganic salt) → **6**: CF_2O + **X** (very common inorganic salt)

Since compound **6** (CF_2O) does not contain Na element, **X** must be a sodium salt. Also, the anion(s) in **X** should come from compound **4**, since fluorine element in NaF ends up into CF_2O. In addition, the oxygen element in CF_2O must come from compound **4**. So, equation (b) can be further re-written as (Y may be a single element or a group of atoms, but we will consider it as a single element first for simplicity):

b) **4**: CO_aY_b (12.1%w/w C) + NaF (45.2%w/w F, common inorganic salt) → **6**: CF_2O + **X**: NaY_cO_d (very common inorganic salt)

$$\frac{12.01}{16.00a + bY} = \frac{12.1\%}{100\% - 12.1\%}$$

Hence, $16a + bY = 87.25$. Mathematically, a can only be up to 5:

a	bY	b	Y	Element Y	Compound **4**
5	7.25	1	7.25	Li (6.941)	$LiCO_5$ (12.14%w/w C)
4	23.25	1	23.25	Na (22.99)	$NaCO_4$ (12.13%w/w C)
3	39.25	1	39.25	K (39.10)	KCO_3 (12.12%w/w C)
		6	6.54	Li (6.941)	Li_6CO_3 (11.81%w/w C)
2	55.25	1	55.25	Fe (55.85)	$FeCO_2$ (12.03%w/w C)
		5	11.05	B (10.81)	CB_5O_2 (12.25%w/w C)
1	71.25	2	35.625	Cl (35.45)	$COCl_2$ (12.14%w/w C)
		3	23.75	Mg (24.31)	Mg_3CO (11.90%w/w C)
		5	14.25	N (14.01)	CON_5 (12.25%w/w C)

Among all these, some have too high (CON_5) or too low (Li_6CO_3 and Mg_3CO) %w/w C value. Some have the correct %w/w C value, but an unreasonable formula ($LiCO_5$, $NaCO_4$, …). In particular, KCO_3 is incorrect as it should be K_2CO_3. The only correct formula is $COCl_2$ with 12.14%w/w C, and this completes equation (b) nicely:

b) **4**: $COCl_2$ (12.1%w/w C) + NaF (45.2%w/w F, common inorganic salt) → **6**: CF_2O + **X**: NaCl (very common inorganic salt)

$COCl_2 + 2NaF \rightarrow CF_2O + 2NaCl$ [including stoichiometry coefficients]

On top of that, NaCl is indeed a very common inorganic salt (more common than NaF).

All equations are now rewritten once more as:

a) **1** (61.7%w/w F) + **2** (element) [1:1 ratio] → **3** (b.p. = −100°C, pale yellow liquid)

b) **4**: $COCl_2$ (12.1%w/w C) + **5**: NaF (45.2%w/w F, common inorganic salt) → **6**: CF_2O + **X**: NaCl (very common inorganic salt)

c) **3** + **6**: CF_2O [1:1 ratio, nucleophilic addition] → **7** (47.3%w/w F)

d) **7** + **8** (binary compound, strong acid) → CF_3OH + **2** (element)

e) CF_3OH → **6**: CF_2O + **9**: HF (binary, 95.0%w/w F)

Compound **3** contains fluorine from compound **1**, hence we can assume that formula of compound **3** is ZF_n (Z may be a combination of multiple elements). Then, the 1:1 ratio addition product of **3** and **6** (equation c) shall give $CZF_{n+2}O$ (compound **7**). Therefore:

$$\frac{19.00(n+2)}{12.01 + Z + 16.00} = \frac{47.3\%}{100\% - 47.3\%}$$

Solving it gives: $Z = 14.33 + 21.17n$. When $n = 1$, $Z = 35.50$, which corresponds to Cl (35.45). This seems to be a good match, since the atomic mass is quite close and chlorine is a possible element in compound **1** (see part 9 above). In addition,

ClF is a pseudohalogen, hence it should have similar properties to F_2 and Cl_2. For example, its colour (pale yellow) is between F_2 (pale yellow) and Cl_2 (yellow-green). Now, we can confirm that compound **3** is ClF (although unfamiliar) and compound **1** is ClF_3. In ClF, Cl is partially positively charged and F is partially negatively charged, hence F atom will add onto carbon and Cl atom will add onto oxygen in the nucleophilic addition reaction (equation c). Thus, the equations are:

a) **1**: ClF_3 (61.7%w/w F) + **2** (element) [1:1 ratio] → **3**: ClF (b.p. = –100°C, pale yellow liquid)

b) **4**: $COCl_2$ (12.1%w/w C) + **5**: NaF (45.2%w/w F, common inorganic salt) → **6**: CF_2O + **X**: $NaCl$ (very common inorganic salt)

c) **3**: ClF + **6**: CF_2O [1:1 ratio, nucleophilic addition] → **7**: $CF_3–O–Cl$ (47.3%w/w F)

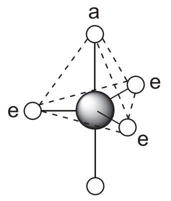
d) **7**: $CF_3–O–Cl$ + **8** (binary compound, strong acid) → CF_3OH + **2** (element)

e) CF_3OH → **6**: CF_2O + **9**: HF (binary, 95.0%w/w F)

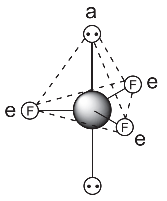
Finally, based on equation (a), element **2** must be Cl_2. Substituting this (**2** = Cl_2) into equation (d) means that compound **8** is HCl.

There is still one more thing that we have not explained — the geometry of compound **1**, ClF_3. This is a typical question that we can apply VSEPR theory (part 3.3.1). Chlorine is the centre atom, using 3 of its valance electrons to form 3 single bonds with 3 fluorine atoms. The remaining 4 electrons on chlorine form 2 lone pairs, thus chlorine has a total of 5 electron regions and 2 lone pairs. By checking Table 3.2, it is T-shaped.

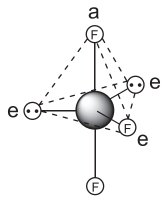
However, why do 5 electron regions and 2 lone pairs give the molecule a T-shape? This may remain unclear to some students. Molecules with 5 electron regions adopt a trigonal bipyramidal geometry, if we consider all the electron regions. In the trigonal bipyrimidal shape, 3 atoms are located in the central horizontal plane (labelled with e) and 2 atoms are located perpendicular to this plane (labelled with a). The 3 coplanar atoms are at the equatorial positions, while the 2 atoms above and below the plane are at the axial positions. The equatorial positions and axial positions are inequivalent. We can simply measure the bond angles: angle e-centre-e is 120°, angle e-centre-a is 90°, and angle a-centre-a is 180°. Also, the repulsion of two electron domains will be the greatest when they are located at e-a positions because this has the smallest bond angle 90°.



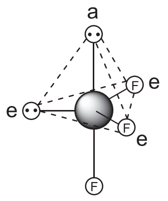
(only one pyramid is drawn for simplicity)



A



B



C

In ClF_3, two lone pairs may occupy two axial positions (structure A), or two equatorial positions (structure B), or one axial & one equatorial position (structure C). Let us examine the electron repulsions in these three structures (L denotes the lone pair):

Repulsion angle	Structure A	Structure B	Structure C
90° (e-center-a)	F-L × 6	F-F × 2 & F-L × 4	F-F × 2 & F-L × 3 & L-L × 1
120° (e-center-e)	F-F × 3	F-L × 2 & L-L × 1	F-F × 1 & F-L × 2
180° (a-center-a)	L-L × 1	F-F × 1	F-L × 1

Each structure has 10 pairs of repulsions, but these repulsions are of different angles. The repulsion is strongest when it is between two lone pairs (L-L), followed by lone pair-bonding pair (F-L), and the weakest between two bonding pairs (F-F). Since the repulsion between 2 electron regions 90° to each other is greater that between those 120° or 180° to each other, the repulsion between electron regions 90° to each other should be dominant. Comparing the 3 structures across the first row of the table above, structure B has the weakest repulsion, and thus is the most stable structure. When we decide the geometry of a molecule, atoms are "observable" but lone pairs are not "observable", hence the geometry of ClF_3 (structure B) is T-shaped.

Comments on Q1:

This question contains both physical chemistry and inorganic chemistry. It also requires some related organic chemistry knowledge to determine the reactivities. Such hybrid questions are actually encouraged by the International Chemistry Olympiad community, because many real chemistry problems are indeed cross-disciplinary, requiring knowledge from all areas of chemistry.

The difficulty in the physical chemistry part is to find out the Hess's Law relationships, e.g. which equations added up (or subtracted) will give which equation. Special attention should be given to whether a species is a radical or an ion. Once such a relationship is established, the Hess's Law calculation should be rather straightforward. The questions are ordered in such a way that the answers of previous questions are used in the following questions. Naturally, students should follow the sequence of the question itself.

The inorganic chemistry part has a lot of given information, but there is no "question sequence" that you have seen in the physical chemistry part. This is quite common in inorganic and organic questions. The first reaction may not be the easiest reaction to decipher. Hints are usually given but almost always hidden. The hints are usually the properties of certain compounds rather than the reaction itself.

Such properties include (but are not limited to) state, colour, smell and composition (binary, ternary, elemental analysis, combustion product). In some questions, stoichiometric ratio is critical in solving the questions. In such questions, some calculations are usually needed, but always bear in mind that calculations should be used as a tool to solve the chemistry problem, and we should still rely on our chemistry knowledge to find out the most reasonable chemistry answer.

Problem 2. *Electrochemistry Puzzles*

2.1.

Answer: $0.137\ \mathrm{mol\cdot dm^{-3}}$

Solution: First, we must find the E^0 of the overall reaction:

$$[\mathrm{Cu(CN)_2}]^-_{(aq)} + \mathrm{Ag}_{(s)} + \mathrm{Cl}^-_{(aq)} \rightarrow \mathrm{AgCl}_{(s)} + \mathrm{Cu}_{(s)} + 2\ \mathrm{CN}^-_{(aq)}$$

Based on the individual equations:

$$\mathrm{Ag} \rightarrow \mathrm{Ag}^+ + \mathrm{e}^- \qquad E^0 = -0.800\ \mathrm{V}$$

$$\mathrm{Cu}^+ + \mathrm{e}^- \rightarrow \mathrm{Cu} \qquad E^0 = +0.518\ \mathrm{V}$$

$$[\mathrm{Cu(CN)_2}]^- \rightarrow \mathrm{Cu}^+ + 2\ \mathrm{CN}^- \qquad E^0 = \frac{RT}{nF}\ln K = -0.946\ \mathrm{V}$$

$$\mathrm{Ag}^+ + \mathrm{Cl}^- \rightarrow \mathrm{AgCl} \qquad E^0 = \frac{RT}{nF}\ln K = +0.576\ \mathrm{V}$$

The overall $E^0 = -0.800 + 0.518 - 0.946 + 0.576 = -0.652\ \mathrm{V}$
Using the Nernst equation:

$$E = E^0 - \frac{RT}{nF}\ln Q$$

$$-0.440 = -0.652 - \frac{(8.314)(298)}{(1)(96485)}\ln\frac{[\mathrm{CN}^-]^2}{[\mathrm{Cl}^-][\mathrm{Cu(CN)}_2^-]}$$

As $K_f([\mathrm{Cu(CN)_2}]^-)$ is large, we may assume that $[\mathrm{Cu}^+] \ll [\mathrm{Cu(CN)}_2^-]$, and that $[\mathrm{Cu(CN)}_2^-] \approx 1.00\times10^{-3}\ \mathrm{mol\cdot dm^{-3}}$. We are thus able to solve for $[\mathrm{CN}^-] = 5.096\times10^{-4}$ $\mathrm{mol\cdot dm^{-3}}$.

From the acid-equilibria of HCN, we are able to find $[\mathrm{H}^+]$:

$$[\mathrm{HCN}] + [\mathrm{CN}^-] = 1.00\times10^{-3}\ \mathrm{mol\cdot dm^{-3}}$$

$$[\mathrm{HCN}] = 4.904\times10^{-4}\ \mathrm{mol\cdot dm^{-3}}$$

$$K_a = 10^{-9.21} = \frac{[\mathrm{H}^+][\mathrm{CN}^-]}{[\mathrm{HCN}]}$$

$$[\mathrm{H}^+] = 5.934\times10^{-10}\ \mathrm{mol\cdot dm^{-3}}$$

Using $[\mathrm{H^+}]$, we are able to find $[\mathrm{X^-}]$:

$$[\mathrm{X^-}]+[\mathrm{HX}]=0.1\ \mathrm{mol\cdot dm^{-3}}$$

$$\frac{[\mathrm{X^-}]}{[\mathrm{HX}]}=\frac{K_a}{[\mathrm{H^+}]}=\frac{10^{-9.50}}{5.934\times10^{-10}}=0.5329$$

$$[\mathrm{X^-}]=0.03476\ \mathrm{mol\cdot dm^{-3}}$$

Applying the charge balance condition to the cell solution, we have:

$$[\mathrm{K^+}]+[\mathrm{H^+}]+[\mathrm{Cu^+}]=[\mathrm{CN^-}]+[\mathrm{Cu(CN)_2^-}]+[\mathrm{X^-}]+[\mathrm{OH^-}]$$

Since the solution is rather basic, we may ignore $[\mathrm{H^+}]$ since $[\mathrm{H^+}]\ll[\mathrm{OH^-}]$. Similarly, we also assume $[\mathrm{Cu^+}]\ll[\mathrm{Cu(CN)_2^-}]$.Thus, we are able to find $[\mathrm{K^+}]=0.03629\ \mathrm{mol\cdot dm^{-3}}$. $\mathrm{K^+}$ ions are formed from KOH, $\mathrm{K[Cu(CN)_2]}$ and KCN.

$$[\mathrm{KOH}]=0.03629-1.00\times10^{-3}-1.00\times10^{-3}=0.03429\ \mathrm{mol\cdot dm^{-3}}$$

Accounting for the dilution from 25.0 mL to 100 mL, the original concentration of KOH is:

$$[\mathrm{KOH}]_0=4\times0.03429=0.137\ \mathrm{mol\cdot dm^{-3}}$$

2.2.

Answer and **Solution:** $\mathrm{CN^-}$ is a soft base as the negative charge is delocalised. $\mathrm{Cu^+}$ and $\mathrm{Ag^+}$ are soft metals as they have low charge density. From the Hard-Soft Acid-Base theory, soft acid-soft base interactions are preferred as they allow the formation of strong covalent interactions. To further stabilise the complexes, $\mathrm{CN^-}$ is a good π-acceptor ligand while $\mathrm{Ag^+}$ and $\mathrm{Cu^+}$ are electron-rich metals. The metal-ligand bond can be further strengthened by $\mathrm{d}\pi\rightarrow\pi^*$ backdonation.

2.3.

Answer: $-0.141\ \mathrm{V}$

Solution:

Applying Nernst Equation:

$$E=E^0-\frac{RT}{nF}\ln Q$$

$$0.222-0.393=E^0-\frac{(8.314)(298)}{(2)(96485)}\ln\frac{1}{0.100}$$

$$E^0=-0.141\ \mathrm{V}$$

2.4.

Answer: $-0.394\ \mathrm{V}$

Solution: $n_{EDTA}=\dfrac{5.00}{336}=0.01488\ \mathrm{mol}$

Using ICE table,

$$K_f = \frac{[\text{Complex}]}{[\text{M}^{2+}][\text{EDTA}]}$$

$$= \frac{x}{(0.1 - x)(0.01488 - x)} = 22.3$$

$$x = 9.934 \times 10^{-3}\ \text{mol} \cdot \text{dm}^{-3}$$

$$[\text{M}^{2+}] = 0.1 - 9.934 \times 10^{-3} = 0.090066\ \text{mol} \cdot \text{dm}^{-3}$$

Applying Nernst Equation again,

$$E = E^0 - \frac{RT}{nF}\ln Q$$

$$E = -0.141 - \frac{(8.314)(298)}{(2)(96485)}\ln\left(\frac{1}{0.090066}\right) = 0.222 + E_{\text{cell}}$$

$$E_{\text{cell}} = -0.394\ \text{V}$$

2.5.

Answer: $\text{X} = +0.492\ \text{V},\ \text{Y} = +0.138\ \text{V}$

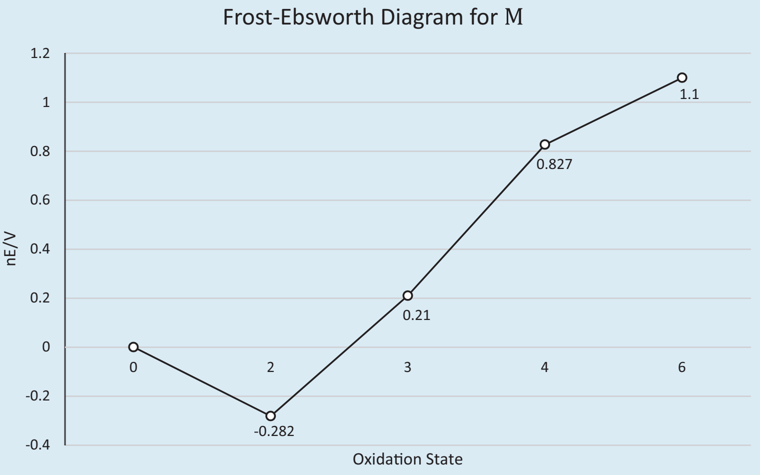
Solution: By applying the shortcut method,

$$0.0700 = \frac{\text{X} + 2 \times (-0.141)}{3},\ \ \text{X} = +0.492\ \text{V}$$

$$0.346 = \frac{2\,\text{Y} + 0.617 + \text{X}}{4},\ \ \text{Y} = +0.138\ \text{V}$$

2.6.

Answer:



Solution: We must find the values of the points using a table:

N	Species	nE/V (relative to $M(0)$)
0	M	0
+2	M^{2+}	$2(-0.141) = -0.282$
+3	M_2O_3	$-0.282 + 0.492 = 0.210$
+4	MO_2	$0.617 + 0.210 = 0.827$
+6	MO_4^{2-}	$0.827 + 2(0.138) = 1.10$

The Frost-Ebsworth diagram can be plotted using values of N as the x-axis and values of nE as the y-axis.

2.7.

Answer: +2

Solution: The most stable oxidation state is the lowest point on Frost-Ebsworth diagram.

2.8.

Answer and **Solution:**

Disproportionation at convex point, where oxidation state is +4: MO_2

Note that disproportionation occurs towards the 2 neighbouring oxidation states (+3 and +6), with the half equation given below:

$$2\ H_2O + MO_2 \rightarrow MO_4^{2-} + 4\ H^+ + 2\ e^- \qquad E^0 = -0.138\ V$$

$$2\ H^+ + 2\ MO_2 + 2\ e^- \rightarrow M_2O_3 + H_2O \qquad E^0 = +0.617\ V$$

Overall disproportionation reaction:

$$3\ MO_2 + H_2O \rightarrow MO_4^{2-} + M_2O_3 + 2\ H^+ \qquad E^0 = 0.617 - 0.138 = +0.479\ V$$

$$K = e^{\frac{2(96485)(0.479)}{(8.314)(298)}} = 1.59 \times 10^{16}$$

Problem 3. *Sulfur Chemistry*

3.1.

Answer: 6.89×10^4 tonnes

Solution:

First, we need to write the balanced equation for the combustion of oil (represented by octane): $2\ C_8H_{18} + 25\ O_2 \rightarrow 16\ CO_2 + 18\ H_2O$

The energy generated from this equation is the enthalpy change ΔH_r. From part 2.1.12, $\Delta H_r^0 = \sum \text{Bond Energy (broken)} - \sum \text{Bond Energy (formed)}$.

In the current reaction, C–C and C–H bonds in octane and O=O bonds in oxygen are broken. Meanwhile, H–O bonds form in water and C=O bonds form in CO_2. Therefore,

$$\begin{aligned}\Delta H_r &= [(348\times 7+412\times 18)\times 2+497\times 25]-[799\times 2\times 16+463\times 2\times 18]\ \text{kJ mol}^{-1}\\ &= -10107\ \text{kJ mol}^{-1}\end{aligned}$$

The enthalpy change is negative, indicating that the reaction is exothermic. Also, this enthalpy of combustion is per mole of reaction but two moles of octane are consumed in each mole of reaction, hence the enthalpy of combustion per mole of octane is $5053.5\ \text{kJ mol}^{-1}$.

The annual energy consumption from oil products is $3.9\times 10^{20}\ \text{J}\times 31.3\% = 1.22\times 10^{20}\ \text{J}$

Since the efficiency of energy utilization is 80%, the combustion of octane must generate $1.22\times 10^{20}\ \text{J}/80\% = 1.525\times 10^{20}\ \text{J}$ of energy, corresponding to $1.525\times 10^{20}/5053.5\times 10^{3} = 3.02\times 10^{13}\ \text{mol}$ of octane. Hence, the mass of octane is $345\times 10^{13}\ \text{g} = 3.45\times 10^{15}\ \text{g} = 3.45\times 10^{12}\ \text{kg} = 3.45\times 10^{9}$ tonnes.

Since octane contains 10 ppm of sulfur by mass, the mass of sulfur in octane is 3.45×10^{4} tonnes. Combustion of the sulfur would produce 6.89×10^{4} tonnes of SO_2.

3.2.

Answer: $a = 1$

Solution:

Among the three curves, only the 3rd curve ($\ln[SO_3^{2-}]$–t) is linear. This means that the reaction is first order with respect to SO_3^{2-}. If the $[SO_3^{2-}]$–t curve is linear, the reaction is zeroth order with respect to SO_3^{2-}. If the $1/[SO_3^{2-}]$–t curve is linear, the reaction is second order with respect to SO_3^{2-}.

3.3.

Answer: $b = 0.5$

Solution:

Since $k' = k[O_2]^b$, taking natural logarithm on both sides gives: $\ln k' = \ln k + b\ln[O_2]$

Now, two more rows can be added to the table:

$[O_2]$	212.0	390.7	652.2	979.2
k'	741.3	955.0	1230.3	1584.9
$\ln[O_2]$	5.357	5.968	6.480	6.887
$\ln k'$	6.608	6.862	7.115	7.368

Hence, $b = \frac{\Delta(\ln k')}{\Delta(\ln[\mathrm{O_2}])}$. Choosing any pair of values should give us the same results and b = 0.5 (after rounding off).

3.4.

Answer: $\frac{\mathrm{d}[\mathrm{SO_4^{2-}}]}{\mathrm{d}t} = \frac{k_2[\mathrm{O_2}]}{2}\sqrt{\frac{k_1[\mathrm{Fe^{3+}}][\mathrm{SO_3^{2-}}]}{2k_5}}$

Solution:

The overall reaction is: $2\ \mathrm{SO_3^{2-}} + \mathrm{O_2} \rightarrow 2\ \mathrm{SO_4^{2-}}$

In order to identify the intermediates in the reaction mechanism, we must first identify the reactants and products.

Reactants: $\mathrm{SO_3^{2-}}$, $\mathrm{O_2}$

Products: $\mathrm{SO_4^{2-}}$ (product), $\mathrm{S_2O_6^{2-}}$ (side product)

Intermediates: $\mathrm{SO_3^{\bullet-}}$, $\mathrm{SO_5^{\bullet-}}$, $\mathrm{SO_5^{2-}}$

We can assume that the intermediates are in steady state, $\frac{\mathrm{d}[I]}{\mathrm{d}t} \approx 0$. Thus, we have

$$\frac{\mathrm{d}[\mathrm{SO_3^{\bullet-}}]}{\mathrm{d}t} = k_1[\mathrm{Fe^{3+}}][\mathrm{SO_3^{2-}}] - k_2[\mathrm{SO_3^{\bullet-}}][\mathrm{O_2}] + k_3[\mathrm{SO_5^{\bullet-}}][\mathrm{SO_3^{2-}}] - 2k_5[\mathrm{SO_3^{\bullet-}}]^2 \approx 0 \qquad (1)$$

$$\frac{\mathrm{d}[\mathrm{SO_5^{\bullet-}}]}{\mathrm{d}t} = k_2[\mathrm{SO_3^{\bullet-}}][\mathrm{O_2}] - k_3[\mathrm{SO_5^{\bullet-}}][\mathrm{SO_3^{2-}}] \approx 0 \qquad (2)$$

$$\frac{\mathrm{d}[\mathrm{SO_5^{2-}}]}{\mathrm{d}t} = k_3[\mathrm{SO_5^{\bullet-}}][\mathrm{SO_3^{2-}}] - k_4[\mathrm{SO_5^{2-}}][\mathrm{SO_3^{2-}}] \approx 0 \qquad (3)$$

Equation (1) + (2) gives:

$$k_1[\mathrm{Fe^{3+}}][\mathrm{SO_3^{2-}}] = 2k_5[\mathrm{SO_3^{\bullet-}}]^2$$

Hence,

$$[\mathrm{SO_3^{\bullet-}}] = \sqrt{\frac{k_1[\mathrm{Fe^{3+}}][\mathrm{SO_3^{2-}}]}{2k_5}} \qquad (4)$$

Substitute (4) into (2):

$$[\mathrm{SO_5^{\bullet-}}] = \frac{k_2\sqrt{\frac{k_1[\mathrm{Fe^{3+}}][\mathrm{SO_3^{2-}}]}{2k_5}}[\mathrm{O_2}]}{k_3[\mathrm{SO_3^{2-}}]} = \frac{k_2[\mathrm{O_2}]}{k_3}\sqrt{\frac{k_1[\mathrm{Fe^{3+}}]}{2k_5[\mathrm{SO_3^{2-}}]}} \qquad (5)$$

Substitute (5) into (3):

$$[\mathrm{SO_5^{2-}}] = \frac{k_3}{k_4}[\mathrm{SO_5^{\bullet-}}] = \frac{k_2[\mathrm{O_2}]}{k_4}\sqrt{\frac{k_1[\mathrm{Fe^{3+}}]}{2k_5[\mathrm{SO_3^{2-}}]}} \qquad (6)$$

Substitute (6) into the comproportionation step:

$$\begin{aligned}\frac{\mathrm{d}[\mathrm{SO_4^{2-}}]}{\mathrm{d}t} &= \frac{k_4}{2}[\mathrm{SO_5^{2-}}][\mathrm{SO_3^{2-}}] \\ &= \frac{k_4}{2}\frac{k_2[\mathrm{O_2}]}{k_4}\sqrt{\frac{k_1[\mathrm{Fe^{3+}}]}{2k_5[\mathrm{SO_3^{2-}}]}}[\mathrm{SO_3^{2-}}] = \frac{k_2[\mathrm{O_2}]}{2}\sqrt{\frac{k_1[\mathrm{Fe^{3+}}][\mathrm{SO_3^{2-}}]}{2k_5}} \qquad (7)\end{aligned}$$

Equation (7) is the rate law of the overall reaction. This rate law shows that the reaction is first order in O_2 and half order in SO_3^{2-}.

3.5.

Answer: $\frac{\mathrm{d}[SO_4^{2-}]}{\mathrm{d}t} = \sqrt{\frac{k_1 k_2 k_3 [O_2][Fe^{3+}]}{8k_6}}\,[SO_3^{2-}]$

Solution:

Part 5 is similar to part 4, and may be solved through a similar method.

The overall reaction is: $2\ SO_3^{2-} + O_2 \rightarrow 2\ SO_4^{2-}$

We can assume that the intermediates are in steady state, $\frac{\mathrm{d}[I]}{\mathrm{d}t} \approx 0$. Thus, we have

$$\frac{\mathrm{d}[SO_3^{\bullet-}]}{\mathrm{d}t} = k_1[Fe^{3+}][SO_3^{2-}] - k_2[SO_3^{\bullet-}][O_2] + k_3[SO_5^{\bullet-}][SO_3^{2-}] - k_6[SO_3^{\bullet-}][SO_5^{\bullet-}] \approx 0 \quad (8)$$

$$\frac{\mathrm{d}[SO_5^{\bullet-}]}{\mathrm{d}t} = k_2[SO_3^{\bullet-}][O_2] - k_3[SO_5^{\bullet-}][SO_3^{2-}] - k_6[SO_3^{\bullet-}][SO_5^{\bullet-}] \approx 0 \quad (9)$$

$$\frac{\mathrm{d}[SO_5^{\bullet-}]}{\mathrm{d}t} = k_3[SO_5^{\bullet-}][SO_3^{2-}] - k_4[SO_5^{2-}][SO_3^{2-}] \approx 0 \quad (10)$$

Equation (8) + (9) gives:

$$k_1[Fe^{3+}][SO_3^{2-}] = 2k_6[SO_3^{\bullet-}][SO_5^{\bullet-}] \quad (11)$$

From (11),

$$[SO_3^{\bullet-}] = \frac{k_1[Fe^{3+}][SO_3^{2-}]}{2k_6[SO_5^{\bullet-}]} \quad (12)$$

Substitute (11) and (12) into (9):

$$k_2[O_2]\frac{k_1[Fe^{3+}][SO_3^{2-}]}{2k_6[SO_5^{\bullet-}]} - k_3[SO_5^{\bullet-}][SO_3^{2-}] - \frac{k_1}{2}[Fe^{3+}][SO_3^{2-}] = 0$$

Rearrange this equation: $k_1k_2[O_2][Fe^{3+}] - 2k_3k_6[SO_5^{\bullet-}]^2 - k_1k_6[Fe^{3+}][SO_5^{\bullet-}] = 0$ (13)

Equation (13) is a quadratic equation with one unknown $[SO_5^{\bullet-}]$. We can solve it by using the quadratic formula, and we have:

$$[SO_5^{\bullet-}] = \frac{-k_1k_6[Fe^{3+}] \pm \sqrt{k_1^2k_6^2[Fe^{3+}]^2 + 8k_1k_2k_3k_6[O_2][Fe^{3+}]}}{4k_3k_6} \quad (14)$$

Equation (14) gives the 2 roots of a quadratic equation, hence it appears very complicated. An assumption should be made here to simplify it. In this reaction, Fe^{3+} is the initiator (which oxidizes SO_3^{2-} to form a radical to kick start the reaction). A reasonable assumption is that $[Fe^{3+}]$ is quite small, such that $[Fe^{3+}]^{1/2} \gg [Fe^{3+}] \gg [Fe^{3+}]^2$. Using this assumption, equation (14) can be simplified:

$$[\mathrm{SO_5^{\bullet-}}] = \frac{-k_1k_6[\mathrm{Fe^{3+}}] \pm \sqrt{k_1^2k_6^2[\mathrm{Fe^{3+}}]^2 + 8k_1k_2k_3k_6[\mathrm{O_2}][\mathrm{Fe^{3+}}]}}{4k_3k_6}$$

$$\approx \frac{-k_1k_6[\mathrm{Fe^{3+}}] \pm \sqrt{8k_1k_2k_3k_6[\mathrm{O_2}][\mathrm{Fe^{3+}}]}}{4k_3k_6} \approx \frac{\sqrt{8k_1k_2k_3k_6[\mathrm{O_2}][\mathrm{Fe^{3+}}]}}{4k_3k_6} \quad (15)$$

In this case, we reject the negative root as concentration can never be negative.

Substituting (15) into (10): $[\mathrm{SO_5^{2-}}] = \dfrac{k_3}{k_4}[\mathrm{SO_5^{\bullet-}}] = \dfrac{\sqrt{8k_1k_2k_3k_6[\mathrm{O_2}][\mathrm{Fe^{3+}}]}}{4k_4k_6}$ (16)

Substitute (16) into the comproportionation step:

$$\frac{\mathrm{d}[\mathrm{SO_4^{2-}}]}{\mathrm{d}t} = \frac{k_4}{2}[\mathrm{SO_5^{2-}}][\mathrm{SO_3^{2-}}]$$

$$= \frac{k_4}{2}\frac{\sqrt{8k_1k_2k_3k_6[\mathrm{O_2}][\mathrm{Fe^{3+}}]}}{4k_4k_6}[\mathrm{SO_3^{2-}}] = \sqrt{\frac{k_1k_2k_3[\mathrm{O_2}][\mathrm{Fe^{3+}}]}{8k_6}}[\mathrm{SO_3^{2-}}] \quad (17)$$

Equation (17) is the rate law of the overall reaction. This rate law shows that the reaction is half order in $\mathrm{O_2}$ and first order in $\mathrm{SO_3^{2-}}$.

Combining the results from parts 2–6, we see that the rate law from part 5 matches the experimental results best. Thus, Termination 2 should be the major pathway for the termination.

3.6.

Answer: $pH = 3.59$

Solution:

First, the analytical concentration of $\mathrm{H_2SO_3}$ should be converted to the standard unit, $\mathrm{mol \cdot dm^{-3}}$.

$\mathrm{c(H_2SO_3) = c(SO_2) = 16.75\,\mu g\,cm^{-3} = 16.75 \times 10^3\,\mu g\,dm^{-3} = 16.75 \times 10^{-3}\,g\,dm^{-3}}$
$= \mathrm{(16.75 \times 10^{-3}/64.07)\,mol\,dm^{-3} = 2.614 \times 10^{-4}\,mol\,dm^{-3}}$

The species in this $\mathrm{H_2SO_3}$ solution are $\mathrm{H^+}$, $\mathrm{OH^-}$, $\mathrm{H_2SO_3}$, $\mathrm{HSO_3^-}$ and $\mathrm{SO_3^{2-}}$.

At equilibrium, we may write the charge and mass balance conditions:

Charge balance: $[\mathrm{H^+}] = [\mathrm{OH^-}] + [\mathrm{HSO_3^-}] + 2\,[\mathrm{SO_3^{2-}}]$ (1)

Mass balance: $c(\mathrm{H_2SO_3}) = [\mathrm{H_2SO_3}] + [\mathrm{HSO_3^-}] + [\mathrm{SO_3^{2-}}]$ (2)

There are three additional relationships:

$$K_1 = [\mathrm{H^+}][\mathrm{HSO_3^-}]/[\mathrm{H_2SO_3}] \quad (3)$$

$$K_2 = [\mathrm{H^+}][\mathrm{SO_3^{2-}}]/[\mathrm{HSO_3^-}] \quad (4)$$

$$K_w = [\mathrm{H^+}][\mathrm{OH^-}] \quad (5)$$

There are five unknown concentrations and five equations, hence solving these equations should reveal the values of the unknown concentrations. However, accurate mathematical solution of these five equations will result in high-ordered equations (higher than quadratic), which are very difficult (or nearly impossible) to solve. As a chemist, we have to make reasonable approximations to simplify the equation. The following discussion will mainly focus on how to make assumptions to simplify the equations using our chemistry knowledge:

H_2SO_3 is definitely acidic, hence we can make assumption {1} that $[H^+] \gg [OH^-]$, thus equation (1) can be simplified to:

$$[H^+] = [HSO_3^-] + 2\,[SO_3^{2-}] \tag{6}$$

Substitute (3) and (4) into (2):

$$\begin{aligned} c(H_2SO_3) &= \frac{[H^+][HSO_3^-]}{K_1} + [HSO_3^-] + [SO_3^{2-}] \\ &= \frac{[H^+]^2[SO_3^{2-}]}{K_1K_2} + \frac{[H^+][SO_3^{2-}]}{K_2[SO_3^{2-}]} \end{aligned}$$

Therefore:

$$[SO_3^{2-}] = \frac{K_1K_2}{[H^+]^2 + K_1[H^+] + K_1K_2}c(H_2SO_3) \tag{7}$$

$$[HSO_3^-] = \frac{K_1[H^+]}{[H^+]^2 + K_1[H^+] + K_1K_2}c(H_2SO_3) \tag{8}$$

Substitute equations (7) and (8) into (6):

$$[H^+] = \frac{K_1[H^+]}{[H^+]^2 + K_1[H^+] + K_1K_2}c(H_2SO_3) + \frac{2K_1K_2}{[H^+]^2 + K_1[H^+] + K_1K_2}c(H_2SO_3) \tag{9}$$

Equation (9) is a cubic equation with one unknown $[H^+]$. We could further simplify it by using our chemistry knowledge on acid dissociation to make assumption {2}:

Since $K_1 \gg K_2$, $[SO_3^{2-}] \ll [HSO_3^-]$.

Therefore, (6) can be further simplified to:

$$[H^+] = [HSO_3^-] \tag{10}$$

Substitute (8) into (10):

$$[H^+] = \frac{K_1[H^+]}{[H^+]^2 + K_1[H^+] + K_1K_2}c(H_2SO_3) \tag{11}$$

Equation (11) is a quadratic equation and can be simplified to:

$$[H^+]^2 + K_1[H^+] + K_1K_2 = K_1c(H_2SO_3) \tag{12}$$

Substitute all the numerical values into (12):

$$[\mathrm{H^+}]^2+1.5\times10^{-2}[\mathrm{H^+}]+1.5\times10^{-2}\times6.8\times10^{-8}=1.5\times10^{-2}\times2.614\times10^{-4} \quad (13)$$

Equation (13) can be simplified even further, because $K_1K_2 \ll K_1c(\mathrm{H_2SO_3})$:

$$[\mathrm{H^+}]^2+1.5\times10^{-2}[\mathrm{H^+}]=1.5\times10^{-2}\times2.614\times10^{-4} \quad (14)$$

Here we will demonstrate to you that all these approximations do not affect the final result.

Equation (13) has two roots: 2.569×10^{-4} and -0.01526. Obviously, only the positive root is valid since $[\mathrm{H^+}]$ can never be negative. Hence, $[\mathrm{H^+}]=2.569\times10^{-4}$ $\mathrm{mol\ dm^{-3}}$ and $pH=3.59(0)$.

Equation (14) also has two roots: 2.570×10^{-4} and -0.01526. Hence, $[\mathrm{H^+}]=2.570\times10^{-4}$ $\mathrm{mol\ dm^{-3}}$ and $pH=3.59(0)$.

Equation (9) is cubic. If we solve it through mathematical analysis, we would find slightly more accurate results: $[\mathrm{H^+}]=2.57061\times10^{-4}$ $\mathrm{mol\ dm^{-3}}$ and $pH=3.58996$.

Mathematically, the root from equation (9) is more accurate than root from equation (13) and (14). However, the high accuracy is not meaningful in chemistry because there is no way to measure a concentration to such a high accuracy. Experimentally, concentrations can be measured to 4 significant figures by titration and pH values can be measured by a pH meter to 2 decimal places. Thus, using any equation, we will obtain the same pH value of 3.59. Solving a simpler equation will thus save a lot of time and effort, and still give us a reasonably accurate pH result.

It is a good habit to check the result by calculating the concentration of all species in this solution and ensuring that all the balances (equations (1) and (2)) are fulfilled. [For simplicity, units are not included in the following calculations.]

$$[\mathrm{H^+}]=2.569\times10^{-4}$$

$$[\mathrm{OH^-}]=K_w/[\mathrm{H^+}]=\frac{1.00\times10^{-14}}{2.569\times10^{-4}}=3.893\times10^{-11}$$

$$[\mathrm{SO_3^{2-}}]=\frac{K_1K_2}{[\mathrm{H^+}]^2+K_1[\mathrm{H^+}]+K_1K_2}c(\mathrm{H_2SO_3})=\frac{1.020\times10^{-9}}{3.921\times10^{-6}}\times2.614\times10^{-4}=6.801\times10^{-8}$$

$$[\mathrm{HSO_3^-}]=\frac{[\mathrm{H^+}][\mathrm{SO_3^{2-}}]}{K_2}=\frac{2.569\times10^{-4}\times6.801\times10^{-8}}{6.8\times10^{-8}}=2.570\times10^{-4}$$

$$[\mathrm{H_2SO_3}]=\frac{[\mathrm{H^+}][\mathrm{HSO_3^-}]}{K_1}=\frac{2.569\times10^{-4}\times2.570\times10^{-4}}{1.5\times10^{-2}}=4.401\times10^{-6}$$

Charge balance: $3.893\times10^{-11}+6.801\times10^{-8}\times2+2.570\times10^{-4}=2.571\times10^{-4}\approx[\mathrm{H^+}]$

Mass balance: $6.801\times10^{-8}+2.570\times10^{-4}+4.401\times10^{-6}=2.615\times10^{-4}\approx c(\mathrm{H_2SO_3})$

As both balances are fulfilled (with a very small error due to rounding), we can confirm that the pH is correct.

From these concentrations, we can also check our assumptions:

Assumption {1}: $[\mathrm{H^+}] \gg [\mathrm{OH^-}]$ is true, since $2.569 \times 10^{-4} \gg 3.893 \times 10^{-11}$

Assumption {2}: $[\mathrm{SO_3^{2-}}] \ll [\mathrm{HSO_3^-}]$ is also true, since $6.801 \times 10^{-8} \ll 2.570 \times 10^{-4}$

3.7.

Answer: $pH = 6.91$

Solution:

The species in the solution are $\mathrm{H^+}$, $\mathrm{OH^-}$, $\mathrm{HSO_4^-}$ and $\mathrm{SO_4^{2-}}$. Note that $\mathrm{H_2SO_4}$ is not present because the first ionisation is complete.

$$c(\mathrm{H_2SO_4}) = 2.0 \times 10^{-8}\ \mathrm{mol\ dm^{-3}}$$

At equilibrium, we may write the charge and mass balance conditions:

Charge balance: $$[\mathrm{H^+}] = [\mathrm{OH^-}] + [\mathrm{HSO_4^-}] + 2\,[\mathrm{SO_4^{2-}}] \qquad (15)$$

Mass balance: $$c(\mathrm{H_2SO_4}) = [\mathrm{HSO_4^-}] + [\mathrm{SO_4^{2-}}] \qquad (16)$$

From equilibrium constants, we have:

$$K_2 = [\mathrm{H^+}][\mathrm{SO_4^{2-}}]/[\mathrm{HSO_4^-}] \qquad (17)$$

$$K_w = [\mathrm{H^+}][\mathrm{OH^-}] \qquad (18)$$

Again, there are four unknowns and four equations, which can be solved mathematically. However, we can still simplify the equation by making the same assumptions as in part 6.

Assumption {3}: $[\mathrm{H^+}] \gg [\mathrm{OH^-}]$

Assumption {4}: $[\mathrm{SO_4^{2-}}] \gg [\mathrm{HSO_4}]$

Thus, equation (15) can be re-written as: $$[\mathrm{H^+}] = 2\,[\mathrm{SO_4^{2-}}] \qquad (19)$$

Similar to part 6, $$[\mathrm{SO_4^{2-}}] = \frac{K_2}{[\mathrm{H^+}] + K_2} c(\mathrm{H_2SO_4}) \qquad (20)$$

Substitute (20) into (19): $$[\mathrm{H^+}] = \frac{2K_2}{[\mathrm{H^+}] + K_2} c(\mathrm{H_2SO_4}) \qquad (21)$$

Equation (21) can be rearranged to: $$[\mathrm{H^+}]^2 + K_2[\mathrm{H^+}] = 2K_2\,c(\mathrm{H_2SO_4}) \qquad (22)$$

This is almost identical (in format) to equation (12). Substitute the numerical values into equation (22) gives:

$$[\mathrm{H^+}]^2 + 1.2 \times 10^{-2}[\mathrm{H^+}] - 2(1.2 \times 10^{-2}) \times 2.0 \times 10^{-8} = 0 \qquad (23)$$

Solving (23) gives two roots: 4.000×10^{-8} and -1.200×10^{-2}

Only the positive root is possible, thus $[\mathrm{H}^+]=4.000\times10^{-8}\ \mathrm{mol\ dm}^{-3}$ and $pH = 7.40$.

You may be happy with this result, but wait a minute. Do you notice something wrong?

The pH is larger than 7, and this is an acidic solution! Obviously the result is incorrect, but why?

Using $[\mathrm{H}^+]=4.000\times10^{-8}\ \mathrm{mol\ dm}^{-3}$, we can calculate the concentrations of other species:

$$[\mathrm{OH}^-]=\frac{K_W}{[\mathrm{H}^+]}=\frac{1.00\times10^{-14}}{4.000\times10^{-8}}=2.500\times10^{-7}\ \mathrm{mol\ dm}^{-3}$$

$$[\mathrm{SO}_4^{2-}]=\frac{K_2}{[\mathrm{H}^+]+K_2}c(\mathrm{H_2SO_4})=\frac{1.2\times10^{-2}}{1.2\times10^{-2}}\times2.0\times10^{-8}=2.000\times10^{-8}\ \mathrm{mol\ dm}^{-3}$$

$$[\mathrm{HSO}_4^-]=\frac{[\mathrm{H}^+][\mathrm{SO}_4^{2-}]}{K_2}=\frac{4.000\times10^{-8}\times2.000\times10^{-8}}{1.2\times10^{-2}}=6.667\times10^{-14}\ \mathrm{mol\ dm}^{-3}$$

Mass balance is fulfilled but charge balance is not.

The error is due to assumption {3} that $[\mathrm{H}^+]\gg[\mathrm{OH}^-]$ being invalid. OH^- can also be formed by the self-ionisation of water. When the acid is reasonably concentrated, the self-ionisation of water is usually insignificant. For example, in a weakly acidic solution of $pH=5$, $[\mathrm{OH}^-]$ from self-ionisation of water is as low as $10^{-9}\ \mathrm{mol\ dm}^{-3}$, which is 10000 times smaller than $[\mathrm{H}^+]$ $(10^{-5}\ \mathrm{mol\ dm}^{-3})$, and can be safely ignored. However, in a solution close to neutral pH, the self-ionisation of water cannot be ignored any more. For example, if a solution has a pH of 6.7, $[\mathrm{OH}^-]=5.012\times10^{-8}\ \mathrm{mol\ dm}^{-3}$ would be comparable to $[\mathrm{H}^+]=1.995\times10^{-7}\ \mathrm{mol\ dm}^{-3}$ and neither should be ignored.

We are facing this situation now, because the maximum concentration of H^+ from $\mathrm{H_2SO_4}$ (assuming full dissociation) is $2\times2.0\times10^{-8}=4.0\times10^{-8}\ \mathrm{mol\ dm}^{-3}$. And the maximum concentration of H^+ from water is $1.0\times10^{-7}\ \mathrm{mol\ dm}^{-3}$. The maximum "sum" is $1.4\times10^{-7}\ \mathrm{mol\ dm}^{-3}$, which is close to neutral.

Without assumption {3}, equation (15) still have four terms. Are we able to ignore any term? We already know $[\mathrm{H}^+]$ and $[\mathrm{OH}^-]$ cannot be ignored, but can we ignore either $[\mathrm{HSO}_4^-]$ or $[\mathrm{SO}_4^{2-}]$? Obviously, we cannot ignore both $[\mathrm{HSO}_4^-]$ and $[\mathrm{SO}_4^{2-}]$ otherwise the solution will be neutral.

We shall look at equation (17) once more:

$$K_2=\frac{[\mathrm{H}^+][\mathrm{SO}_4^{2-}]}{[\mathrm{HSO}_4^-]} \qquad (17)$$

We already confirmed that $[\mathrm{H}^+]<1.4\times10^{-7}$, thus $[\mathrm{H}^+]\ll K_2$. Hence, $[\mathrm{HSO}_4^-]\ll[\mathrm{SO}_4^{2-}]$. This proves that assumption {4} is correct.

Finally, we can simplify equation (15) to: $[\mathrm{H}^+] = [\mathrm{OH}^-] + 2\,[\mathrm{SO}_4^{2-}]$ (24)

Substitute (18) and (20) into (24):

$$[\mathrm{H}^+] = \frac{K_w}{[\mathrm{H}^+]} + \frac{2K_2}{[\mathrm{H}^+]+K_2}c(\mathrm{H_2SO_4}) \tag{25}$$

Equation (25) is still a cubic equation, and can be further simplified. We have proved just now that $[\mathrm{H}^+] \ll K_2$, thus $\frac{2K_2}{[\mathrm{H}^+]+K_2} \approx \frac{2K_2}{K_2} = 2.$

Hence,

$$[\mathrm{H}^+] = \frac{K_w}{[\mathrm{H}^+]} + 2\,c(\mathrm{H_2SO_4}) \tag{26}$$

Equation (26) is quadratic now: $[\mathrm{H}^+]^2 - 2\,c(\mathrm{H_2SO_4})[\mathrm{H}^+] - K_w = 0$ (27)

Substitution of numerical values: $[\mathrm{H}^+]^2 - 4.0\times10^{-8}[\mathrm{H}^+] - 1.0\times10^{-14} = 0$ (28)

The roots are: 1.220×10^{-7} and -8.198×10^{-8}. Hence, $[\mathrm{H}^+] = 1.220 \times 10^{-7}$ mol dm^{-3} and $pH = 6.91$.

We can check our new assumptions:

$$[\mathrm{OH}^-] = \frac{K_w}{[\mathrm{H}^+]} = \frac{1.00\times10^{-14}}{1.220\times10^{-7}} = 8.197\times10^{-8}\ \mathrm{mol\ dm^{-3}}$$

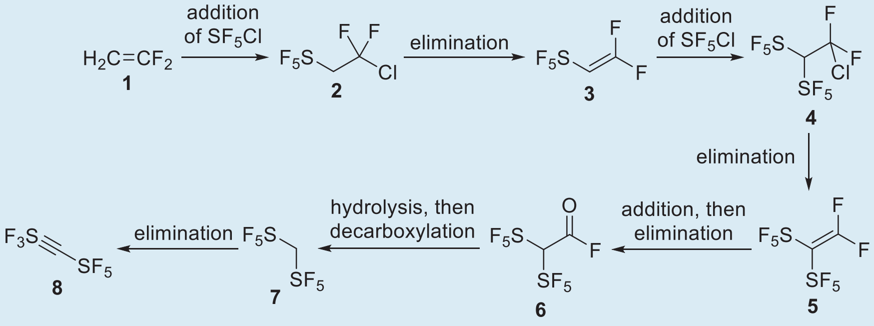
$$[\mathrm{SO}_4^{2-}] = \frac{K_2}{[\mathrm{H}^+]+K_2}c(\mathrm{H_2SO_4}) = \frac{1.2\times10^{-2}}{1.2\times10^{-2}}\times2.0\times10^{-8} = 2.000\times10^{-8}\ \mathrm{mol\ dm^{-3}}$$

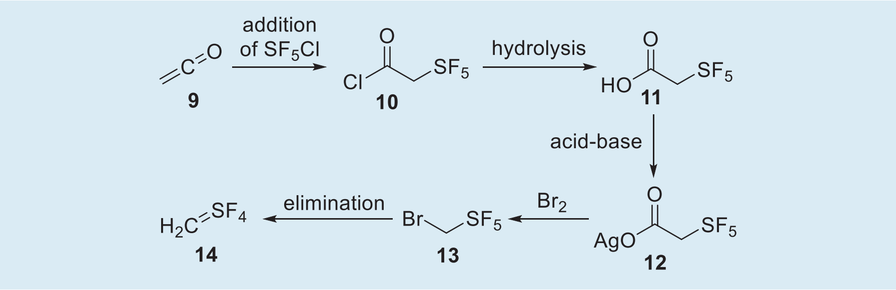
$$[\mathrm{HSO}_4^-] = \frac{[\mathrm{H}^+][\mathrm{SO}_4^{2-}]}{K_2} = \frac{1.220\times10^{-7}\times2.000\times10^{-8}}{1.2\times10^{-2}} = 2.033\times10^{-13}\ \mathrm{mol\ dm^{-3}}$$

Both charge balance and mass balance are fulfilled now.

3.8.

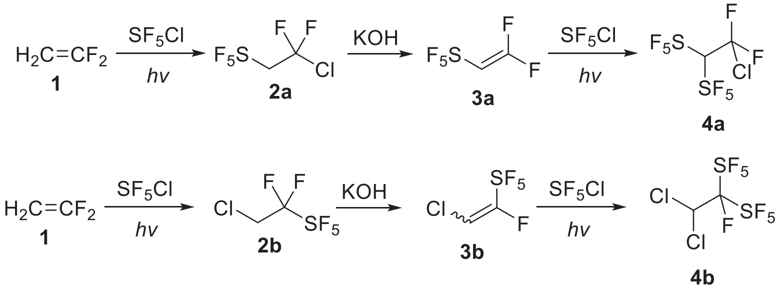
Answer:



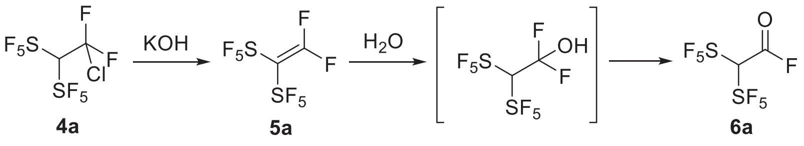


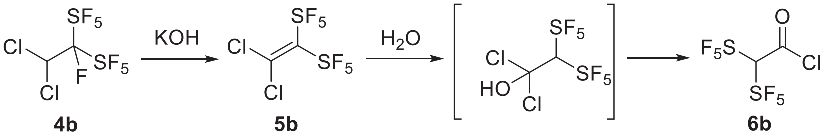
Solution:

Compound **1** is an alkene, hence reaction **1** → **2** is likely an addition reaction. The reaction condition is photochemical, so the reaction most likely proceeds through a radical mechanism. Reaction **3** → **4** has exactly the same condition, and should be a second addition reaction. This means that **2** → **3** is an elimination reaction. In SF_5Cl, the bond that breaks should be the weaker $S{-}Cl$ bond, thus the SF_5 group shall add to one carbon while the Cl atom adds to the other carbon. There is only one remaining question now — the regioselectivity of the addition reaction. Since the addition reaction might be radical in nature, its regioselectivity may not be easily determined. We shall try to draw the reactions using both regioselectivies (**1** → **2** and **3** → **4** should have identical regioselectivity as they are carried out in identical conditions):

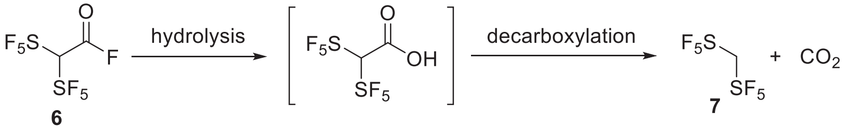


Reaction of **4** → **5** is another basic elimination of HX, generating alkene **5**. **5** → **6** is a hydration, forming a 1,1-haloalcohol intermediate, which eliminates the halide to form the carbonyl compound **6**. The intermediate cannot be a 1,2-haloalcohol because the following elimination would not occur. By comparison with the given formula of **6** ($C_2HF_{11}OS_2$), we can conclude that **6a** (and hence **2a**–**5a**) is the correct structure.

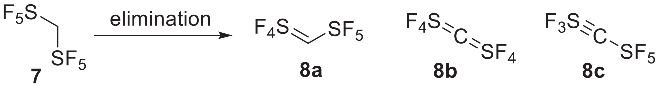




Compound **6** is an acyl halide, which reacts easily with water to form a carboxylic acid **7**. **7** will lose a gas according to the reaction scheme, and the only possibility is CO_2 by a decarboxylation reaction.

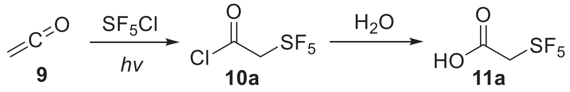


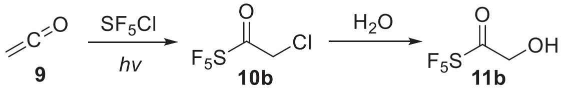
The last step should be an elimination reaction again, since it is conducted at a high temperature of 80°C. Because the molecule is symmetrical, three products are possible:

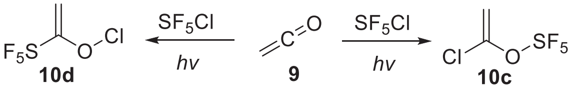


No clue is given in the reaction scheme for us to determine which is the correct product, but the text has mentioned a rare bond in **8** with a bond length of 139.2 pm. At the same time, compound **14** has a more common bond with a bond length of 155.3 pm. These are hints for sure, but we may not understand them at the moment. What is the "rare bond" and what is the "more common bond"? We could first continue to the second reaction scheme and see whether we can find more clues.

9 → **10** is a similar addition reaction and **10** → **11** is probably another hydrolysis.



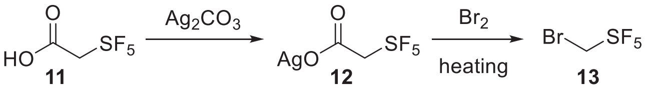




Will the SF_5 and Cl add to the $C{=}C$ bond or $C{=}O$ bond? Addition to $C{=}O$ gives either **10c** or **10d**, which are less stable than **10a** and **10b** due to weak $O{-}Cl$ and

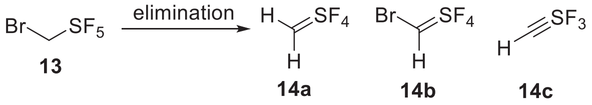
$O{-}S$ bonds. Both **10a** and **10b** seem fine, but the hydrolysis product **11a** is a carboxylic acid while **11b** is an alcohol. The next reaction **11** → **12** is with a base, Ag_2CO_3, hence **11** should be the more acidic carboxylic acid **11a**.

Compound **12** is naturally the corresponding silver salt of acid **11**. By using bromine, $AgBr$ solid will precipitate, driving the reaction. By heating, a decarboxylation reaction should occur, leaving only one carbon in **13**.

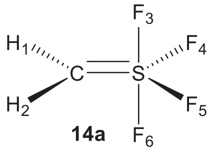


How does the alkyl halide **13** form? The bromine molecule Br_2 can be temporarily polarised, forming one partially positive-charged Br ($\delta+$) and one partially negative-charged Br ($\delta-$). Upon the reaction, the "Br^-" will first combine with Ag^+, forming the stable $AgBr$ solid. The stability of $AgBr$ will drive the reaction to proceed, leaving a carboxylate anion $SF_5CH_2COO^-$. Decarboxylation occurs next upon heating and is driven by entropy, forming CO_2 gas and $SF_5CH_2^-$. The $SF_5CH_2^-$ then combines with the "Br^+", forming SF_5CH_2Br.

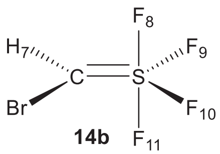
The condition for the last reaction **13** → **14** is n-pentyl lithium, which is homologous to the common strong base n-butyl lithium. Thus, this reaction should be an elimination reaction, forming either double bond or triple bond between carbon and sulfur.



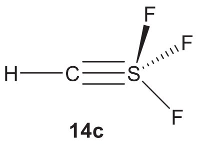
3 elimination products are possible, 2 with $C{=}S$ bond and 1 with $C{\equiv}S$ bond. For the 2 compounds with $C{=}S$ bond, carbon is trigonal planar and sulfur is trigonal bipyramidal (by VSEPR theory). Thus, **14a–14c** will have the following structures:



14a



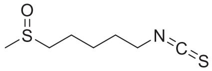
14b

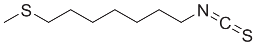


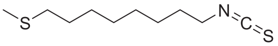
14c

From the structures, **14a** has a higher symmetry than **14b**. In **14a**, H_1 and H_2 are equivalent; F_3 and F_6 are equivalent; F_4 and F_5 are equivalent. Thus, **14a** has 1 hydrogen signal and 2 fluorine signals in NMR. On the other hand, in **14b**, F_9 and F_{10} are inequivalent, because F_9 is syn to H_7 but F_{10} is anti to H_7. Whether F_8 and F_{11} are equivalent is probably debatable, but there are at least 3 fluorine signals in the NMR of **14b**. For **14c**, the 3 fluorine atoms are equivalent. Thus, only **14a** fulfils the description in the question.

Now, we have found the structure of **14**, having a $C{=}S$ bond. This will give us a hint to deduce the structure of compound **8**. It is known that **14** has a bond of 155.3 pm and **8** has a bond of 139.2 pm. First, we should identify the 155.3 pm bond in **14**. Compound **14** has $C{-}H$ (109 pm), $C{=}S$ (not in table) and $S{-}F$ (158 pm) bonds. Thus, the 155.3 pm bond in **14** must be from the $C{=}S$ bond. The 139.2 pm bond in **8** is significantly shorter than the $C{=}S$ (155.3 pm) bond. Thus, it can only be the $C{\equiv}S$ bond, meaning that **8c** is the correct structure. This is also confirmed by the fact that $C{\equiv}S$ bond is much rarer than $C{=}S$ bond in organic chemistry. For example, the unique flavour of wasabi comes from the following isothiocyanates ($R{-}N{=}C{=}S$) with $C{=}S$ bond.


6-(methylsulfinyl)hexyl isothiocyanate


7-methylthioheptyl isothiocyanate


8-methylthiooctyl isothiocyanate

Problem 4. *Safer is Better*

4.1.

Answer: 5.95 g

Solution:

We can write the reaction equation for preparation of **A** (stoichiometric ratio is unknown):

$$\begin{array}{ccccccccc} \mathrm{X} & + & \mathrm{Y} & \rightarrow & \text{gas} & + & \mathrm{A} \\ 10.00\text{ g} & & 27.02\text{ g} & & & & 31.07\text{ g} \end{array}$$

Since the yield is quantitative, there is no side product or by-product.

$$\mathrm{m(gas)} = \mathrm{m(X)} + \mathrm{m(Y)} - \mathrm{m(A)} = 10.00 + 27.02 - 31.07 = 5.95\text{ g}$$

4.2.

Answer: CO_2

Solution:

Using perfect gas law, $n = \frac{pV}{RT} = \frac{1.013\times10^{5}\times13.01\times10^{-3}}{8.314\times(273.15+900)} = 0.1351\ \mathrm{mol}$

Thus, the molar mass of this gas is: $M_r = \frac{\mathrm{m}}{n} = \frac{5.95}{0.1351} = 44.04\ \mathrm{g\ mol^{-1}}$

From the molar mass, we can immediately deduce that the gas is CO_2. This requires familiarity with the molecular masses of common chemicals, such as H_2O, O_2, CO_2, CO, N_2, H_2SO_4, HCl and more.

4.3.

Answer: Li_2CO_3

Solution:

The CO_2 gas must come from the reaction of **X** and **Y**. It is known that **Y** is an oxide, which does not contain carbon. The carbon must come from mineral **X**. Most likely, **X** is a metal carbonate, because thermal reaction/decomposition of carbonates will release CO_2. We will draw a table to analyse all possible oxidation states of the metal in the metal carbonate (mass of carbonate is 10.00 g):

Oxidation state	Formula of **X**	$n(CO_2)$ mol	$n(\mathbf{X})$ mol	$M_r(\mathbf{X})$ g mol^{-1}	$M_r(M)$ g mol^{-1}	Possible metal M
+1	M_2CO_3	0.1351	0.1351	74.02	7.00	Li
+2	MCO_3	0.1351	0.1351	74.02	13.99	N (not a metal)
+3	$M_2(CO_3)_3$	0.1351	0.04503	222.07	20.99	Ne/Na
+4	$M(CO_3)_2$	0.1351	0.06755	148.04	27.98	Si
+5 (rare)	$M_2(CO_3)_5$	0.1351	0.02702	370.10	34.98	Cl (not a metal)
+6 (rare)	$M(CO_3)_3$	0.1351	0.04503	222.07	41.98	No possible element

The table list possible oxidation states from +1 to +6. Do note that the oxidation states of +5 and +6 are rare for cations in salts, and +7/+8 are even more rare, if ever possible. For a student, you should probably start by trying +1, +2 and +3. Most of the time, you will find a reasonable answer. However, there are rare questions where the oxidation state is +4 or higher, that is why the above table is until +6.

From the table, the only "possibilities" are Li_2CO_3 and $Si(CO_3)_2$. The others are either non-metals, or lead to impossible oxidation states. Between Li_2CO_3 and $Si(CO_3)_2$, the correct answer is quite obvious: Li_2CO_3. On top of that, the product **A** should contain lithium, because it is a potential electrode material in lithium-ion battery.

4.4.

Answer: TiO_2

Solution:

With the known information, we can rewrite the reaction equations, with oxide Y written as Q_aO_b:

$$\begin{array}{ccccccccc} \mathrm{Li_2CO_3} & + & \mathrm{Y\ (Q_aO_b)} & \rightarrow & \mathrm{CO_2} & + & \mathrm{A} \\ 10.00\text{ g} & & 27.02\text{ g} & & 5.95\text{ g} & & 31.07\text{ g} \\ 0.1353\text{ mol} & & & & 0.1351\text{ mol} & & \end{array} \tag{1}$$

$$\begin{array}{ccccccccc} \mathrm{Li_2CO_3} & + & \mathrm{Y\ (Q_aO_b)} & \rightarrow & \mathrm{CO_2} & + & \mathrm{Z} \\ 10.00\text{ g} & & 10.81\text{ g} & & 5.95\text{ g} & & 14.85\text{ g} \\ 0.1353\text{ mol} & & & & 0.1351\text{ mol} & & \end{array} \tag{2}$$

$$\begin{array}{ccccccccc} \mathrm{Z} & + & \mathrm{Y\ (Q_aO_b)} & + & \mathrm{M} & \rightarrow & \mathrm{B} \\ 14.85\text{ g} & & 27.02\text{ g} & & 3.24\text{ g} & & 45.11\text{ g} \end{array} \tag{3}$$

From the question, both **A** and **B** are ternary oxides. First, we need to know the meaning of "ternary" (not "tertiary"). "Ternary" comes from Latin "ternarius" and it means to be composed of three items. Here, each ternary oxide should be composed of three elements, one of which is oxygen. From the equations, we can see that the lithium element in $\mathrm{Li_2CO_3}$ goes to compound **A** and **B** (via **Z**). The element Q in **Y** also ends up in compound **A** and **B**. Thus, both **A** and **B** should have a formula of $\mathrm{Li_cQ_dO_e}$, where c, d and e are integers.

It is stated that "When arranged in a certain order, the number of atoms in **B** are described by geometric progression". Therefore, the 3 stoichiometric numbers should be in the form of x, xq, $\mathrm{xq^2}$, but we do not know their corresponding element. Since these 3 numbers have a common factor x, we can always simplify the stoichiometric number to 1, q, $\mathrm{q^2}$.

Again, we will use a table to find out which combination(s) is more possible:

Entry	Stoichiometric number for Li	Stoichiometric number for Q	Stoichiometric number for O	Average oxidation state of Li & Q
1	1	q	$\mathrm{q^2}$	$2\mathrm{q}^2/(\mathrm{q}+1)$
2	1	$\mathrm{q^2}$	q	$2\mathrm{q}/(\mathrm{q}^2+1)$
3	q	1	$\mathrm{q^2}$	$2\mathrm{q}^2/(\mathrm{q}+1)$
4	$\mathrm{q^2}$	1	q	$2\mathrm{q}/(\mathrm{q}^2+1)$
5	q	$\mathrm{q^2}$	1	$2/(\mathrm{q}+\mathrm{q}^2)$
6	$\mathrm{q^2}$	q	1	$2/(\mathrm{q}+\mathrm{q}^2)$

We do know that the oxidation state of Li is +1. On the other hand, we do not know the oxidation state of Q, but it is definitely positive. Since oxygen has an oxidation state of –2 in this oxide B, we can calculate the average oxidation state of the positive elements Li and Q. Mathematically, there are 3 possible expressions and we shall try to calculate them by substituting q with integers: 1, 2, 3, 4, …

q	$2q^2/(q+1)$	$2q/(q^2+1)$	$2/(q+q^2)$
1	1	1	1
2	8/3 = 2.67	4/5 = 0.8	2/6 = 0.333
3	18/4 = 4.5	6/10 = 0.6	2/12 = 0.167
4	32/5 = 6.4	8/17 = 0.47	2/20 = 0.1

The smallest possible oxidation state of Q is +1, hence the minimum average oxidation state of Li and Q is +1. Thus, we can eliminate $2q/(q^2+1)$ and $2/(q+q^2)$, as the values will be even smaller as q further increases.

So far, we have confirmed that the formula of **B** is either $\mathrm{LiQ_qO_{q^2}}$ or $\mathrm{QLi_qO_{q^2}}$.

We will calculate the corresponding oxidation state of Q:

q	Formula of $\mathrm{LiQ_qO_{q^2}}$	Oxidation state of Q in $\mathrm{LiQ_qO_{q^2}}$	Formula of $\mathrm{QLi_qO_{q^2}}$	Oxidation state of Q in $\mathrm{QLi_qO_{q^2}}$
1	LiQO	+1	QLiO	+1
2	$\mathrm{LiQ_2O_4}$	+3.5	$\mathrm{QLi_2O_4}$	+6
3	$\mathrm{LiQ_3O_9}$	+5.67	$\mathrm{QLi_3O_9}$	+15
4	$\mathrm{LiQ_4O_{16}}$	+7.75	$\mathrm{QLi_4O_{16}}$	+28

Only 4 formulae of **B** are reasonable: LiQO, $\mathrm{LiQ_2O_4}$, $\mathrm{LiQ_3O_9}$, $\mathrm{QLi_2O_4}$. From these formulae, we know that the stoichiometric ratio of Li:Q can only be 1:1, 1:2, 1:3 and 2:1.

Addition of equation (2) and (3) gives a new equation (4):

$$\begin{array}{ccccccccc} \mathrm{Li_2CO_3} & + & \mathrm{Y\ (Q_aO_b)} & + & \mathrm{M} & \rightarrow & \mathrm{CO_2} & + & \mathrm{B} \\ 10.00\ \text{g} & & 37.83\ \text{g} & & 3.24\ \text{g} & & 5.95\ \text{g} & & 45.11\ \text{g} \\ 0.1353\ \text{mol} & & & & & & 0.1351\ \text{mol} & & \end{array} \qquad (4)$$

The identify of metal **M** is yet another problem. 3.24 g of metal **M** is used in equation (4), but we do not know which metal is this. Since **B** is a ternary oxide, containing elements Li, O and Q, the metal **M** has no choice but to be either Li or Q. To confirm which is **M**, we have to analyse both scenarios.

Scenario 1: If **M** is Li, then 3.24 g of Li is 0.4668 mol of Li.

We can calculate the molar ratio of Li, Q and O in compound **B** now:

$$n(\mathrm{Li}) = 0.1353 \times 2 + 0.4668 = 0.7374 \text{ mol}$$

$$n(\mathrm{Q}) = \frac{37.83}{M_r} \times a \text{ mol}$$

$$n(\mathrm{O}) \;=\; 0.1353 + \frac{37.83}{M_r} \times b \text{ mol}$$

[M_r is the molar mass of Q_aO_b.]

Although 1 mole of Li_2CO_3 contains 3 moles of oxygen, only 1 mole of oxygen ends up into compound **B**, because the other 2 moles of oxygen are in CO_2.

Formula of **B**	By Li:Q ratio	By Li:O ratio	a:b ratio
LiQO	$M_r(Y) = 51.30a$	$M_r(Y) = 62.83b$	$a{:}b = 1.2248{:}1 \approx 11{:}9$ or $5{:}4$
LiQ_2O_4	$M_r(Y) = 25.65a$	$M_r(Y) = 13.44b$	$a{:}b = 0.5240{:}1 \approx 11{:}21$ or $1{:}2$
LiQ_3O_9	$M_r(Y) = 17.10a$	$M_r(Y) = 5.82b$	$a{:}b = 0.3404{:}1 \approx 1{:}3$
QLi_2O_4	$M_r(Y) = 102.60a$	$M_r(Y) = 28.24b$	$a{:}b = 0.2752{:}1 \approx 1{:}4$

The molar mass of oxide **Y** (Q_aO_b) might be calculated by either Li:Q ratio or Li:O ratio, as shown in the table above. The ratio of a:b can thus be calculated. Obviously, the ratio of 11:9 and 11:21 for an oxide Q_aO_b is unlikely. Also, Q_5O_4 is uncommon, if ever possible. The other three are possible: QO_2, QO_3 and QO_4. Do note that there are some rounding-off and approximation, because the calculation might carry some error depending on the number of significant numbers used.

For each formula of oxide **Y**, the atomic mass of metal Q can be calculated:

Formula of **B**	Formula of **Y**	M_r of **Y**	Atomic mass of Q	Identity of Q
LiQO	No possible formula			
LiQ_2O_4	QO_2	25.65 or 26.88	−6.35 or −5.12	No possible element
LiQ_3O_9	QO_3	17.10 or 17.46	−30.90 or −30.54	No possible element
QLi_2O_4	QO_4	102.60 or 112.96	38.60 or 48.96	K or Ti or V

Obviously, the negative atomic masses do not correspond to any element. The positive atomic mass 38.59 is from Li:Q ratio ($M_r = 102.60a$), while the other value 48.96 is from the Li:O ratio ($M_r = 28.24b$). Indeed, judging from these two values, we can already suspect that QO_4 is probably not the correct answer, because the two numbers are quite different from one another. Nevertheless, if we still try to find the corresponding element Q, we will find K (calculated atomic mass 38.60, actual atomic mass 39.10), Ti (calculated atomic mass 48.96, actual atomic mass 47.87) and V (calculated atomic mass 48.96, actual atomic mass 50.94). None of the three metals have an oxidation state of +8 for QO_4. In addition, the actual atomic mass of Ti and V are also far away from the calculated value.

We seem to have reached a dead end now: none of our guesses match the descriptions in the question. You can try to check our thinking process as a practice for your understanding.

After checking, you should find out that we have made no mistakes. Rather, we have only considered scenario 1 (**M** is Li) so far. There is a second scenario to be considered as well: **M** is Q.

It is quite common for students to miss out on other possible scenarios and feel frustrated, giving up on the question. This can be avoided by listing down all the possible scenarios from the beginning. Now we will consider scenario 2.

Scenario 2: If **M** is metal Q.

This scenario is a little bit more difficult, since we do not know the atomic mass of Q. However, we can still calculate the molar ratio of Li, Q and O in compound **B**:

$$n(\mathrm{Li}) = 0.1353 \times 2 = 0.2706 \text{ mol}$$

$$n(\mathrm{Q}) = \frac{37.83}{M_r} \times a + \frac{3.24}{Q} \text{ mol}$$

$$n(\mathrm{O}) = 0.1353 + \frac{37.83}{M_r} \times b \text{ mol}$$

[M_r is the molecular mass of Q_aO_b, and Q is the atomic mass of element Q.]

Formula of **B**	By Li:Q ratio	By Li:O ratio
LiQO	Not a simple relationship because $n(\mathrm{Q})$ is expressed by unknowns M_r and Q	$M_r(\mathrm{Y}) = 279.60\mathrm{b}$
LiQ_2O_4		$M_r(\mathrm{Y}) = 39.94\mathrm{b}$
LiQ_3O_9		$M_r(\mathrm{Y}) = 16.45\mathrm{b}$
QLi_2O_4		$M_r(\mathrm{Y}) = 93.20\mathrm{b}$

From the molar mass of Y, we can calculate the atomic mass of Q, assuming that Q has an oxidation state from +1 to +6:

Formula of **B**	Q is +1: $a = 2, b = 1$	Q is +2: $a = 1, b = 1$	Q is +3: $a = 2, b = 3$	Q is +4: $a = 1, b = 2$	Q is +5: $a = 2, b = 5$	Q is +6: $a = 1, b = 3$
$LiQO$	$Q = 131.80$	$Q = 263.60$	$Q = 395.40$	$Q = 527.20$	$Q = 659.00$	$Q = 790.80$
LiQ_2O_4	$Q = 11.97$	$Q = 23.94$	$Q = 35.91$	$Q = 47.88$	$Q = 59.85$	$Q = 71.82$
LiQ_3O_9	$Q = 0.225$	$Q = 0.45$	$Q = 0.675$	$Q = 0.90$	$Q = 1.125$	$Q = 1.35$
QLi_2O_4	$Q = 38.60$	$Q = 77.20$	$Q = 115.80$	$Q = 154.40$	$Q = 193.00$	$Q = 231.60$

Among all the calculated atomic masses, only 131.80 (Xe, 131.29), 11.97 (C, 12.01), 23.94 (Mg, 24.31), 35.91 (Cl, 35.45), 47.88 (Ti, 47.87), 231.60 (Pa, 231.04) are close enough to a real element. They correspond to these oxides: Xe_2O, C_2O, MgO, Cl_2O_3, TiO_2 and PaO_3. Using our chemistry knowledge, the only compounds that are possibly **Y** are MgO and TiO_2, and they correspond to $LiMg_2O_4$ and $LiTi_2O_4$ as compound **B**, respectively. In both ternary compounds, Li is +1, O is −2, and Mg/Ti is +3.5. As the maximum oxidation state of Mg is +2, $LiMg_2O_4$ is impossible and only $LiTi_2O_4$ is possible to be compound **B** (maximum oxidation state of Ti is +4). Thus, the metal **M** (Q) is Ti and oxide **Y** is TiO_2.

It is always a good habit to confirm the results by checking the stoichiometric ratios of the reactions described in the question, and we will do this in part 5.

4.5.

Answer:

$$2\ Li_2CO_3 + 5\ TiO_2 \rightarrow 2\ CO_2 + Li_4Ti_5O_{12} \qquad (1)$$

$$Li_2CO_3 + TiO_2 \rightarrow CO_2 + Li_2TiO_3 \qquad (2)$$

$$2\ Li_2TiO_3 + 5\ TiO_2 + Ti \rightarrow 4\ LiTi_2O_4 \qquad (3)$$

Solution:

Since we now know the identity of all the reactants, we can rewrite the equations one more time:

Li_2CO_3	+	TiO_2	→	CO_2	+	A	(1)
10.00 g		27.02 g		5.95 g		31.07 g	
0.1353 mol		0.3383 mol		0.1351 mol			

Li_2CO_3	+	TiO_2	→	CO_2	+	Z	(2)
10.00 g		10.81 g		5.95 g		14.85 g	
0.1353 mol		0.1353 mol		0.1351 mol			

$$\begin{array}{ccccccc} \mathrm{Z} & + & \mathrm{TiO_2} & + & \mathrm{M} & \rightarrow & \mathrm{B} \\ \text{14.85 g} & & \text{27.02 g} & & \text{3.24 g} & & \text{45.11 g} \\ & & \text{0.3383 mol} & & \text{0.06768 mol} & & \end{array} \qquad (3)$$

Compound **A** contains the following elements:

$$n(Li) = 0.1353 \times 2 = 0.2706\ \mathrm{mol}$$
$$n(\mathrm{Ti}) = 0.3383\ \mathrm{mol}$$
$$n(\mathrm{O}) = 0.1353 + 0.3383 \times 2 = 0.8119\ \mathrm{mol}$$

The molar ratio of Li:Ti:O is 1:1.25:3 = 4:5:12, thus compound **A** is $\mathrm{Li_4Ti_5O_{12}}$.

Compound **Z** contains the following elements:

$$n(Li) = 0.1353 \times 2 = 0.2706\ \mathrm{mol}$$
$$n(\mathrm{Ti}) = 0.1353\ \mathrm{mol}$$
$$n(\mathrm{O}) = 0.1353 + 0.1353 \times 2 = 0.4059\ \mathrm{mol}$$

The molar ratio of Li:Ti:O is 2:1:3, thus compound **Z** is $\mathrm{Li_2TiO_3}$.

Compound **B** contains the following elements:

$$n(Li) = 0.2706\ \mathrm{mol}$$
$$n(\mathrm{Ti}) = 0.1353 + 0.3383 + 0.06768 = 0.5413\ \mathrm{mol}$$
$$n(\mathrm{O}) = 0.4059 + 0.3383 \times 2 = 1.0825\ \mathrm{mol}$$

The molar ratio of Li:Ti:O is 1:2:4, thus compound **B** is $\mathrm{LiTi_2O_4}$.

Therefore, the equations are:

$$\begin{array}{ccccccccc} 2\ \mathrm{Li_2CO_3} & + & 5\ \mathrm{TiO_2} & \rightarrow & 2\ \mathrm{CO_2} & + & \mathrm{Li_4Ti_5O_{12}} \\ \text{10.00 g} & & \text{27.02 g} & & \text{5.95 g} & & \text{31.07 g} \\ \text{0.1353 mol} & & \text{0.3383 mol} & & \text{0.1351 mol} & & \text{0.06767 mol} \end{array} \qquad (1)$$

$$\begin{array}{ccccccc} \mathrm{Li_2CO_3} & + & \mathrm{TiO_2} & \rightarrow & \mathrm{CO_2} & + & \mathrm{Li_2TiO_3} \\ \text{10.00 g} & & \text{10.81 g} & & \text{5.95 g} & & \text{14.85 g} \\ \text{0.1353 mol} & & \text{0.1353 mol} & & \text{0.1351 mol} & & \text{0.1353 mol} \end{array} \qquad (2)$$

$$\begin{array}{ccccccc} 2\ \mathrm{Li_2TiO_3} & + & 5\ \mathrm{TiO_2} & + & \mathrm{Ti} & \rightarrow & 4\ \mathrm{LiTi_2O_4} \\ \text{14.85 g} & & \text{27.02 g} & & \text{3.24 g} & & \text{45.11 g} \\ \text{0.1353 mol} & & \text{0.3383 mol} & & \text{0.06768 mol} & & \text{0.2706 mol} \end{array} \qquad (3)$$

Comments on Q4:

This is a question testing students on stoichiometry. Many students consider this type of question as inorganic chemistry, but such questions only require relatively little inorganic chemistry knowledge. In this case, students do not need to have in-depth prior knowledge on lithium ion batteries or titanium chemistry, although it might be helpful.

You may think that reading inorganic textbooks and knowing more inorganic reactions will help you to solve such questions, but it is a common myth. There are at least 10^5–10^6 inorganic compounds and many more inorganic reactions. Even if you memorise each inorganic reaction that you have encountered, you will probably remember up to a few thousand, but this number is still only a small percentage of all the inorganic reactions. Chances that such a "stoichiometry question" contains reactions that you have seen before are actually quite low.

On the other hand, we rarely see any students trying to memorise all the organic reactions. There are millions of organic compounds and even more organic reactions. Nobody can remember all of them, but does it matter? No, because we can always deduce the organic reactions based on the reactivity and mechanism. Same rationale applies to inorganic chemistry. Instead of trying to memorise all inorganic reactions and the properties of every element, a Chemistry Olympiad student should be able to use minimum basic knowledge (e.g. common oxidation states of elements, atomic mass, colour of common ions, solubility of common salts, etc.) to deduce the inorganic reactions. Also, in many cases, calculation based on stoichiometry is very useful, as demonstrated in our current question.

The difficulty level of the questions can also be easily modified. Take our current question as an example:

The question can be more difficult if this sentence "the number of atoms in **B** are described by geometric progression" is rephrased to "the number of atoms in **A** or **B** are described by geometric progression". The answer to the question is still the same, but more working is needed to analyse compound **A** as well.

The question can be easier if more information is added. For example, "The metal in oxide **Y** has an oxidation state of +4". With this information, we can rule out two more formulae of compound **B**: $\mathrm{LiQ_3O_9}$ and $\mathrm{QLi_2O_4}$. Equation (4) is a redox reaction, because metal **M** is oxidised from 0 oxidation state to a positive oxidation state in **B**. Which element is reduced? The +1 Li (from $\mathrm{Li_2CO_3}$) should still remain +1 in **B**. The −2 O (from $\mathrm{Li_2CO_3}$ and $\mathrm{Q_aO_b}$) cannot be further reduced. The only element that can be reduced is Q in compound **Y**. Since Q has an oxidation state of +4 in **Y**, it must be reduced to an oxidation state lower than +4, e.g. +1 in LiQO and +3.5 in $\mathrm{LiQ_2O_4}$.

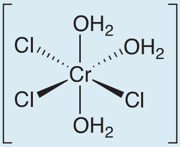
The question can become even easier if this information is added: "Oxide **Y** is widely used as a pigment and the metal in it has an oxidation state of +4". Students familiar with inorganic elements may immediately identify this oxide as TiO_2, which is a widely used white pigment (titanium white) in paint, sunscreen and food colouring.

Problem 5. *Chromium Complexes*

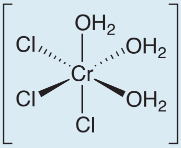
5.1.

Answer: There are a total of 6 different complexes, as shown below:

$[CrCl_3(H_2O)_3]$



mer



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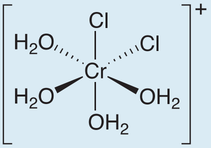
$[CrCl_2(H_2O)_4]Cl$



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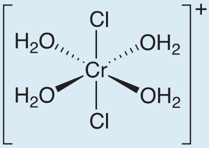
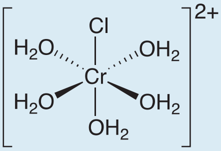
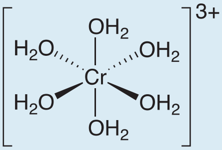


trans

$[CrCl(H_2O)_5]Cl_2$



$[Cr(H_2O)_6]Cl_3$



Solution:

In this question, we must first consider the formulae of all the different constitutional isomers, depending on the number of chloro ligands in the coordination sphere. This will lead us to the 4 possible formulae with 0, 1, 2 and 3 chloro ligands. For the formulae with 2 and 3 chloro ligands in the coordination sphere, they each have 2 different geometric isomers. This leads to the total of 6 different isomers.

5.2.

Answer and **Solution:** The colour change is due to the ligand substitution reaction of the aqua ligand substituting the chloro ligand:

$$\underset{\text{Green}}{[CrCl_3(H_2O)_3]} + 3\ H_2O \rightarrow \underset{\text{Violet}}{[Cr(H_2O)_6]Cl_3}$$

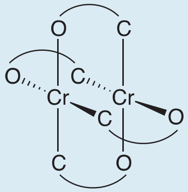
Using the colour wheel, we note that the complementary colour to green is red while the complementary colour to violet is yellow. This indicates that $[CrCl_3(H_2O)_3]$ absorbs light of higher wavelength than $[Cr(H_2O)_6]^{3+}$. As wavelength is inversely proportional to energy, the energy gap (Δ_0) is larger for $[Cr(H_2O)_6]^{3+}$ than $[CrCl_3(H_2O)_3]$. This is because H_2O is a stronger-field ligand than Cl^-, as Cl^- is a π-donor ligand. Refer to part 3.7.4 for details on how different types of ligands affect Δ_0.

5.3.

Answer and **Solution:** Ligand substitution on Cr(III) complexes is extremely slow due to the exceptional stability of d^3 octahedral complexes. This is because octahedral complexes with d^3 configuration are very stable with a crystal field stabilisation energy of −1.2 Δ_0 without any interelectronic repulsion.

5.4.

Answer:



Solution: The structure of $Cr_2(DMP)_4$ can be drawn accounting for the fact that each DMP ligand bridges the 2 chromium centres. The orientation of the DMP ligands may be determined by ensuring that the bulky sides of the ligand point away from each other.

5.5.

Answer: DMP acts as a polyatomic bridging ligand in $Cr_2(DMP)_4$.

Solution: As DMP bridges 2 metal centres, we must look under bridging ligands to classify DMP. DMP is a small polyatomic ligand with different binding sites. Refer to part 3.7.2 for ligand classification.

5.6.

Answer and **Solution:** DMP is a good chelating ligand, bringing the 2 Cr centres close together for interaction through the formation of 5-membered chelate rings. It also stabilises the complex through chelation effect.

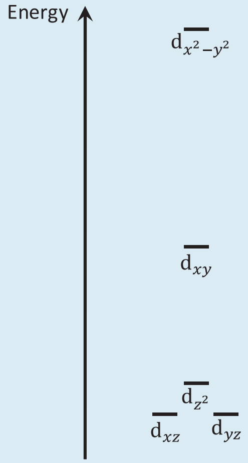
5.7.

Answer: Coordination number = 4, coordination geometry is square planar

Solution: If we look at each chromium centre from chapter 5.5, we can see that it is bonded to 4 donor atoms with square planar geometry.

5.8.

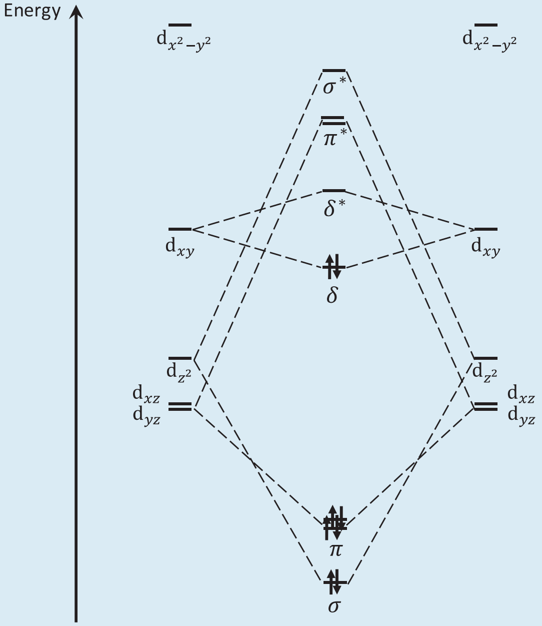
Answer: The crystal field diagram for square planar complexes is:



Solution: The crystal field diagram for square planar complexes may be derived by considering how the different d-orbitals interact with the ligands (on the xy-plane). It can also be derived from the octahedral crystal field, after removing 2 ligands on the z-axis. However, it is best to remember the common crystal field splitting diagrams as the exact energies are calculated and difficult to obtain by a purely theoretical method. Refer to part 3.7.4 for crystal field theory and diagrams.

5.9.

Answer:



Solution:

The molecular orbital diagram may be constructed by considering how the different d-orbitals interact with each other. d_{z^2}-orbitals will overlap head on, forming σ-interactions. d_{xz} and d_{yz}-orbitals will overlap sideways to form π-interactions. d_{xy}-orbitals overlap face-on to form δ-interactions. $d_{x^2-y^2}$-orbitals are used to bond with the DMP ligands and are not involved in $Cr{-}Cr$ interactions. Since the order of strength of interactions is: $\sigma > \pi > \delta$, we can obtain the molecular orbital diagram. The molecular orbitals may be filled using the d-electrons from chromium(II). Chromium(II) is d^4, thus there are a total of 8 d-electrons shared between the chromium centres to be filled into the molecular orbital diagram.

5.10.

Answer: 4

Solution: Bond order is the total number of electrons in bonding orbitals minus the total number of electrons in antibonding orbitals divided by 2. As there are 8 electrons filled into bonding orbitals, the bond order is $\frac{8}{2} = 4$.

5.11.

Answer and **Solution:** Due to the steric hindrance caused by bulky isopropyl groups on the aromatic ring in the guanidate ligand, the $\mathrm{Cr{-}Cr}$ internuclear distance is shortened, allowing for enhanced internuclear interactions.

5.12.

Answer: 5

Solution: As all five d-orbitals participate in the $\mathrm{Cr{-}Cr}$ interaction, there will be a total of 5 bonding and 5 antibonding molecular orbitals formed. In fact, the extra bonding molecular orbital is a δ^{sd}-orbital originating from both the $3d_{x^2-y^2}$ and $4s$-orbitals. As chromium(I) is d^5, the total number of d-electrons shared between the 2 chromium(I) centres is 10. This will allow all the 5 bonding molecular orbitals to be filled, giving a bond order of 5.

Comments on Q5:

This is another common type of question in IChO. These questions are inspired by modern research and taken from recent publications. They often aim to expose students to the newer discoveries in chemistry and pique interest in niche areas.

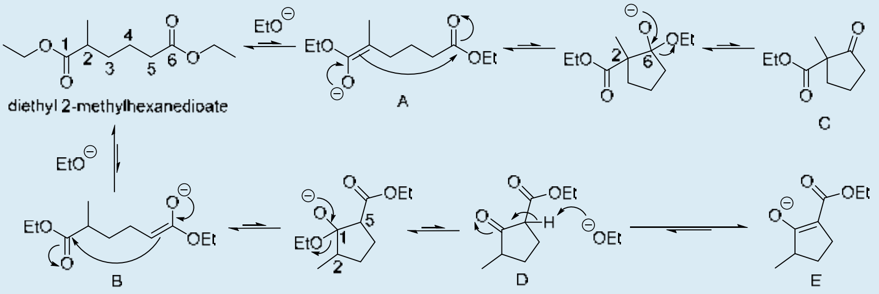
Such questions are usually challenging as they are a large leap from classical chemistry concepts listed in textbooks. They test the students' ability to understand current research with their fundamental knowledge. It is definitely not required, nor is it possible, for students to read through all the published literature in modern chemistry. Instead, these questions start off from the basic knowledge and guide the student towards the new discoveries. Students should try to follow the question and use the hints given to work out the solution.

Problem 6. *Cats' Favourite*

6.1.

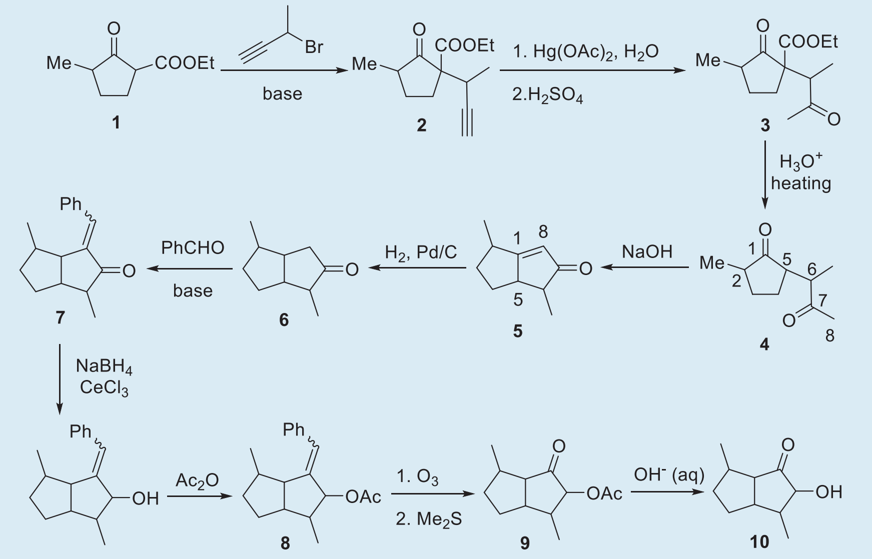
Answer and **Solution:**
We should first know how to convert the IUPAC name into a chemical structure. The diester is not symmetric with two enolisable positions — $\mathrm{C2}$ and $\mathrm{C5}$, forming enolates $\mathbf{A}$ and $\mathbf{B}$, respectively. Each enolate may undergo an intramolecular Claisen condensation, forming ketoester $\mathbf{C}$ and $\mathbf{D}$. Note that the base used in this process is sodium ethoxide because it is the alkoxide corresponding to the ester. Since ethoxide is a moderate-strength base, it only partially enolises the ester, forming a small amount of enolate.

The first three steps (enolisation, nucleophilic addition and elimination of EtO^-) all favour the reactant. Therefore, the driving force for Claisen condensation is the 4th step — deprotonation of the 1,3-dicarbonyl compound. Ketoester D has a hydrogen atom attached to the centre carbon, and can be enolised by ethoxide. However, ketoester C does not have a hydrogen atom attached to the centre carbon, and cannot be enolised by ethoxide. Thus, ketoester C will revert back to the diester by Le Chatelier's principle. The other reaction pathway is favoured because the last step forms the enolate E irreversibly. This mechanism explains why only ketoester D is formed, but not ketoester C.



6.2.

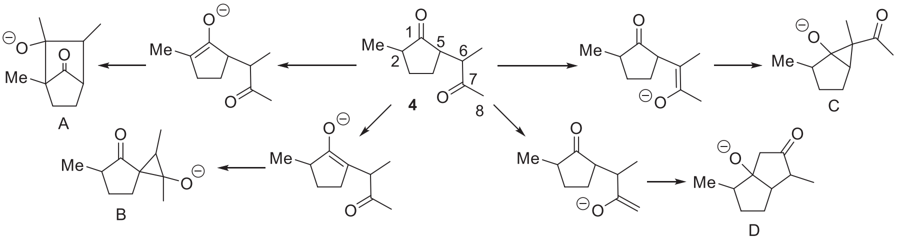
Answer:



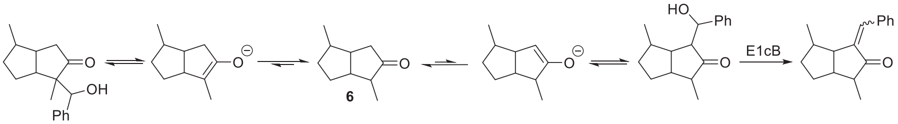
Solution:

Step 1 is an α-alkylation. The enolate preferably forms at the centre carbon of the 1,3-dicarbonyl compound, because it can be stabilised by both carbonyl groups. Compound **2** has 13 carbons whereas compound **4** has 10 carbons, indicating a loss of 3 carbons. Therefore, step 2 is the regioselective oxymercuration of alkyne to form a ketone (rather than aldehyde), and step 3 is the acidic hydrolysis of ester followed by decarboxylation (removing 3 carbons).

Compound **4** is a diketone with 4 possible enolisable positions, which leads to many possible aldol reactions. Forming the enolate at $C2$ will lead to a bridged bicyclic system A, which will not undergo further elimination because the bridgehead carbon ($C2$) cannot adopt sp^2-hybridisation. Forming the enolate at $C5$ will lead to spiro bicyclic compound B with an unfavourable 3-membered ring. Forming the enolate at $C6$ also leads to an unfavourable new 3-membered ring (compound C). Only when the enolate is formed at $C8$, we have a fused bicyclic system with a new 5-membered ring. The ring size is favourable and further elimination via $E1cb$ mechanism occurs to form the conjugated ketone product **5**. The elimination is the driving force for this reaction as it is irreversible.

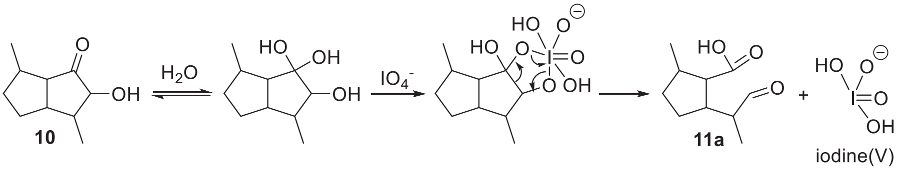


Step 5 is a catalytic hydrogenation reaction, which reduces the $C{=}C$ double bond to a $C{-}C$ single bond. The reaction from **6**→**7** is another aldol condensation. The benzaldehyde is non-enolisable, acting only as an electrophile. The ketone is enolisable on both sides, forming 2 possible aldol addition products. However, the reaction is driven by the $E1cb$ elimination, and only the one that has a hydrogen on the centre carbon can participate. Hence, **7** is formed regioselectively:

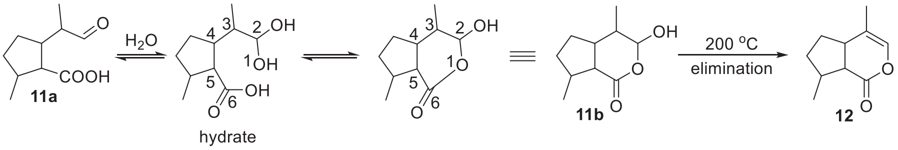


The next step is a Luche reduction, which selectively reduces the $C{=}O$ double bond of the conjugated ketone **7**. The Ce^{3+} ion coordinates to the carbonyl oxygen atom through a hard-hard interaction to ensure that the $NaBH_4$ only reduces the $C{=}O$ bond but not the $C{=}C$ bond. The obtained allylic alcohol then reacts with acetic anhydride to form the ester **8**. The reaction from **8**→**9** is ozonolysis, which also confirms that the Luche reduction only reduces the $C{=}O$ bond, leaving the $C{=}C$ bond in **8**. Step 9 is simply the basic hydrolysis of ester **9** to alcohol **10**.

Compound **10** is an α-hydroxyketone. The ketone is in equilibrium with its hydrate, and the hydrate is actually a 1,1,2-triol, which can be oxidised by periodate to 2 carbonyl groups with the cleavage of the $C{-}C$ bond. For this transformation, the iodine in periodate is reduced from +7 to +5.



11b is a bicyclic isomer of **11a**. Based on the structure of **12**, a new 6-membered ring should be formed in **11b**. One possible mechanism is based on an indirect hint that the aldehyde is in equilibrium with its hydrate (the original hint is about the aldehyde group in compound **10**). In the aldehyde hydrate of **11a**, the $-OH$ group of the 1,1-diol can react with the carboxylic acid to form a new 6-membered ring, with a "hemiacetal-like" structure. Another possible mechanism is that the carboxylate anion carries out a nucleophilic attack on the aldehyde to generate the lactone ring. Structure **11b** is an isomer of **11a** as they have the same chemical formula.

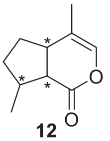


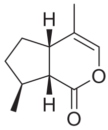
6.3.

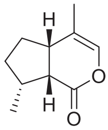
Answer: 3 chiral centres and 8 stereoisomers.

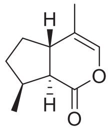
Solution:

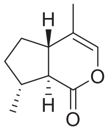
The question does not ask the students to label the chiral centres and draw all the stereoisomers, but doing so will facilitate our following discussion:

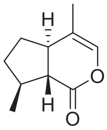

12

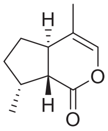

12a

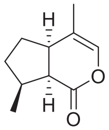

12b

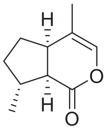

12c


12d


12e


12f


12g


12h

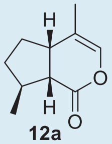
For any chiral molecule with n chiral centres, the maximum possible number of stereoisomers is 2^n. However, the actual number might be smaller than 2^n depending on the symmetry of the molecule.

In our current molecule, the possible number is indeed $2^3 = 8$, but not all the 8 stereoisomers are equally stable. Compound **12** is have a 5,6-fused bicyclic system. For such bicyclic systems, trans-isomers do exist, but are less stable than the cis-isomers (cis–trans isomers are defined based on the stereochemistry of the hydrogens at the ring junctions). Therefore, stereoisomers **12c**, **12d**, **12e** and **12f** are relatively less stable than the other 4 isomers. Generally, fused bicyclic systems with at least one 3-membered ring can only form cis-isomers. 4,4-fused and 4,5-fused bicyclic systems can only be cis too. 4,6-fused, 5,5-fused and 5,6-fused bicyclic systems can be either cis or trans, but their cis-isomers are more stable, therefore if the formation of such ring systems is under thermodynamic control, the predominant product will have a cis-configuration. On the other hand, fused bicyclic systems of 6,6- or larger actually prefer trans over cis, although both types of isomers are possible.

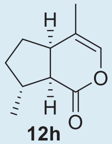
6.4.

Answer:

No. Only two isomers are major:



12a

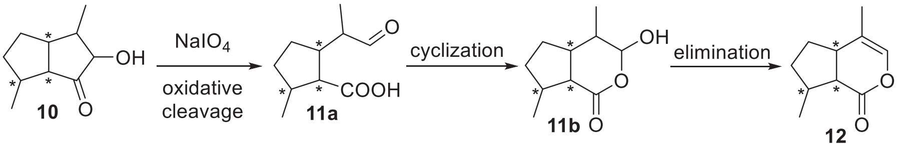


12h

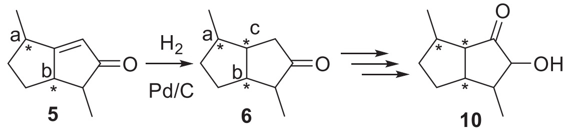
Solution:

From our analysis of part 3, the answer to part 4 is definitely a "no", because the trans bicyclic rings are less stable than the cis ones. However, we should look at the scheme to better understand which reaction step resulted in the preferential formation of cis isomers.

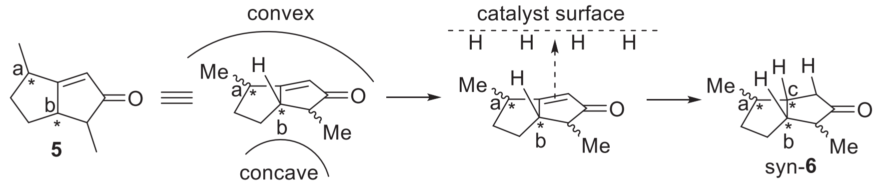
If we revisit the formation of the 6-membered ring in **12**, we can find retention of all the three chiral centres in all the reaction steps from **10** to **12**, since the reactions are not occurring at any of these chiral centres. The other two chiral centres in compound **10** do not matter, because both become sp^2-hybridised in the transformation from **11b** → **12**.



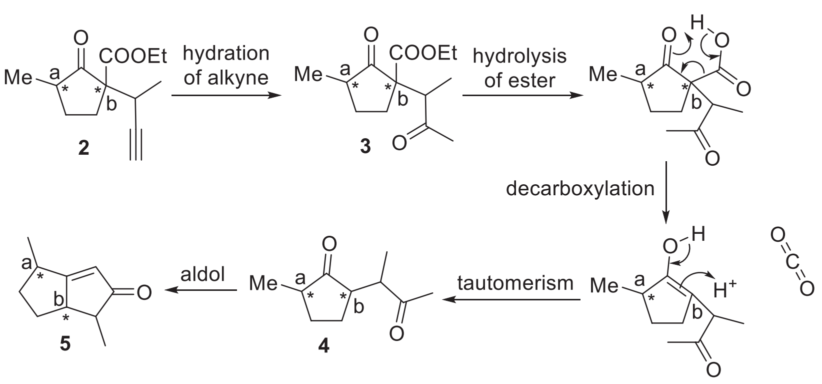
If we continue tracing backwards from **10**, compound **6** has the same three chiral centres in **10**, but compound **5** has only two out of the three. Chiral centre c in compound **6** is a newly formed chiral centre during the hydrogenation reaction.



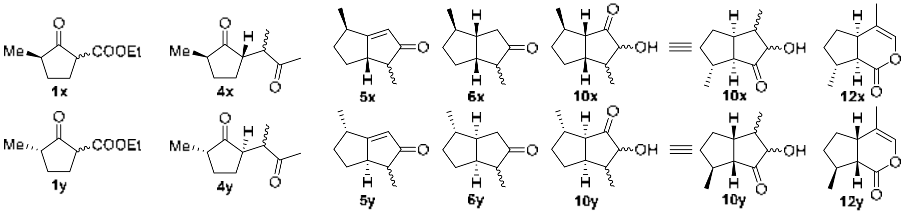
This hydrogenation step (**5**→**6**) is stereoselective due to steric hindrance. Compound **5** is a 5,5-fused bicyclic system, hence having a convex side (syn with the hydrogen on carbon b) and a concave side. The convex side has less steric hindrance; hence molecules of **5** would approach the flat catalyst surface with the convex side. Eventually, the two hydrogen atoms add onto the $C{=}C$ from the convex surface, resulting in a syn-addition product **6**. The newly-formed chiral centre c in **6** is thus dependant on existing chiral centre b in compound **5**.



Is there any relationship between chiral centres a and b in compound **5** then? Throughout the reactions from **2** to **5**, there is a retention of chiral centre a, but chiral centre b has disappeared and reappeared during the decarboxylation step. In the tautomerism step, the enol carbon b is sp^2-hybridised and may react with H^+ from either side. The tautomerism will result in trans-**4** as the major product, because the trans isomer is more stable than the cis isomer. The chiral centre b in compound **1** and **2** is not critical because it becomes sp^2-hybridised in the decarboxylation step.

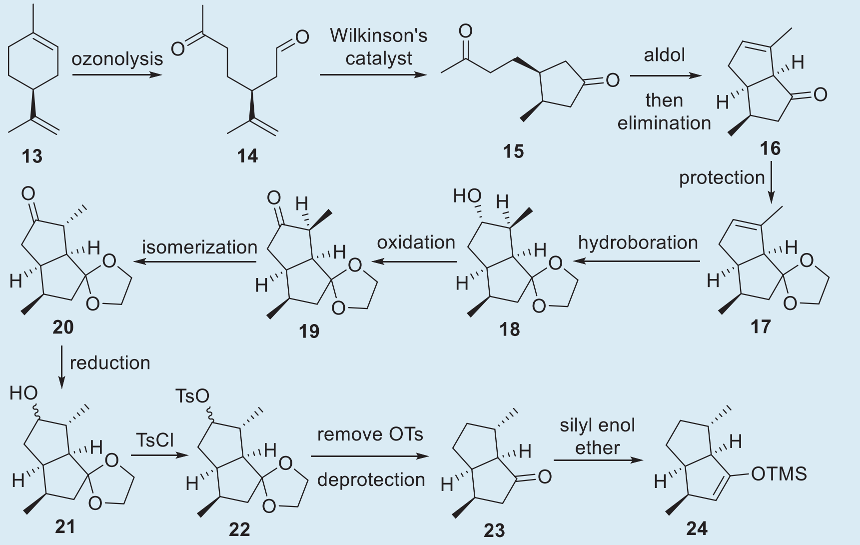


Hence, starting from two isomers of **1x** and **1y**, products **12x** and **12y** will be obtained.



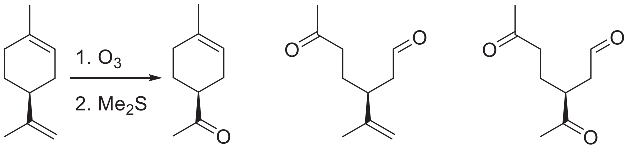
6.5.

Answer:



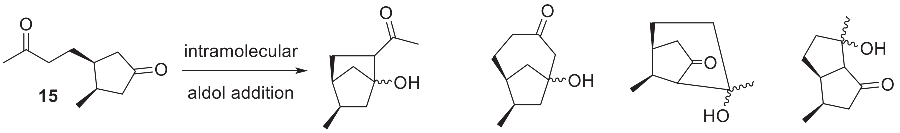
Solution:

Compound **13** has two alkene groups, hence ozonolysis may break either one or both C=C bonds, therefore forming three possible carbonyl compounds **14a**–**14c**. Based on the reaction condition (O_3/Me_2S), it is not easy to tell which product forms. The decision is actually based on the hint that "Wilkinson's catalyst catalyses the cyclization reaction of (substituted) pent-4-enal". Structure **14a** is a ketone. Structure **14c** has an aldehyde, but no alkene group. Only structure **14b** is both an aldehyde and an alkene, also the C=C bond is between C4 and C5. Hence, the answer must be **14b**.

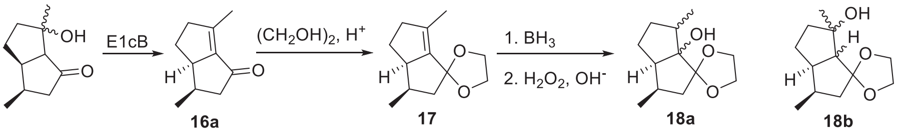


13 **14a** **14b** **14c**

Compound **15** has a formula of $C_{10}H_{16}O_2$, whereas compound **16** is $C_{10}H_{14}O$. Therefore, the reaction of **15→16** must be an aldol condensation reaction of the diketone with a loss of H_2O. Diketone **15** has four enolisable positions, resulting in four possible aldol addition products. However, the first three products are bridged bicyclic systems, unable to eliminate H_2O because the bridgehead carbon cannot become sp^2-hybridised. Only the last product is a fused bicyclic system that is able to eliminate H_2O.

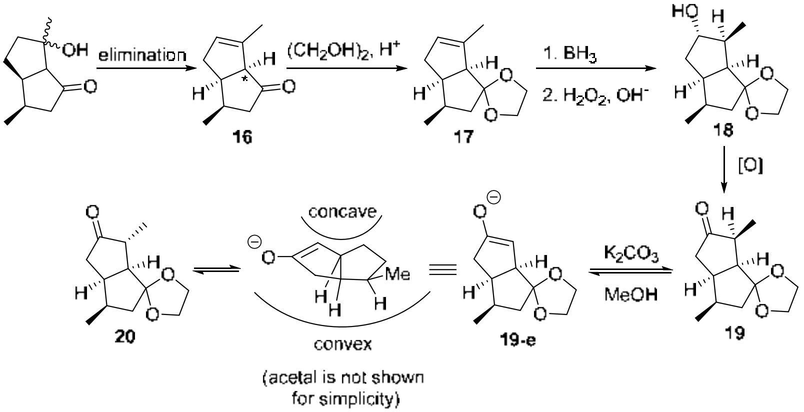


From the last aldol addition product, the corresponding aldol condensation product **16a** can be easily deduced. The C=O group in **16a** is then protected as an acetal to form **17**. As compound **17** is an alkene, its hydroboration will produce an alcohol. The alkene is unsymmetrical, but both sides have two alkyl groups attached, hence both regioisomers **18a** and **18b** may form (stereochemistry is not considered yet). If we look at the following step, we realise that it is Swern oxidation. However, a tertiary alcohol cannot be further oxidised (only primary and secondary alcohols can be oxidised).



There must be something wrong, but where? The protection condition is very standard and there is only one C=O group in **16a**, so **16a→17** must be correct. **17→18a/b** is a standard hydroboration and must be correct as well. $(COCl)_2$/DMSO/Et_3N is also a standard condition for Swern oxidation. It is clear that our aldol elimination product is incorrect. The formula of **16** still indicates a loss of H_2O molecule from **15**, but how does the elimination occur? Following the standard mechanism of aldol addition and E1cB, an aldol condensation product **16a** indeed forms, but is this correct? You should pause here and go back to check the question and your answer one more time before continuing.

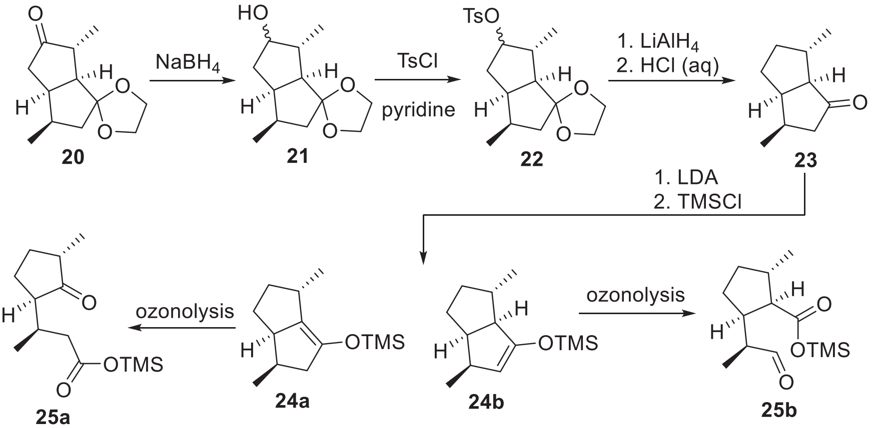
In fact, the product is NOT an aldol condensation product. A hint has been given that "Compound **16** is not conjugated". You may or may not have noticed this hint, but it is critical to our current discussion. It is now clear that **16** is indeed formed via elimination from the other side of the aldol addition product. The mechanism is also not $\mathrm{E1cB}$ because the reaction condition is acidic.



Now that we have the correct structure of **16**, we still need to determine the configuration of the newly formed chiral centre (labelled with *). Compound **16** is a 5,5-fused bicyclic compound. For 5,5-fused system, both trans and cis compound can form but cis is more stable than trans. As the aldol addition is a reversible reaction that favours the more thermodynamically stable isomer, the two hydrogens are cis to each other in **16**. In compound **17**, the ketone is protected as an acetal. Hydroboration of **17** is regioselective, forming the anti-Markovnikov product with $-\mathrm{OH}$ added on the less substituted carbon. This reaction is also stereoselective, because $\mathrm{BH_3}$ prefers to approach the alkene from the convex side of the 5,5-fused system. Now that **18** is a secondary alcohol, it can be smoothly oxidised by the Swern oxidation to ketone **19**.

Conversion from **19** to **20** seems redundant because the two structures look the same. However, a careful examination should tell you the difference — the chirality of the α-C of the ketone. $\mathrm{K_2CO_3}$ provides a weakly basic environment, which can partially enolise ketone **19** to form a small amount of enolate **19-e** via equilibrium. Enolate **19-e** is unstable and will gain a proton to revert the keto form. This time, the proton may approach the enolate **19-e** from either side. If the proton is coming from the less hindered convex side (bottom), the methyl group is forced into the more hindered concave side (top), and this reaction forms back **19**. On the other hand, if the proton is coming from the more hindered concave side (top), the methyl group can then adopt the less hindered convex side (bottom), and the product is **20**. The interconversions of **19**→**19e** and **19e**→**20** are reversible; hence the most stable structure among the three will predominate after sufficient time (by thermodynamic control). Between the keto forms (**19/20**) and the enolate form (**19e**), the keto forms are more stable. Between the two keto forms, **20** is more stable than **19**, because the bulkier methyl group is at the less hindered convex side. The conversion of **19** to **20** is necessary because only **20** has the correct configuration for the final product.

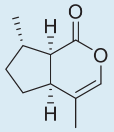
After **20** is formed with the correct stereochemistry, the following steps are just simple functional group conversions. Ketone **20** is reduced to alcohol **21**, which is further converted to tosylate **22**. Whenever an alcohol is converted to a tosylate (or mesylate/triflate), the next reaction will be a nucleophilic substitution or an elimination, as the tosylate is a good leaving group. This is indeed the case, since an S_N2 reaction occurs on tosylate **22** to remove the tosylate, forming an alkane. Aqueous acid simply removes the acetal protecting group, yielding ketone **23**. The three chiral centres in **23** are all in the correct configuration for the formation of the final product in its single enantiopure form.



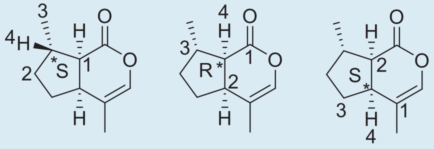
Ketone **23** is then fully enolised by LDA and the less stable lithium enolate is trapped by TMSCl to form a more stable silyl enol ether. There is an interesting regioselectivity issue here in the formation of the silyl enol ether. Silyl enol ether **24a** is formed by enolisation of the more substituted side of the ketone, hence a thermodynamic enol equivalent. On the other hand, **24b** is formed on the less substituted side, hence a kinetic enol equivalent. To determine which enolate is formed, we can look at the next step of ozonolysis. Ozonolysis of **24a** gives a ketone **25a**, which has a different carbon skeleton compared to the given structure of **25**. On contrary, the ozonolysis product (**25b**) of kinetic silyl enol ether **24b** indeed matches with the given structure of **25**. This means that the correct structure of **24** is the kinetic enolate **24b**. One equivalent of LDA first fully converts ketone **23** to its kinetic lithium enolate. Since the keto form is already fully consumed, there is no keto-enol equilibrium, hence the thermodynamic enol equivalent will not form. This kinetic lithium enolate then reacts with TMSCl with retention of the regioselectivity, resulting in a kinetic silyl enol ether product. The choice of base is thus critical to the regioselectivity. The common method to prepare silyl enol ethers use a weak base (usually Et_3N), allowing equilibria between the keto form and both enol forms. Thus, the more thermodynamically stable silyl enol ether (with more substitution on C=C) will predominate. If the kinetic silyl enol ether is needed, then a strong, bulky base (such as LDA) is needed to form the kinetic enolate without equilibrium. **25b** is a silyl ester that can be easily hydrolysed to afford a carboxylic acid.

6.6.

Answer:



(+)-**12**

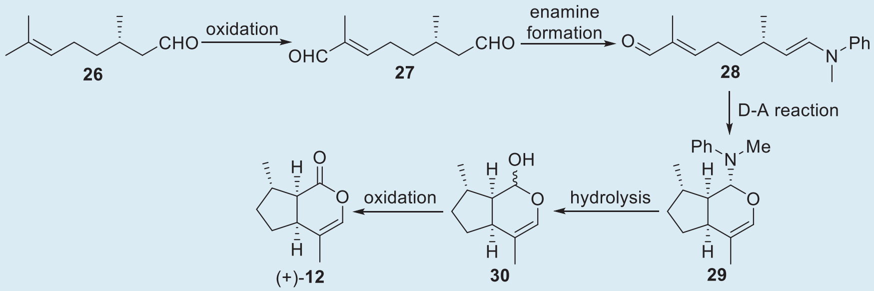


Solution:

25 is one specific enantiomer of **11a**, therefore the conversion of **25** to (+)-**12** follows exactly the same mechanism as **11a**→**12**. The configurations of the three chiral centres in (+)-**12** are simply retained from **25**.

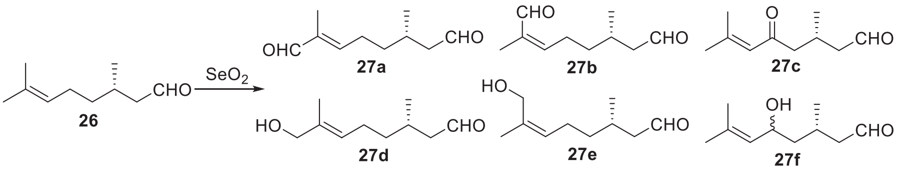
6.7.

Answer:

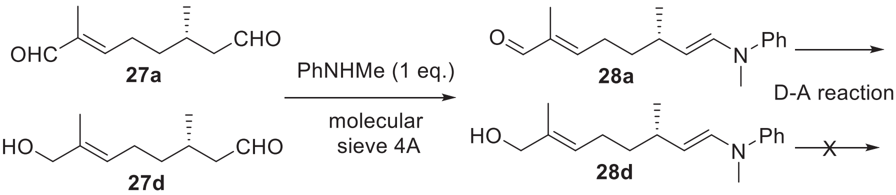


Solution:

Oxidation of **26** by SeO_2 is regioselective for the allylic position of alkenes, forming either allylic alcohol or conjugated ketone/aldehyde products. There are 3 allylic positions in **26**, leading to 6 possible oxidisation products.

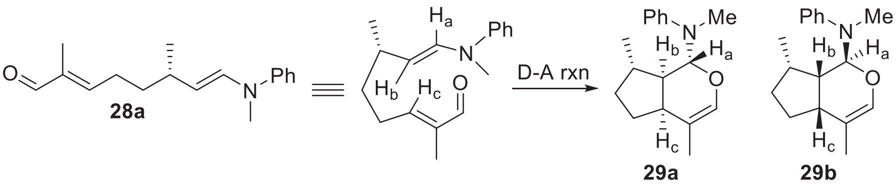


Among these 6 products, **27a/d** are (*E*)-isomers but **27b/e** are (*Z*)-isomers. **27f** is either (*R*)- or (*S*)-isomer and **27c** has no isomer.



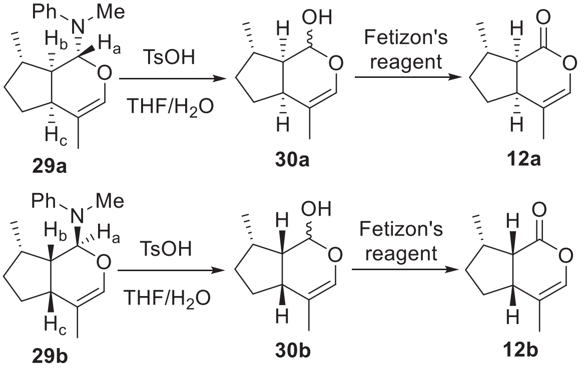
Continuing from **27a/d**, PhNHMe is a secondary amine, which only reacts with aldehydes (to form an enamine) and not alcohols. Between the two aldehyde groups in **27a**, the conjugated one is more stable and less reactive. Therefore, the enamine from **27a** will be formed on the non-conjugated aldehyde since only 1 equivalent of secondary amine is used. The following Diels–Alder reaction requires a diene and a dienophile, requiring a total of 3 double bonds. This can only occur on **28a**, using the conjugated aldehyde as a diene. Such Diels–Alder reactions are known as hetero-Diels–Alder reactions, as they involve heteroatoms in the reaction.

We need to redraw **28a** to a conformation suitable for Diels–Alder reaction — conjugated aldehyde taking s-cis conformation. When the Diels–Alder reaction is occurring, $\mathrm{H_a}$ and $\mathrm{H_b}$ will become anti in the product because they are anti in **28a**. $\mathrm{H_b}$ and $\mathrm{H_c}$ will become syn in the product, because they are pointing towards each other in **28a**. You may refer to chapter 4.14.4 for the details on the stereoselectivity of Diels-Alder reaction. Following such stereoselectivity, 2 possible Diels–Alder products may be formed **29a** and **29b**.



Clearly, the Diels–Alder reaction is not only diastereoselective, but also enantioselective due to the existing chiral centre in **28a**. However, determining which one (**29a** or **29b**) is the major enantiomer by the Diels-Alder mechanism is beyond the

Chemistry Olympiad scope. We have to deduce this from the following reactions. Both **29a** and **29b** will undergo the same type of reaction when treated with TsOH in THF/H_2O solvent. TsOH is obviously an acid catalyst, which will not end up in the product **30**. By comparison of the formulae of **29** ($C_{17}H_{23}NO$) and **30** ($C_{10}H_{16}O_2$), a 7-carbon-1-nitrogen fragment will be lost from **29**, and this should be the Ph(Me)N–moiety. This conversion is an acid-catalysed hydrolysis of hemiaminal ether to hemiacetal, via the oxonium intermediate. The question has mentioned that "**30** is a mixture of two stereoisomers", hence a wavy line is used on the –OH group. The structure of **30a/b** also matches with another clue in the question that "Fetizon's reagent (Ag_2CO_3/celite) is a mild oxidiser, usually oxidises primary alcohol, secondary alcohol or lactol", because **30a/b** is a lactol (cyclic hemiacetal). Thus, with Fetizon's reagent, the lactol is oxidised to a lactone (cyclic ester) and that is why the stereochemistry of –OH group in **30** is not important. Following the hydrolysis and oxidation, we obtain **12a** and **12b** from **29a** and **29b**, respectively. Since we have already determined the structure of (+)-**12** in part 6, it is easy to tell that **12a** (as well as **29a** and **30a**) is the correct answer.



29a **30a** **12a**

29b **30b** **12b**

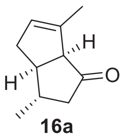
6.8.

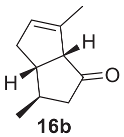
Answer:

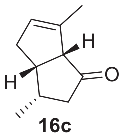
	(+)-**12**	(–)-**12**	neither (+)-**12** nor (–)-**12**
15a	Y		
15b		Y	
15c		Y	

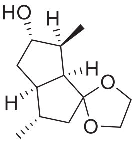
Solution:

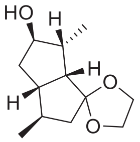
A few key intermediates from **15a/b/c** to **12a/b/c** are shown. **12a** is identical to (+)-**12**. **12b/c** (identical) is the non-superimposable mirror image of (+)-**12**.

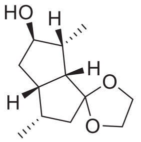

16a

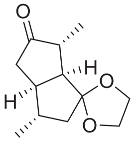

16b

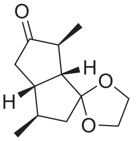

16c

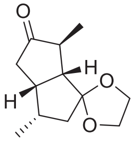

18a

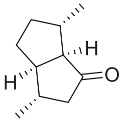

18b

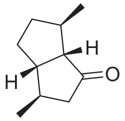

18c

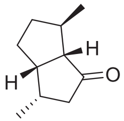

20a

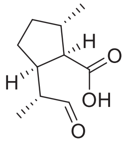

20b

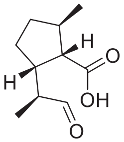

20c

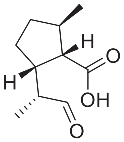

23a

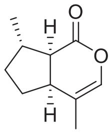

23b

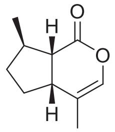

23c

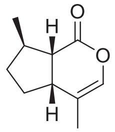

25a


25b


25c


12a


12b

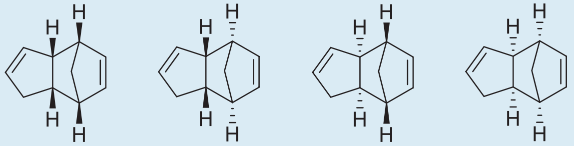

12c

From these synthetic routes, you can see that different stereoisomers of **12** may be prepared from starting materials with different chirality. A group of scientists have also chosen commercially available (*R*)-(+)-citronellal **26** as the starting material to synthesize the unnatural enantiomer (–)-**12**. Also, the natural enantiomer (+)-**12** was obtained from commercially available (*S*)-(–)-citronellal **26**. Each enantiomer was tested on cats of several different breeds and it was found that "both enantiomers were extremely attractive to mature cats". The attraction threshold was as low as 0.01 mg.

Problem 7. *Alkaloids from Africa*

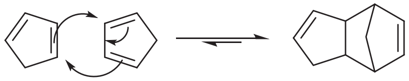
7.1.

Answer:

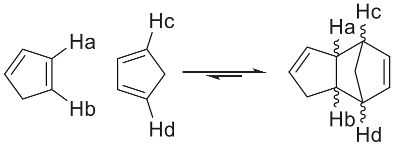


Solution:

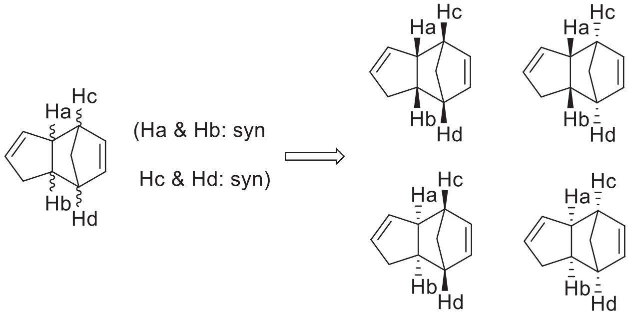
Dicyclopentadiene is the dimer of cyclopentadiene. The dimerisation of cyclopentadiene is a Diels–Alder reaction ([4 + 2] cycloaddition). Thermodynamically, dicyclopentadiene is more stable, and the commercial source of cyclopentadiene is actually dicyclopentadiene. Dicyclopentadiene can be cracked under heat to cyclopentadiene via a retro-Diels–Alder reaction when it is needed in synthesis.



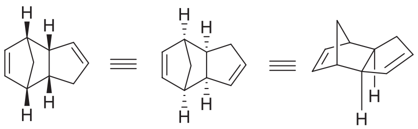
There are 4 chiral centres in dicyclopentadiene, with $2^4 = 16$ possible stereoisomers. However, the actual number is limited by the geometry of cyclopentadiene. In the cyclopentadiene acting as dienophile, the two hydrogen atoms on C1 and C2 (H_a and H_b) are permanently syn to each other, hence H_a and H_b are also syn in dicyclopentadiene. Likewise, in the cyclopentadiene acting as diene, the two hydrogen atoms on C1 and C4 (H_c and H_d) have a cis–cis relationship, leading to a syn product. You can refer to chapter 4.14.4 for the stereoselectivity of Diels–Alder reaction.

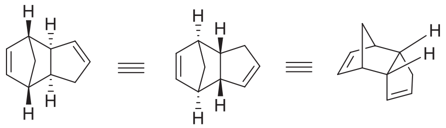


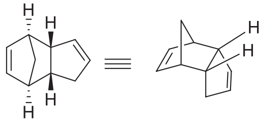
Thus, there are only four possible stereoisomers of dicyclopentadiene, forming two pairs of enantiomers (try to identify by yourself which are enantiomers):

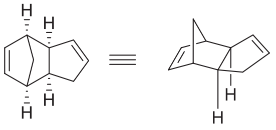


Shown here are the 2D projections with stereochemistry shown. If you prefer the 3D drawings, you may also draw the following structures, which makes it easier to identify the endo and exo compounds:





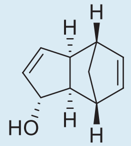




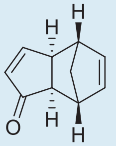
If you feel that some structures are identical, pay special attention to the position of C=C bonds.

7.2.

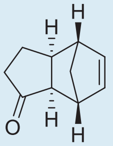
Answer:



(-)-**2**

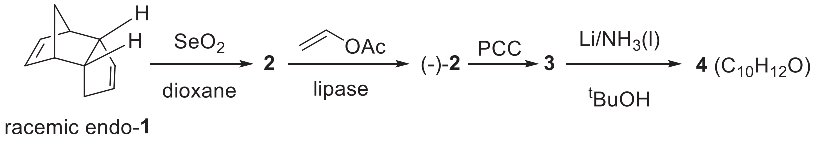


3



4

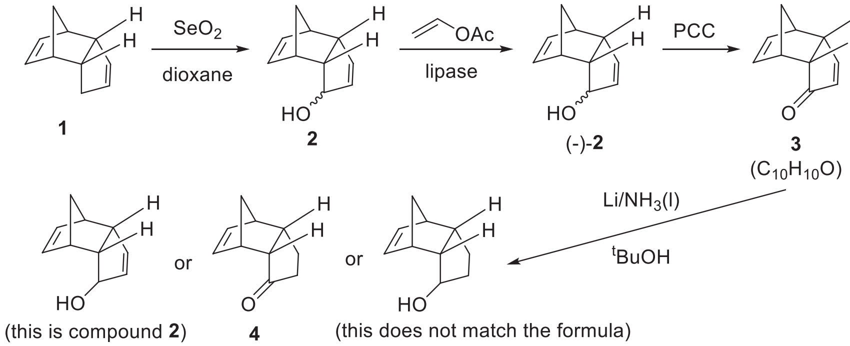
Solution:



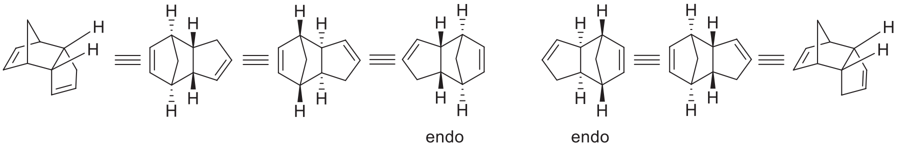
SeO$_2$ selectively oxidises the allylic position of an alkene, forming either an allylic alcohol or a α,β-unsaturated carbonyl compound. There are two alkenes and a total of 4 possible allylic positions to be oxidised. However, reaction only occurs on the more reactive secondary carbon rather than the tertiary carbons.

Lipase is an enzyme; hence the second step is an enzyme-catalysed transesterification reaction, where compound **2** reacts with the vinyl acetate. Thus, compound **2** must be an allylic alcohol and not a ketone, since only alcohol can undergo transesterification.

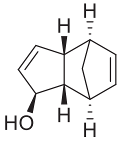
PCC will oxidise the allylic alcohol to a α,β-unsaturated ketone **3** (formula $C_{10}H_8O$). Since compound **4** has 2 more hydrogen atoms than compound **3**, the last step should be a reduction reaction using free electrons generated from lithium in liquid ammonia. There are 2 possible ways that **3** can be reduced, forming either an allylic alcohol ($C{=}O$ is reduced) or a saturated ketone ($C{=}C$ is reduced). **4** should be the saturated ketone, as the allylic alcohol is actually **2**. Note that the saturated alcohol is not possible for compound **4**, since it has 4 additional hydrogens compared to compound **3**. The reactions are shown below without consideration of stereochemistry yet:

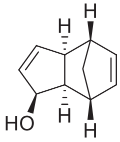


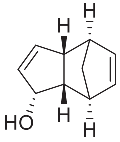
Now, we need to determine the stereochemistry of these compounds. On paper, it is usually easier to draw the structures in 2D. The racemic endo-**1** contains two enantiomers in 1:1 ratio (definition of endo can be found at chapter 4.14.4):

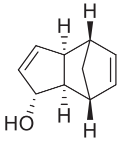


From the two endo-**1** stereoisomers, 4 possible secondary allylic alcohols can be formed through the oxidation:

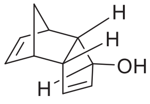

2a

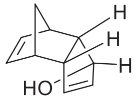

2b

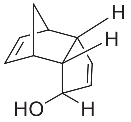

2c

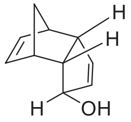

2d

However, among the four stereoisomers, two are more stable than the other two due to steric hindrance. Redrawing the structures into 3D can demonstrate the steric hindrance more clearly:

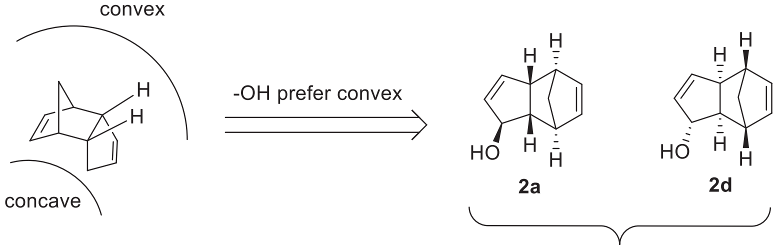

2a


2b


2c

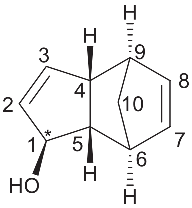

2d

The steric hindrance of the tricyclic system is different on either side. The hydrogen atoms (and any substituents) on the concave side are closer to each other, having more steric hindrance. On the other hand, the convex side is less steric hindered. Thus, when SeO_2 (or any other reagents in other reactions) is approaching this tricyclic system, it will preferably attack from the convex side, thus the major products will have $-OH$ on the convex side. Hence, the structure of product **2** will be **2a** and **2d**, which are actually a pair of enantiomers.

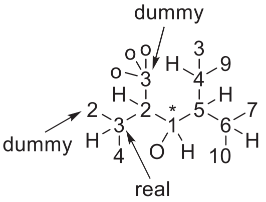


2 is a recemic mixture of **2a** and **2d**

In order to determine which stereoisomer (**2a** or **2d**) is (–)-**2**, we need to assign absolute configuration of the alcohol. We will use **2a** as an example. The carbons in **2a** are labelled from 1 to 10 to facilitate the discussion.



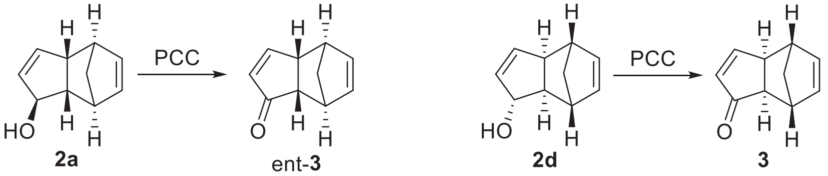
2a



The normal Cahn-Ingold-Prelog (CIP) rules still apply. Chiral centre C1 is attached to hydrogen (4th priority), oxygen (1st priority), C2 and C5. We need to decide the priority of C2 and C5 by examination of the atoms further attached to C2 and C5. C5 is attached to C4, C6 and hydrogen, but C2 is attached to hydrogen and C3 twice. How shall we count the double bond between C2 and C3? C3 should be counted attached to C2 twice, one as a real atom, the other as a dummy atom. When counting further from C3, the real atom C3 is considered to be attached to further real atoms (C2, C4 and hydrogen), while the dummy atom C3 is attached to 3 dummy atoms with zero atomic number (denoted by "o"). Since "o" has an atomic number of zero, C2 will have a lower priority than C5. Thus, the chiral centre in **2a** should be assigned with an (*S*)-configuration. Hence, the (*R*)-alcohol should be **2d**. Note that the dummy C2 should also be attached to 3 dummy atoms if the need for further analysis arises.

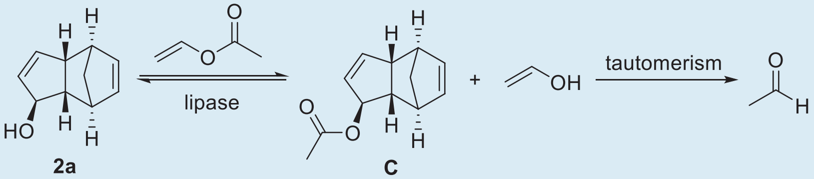
Conversion from (–)-**2** to **3** is simply an oxidation of secondary alcohol to ketone. And the following reduction just reduces C=C to C–C bond.

You may have a query on why the resolution of racemic-**2** is necessary. By the following reaction scheme, you can see that the oxidation product of **2a** is actually the mirror image of **3**. Thus, if the oxidation is conducted without resolution, the obtained ketone is still a racemic mixture, which will continue to form racemic products in all the following steps until the final product.



7.3.

Answer:



The transesterification reaction is irreversible (because the tautomerism from enol to aldehyde is irreversible).

Solution:

Transesterification is an analogue of ester hydrolysis, except that the nucleophile is an alcohol instead of water. Acidic ester hydrolysis is reversible, but basic ester hydrolysis becomes irreversible due to the deprotonation of carboxylic acid product. Transesterification is more often acid-catalysed and reversible. In order to push the transesterification reaction forward, Le Chatelier's principle may be applied to remove one of the products (usually via distillation). In our current enzyme-catalysed reaction, the transesterification step is also reversible, but the reverse reaction will affect the efficiency of the kinetic resolution, decreasing the enantiopurity of the alcohol obtained. In order to render the reaction irreversible, a special ester — vinyl acetate, is used. The alcohol product after transesterification is enol, which readily tautomerises to acetaldehyde ($\mathrm{K} \approx 10^6$).

7.4.

Answer: 52.77%

Solution:

Since no side reactions occur and there is no loss of any materials, $[R\text{-ester}] + [S\text{-ester}] + [R\text{-alcohol}] + [S\text{-alcohol}] = \mathrm{c}_0(\text{rac-2}) = 0.01\ \mathrm{mol\ dm^{-3}}$.

When the conversion of ester **C** is 65%: $[R\text{-ester}] + [S\text{-ester}] = 65\% \times 0.01\ \mathrm{mol\ dm^{-3}} = 6.5 \times 10^{-3}\ \mathrm{mol\ dm^{-3}}$.

Therefore, $[R\text{-alcohol}] + [S\text{-alcohol}] = 0.01 - 6.5 \times 10^{-3}\ \mathrm{mol\ dm^{-3}} = 3.5 \times 10^{-3}\ \mathrm{mol\ dm^{-3}}$.

The *ee* of the obtained alcohol is 98%, containing 99% $R\text{-alcohol}$ and 1% $S\text{-alcohol}$. Hence, $[S\text{-alcohol}] = 3.5 \times 10^{-5}\ \mathrm{mol\ dm^{-3}}$ and $[R\text{-alcohol}] = 3.465 \times 10^{-3}\ \mathrm{mol\ dm^{-3}}$.

Also, the starting material is a racemic mixture of **2**, containing equal amounts of R- and S-isomers, thus: $[R\text{-ester}] + [R\text{-alcohol}] = [S\text{-ester}] + [S\text{-alcohol}] = 5 \times 10^{-3}\ \mathrm{mol\ dm^{-3}}$.

Since we have already calculated the concentration of S- and R-alcohol, $[S\text{-ester}] = 5\times10^{-3} - 3.5\times10^{-5} = 4.965\times10^{-3}\ \text{mol dm}^{-3}$ and $[R\text{-ester}] = 5\times10^{-3} - 3.465\times10^{-3} = 1.535\times10^{-3}\ \text{mol dm}^{-3}$.

Finally, we can calculate the enantiomeric excess:

$$ee = \frac{4.965\times10^{-3} - 1.535\times10^{-3}}{4.965\times10^{-3} + 1.535\times10^{-3}} \times 100\% = 52.77\%$$

7.5.

Answer: k_+ is larger. $s = 13.5$

Solution:

The alcohol after resolution is predominantly (–)-alcohol. This means that (+)-alcohol is mostly converted into the ester form, hence $k_+ > k_-$. Also, (–)-alcohol is (R) and (+)-alcohol is (S).

Since the reaction is pseudo-first-order to the alcohol, we have the integrated rate law as:

$$\ln\frac{[\text{alcohol}]_0}{[\text{alcohol}]_t} = kt$$

Substitute the values obtained from question 4 into the equation:

$$k_+ t = \ln\frac{5\times10^{-3}}{3.5\times10^{-5}} = 4.96$$

$$k_- t = \ln\frac{5\times10^{-3}}{3.465\times10^{-3}} = 0.367$$

Therefore: $s = k_{faster}/k_{slower} = k_+/k_- = 4.96/0.367 = 13.5$

7.6.

Answer: $6.45\ \text{kJ mol}^{-1}$

Solution:

According to Arrhenius equation, rate constant $k = Ae^{\frac{-E_a}{RT}}$

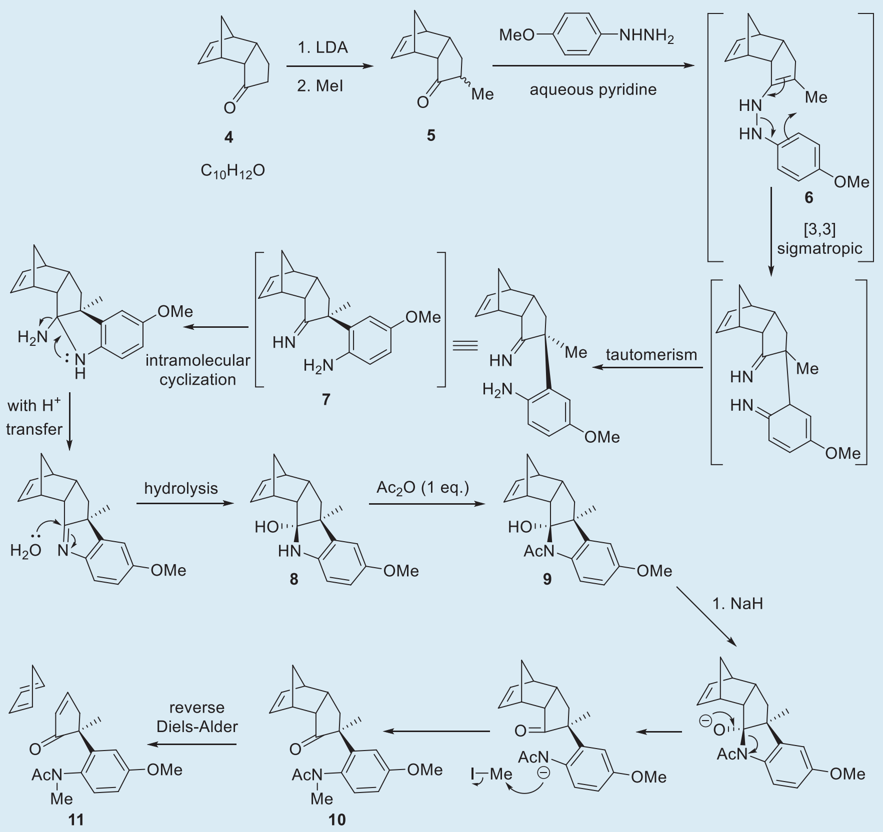
Taking logarithm of both sides gives: $\ln k = \ln A - \frac{E_a}{RT}$

Thus, $\ln k_+ - \ln k_- = \left(-\frac{(E_a)_+}{RT}\right) - \left(-\frac{(E_a)_-}{RT}\right) = \frac{(E_a)_- - (E_a)_+}{RT} = \frac{\Delta E_a}{RT}$

Hence, $\Delta E_a = RT\ln\frac{k_+}{k_-} = 8.314\times(273.15+25)\times\ln(13.5) = 6452\,\text{J}\,\text{mol}^{-1} = 6.45\,\text{kJ}\,\text{mol}^{-1}$

7.7.

Answer:



Solution:

LDA completely deprotonates the α-H of ketone **4**, forming a lithium enolate. Reaction of this lithium enolate with methyl iodide attaches the methyl group to the α-position. The stereoselectivity of this methylation step is not important because the chiral centre becomes planar (sp^2) in the next step.

Ketone **5** reacts with the primary amine in hydrazine, forming an imine which tautomerises to enamine **6**. Enamine **6** has 2 double bonds in a 1,5-relationship, allowing a [3,3]-sigmatropic reaction to occur, breaking a weak N–N bond to form a new C–C bond. The product immediately after sigmatropic rearrangement is a diimine. One imine tautomerises to enamine in order to restore aromaticity, forming compound **7**. The stereochemistry of **7** can be deduced backwards from compound **11**. Also, considering the steric hindrance, the bulkier aromatic group (rather than the methyl group) is at the convex side in **7**.

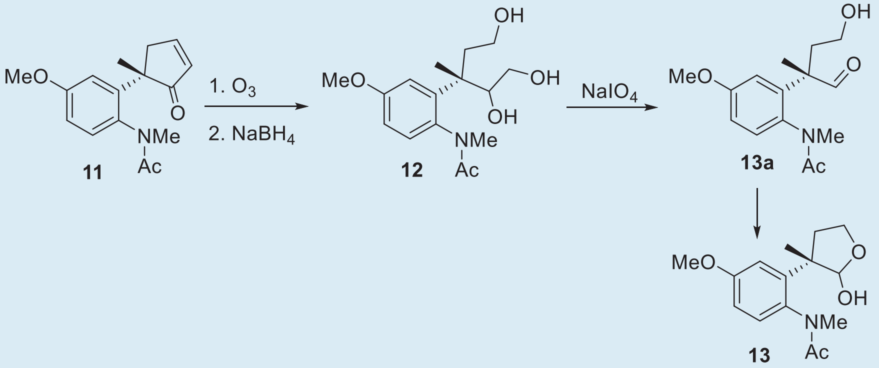
Compound **7** has a nucleophilic amine nitrogen and an electrophilic imine group, allowing an intramolecular cyclisation to occur, forming a new 5-membered ring. As the 5,5-fused system can only be cis, the $-\mathrm{OH}$ group and the $-\mathrm{Me}$ group has to be syn to each other in product **8**.

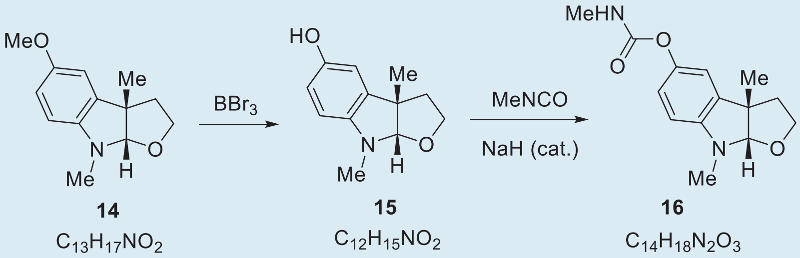
Compound **8** has two nucleophilic centres: hydroxyl oxygen atom and amine nitrogen atoms. When reacting with only 1 equivalent of acetic anhydride, the more reactive N atom will react first, forming an amide **9**. Deprotonation of **9** will form an alkoxide, which expels nitrogen as a leaving group to form a ketone **10** after methylation at nitrogen atom.

Finally, ketone **10** has a formula of $C_{21}H_{25}NO_3$, while ketone **11** has a formula of $C_{16}H_{19}NO_3$. This means that ketone **10** has lost a fragment of C_5H_6 to form ketone **11**. This fragment (C_5H_6) has a double bond equivalence (DBE) of 3. Based on the previous information, it is cyclopentadiene. Therefore, the last step is actually a retro-Diels–Alder reaction.

7.8.

Answer:





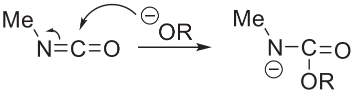
Solution:

First step is an ozonolysis (with reducing reagent $NaBH_4$), cleaving the $C{=}C$ bond and attaching $-OH$ to each carbon. This will produce a diol-ketone, which will be further reduced by $NaBH_4$ to a triol. How do we ensure that compound **12** is a triol rather than a diol-ketone? We should look at the next step using $NaIO_4$. $NaIO_4$ is an oxidising reagent which can cleave the $C–C$ bond in a 1,2-diol. Hence, **12** must be the triol with two $-OH$ groups on adjacent carbons.

Oxidation of the triol by $NaIO_4$ will cleave the $C–C$ bond and convert each carbon into a carbonyl, forming the aldehyde intermediate **13a**. As the question gives a hint that **13** is a bicyclic compound, **13a** must undergo a further cyclisation reaction. Both **13a** and **13** have the same formula $C_{15}H_{21}NO_4$. Therefore, the cyclisation is the intramolecular formation of hemiacetal by the nucleophilic attack of primary alcohol on aldehyde.

It is not easy to deduce the next step since the reaction condition ($MeOH$, H^+) is too general. If we have difficulty working forward from **13**, we could try to work backwards from **16**.

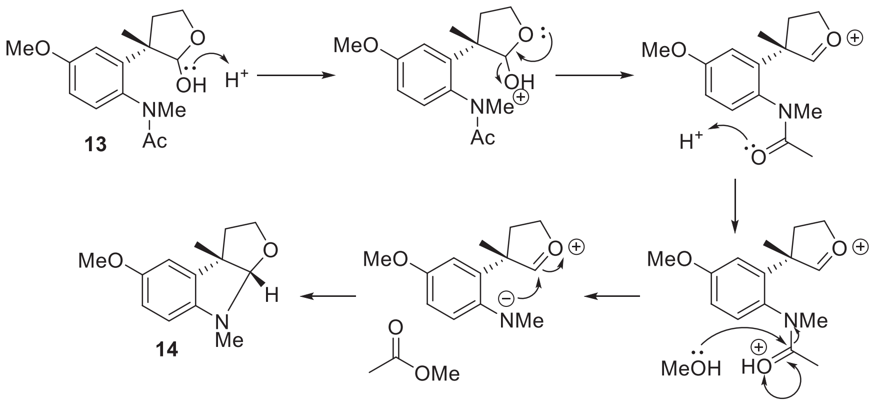
Compound **16** is a carbamate, which is both an ester and an amide on the same $C{=}O$ group. It is clear that the $MeNHCO–$ group in **16** is coming from the reagent $MeNCO$. What is this reagent and how does it react?



The reagent $MeNCO$ is methyl isocyanate, having a $C{=}N$ and a $C{=}O$ at the same carbon. Carbamate can be formed when an alkoxide (RO^-) is attacking the $C{=}N$ of isocyanate. Thus, we can work backwards to deduce compound **15** to be the corresponding phenol with formula $C_{12}H_{15}NO_2$.

Comparing the formula of **14** ($C_{13}H_{17}NO_2$) with **15** ($C_{12}H_{15}NO_2$), we can tell that BBr_3 has triggered a demethylation reaction. This simply means that **14** has one more methyl group than **15**. The position of this methyl group on **14** can be deduced from the structure of **13**.

Now that we have managed to deduce all the unknown structures, we can try to understand how compound **14** is formed. The formula of **13** is $C_{15}H_{21}NO_4$, while the formula of **14** is $C_{13}H_{17}NO_2$. There is a loss of two carbons from **13** when **14** is formed. By checking the structures of **13** and **14**, the two carbons should be from the acetyl group (Ac). Also, a new $C–C$ bond is formed between the nitrogen atom (nucleophile) and the acetal carbon atom (electrophile). Thus, the reaction mechanism is as follows:



Problem 8. *Treasures from the Ocean*

8.1.

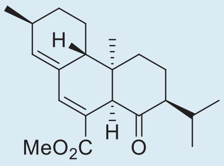
Answer: E

Solution:

This is to test students' basic understanding about the *R*/*S* and (+)/(–) nomenclature used for chiral molecules. *R* and *S* are used to assign absolute configuration for each individual chiral centre. (+) and (–) are referring to the optical property of the entire molecule. The (+)-isomer rotates plane-polarised light clockwise while the (–)-isomer rotates it anticlockwise. *R*/*S* is only used for nomenclature and has no impact on the optical properties of a chiral molecule. Therefore, *R*/*S* and (+)/(–) are totally irrelevant.

8.2.

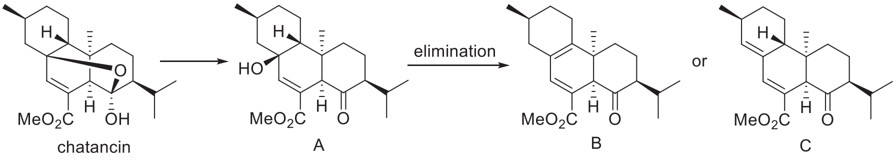
Answer:



Solution:

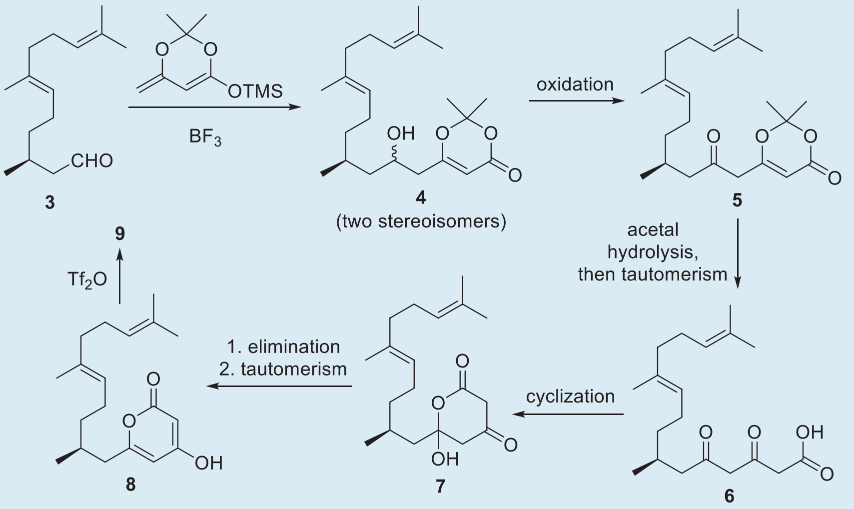
The formula of chatancin is $C_{21}H_{32}O_4$, while the formula of anhydrochatancin is $C_{21}H_{30}O_3$. Thus, anhydrochatancin is the dehydration product of chatancin, which can be confirmed from its name ("anhydro" means "no water"). Now, the question is where and how is water lost?

Chatancin is acid sensitive as it contains a hemiacetal. After the hydrolysis of the hemiacetal group, intermediate A will form, with a ketone and a 3° alcohol. A is only an intermediate, because A has the same formula as chatancin. Next, dehydration of A should be on the 3° alcohol, but there are two possible elimination products B and C. B has 4 chiral centres and C has 5 chiral centres, which means that C must be the correct structure.



8.3.

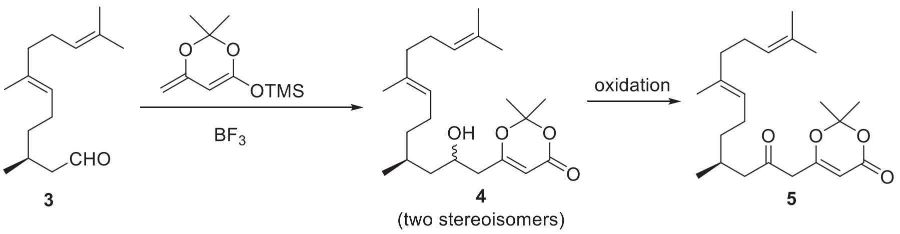
Answer:



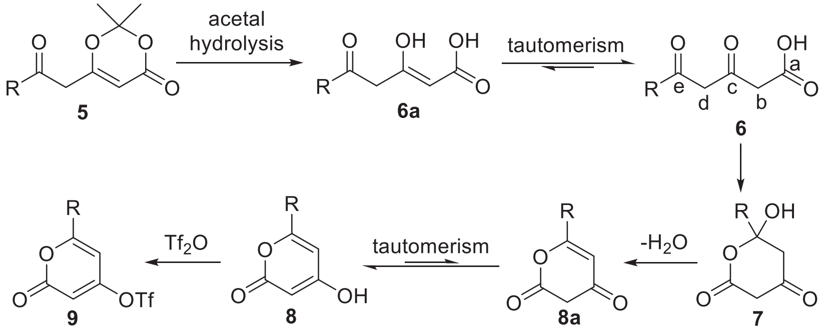
Solution:

In the conversion **3**→**4**, the reactant is a silyl enol ether. The 2 alkenes in this silyl enol ether are conjugated; hence this silyl enol ether has two possible nucleophilic centres: the α-carbon (of the ketone before silyl enol ether) and the terminal carbon. The terminal carbon has higher reactivity as it is less sterically hindered. Product **4** is thus the aldol addition product, with the alcohol having 2 possible configurations.

Dess-Martin Periodinane (DMP) is a selective oxidant to oxidise 1° alcohols to aldehydes, but it can also oxidise 2° alcohols to ketones. This confirms that **4** is the aldol addition product rather than the aldol condensation product. This also explains why the two stereoisomers of **4** are not separated because both are oxidised to the same ketone **5**.



Comparing the structures of **5** and **9** show that the reaction must occur at the ketone and acetal part of **5**, since the long side chain remains unchanged in **9**. For simplicity, we can represent the long side chain with R in **5**–**9**.

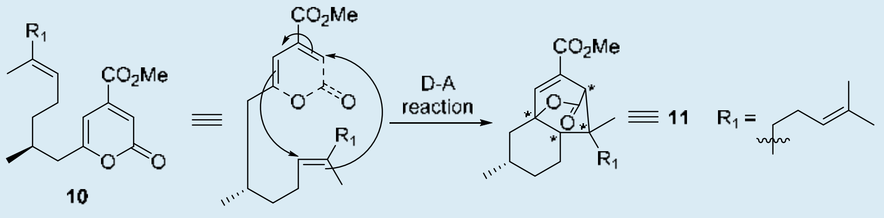


With trace amounts of water and acid (which will be regenerated later), acetal in **5** is hydrolysed to the enol intermediate **6a**, which quickly tautomerises to compound **6**. **6** is an acyclic tricarbonyl compound, fulfilling the description in the question.

Since **7** is a cyclic dicarbonyl compound, the reaction **6**→**7** must be an intramolecular cyclisation. In compound **7**, there are 3 $\mathrm{C{=}O}$ groups (carbon a, c and e), while there is only one nucleophile — the OH group of the carboxylic acid. If the OH group attacks carbon c, a 4-membered ring is formed; while a 6-membered ring is formed when the OH group attacks carbon e. As 6-membered rings are more favourable, compound **7** is the 6-membered cyclic hemiacetal. We could confirm this by comparing the structure of **7** with that of **9**. Comparing the formula of **7** ($\mathrm{C_{19}H_{30}O_4}$) and **8** ($\mathrm{C_{19}H_{28}O_3}$), the process **7**→**8** is a dehydration (elimination) reaction, forming **8a**. **8a** is a ketone, which tautomerises to the enol form **8**. Enol **8** is more stable in this case, because **8** is aromatic (in one of its resonance structures). Finally, the OH group of phenol **8** reacts with $\mathrm{Tf_2O}$ (an anhydride) to form the triflate ester **9**.

8.4.

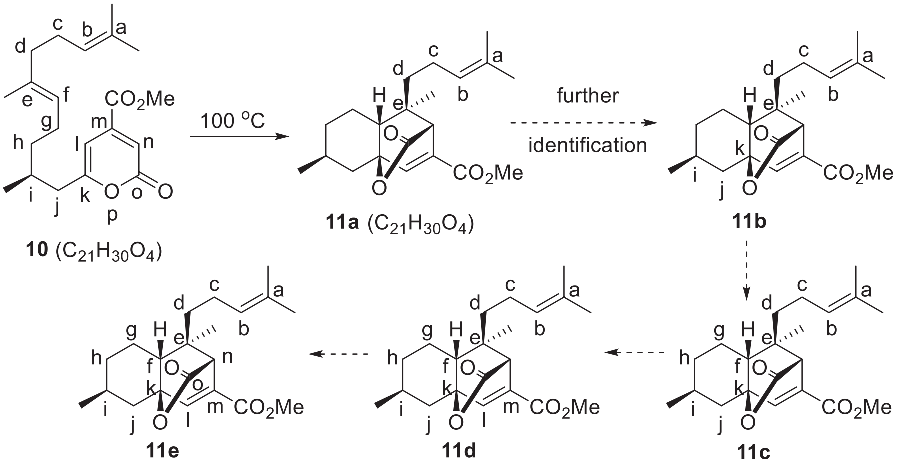
Answer:



Solution:

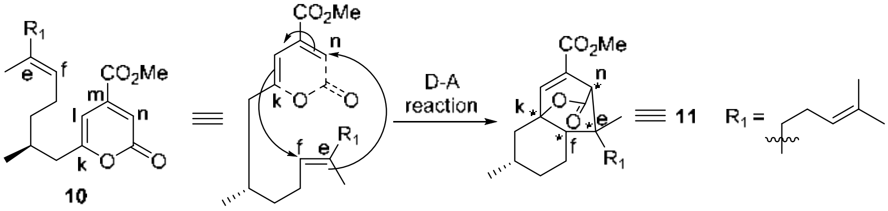
The formulae of both **10** and **11** are $C_{21}H_{30}O_4$, therefore this conversion is an intramolecular cyclisation reaction. It is not easy to see the reaction mechanism directly, so we will first label the corresponding carbons (a to p) to identify the reaction centres. In compound **11**, we can easily identify carbons a to e, since sp^2-carbon a has 2 methyl groups attached (see structure **11a**). The π-bond between carbon e and f breaks and a new bond forms on carbon e. Carbon e is probably a nucleophile (since C=C is electron rich), but which carbon (in **10**) is the electrophile?

If we cannot continue our analysis from carbon e, then let's try to find some other clues. Carbon i is a chiral centre with a methyl group, which can be identified in **11**. On one side of i (in **10**), we can find carbons h, g and f (alkene). On the other side of i, we have carbons j and k (attached to oxygen). In **11**, we can locate an oxygen atom three bonds away from carbon i, allowing us to assign the atoms j and k (structure **11b**). Thus, the carbons on the opposite side of i can also be confirmed as h, g and f (structure **11c**).



The ester group (CO_2Me) is attached to carbon m, hence we can identify m in **11d**, as well as l (between k and m). The remaining two carbons are n and o, just beside m (structure **11e**). There is no change to carbonyl carbon o.

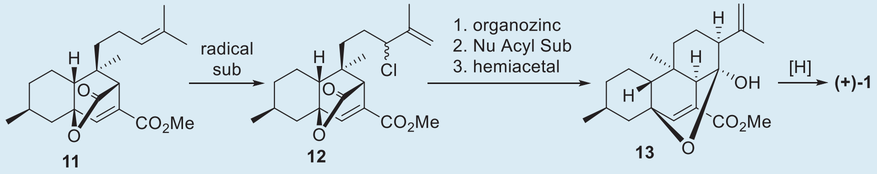
Now, we have successfully identified the corresponding atoms in **10** and **11**. The new bonds formed in **11** are: e–n, f–k, l–m (π-bond). The bonds broken in **10** are: e–f (π-bond), k–l (π-bond), m–n (π-bond). Overall, two σ-bonds are broken and two π-bonds are formed, with one π-bond shift. This is typical for a Diels–Alder reaction (chapter 4.14.4), with carbons k–l–m–n being the diene and e–f double bond being the dienophile.



We need to redraw **10** to show the relationship of the diene and the dienophile. During this Diels–Alder reaction, a new 6-membered ring (e–f–k–l–m–n) is formed between the diene and the dienophile. Another new 6-membered ring (f–g–h–i–j–k) is also formed, due to the formation of f–k bond and the existing chain between f and k. Therefore, compound **11** has a total of three rings. Stereochemistry of **11** is not shown for simplicity, but the stereochemistry is induced by chiral centre i.

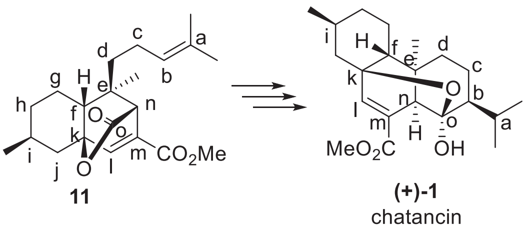
8.5.

Answer:



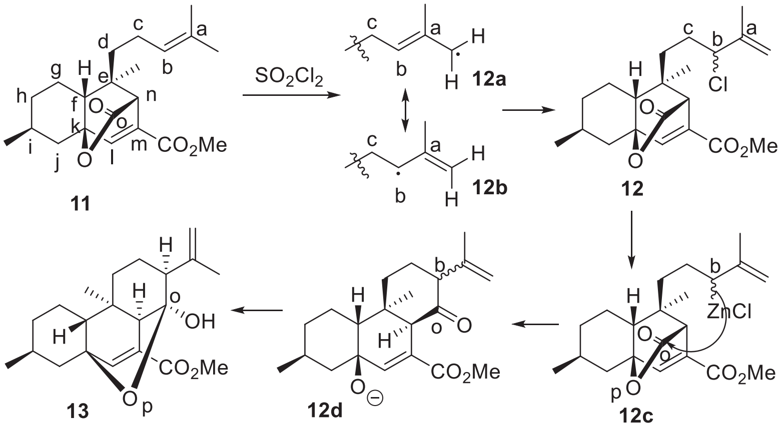
Solution:

Some atoms in (+)-**1** have been labelled by comparison of **11** and (+)-**1**. The isopropyl group in (+)-**1** must come from the alkene carbon a, because this is the only carbon bonded to 2 methyl groups in **11**. Thus, the reaction site is carbon b. A new bond is formed between carbon b and carbon o. Carbon o is an electrophilic carbonyl carbon, which makes carbon b the nucleophilic site.



Looking at the reaction conditions, allylic chloride **12** is converted by Zn to an organozinc reagent, which then attacks the carbonyl carbon o. The organozinc must be on carbon b according to our previous analysis and the b–o bond formation will generate the new 6-membered ring.

Organozinc at carbon b must come from the corresponding allylic chloride at carbon b. However, how does the sp^2 carbon b (in **11**) become the allylic chloride in **12**? The key is actually in the reagent $\mathrm{SO_2Cl_2}$. This reagent is sulfuryl chloride, having two $\mathrm{S{=}O}$ bonds instead of one in thionyl chloride ($\mathrm{SOCl_2}$). You should have met thionyl chloride before, in the conversion of alcohol → alkyl chloride and acid → acyl chloride. In these reactions, $\mathrm{SOCl_2}$ is a $\mathrm{Cl^-}$ resource. On the other hand, $\mathrm{SO_2Cl_2}$ is actually a $\mathrm{Cl_2}$ resource; hence we can deduce that the allylic chlorination is through a radical mechanism. **12a** is first formed through hydrogen abstraction, which has resonance form **12b** that reacts to form the allylic chloride **12**. Students do not necessarily need to know the reactivity of $\mathrm{SO_2Cl_2}$, but can still deduce the structure of **12** because the chloride must be on carbon b.

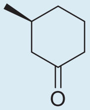


12 is then converted by Zn to the nucleophilic organozinc reagent **12c**, which attacks the ester carbon o. The mechanism of this nucleophilic acyl substitution step is not fully drawn, but the product **12d** (oxygen p as the leaving group) is clearly shown. The alkoxide in **12d** then attacks the ketone carbon o to form the hemiacetal

13. The formulae of **12** and **13** also confirmed that **12**→**13** is an addition reaction without any loss of carbon. Note that the stereochemistry of carbon o and carbon b in **13** can be deduced from the final product (+)**-1**. The last step is a simple catalytic hydrogenation of the acyclic alkene. This is chemoselective because the other alkene is conjugated and more hindered.

8.6.

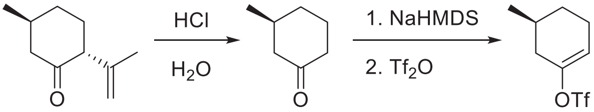
Answer:



15

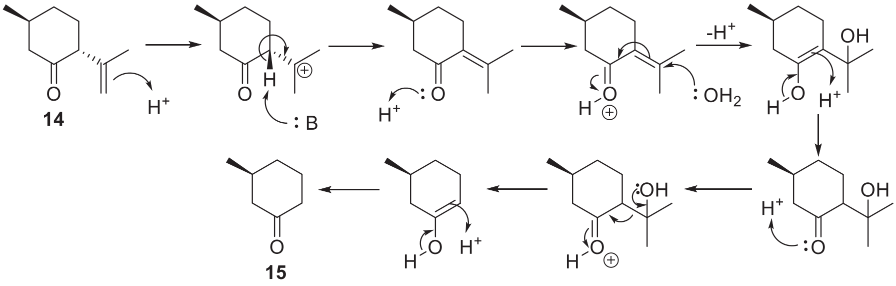
Solution:

Compound **16** is a triflate (ROTf). Triflate is an analogue of tosylate and mesylate, all of which are sulfonic esters. NaHMDS (and KHMDS) is a typical strong, bulky base (similar to LDA), which converts ketone **15** into its enolate form. The obtained enolate then reacts with triflic anhydride (Tf_2O) to form the enol ester **16**. Therefore, it is quite simple to deduce the structure of ketone **15** backwards from enol triflate **16**.



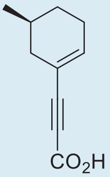
14 **15** **16**

Compound **14** is converted to **15** via the loss of the 3-carbon side chain, but how? The question has mentioned "acid-catalysed isomerisation of **14**, followed by hydrolysis". Thus, the hydrolysis should be a retro-aldol condensation:



8.7.

Answer:



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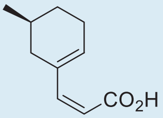

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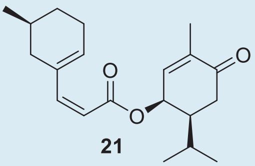
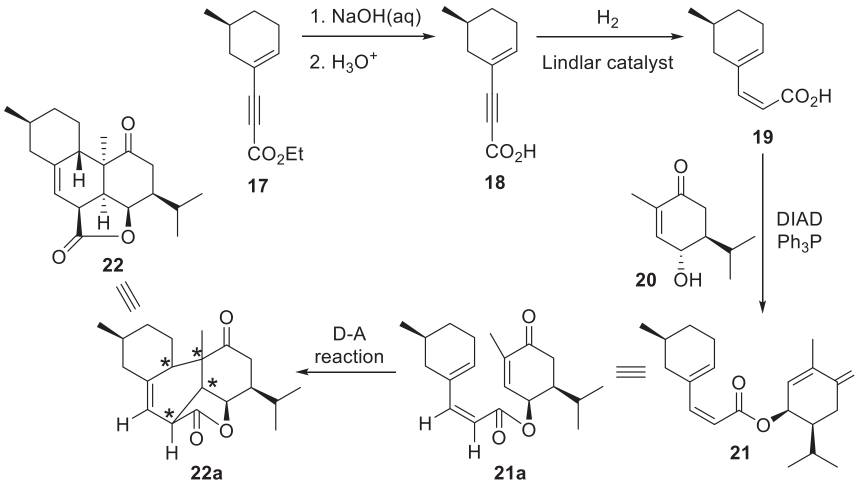


21

Solution:

Basic hydrolysis of ester **17** forms carboxylic acid **18**. Catalytic hydrogenation of the alkyne group in **18** using Lindlar catalyst forms cis-alkene **19**. The formula of **19** is $C_{10}H_{14}O_2$, **20** is $C_{10}H_{16}O_2$, while **21** is $C_{20}H_{28}O_3$. The reaction **19** + **20** → **21** should be a condensation reaction, with loss of H_2O.

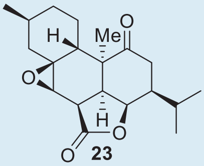
The reaction condition of **19** + **20** → **21** is DIAD (diisopropyl azodicarboxylate), a homologue of DEAD (diethyl azodicarboxylate). Both DEAD and DIAD are typical conditions for the Mitsunobu reaction (part 4.7.1) on alcohols. The Mitsunobu reaction is an S_N2 reaction with a $Ph_3P{=}O$ leaving group. Therefore, an inversion in stereochemistry occurs, with the carboxylate of **19** being the nucleophile.



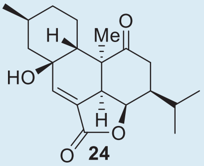
The mechanism of the Diels–Alder reaction is not required in the current question, but we shall still analyse it as a practice. First, we need to redraw ester **21** to **21a**. In **21a**, the diene is in s-cis conformation, and the dienophile is close to the diene. After the Diels–Alder reaction, two new σ-bonds are formed, together with four new chiral centres in the 6-membered ring. The stereochemistry in **22a** is not shown, but is the same as **22**.

8.8.

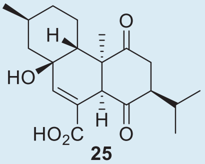
Answer:



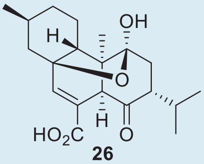
23



24



25

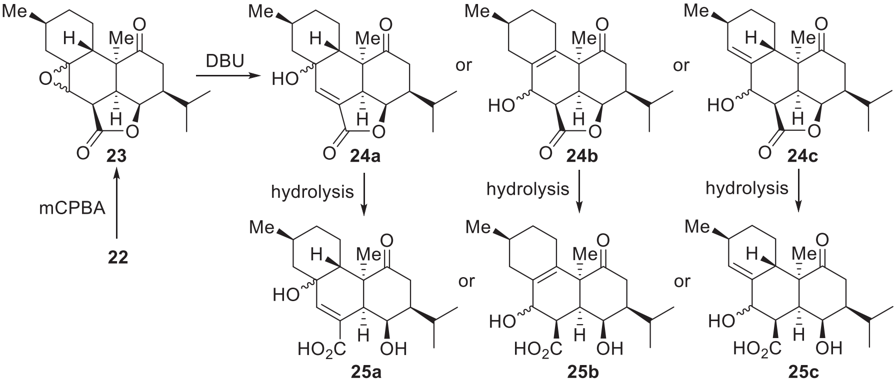


26

Solution:

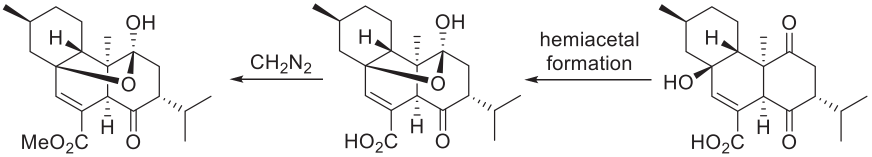
m-CPBA is an epoxidation reagent for the alkene in **22** ($C_{20}H_{28}O_3$). **23** has a formula of $C_{20}H_{28}O_4$ and is thus the corresponding epoxide from the alkene. The stereochemistry of the new epoxide may not be determined at the moment, but should be deduced later on.

DBU is a typical base, thus reaction **23**→**24** should be an elimination of the epoxide. There are three possible β-positions of the epoxide, thus three possible elimination products (allylic alcohols) **24a–c**.



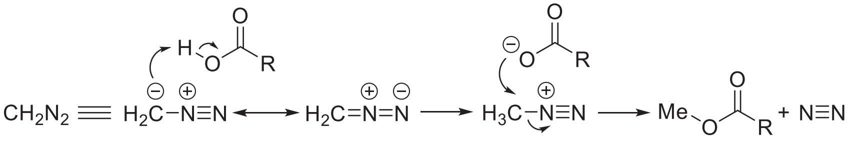
Hydrolysis of **24a–c** will break the lactone, forming a secondary alcohol and a carboxylic acid in **25a–c**. Which one will undergo oxidation by K_2RuO_4 to form intermediate **25**? It is not easy to determine, since **25b** and **25c** both have two secondary alcohols that can be oxidised.

We can try to analyse backwards from (+)-sarcophytin **2** backwards. The formula of **2** is $C_{21}H_{30}O_5$ while the formula of **26** is $C_{20}H_{28}O_5$. This means that **2** has one more carbon (methyl group) than **26**. The only methyl group in **2** is the methyl ester, which means that **26** is the corresponding carboxylic acid.

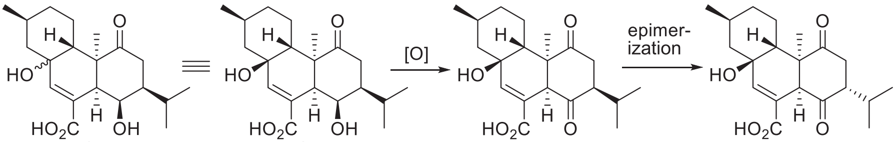


2 ($C_{21}H_{30}O_5$) **26** ($C_{20}H_{28}O_5$) **26a**

What is the reaction mechanism of **26**→**2** then? The reagent CH_2N_2 is called diazomethane, having two resonance structures. It is typically used to convert a carboxylic acid to its methyl ester, by the following mechanism:



26 is not only a carboxylic acid, but also a hemiacetal. This hemiacetal is formed during the reaction of **25**→**26**. Thus, **25** should have the corresponding alcohol and ketone for the formation of the hemiacetal. The intermediate **26a** should thus be the tertiary alcohol, which can form the 5-membered ring hemiacetal with one of the two ketones.



25a **25a** **25** **26a**

Now, the intermediate **26a** is already very close to the intermediates **25a–c**. Both **25b** and **25c** only have secondary alcohols, thus only **25a** is the correct intermediate. The stereochemistry of the tertiary $-OH$ group in **25a** is not shown, but can be deduced from **26a**: this $-OH$ group is pointing towards us. **25** is a diketone, the oxidation product of **25a**.

The diketone **25** undergoes an epimerisation, changing the stereochemistry of the isopropyl group. This epimerisation occurs under basic condition (KOH), via the enolate. **26a** is thermodynamically more stable than **25** because isopropyl is on the less hindered convex side in the cis-fused system of **26a**.

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