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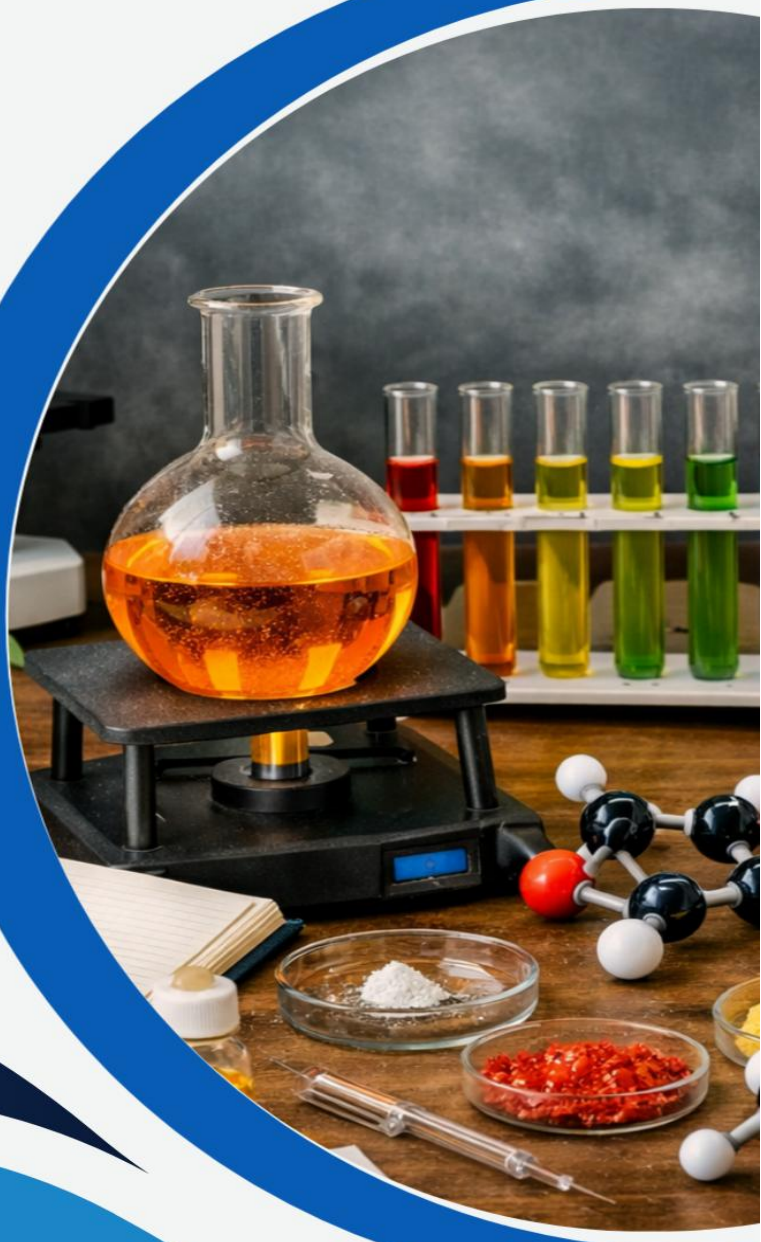
CHM211

ORGANIC CHEMISTRY I



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Course code: CHM 211

Course title: Organic Chemistry I

Course unit: 2 Units

Series 1: Aromatic Compounds and Their Chemistry

Part 1 Fundamentals of Aromatic Compounds

- 1.1.1 Definition and general features of aromatic compounds
- 1.1.2 Structure and resonance in benzene
- 1.1.3 Criteria for aromaticity (Hückel's rule)

Part 2 Reactions of Aromatic Compounds

- 1.2.1 Electrophilic substitution reactions: nitration, halogenation, sulphonation, Friedel–Crafts reactions
- 1.2.2 Orientation and reactivity in substituted aromatics
- 1.2.3 Other reactions of aromatic compounds: oxidation and reduction

Part 3 Applications and Problem-Solving in Aromatic Chemistry

- 1.3.1 Industrial importance of aromatic compounds
- 1.3.2 Worked examples and problem-solving in aromatic chemistry

Introduction

Aromatic compounds occupy a central place in organic chemistry because of their unique stability and widespread occurrence in everyday life. From the fragrance of perfumes to the structure of many pharmaceuticals, these compounds demonstrate the importance of understanding how ring systems behave and react. This Series will set the foundation for appreciating the chemistry of aromatic compounds, preparing you to tackle more complex reactions and applications later in the course.

The aim of this Series is to equip you with the knowledge and skills to define, explain, and analyse the structures, properties, and reactions of aromatic compounds, as well as to apply these concepts in solving practical problems.

We shall commence this Series by exploring the fundamentals of aromatic compounds, including their definition, general features, and the resonance structure of benzene, followed by the criteria for aromaticity. Next, we will move on to the reactions of aromatic compounds, focusing on electrophilic substitution, orientation effects, and other important transformations such as oxidation and reduction. Finally, we will wrap up by considering the industrial importance of aromatic compounds and engaging with worked examples that will strengthen your problem-solving skills in aromatic chemistry.

Series Learning Outcomes

Upon completing this Series, you should be able to:

define the general features of aromatic compounds,
explain the resonance structure of benzene,
analyse aromaticity using Hückel's rule,
describe the major electrophilic substitution reactions of aromatic compounds,
evaluate orientation and reactivity patterns in substituted aromatic compounds,
explain other important reactions of aromatic compounds such as oxidation and reduction,
assess the industrial importance of aromatic compounds, and
apply problem-solving strategies to worked examples in aromatic chemistry.

1.1 Fundamentals Of Aromatic Compounds

1.1.1 Definition and general features of aromatic compounds

An **aromatic compound** is an organic molecule that contains one or more planar ring systems with delocalised π-electrons, which confer unusual stability compared to non-aromatic compounds. The most common example is **benzene**, a six-membered ring with alternating double bonds that are not localised but shared across the ring. This delocalisation leads to a property known as **aromatic stability**, making these compounds resistant to addition reactions that are typical of alkenes.

Aromatic compounds are characterised by their cyclic structure, planarity, and electron delocalisation. They often exhibit unique chemical behaviour, such as undergoing substitution rather than addition reactions.

Fill in the blank: Aromatic compounds are unusually stable because of _____ of π-electrons across the ring.

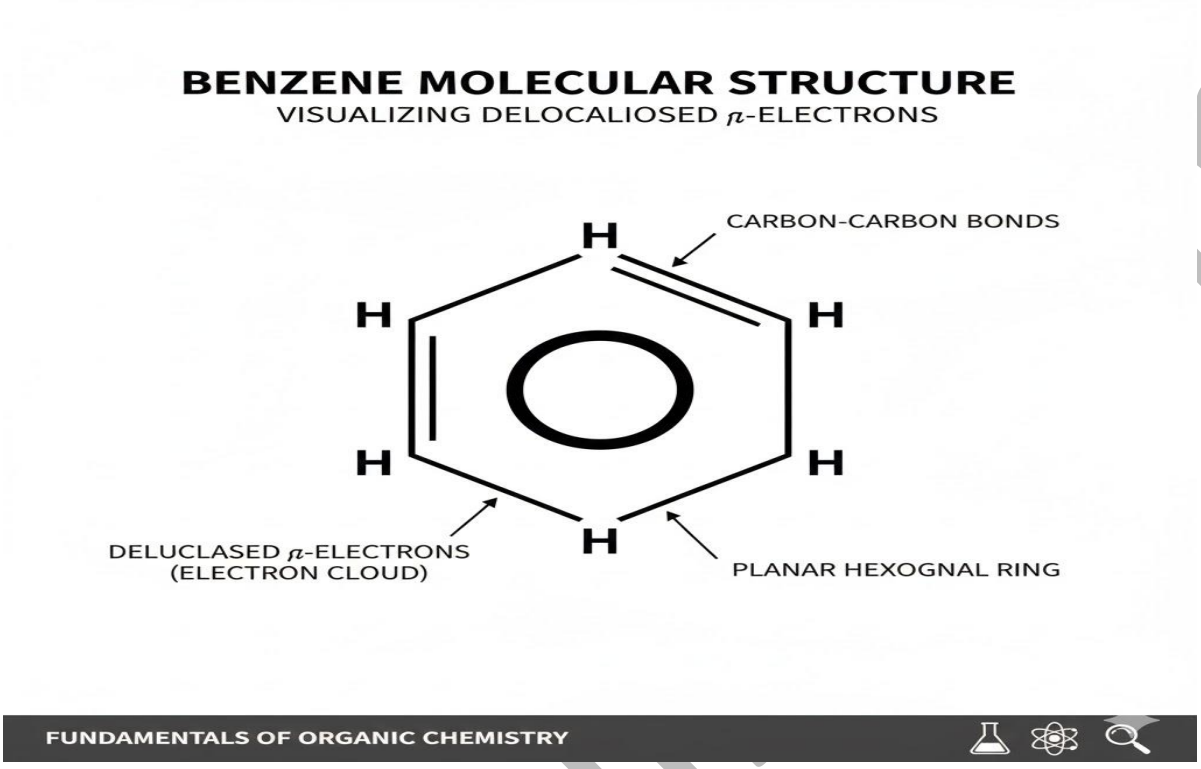


Figure 1.1 Benzene structure with delocalised electrons

1.1.2 Structure and resonance in benzene

The **resonance structure** of benzene refers to the representation of its bonding as alternating single and double bonds. However, in reality, the electrons are delocalised, and all carbon–carbon bonds are of equal length. This concept is explained using resonance theory, where benzene is depicted as a hybrid of two canonical structures.

This resonance stabilisation explains why benzene does not behave like a typical alkene. Instead of undergoing addition reactions, it prefers substitution reactions that preserve the aromatic ring.

Fill in the blank: In benzene, all carbon–carbon bonds are of equal _____ due to resonance stabilisation.

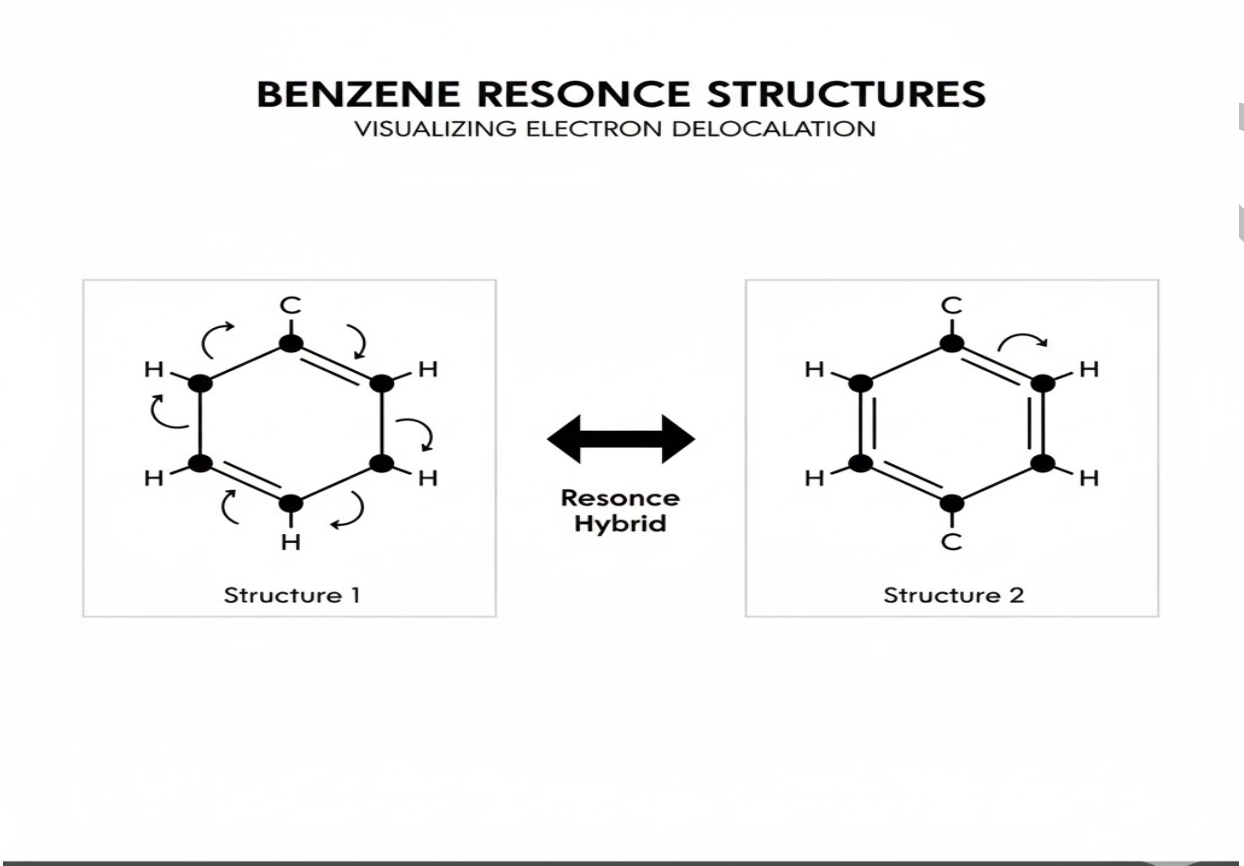


Figure 1.2 Resonance structures of benzene

1.1.3 Criteria for aromaticity (Hückel's rule)

To determine whether a compound is aromatic, chemists use **Hückel's rule**, which states that a planar, cyclic, conjugated molecule is aromatic if it contains (4n + 2) π-electrons, where (n) is a non-negative integer. For benzene, (n = 1), giving 6 π-electrons, which satisfies the rule.

Other compounds, such as naphthalene and anthracene, also follow Hückel's rule, making them aromatic. Compounds that fail to meet these criteria are either non-aromatic or anti-aromatic, depending on their electron count and structure.

Fill in the blank: According to Hückel's rule, a molecule is aromatic if it contains _____ π-electrons, where n is a non-negative integer.

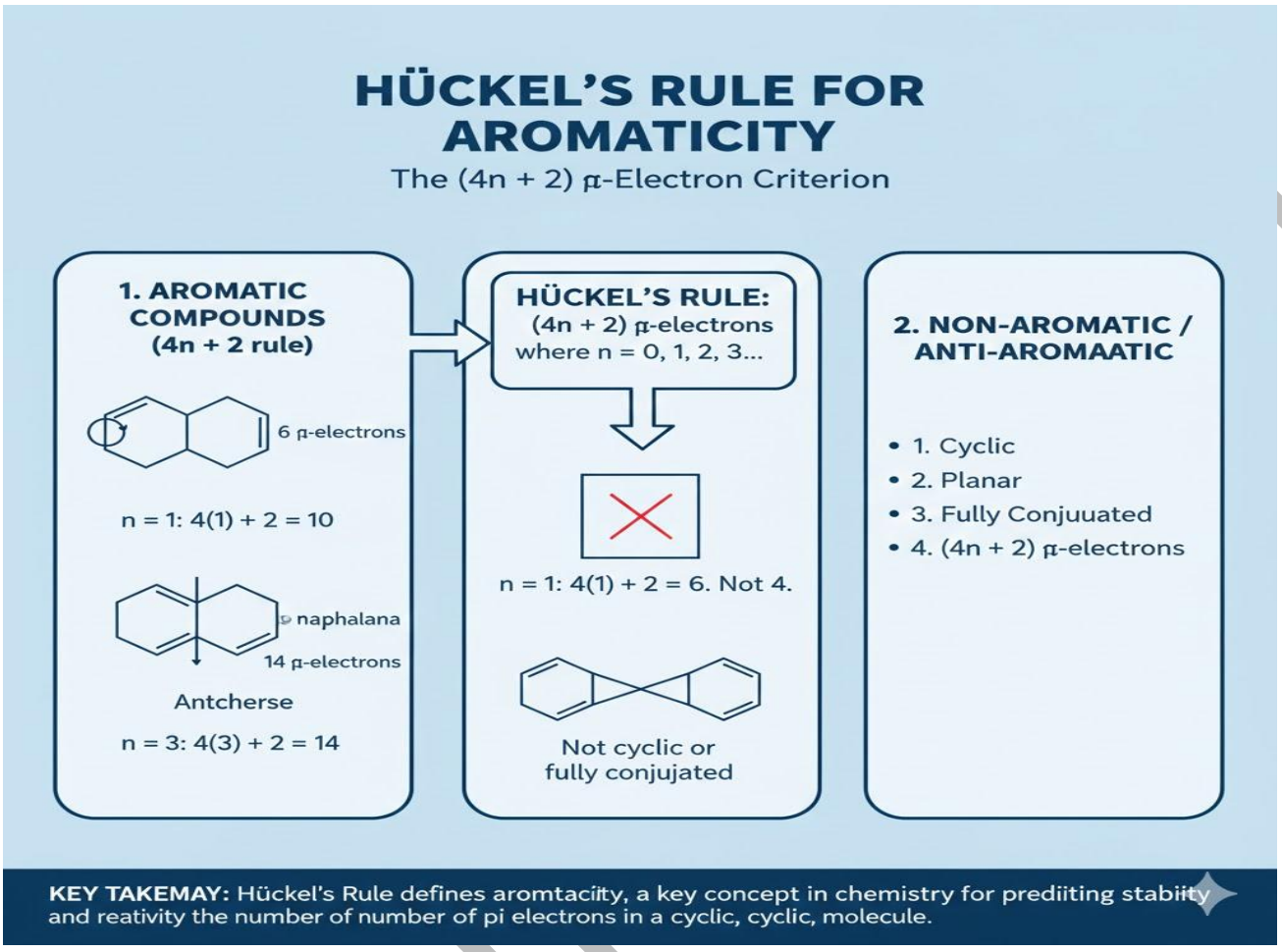


Figure 1.3 – Hückel's Rule and Aromaticity

Pilot questions 1.1

Which property of aromatic compounds explains their resistance to addition reactions?
What feature of benzene's structure makes all its carbon–carbon bonds equal in length?
State Hückel's rule for aromaticity.
How many π-electrons are present in benzene?
Why do aromatic compounds prefer substitution reactions over addition reactions?

1.2 Reactions Of Aromatic Compounds

1.2.1 Electrophilic substitution reactions: nitration, halogenation, sulphonation, Friedel–Crafts reactions

Aromatic compounds typically undergo **electrophilic substitution reactions**, which are reactions where an **electrophile** (an electron-deficient species that seeks electrons) replaces a

hydrogen atom on the aromatic ring. This type of reaction preserves the aromaticity of the ring, which is why it is preferred over addition reactions.

Common examples include:

Nitration, where a nitro group (-NO_2) is introduced using concentrated nitric acid and sulphuric acid.
Halogenation, where halogens such as chlorine or bromine are introduced in the presence of a Lewis acid catalyst like $FeCl_3$.
Sulphonation, where a sulphonyl group (-SO_3H) is introduced using concentrated sulphuric acid.
Friedel–Crafts reactions, which involve alkylation or acylation of the aromatic ring using alkyl or acyl halides with a Lewis acid catalyst.

Fill in the blank: In electrophilic substitution reactions, the aromatic ring retains its _____ because the π-electrons remain delocalised.

1.2.2 Orientation and reactivity in substituted aromatics

When an aromatic ring already contains a substituent, the position at which a new substituent enters is influenced by the nature of the existing group. This is known as **orientation**. Substituents can be classified as **activating groups** (which increase reactivity and direct substitution to the ortho and para positions) or **deactivating groups** (which decrease reactivity and often direct substitution to the meta position).

For example, a methyl group activates the ring and directs substitution to ortho and para positions, while a nitro group deactivates the ring and directs substitution to the meta position.

Fill in the blank: Activating groups generally direct new substituents to the _____ and _____ positions of the aromatic ring.

*Here's a clear table that organises common substituents on benzene, showing whether they are **activating** or **deactivating**, and their typical **orientation effects**:*

Substituent	Classification	Orientation effect
–OH (hydroxyl)	Activating	Ortho/para-directing
–NH_2 (amino)	Activating	Ortho/para-directing
–CH_3 (methyl)	Activating	Ortho/para-directing
–OCH_3 (methoxy)	Activating	Ortho/para-directing
–Cl, –Br (halogens)	Deactivating	Ortho/para-directing
–NO_2 (nitro)	Deactivating	Meta-directing
–CN (cyano)	Deactivating	Meta-directing
–COOH (carboxyl)	Deactivating	Meta-directing

Substituent	Classification	Orientation effect
–CHO (formyl)	Deactivating	Meta-directing
–SO_3H (sulphonyl)	Deactivating	Meta-directing

Table 1.1 Orientation effects of common substituents

1.2.3 Other reactions of aromatic compounds: oxidation and reduction

Apart from substitution, aromatic compounds can also undergo **oxidation** and **reduction** reactions. Oxidation often occurs at side chains rather than the ring itself. For example, toluene can be oxidised to benzoic acid using strong oxidising agents. Reduction reactions, on the other hand, may involve hydrogenation of the ring under high pressure and in the presence of a catalyst, converting benzene into cyclohexane.

These reactions are important in industrial processes, such as the production of polymers and intermediates for pharmaceuticals.

Fill in the blank: Oxidation of toluene typically produces _____ acid as the major product.

Pilot questions 1.2

What type of reaction allows aromatic compounds to retain their aromaticity while introducing new substituents?
Name two common electrophilic substitution reactions of benzene.
Which type of substituents direct new groups to the ortho and para positions?
What is the major product when toluene undergoes oxidation?
Why do aromatic compounds prefer substitution reactions over addition reactions?

1.3 Applications And Problem-Solving In Aromatic Chemistry

1.3.1 Industrial importance of aromatic compounds

Aromatic compounds play a vital role in industry due to their stability and versatility. They are used as raw materials in the manufacture of dyes, plastics, pharmaceuticals, and explosives. For example, **benzene** is a precursor for styrene, which is polymerised to form polystyrene, a widely used plastic. Similarly, **toluene** is employed in the production of solvents and explosives such as trinitrotoluene (TNT).

The importance of aromatic compounds extends to the pharmaceutical industry, where many drugs contain aromatic rings that contribute to their biological activity. Aspirin, paracetamol, and many antibiotics are examples of medicines derived from aromatic chemistry.

Fill in the blank: Benzene is used as a precursor for _____, which is polymerised to form polystyrene.

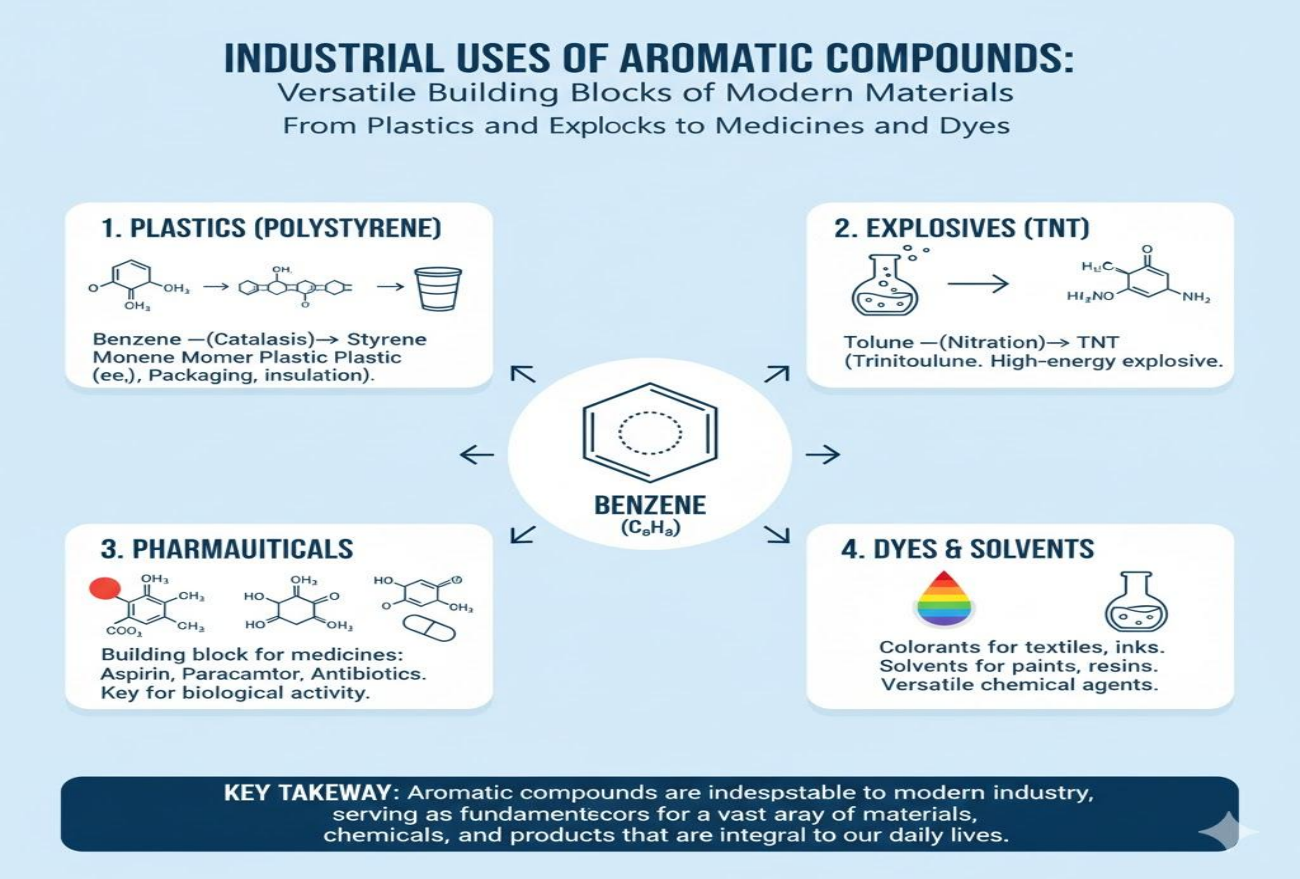


Figure 1.4 – Industrial Importance of Aromatic Compounds

1.3.2 Worked examples and problem-solving in aromatic chemistry

Problem-solving in aromatic chemistry involves applying knowledge of structure, reactivity, and orientation to predict products of reactions. For instance, when benzene undergoes nitration, the product is nitrobenzene. However, if methylbenzene (toluene) undergoes nitration, the methyl group directs the nitro group to the ortho and para positions.

Worked examples help learners practise predicting outcomes and reinforce the principles of electrophilic substitution and orientation effects. By solving problems step by step, you develop confidence in applying theoretical knowledge to practical scenarios.

Fill in the blank: In nitration of methylbenzene, the nitro group is directed to the _____ and _____ positions.

Pilot questions 1.3

Name two industrial products derived from benzene.
Which aromatic compound is used in the manufacture of TNT?
What is the major product when benzene undergoes nitration?
In nitration of methylbenzene, which positions are favoured for substitution?

Why are worked examples important in learning aromatic chemistry?

Series Summary

This Series has introduced you to the chemistry of aromatic compounds, highlighting their importance in organic chemistry and their relevance in both academic study and industrial applications. We began by examining the fundamental features of aromatic compounds, including the resonance structure of benzene and the criteria for aromaticity. We then moved on to explore the major reactions of aromatic compounds, focusing on electrophilic substitution, orientation effects, and other transformations such as oxidation and reduction. Finally, we considered the industrial importance of aromatic compounds and engaged with worked examples to strengthen your problem-solving skills.

By completing this Series, you should now be able to define the general features of aromatic compounds, explain resonance and aromaticity, describe and evaluate their reactions, and apply these principles to practical problems. These abilities directly align with the Series Learning Outcomes (SLOs), ensuring that you are well prepared to analyse aromatic chemistry and apply it confidently in both theoretical and applied contexts.

Concept Check Questions [Series 1]

Objective questions (single-response, not multiple choice)

State Hückel's rule for aromaticity. (Linked to SLO 1.3)
Identify the major product formed when benzene undergoes nitration. (Linked to SLO 1.4)
Name one activating substituent on an aromatic ring. (Linked to SLO 1.5)

Short-answer questions

4. Define aromatic compounds and mention one feature that distinguishes them from alkenes. (Linked to SLO 1.1)
5. Explain why all carbon–carbon bonds in benzene are of equal length. (Linked to SLO 1.2)
6. Describe the orientation effect of a nitro group on benzene. (Linked to SLO 1.5)
7. State one industrial application of benzene. (Linked to SLO 1.7)
8. Predict the product of oxidation of toluene. (Linked to SLO 1.6)

Long-answer questions

9. Analyse the mechanism of electrophilic substitution in benzene, highlighting the role of resonance stabilisation. (Linked to SLO 1.4)
10. Evaluate the importance of orientation effects in substituted aromatics, using methylbenzene and nitrobenzene as examples. (Linked to SLO 1.5)
11. Assess the industrial significance of aromatic compounds, with reference to at least two examples. (Linked to SLO 1.7)

12. Apply problem-solving strategies to predict the major products of nitration of methylbenzene and chlorobenzene. (Linked to SLO 1.8)

Answers to Concept Check Questions [Series 1]

Objective questions

A planar, cyclic, conjugated molecule is aromatic if it contains (4n + 2) π-electrons.
Nitrobenzene.
Methyl group.

Short-answer questions

4. Aromatic compounds are cyclic, planar molecules with delocalised π-electrons. Unlike alkenes, they resist addition reactions.
5. Resonance stabilisation causes delocalisation of electrons, making all carbon–carbon bonds equal in length.
6. A nitro group deactivates the ring and directs substitution to the meta position.
7. Benzene is used to produce styrene, which is polymerised into polystyrene plastics.
8. Oxidation of toluene produces benzoic acid.

Long-answer questions

9. **Basic response:** Electrophilic substitution in benzene involves attack by an electrophile, formation of a carbocation intermediate, and loss of a proton to restore aromaticity. Resonance stabilisation of the intermediate explains the preference for substitution.
Value-added response: Resonance stabilisation distributes the positive charge across the ring, lowering the energy of the intermediate. This explains why benzene undergoes substitution rather than addition, preserving aromaticity.

Basic response: Orientation effects determine where new substituents enter the ring. Methyl groups activate the ring and direct substitution to ortho and para positions, while nitro groups deactivate the ring and direct substitution to the meta position.
Value-added response: These effects are explained by resonance and inductive influences. Electron-donating groups stabilise carbocation intermediates at ortho and para positions, while electron-withdrawing groups destabilise them, favouring meta substitution.

Basic response: Aromatic compounds are important in industry. Benzene is used to produce styrene for plastics, and toluene is used in explosives.
Value-added response: Beyond plastics and explosives, aromatic compounds are central to pharmaceuticals, dyes, and agrochemicals. Their stability and reactivity make them versatile building blocks in industrial chemistry.

Basic response: Nitration of methylbenzene gives ortho- and para-nitrotoluene as major products. Nitration of chlorobenzene gives ortho- and para-nitrochlorobenzene.
Value-added response: The directing effects are explained by the electron-donating nature of the methyl group and the electron-withdrawing but ortho/para-directing nature of the chlorine substituent. This highlights the complexity of predicting products in substituted aromatics.

Answers to Pilot Questions [Series 1]

Part 1 Fundamentals of Aromatic Compounds

Delocalisation of π-electrons across the ring.
Resonance stabilisation.
A planar, cyclic, conjugated molecule with (4n + 2) π-electrons.
Six π-electrons.
Because substitution reactions preserve aromaticity, whereas addition reactions would disrupt it.

Part 2 Reactions of Aromatic Compounds

Electrophilic substitution reactions.
Nitration and halogenation.
Activating groups.
Benzoic acid.
Because substitution reactions maintain the delocalised electron system of the ring.

Part 3 Applications and Problem-Solving in Aromatic Chemistry

Styrene and phenol.
Toluene.
Nitrobenzene.
Ortho and para positions.
They provide practice in applying theoretical knowledge to predict products and solve problems.

Series 2: Structures of Biomolecules: Sugars, Starch, Cellulose, Peptides, and Proteins

Part 1 Carbohydrates: Monosaccharides and Disaccharides

2.1.1 Definition and classification of carbohydrates
2.1.2 Structures and properties of monosaccharides (e.g., glucose, fructose)
2.1.3 Structures and properties of disaccharides (e.g., sucrose, lactose, maltose)

Part 2 Polysaccharides: Starch and Cellulose

2.2.1 Structure and bonding in starch (amylose and amylopectin)
2.2.2 Structure and bonding in cellulose
2.2.3 Comparative properties and functions of starch and cellulose

Part 3 Peptides: Structure and Bonding

2.3.1 Formation of peptide bonds
2.3.2 Primary structure of peptides
2.3.3 Importance of peptide linkages in biomolecules

Part 4 Proteins: Levels of Structure and Functions

2.4.1 Primary, secondary, tertiary, and quaternary structures
2.4.2 Structural examples (α-helix, β-sheet, globular and fibrous proteins)
2.4.3 Biological functions of proteins

Introduction

Biomolecules are the building blocks of life, forming the structures and systems that sustain every living organism. From the sugars that provide quick energy to the proteins that carry out complex biological functions, understanding their structures is essential for appreciating how chemistry connects to biology. This Series will guide you through the organisation and bonding patterns of carbohydrates and proteins, helping you see how their structures underpin their roles in living systems.

The aim of this Series is to introduce you to the structural features of carbohydrates and proteins, and to equip you with the knowledge needed to explain their organisation, bonding, and biological significance.

We shall commence this Series by exploring carbohydrates, beginning with the structures and properties of monosaccharides and disaccharides. Next, we will move on to polysaccharides, focusing on starch and cellulose and comparing their bonding and functions. Following that, we will examine peptides, considering how peptide bonds form and how they contribute to primary structures. Finally, we will wrap up by studying proteins in detail, looking at their levels of structure and the diverse functions they perform in biological systems.

Series Learning Outcomes

Upon completing this Series, you should be able to:

define carbohydrates and classify them into monosaccharides, disaccharides, and polysaccharides,
explain the structural features and properties of common monosaccharides such as glucose and fructose,
describe the bonding and properties of disaccharides including sucrose, lactose, and maltose,
analyse the structural organisation of starch, distinguishing between amylose and amylopectin,
explain the structural organisation of cellulose and its functional role in plants,
compare the properties and biological functions of starch and cellulose,
demonstrate how peptide bonds are formed and explain their importance in biomolecules,
describe the primary structure of peptides and its significance,
explain the levels of protein structure (primary, secondary, tertiary, and quaternary),
identify structural examples such as α-helix, β-sheet, globular proteins, and fibrous proteins, and
evaluate the biological functions of proteins in living systems.

2.1 Carbohydrates: Monosaccharides And Disaccharides

2.1.1 Definition and classification of carbohydrates

Carbohydrates are organic compounds made up of carbon, hydrogen, and oxygen, usually in the ratio of 1:2:1. They are a primary source of energy in living organisms and also serve structural roles. Carbohydrates are classified into **monosaccharides** (simple sugars), **disaccharides** (two sugar units), and **polysaccharides** (many sugar units).

Fill in the blank: Carbohydrates generally contain carbon, hydrogen, and oxygen in the ratio _____.

Type of carbohydrate	Description	Examples
Monosaccharides	Simplest carbohydrates consisting of a single sugar unit	Glucose, fructose, galactose
Disaccharides	Formed when two monosaccharides join via a glycosidic bond	Sucrose (glucose + fructose), lactose (glucose + galactose), maltose (glucose + glucose)
Polysaccharides	Large molecules made of many monosaccharide units linked together	Starch, cellulose, glycogen

Box 2.1 Classification of carbohydrates

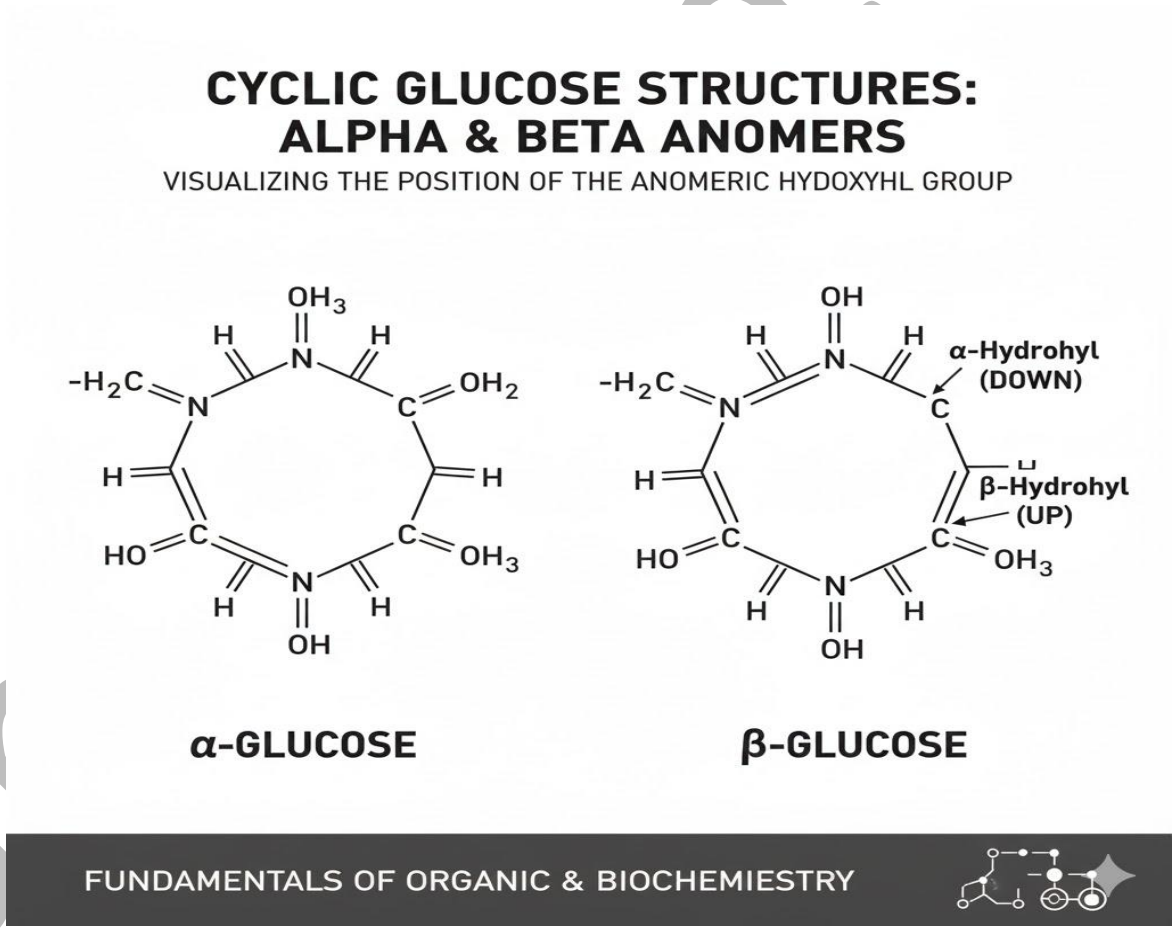
2.1.2 Structures and properties of monosaccharides (e.g., glucose, fructose)

Monosaccharides are the simplest carbohydrates, consisting of a single sugar unit. They are classified based on the number of carbon atoms (triose, pentose, hexose) and the functional group present (aldoses with an aldehyde group, ketoses with a ketone group).

Glucose is a hexose aldose and the most important monosaccharide in metabolism. It can exist in linear form or as a cyclic structure (α- and β-glucose). **Fructose** is a hexose ketose found in fruits and honey.

Fill in the blank: Glucose is classified as a _____ because it contains an aldehyde group.

Figure 2.1 Cyclic structures of α-glucose and β-glucose



2.1.3 Structures and properties of disaccharides (e.g., sucrose, lactose, maltose)

Disaccharides are carbohydrates formed when two monosaccharides join through a **glycosidic bond**, which is a covalent bond formed by condensation (removal of water).

Sucrose is composed of glucose and fructose.
Lactose is composed of glucose and galactose.
Maltose is composed of two glucose units.

These disaccharides differ in their glycosidic linkages, which determine their properties and digestibility. For example, lactose requires the enzyme lactase for digestion, and deficiency leads to lactose intolerance.

Fill in the blank: A disaccharide is formed when two monosaccharides join through a _____ bond.

Disaccharide	Monosaccharide components	Glycosidic bond type
Sucrose	Glucose + Fructose	α-1,2-glycosidic bond
Lactose	Glucose + Galactose	β-1,4-glycosidic bond
Maltose	Glucose + Glucose	α-1,4-glycosidic bond

Box 2.2 Common disaccharides and their components

Pilot questions 2.1

State the general formula ratio of elements in carbohydrates.
Classify glucose and fructose based on their functional groups.
What is the difference between α-glucose and β-glucose?
Name the monosaccharide units that make up sucrose.
Which enzyme is required to digest lactose?

2.2 Polysaccharides: Starch And Cellulose

2.2.1 Structure and bonding in starch (amylose and amylopectin)

Starch is a polysaccharide made up of glucose units and serves as the primary storage carbohydrate in plants. It consists of two components: **amylose** and **amylopectin**.

Amylose is a linear polymer of glucose linked mainly by α-1,4-glycosidic bonds. It tends to form a helical structure, which makes it less soluble in water. **Amylopectin**, on the other hand, is a branched polymer with both α-1,4-glycosidic bonds and α-1,6-glycosidic bonds at the branch points. This branching makes amylopectin more soluble and easier to digest.

Fill in the blank: Amylopectin differs from amylose because it contains _____ bonds at its branch points.

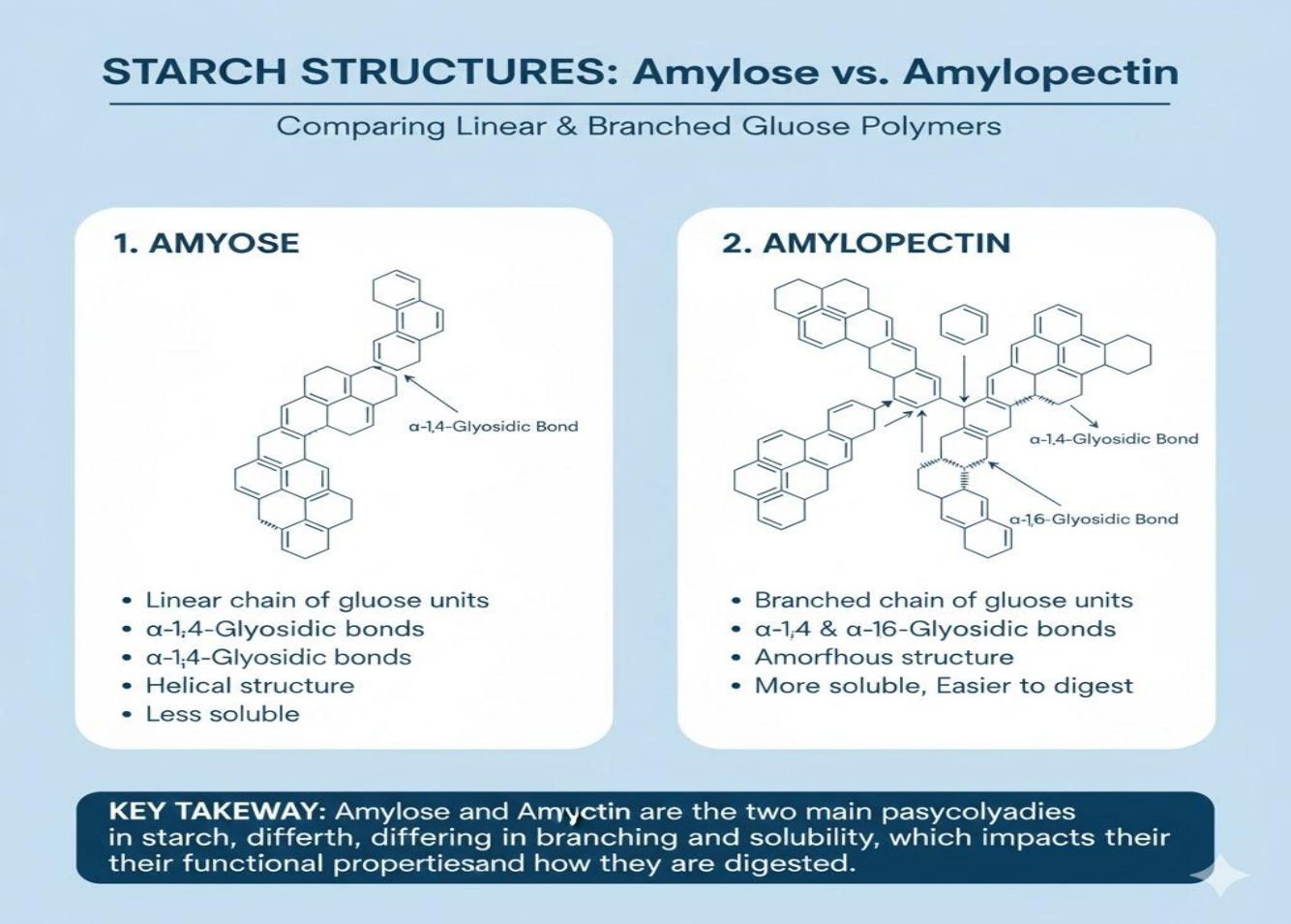


Figure 2.2 – Structure of Amylose and Amylopectin

2.2.2 Structure and bonding in cellulose

Cellulose is a polysaccharide composed of glucose units linked by β-1,4-glycosidic bonds. Unlike starch, cellulose forms long, straight chains that align parallel to each other. These chains are held together by hydrogen bonds, creating strong fibres that provide structural support in plant cell walls.

Because of the β-linkages, cellulose cannot be digested by humans, although it is an important source of dietary fibre. Certain animals, such as ruminants, can digest cellulose due to the presence of symbiotic microorganisms that produce cellulase.

Fill in the blank: Cellulose is composed of glucose units linked by _____ glycosidic bonds.

2.2.3 Comparative properties and functions of starch and cellulose

Although both starch and cellulose are polysaccharides made of glucose, their structures give them very different properties and functions. Starch is mainly used for energy storage in plants, while cellulose provides mechanical strength and rigidity to plant cell walls.

Starch is digestible by humans because of the α-linkages, whereas cellulose is indigestible due to the β-linkages. This difference explains why starch-rich foods such as rice and potatoes are energy sources, while cellulose contributes to dietary fibre.

Fill in the blank: Starch serves as an energy storage molecule, while cellulose provides _____ in plant cell walls.

Feature	Starch	Cellulose
Structure	Composed of glucose units; mixture of amylose (linear) and amylopectin (branched)	Composed of glucose units; long, straight chains
Bonding	α-1,4-glycosidic bonds (amylose) and α-1,6-glycosidic bonds (amylopectin branches)	β-1,4-glycosidic bonds with hydrogen bonding between chains
Digestibility	Digestible by humans due to enzymes like amylase	Indigestible by humans (lack of cellulase); provides dietary fibre
Functions	Energy storage in plants; major food source for humans	Structural support in plant cell walls; contributes to rigidity and strength

Table 2.2 Comparison of starch and cellulose

Pilot questions 2.2

Name the two components of starch.
Which glycosidic bonds are present in amylose?
What type of glycosidic bonds are found in cellulose?
Why is cellulose indigestible to humans?
State one key difference in the biological role of starch and cellulose.

2.3 Peptides: Structure And Bonding

2.3.1 Formation of peptide bonds

Peptides are short chains of amino acids linked together by **peptide bonds**, which are covalent bonds formed between the carboxyl group of one amino acid and the amino group of another.

This reaction is a condensation process, as a molecule of water is released during bond formation.

The peptide bond is rigid and planar due to resonance, which restricts rotation and contributes to the stability of peptide chains. This structural feature is crucial for the folding and function of proteins.

Fill in the blank: A peptide bond is formed between the _____ group of one amino acid and the amino group of another.

2.3.2 Primary structure of peptides

The **primary structure** of a peptide refers to the linear sequence of amino acids joined by peptide bonds. This sequence determines the chemical properties and biological function of the peptide. Even a small change in the sequence can alter the peptide's behaviour significantly.

For example, the difference between haemoglobin and sickle-cell haemoglobin arises from a single amino acid substitution in the peptide chain.

Fill in the blank: The primary structure of a peptide is defined by the _____ of amino acids in the chain.

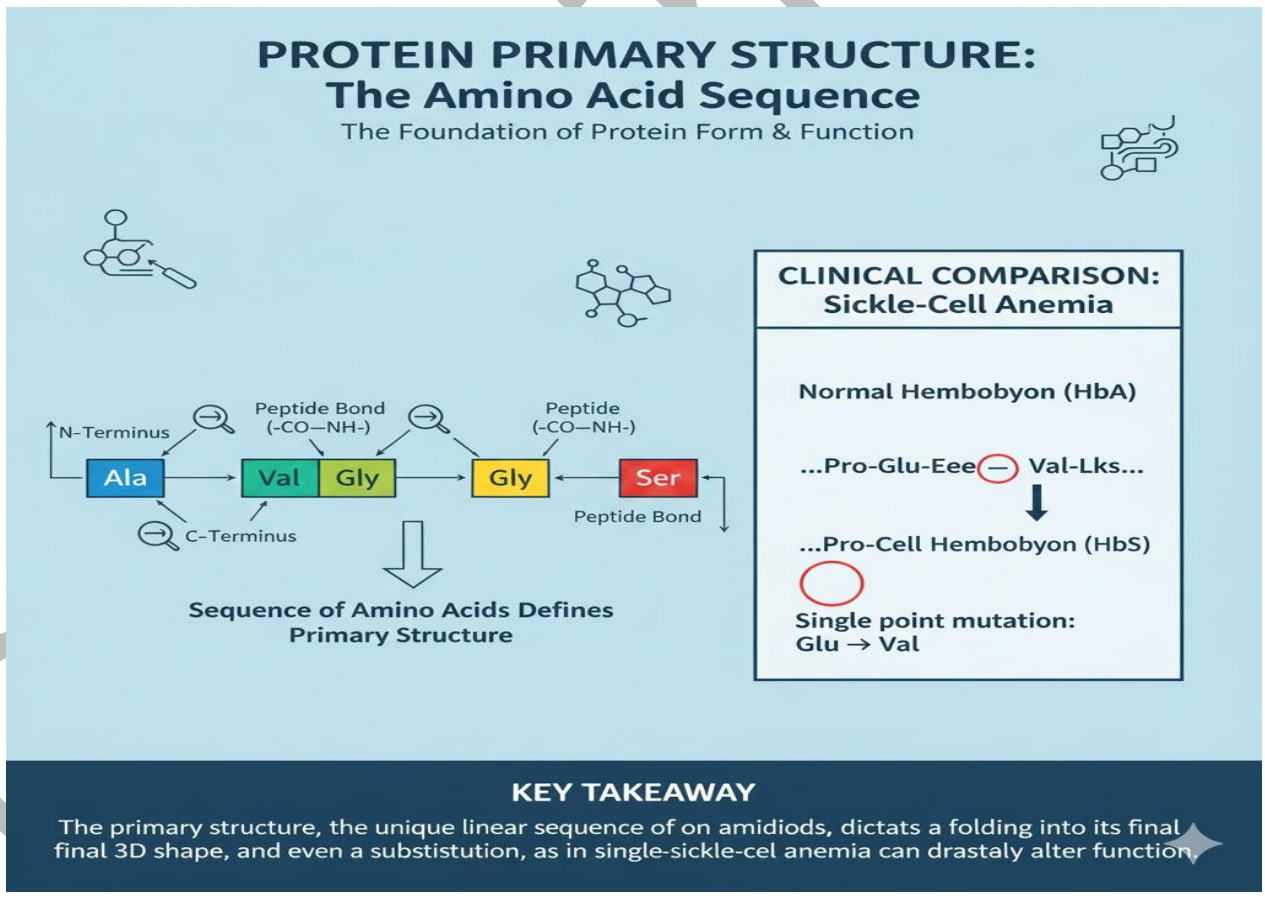


Figure 2.3 – Primary Structure of Peptides

2.3.3 Importance of peptide linkages in biomolecules

Peptide linkages are fundamental to the structure of proteins, which are long chains of peptides folded into complex shapes. These linkages provide stability and continuity, allowing proteins to perform diverse biological functions such as catalysis, transport, and structural support.

Without peptide bonds, proteins could not form, and many essential processes in living organisms would not occur.

Fill in the blank: Proteins are formed when many peptides join together through _____ linkages.

Pilot questions 2.3

What type of bond links amino acids together in peptides?
What reaction occurs during peptide bond formation?
Define the primary structure of a peptide.
Give one example of how a change in peptide sequence can affect biological function.
Why are peptide linkages important in biomolecules?

2.4 Proteins: Levels Of Structure And Functions

2.4.1 Primary, secondary, tertiary, and quaternary structures

Proteins are complex biomolecules composed of amino acid chains linked by peptide bonds. Their function depends on their structure, which is organised into four levels.

The **primary structure** is the linear sequence of amino acids in a polypeptide chain. This sequence dictates how the protein will fold and ultimately determines its function. The **secondary structure** refers to local folding patterns such as the **α-helix** (a coiled structure stabilised by hydrogen bonds) and the **β-sheet** (a pleated arrangement also stabilised by hydrogen bonds).

The **tertiary structure** is the overall three-dimensional shape of a single polypeptide chain, formed by interactions such as hydrogen bonding, ionic interactions, hydrophobic effects, and disulphide bridges. Finally, the **quaternary structure** describes how multiple polypeptide chains (subunits) assemble into a functional protein, as seen in haemoglobin.

Fill in the blank: The _____ structure of a protein refers to its overall three-dimensional shape formed by interactions among side chains.

2.4.2 Structural examples (α-helix, β-sheet, globular and fibrous proteins)

The **α-helix** and **β-sheet** are the two most common secondary structures. The α-helix resembles a coiled spring, while the β-sheet looks like folded pleats. These structures provide stability and flexibility to proteins.

Proteins can also be classified as **globular proteins**, which are compact and soluble (e.g., enzymes, haemoglobin), or **fibrous proteins**, which are elongated and insoluble (e.g., collagen, keratin). Globular proteins are typically involved in dynamic functions such as catalysis and transport, while fibrous proteins provide structural support.

Fill in the blank: Collagen is an example of a _____ protein that provides structural support.

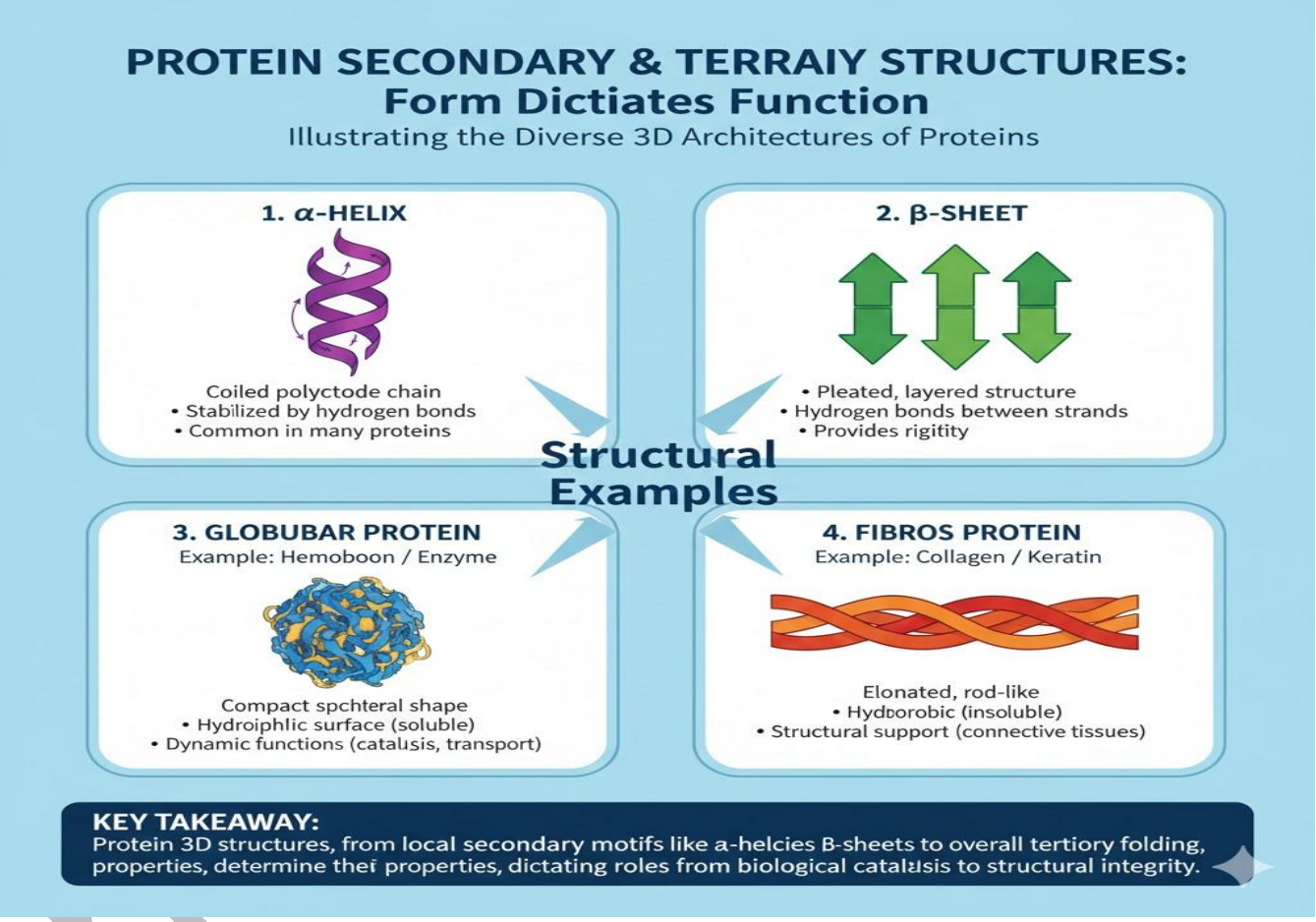


Figure 2.4 – Structural Examples of Proteins

2.4.3 Biological functions of proteins

Proteins perform a wide range of biological functions essential for life. **Enzymes** act as catalysts, speeding up biochemical reactions. **Transport proteins** such as haemoglobin carry oxygen, while **structural proteins** like collagen provide support. **Defensive proteins** such as antibodies protect the body against pathogens, and **regulatory proteins** such as hormones help control processes in cells and tissues.

The diversity of protein functions arises from their structural complexity, which allows them to interact specifically with other molecules.

Fill in the blank: Haemoglobin is a _____ protein that transports oxygen in the blood.

Pilot questions 2.4

What determines the primary structure of a protein?
Name the two most common secondary structures in proteins.
Give one example each of a globular protein and a fibrous protein.
Which protein transports oxygen in the blood?
State two biological functions of proteins.

Series Summary

This Series has introduced you to the structures of essential biomolecules, emphasising their importance in energy storage, structural support, and biological function. We began with carbohydrates, exploring the organisation of monosaccharides and disaccharides, before moving on to polysaccharides such as starch and cellulose, where differences in bonding explain their distinct roles in plants and nutrition. We then examined peptides, focusing on how peptide bonds form and how the primary sequence of amino acids determines biological properties. Finally, we studied proteins in detail, considering their levels of structure and the wide range of functions they perform in living systems.

By completing this Series, you should now be able to define and classify carbohydrates, explain the structural features of sugars, analyse the organisation of starch and cellulose, demonstrate how peptide bonds are formed, and evaluate the structural and functional roles of proteins. These abilities directly align with the Series Learning Outcomes (SLOs), ensuring that you are well prepared to describe, analyse, and apply knowledge of biomolecular structures confidently in both theoretical and applied contexts.

Concept Check Questions [Series 2]

Objective questions

State the general ratio of carbon, hydrogen, and oxygen atoms in carbohydrates. (Linked to SLO 2.1)
Identify the functional group present in glucose. (Linked to SLO 2.2)
Name the monosaccharide units that make up sucrose. (Linked to SLO 2.3)
Specify the glycosidic bond present in cellulose. (Linked to SLO 2.5)
Define the bond that links amino acids together in peptides. (Linked to SLO 2.7)

Short-answer questions

6. Explain why amylopectin is more soluble than amylose. (Linked to SLO 2.4)

7. Describe one reason why cellulose is indigestible to humans. (Linked to SLO 2.5)
8. Give one example of a globular protein and one example of a fibrous protein. (Linked to SLO 2.10)
9. State one biological function of proteins in living systems. (Linked to SLO 2.11)
10. Describe the primary structure of a peptide. (Linked to SLO 2.8)

Long-answer questions
11. Analyse the structural differences between starch and cellulose and explain how these differences affect their biological roles. (Linked to SLO 2.6)
12. Evaluate the importance of peptide bonds in protein formation and stability. (Linked to SLO 2.7)
13. Explain the four levels of protein structure, giving examples at each level. (Linked to SLO 2.9)
14. Assess the functional diversity of proteins, highlighting at least three distinct roles. (Linked to SLO 2.11)

Answers to Concept Check Questions [Series 2]

Objective questions

1:2:1 ratio.
Aldehyde group.
Glucose and fructose.
β-1,4-glycosidic bond.
Peptide bond.

Short-answer questions
6. Amylopectin is branched with α-1,6-glycosidic bonds, making it more soluble and easier to digest.
7. Humans lack cellulase, the enzyme required to break β-1,4-glycosidic bonds.
8. Globular protein: haemoglobin; fibrous protein: collagen.
9. Proteins act as enzymes, catalysts, transporters, structural components, or defensive molecules.
10. The primary structure is the linear sequence of amino acids joined by peptide bonds.

Long-answer questions
11. **Basic response:** Starch contains α-linkages, making it digestible and suitable for energy storage, while cellulose contains β-linkages, forming strong fibres for structural support.
Value-added response: Starch's branched amylopectin allows rapid energy release, whereas cellulose's hydrogen-bonded chains provide rigidity in plant cell walls and dietary fibre benefits in humans.

Basic response: Peptide bonds link amino acids, forming stable chains that are essential for protein structure.
Value-added response: The resonance of peptide bonds restricts rotation, giving rigidity and stability, which is crucial for protein folding and function.

Basic response: Primary structure is the amino acid sequence; secondary structure includes α-helices and β-sheets; tertiary structure is the 3D folding; quaternary structure involves multiple polypeptide chains.
Value-added response: Examples include sickle-cell haemoglobin (primary change), keratin (secondary α-helix), enzymes with complex tertiary folds, and haemoglobin with quaternary subunits.

Basic response: Proteins function as enzymes, structural components, and transport molecules.
Value-added response: Beyond these, proteins also act as antibodies for defence, hormones for regulation, and signalling molecules, demonstrating their vast functional diversity in living systems.

Answers to Pilot Questions [Series 2]

Part 1 Carbohydrates: Monosaccharides and Disaccharides

1:2:1 ratio of carbon, hydrogen, and oxygen.
Glucose is an aldose; fructose is a ketose.
The difference lies in the position of the hydroxyl group on carbon 1.
Glucose and fructose.
Lactase.

Part 2 Polysaccharides: Starch and Cellulose

Amylose and amylopectin.
α-1,4-glycosidic bonds.
β-1,4-glycosidic bonds.
Humans lack cellulase enzyme.
Starch stores energy, while cellulose provides structural support.

Part 3 Peptides: Structure and Bonding

Peptide bond.
Condensation reaction with water released.
The linear sequence of amino acids.
Sickle-cell anaemia caused by substitution of valine for glutamic acid.
They provide stability and continuity in proteins.

Part 4 Proteins: Levels of Structure and Functions

The amino acid sequence.
α-helix and β-sheet.
Globular protein: haemoglobin; fibrous protein: collagen.
Haemoglobin.
Catalysis, transport, structural support, defence, and regulation.

Series 3: Bifunctional Compounds and Reaction Mechanisms

Part 1 Introduction to bifunctional compounds

3.1.1 Definition and classification of bifunctional compounds
3.1.2 Common examples and their importance in organic chemistry

Part 2 Alcohols, acids, and esters as bifunctional compounds

3.2.1 Structures and properties of hydroxy acids
3.2.2 Structures and properties of amino acids
3.2.3 Esterification and hydrolysis reactions

Part 3 Reaction mechanisms of bifunctional compounds

3.3.1 Nucleophilic substitution mechanisms
3.3.2 Elimination mechanisms
3.3.3 Addition mechanisms

Part 4 Applications and biological relevance

3.4.1 Role of amino acids in proteins
3.4.2 Role of hydroxy acids in metabolism
3.4.3 Industrial and pharmaceutical applications

Introduction

Organic molecules often contain more than one functional group, and these **bifunctional compounds** play a central role in both synthetic chemistry and biological systems. Their dual reactivity makes them versatile, allowing for a wide range of transformations and applications. Understanding how these compounds behave and the mechanisms behind their reactions is essential for building a strong foundation in organic chemistry and for appreciating their relevance in everyday life, from pharmaceuticals to metabolism.

The aim of this Series is to introduce you to the structures and properties of bifunctional compounds and to equip you with the ability to explain and analyse the mechanisms through which they undergo chemical reactions.

We shall commence this Series by defining bifunctional compounds and examining their classification and importance. Next, we will explore alcohols, acids, and esters as examples of bifunctional compounds, focusing on their structures and reactions. Following that, we will study the mechanisms of key reactions such as nucleophilic substitution, elimination, and addition. Finally, we will wrap up by considering the applications and biological relevance of these compounds, including their roles in proteins, metabolism, and industry.

Series Learning Outcomes

Upon completing this Series, you should be able to:

define bifunctional compounds and classify them according to their functional groups,
explain the structures and properties of hydroxy acids,
describe the structural features and importance of amino acids,
demonstrate the processes of esterification and hydrolysis in bifunctional compounds,
analyse nucleophilic substitution mechanisms in bifunctional compounds,
explain elimination mechanisms and their outcomes,
describe addition mechanisms relevant to bifunctional compounds,
evaluate the role of amino acids in protein formation,
explain the biological relevance of hydroxy acids in metabolism, and
assess the industrial and pharmaceutical applications of bifunctional compounds.

3.1 Introduction To Bifunctional Compounds

3.1.1 Definition and classification of bifunctional compounds

Bifunctional compounds are organic molecules that contain two distinct functional groups within the same structure. These groups may be similar or different, and their presence gives the compound unique chemical properties and reactivity. For example, amino acids contain both an amino group (–NH_2) and a carboxyl group (–COOH), making them bifunctional.

The classification of bifunctional compounds is usually based on the types of functional groups present. Common categories include **hydroxy acids** (containing hydroxyl and carboxyl groups), **amino acids** (containing amino and carboxyl groups), and **esters** (formed from alcohol and acid groups).

Fill in the blank: A compound that contains both an amino group and a carboxyl group is called an _____.

3.1.2 Common examples and their importance in organic chemistry

Bifunctional compounds are important because the presence of two functional groups allows them to participate in a wider range of chemical reactions. For instance, **hydroxy acids** can undergo both oxidation and esterification, while **amino acids** are the building blocks of proteins. **Esters** are widely used in industry for fragrances, flavourings, and solvents.

Their dual reactivity also makes bifunctional compounds central to biological processes. In metabolism, they serve as intermediates, while in synthetic chemistry, they provide pathways to more complex molecules.

Fill in the blank: Amino acids are important because they serve as the building blocks of _____.

Table 3.1 Examples of hydroxy acids, amino acids, and esters with their uses

Compound type	Example(s)	Uses
Hydroxy acids	Lactic acid, citric acid	Lactic acid in food preservation and skincare; citric acid in metabolism and as a flavouring agent
Amino acids	Glycine, alanine, valine	Building blocks of proteins; nutritional supplements; precursors in pharmaceuticals
Esters	Ethyl ethanoate, methyl salicylate	Solvents in industry; flavourings and fragrances; medicinal applications such as topical analgesics

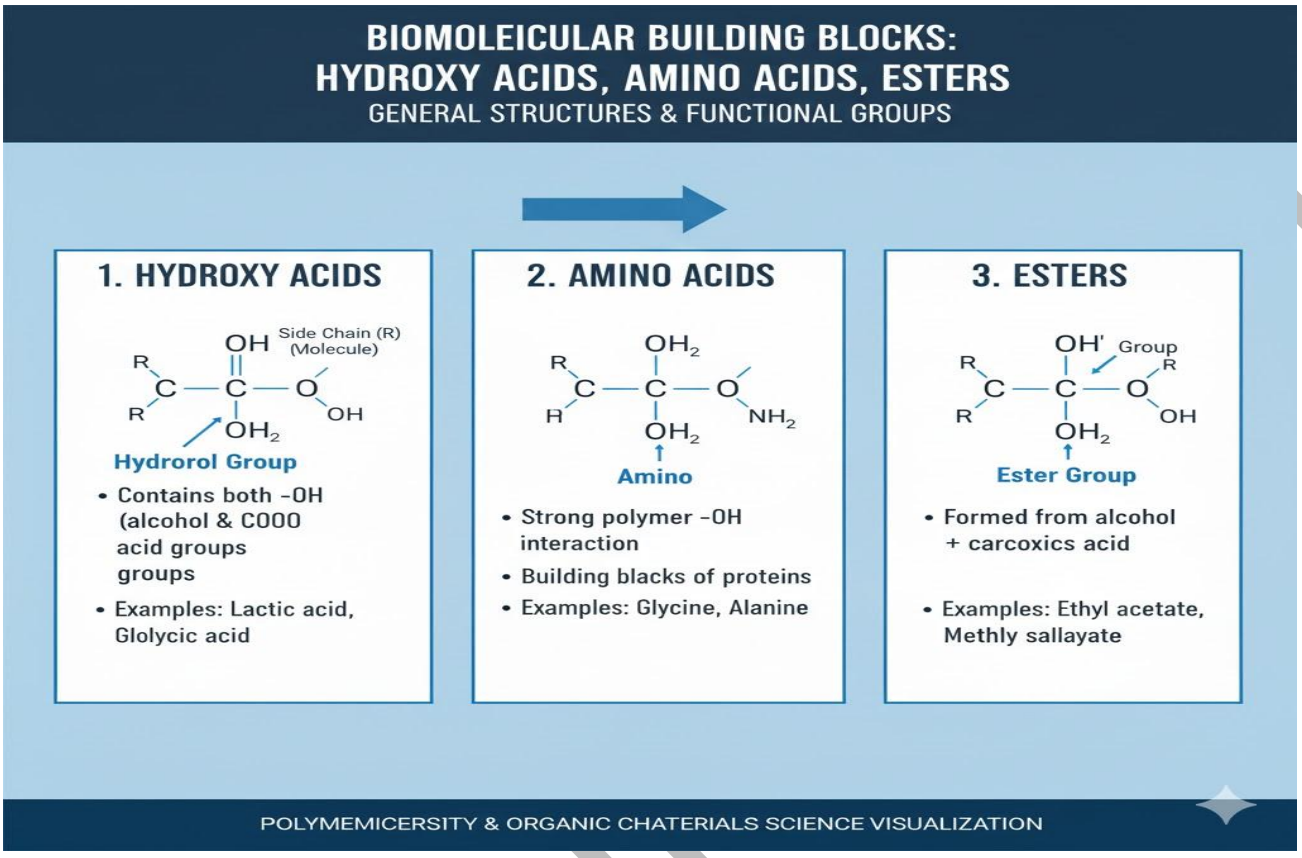


Figure 3.1 General structures of common bifunctional compounds

Pilot questions 3.1

Define bifunctional compounds.
Give two examples of bifunctional compounds.
What functional groups are present in amino acids?
Why are bifunctional compounds important in organic chemistry?
State one industrial use of esters.

3.2 Alcohols, Acids, And Esters As Bifunctional Compounds

3.2.1 Structures and properties of hydroxy acids

Hydroxy acids are compounds that contain both a hydroxyl group (–OH) and a carboxyl group (–COOH) within the same molecule. The presence of these two functional groups makes hydroxy acids reactive in multiple ways. They can undergo oxidation, esterification, and hydrogen bonding, which influences their solubility and acidity.

A common example is **lactic acid**, found in sour milk and produced in muscles during anaerobic respiration. Another is **citric acid**, which plays a central role in the citric acid cycle in metabolism.

Fill in the blank: Hydroxy acids contain both a _____ group and a carboxyl group in the same molecule.

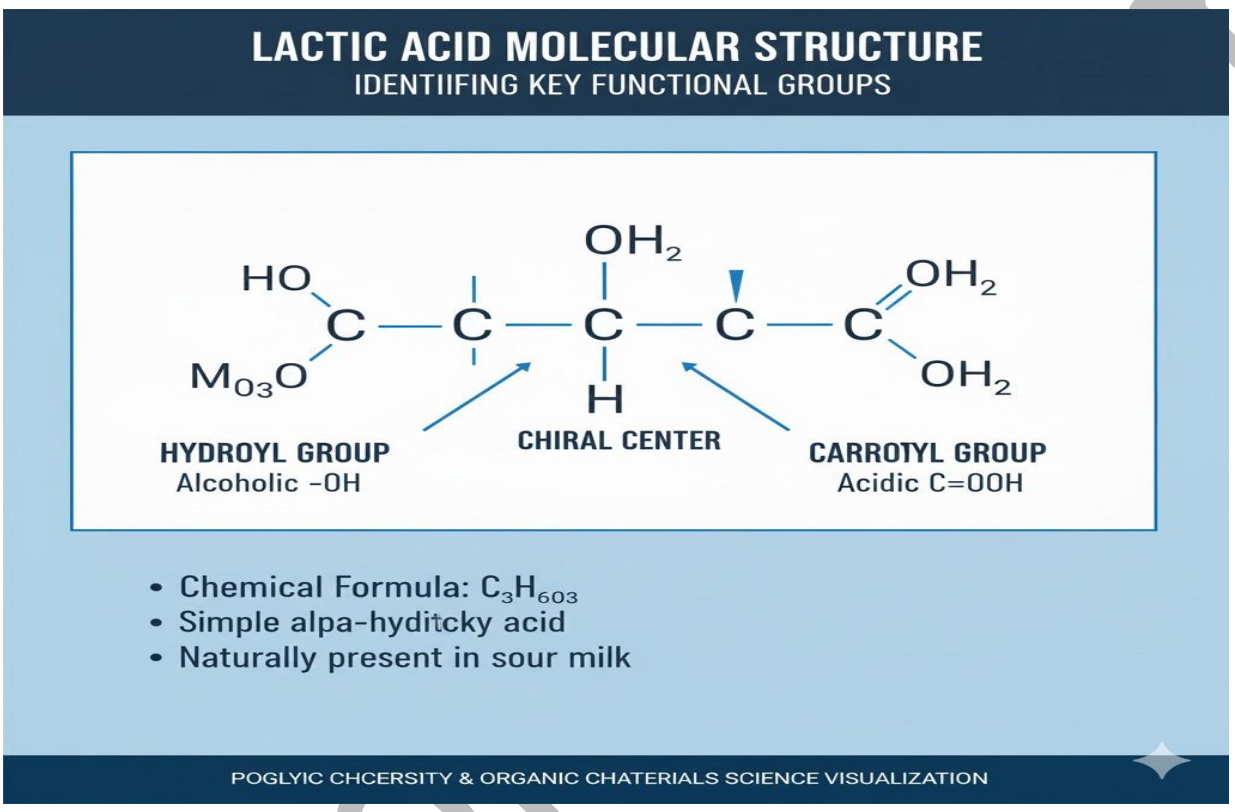


Figure 3.2 Structure of lactic acid as a hydroxy acid

3.2.2 Structures and properties of amino acids

Amino acids are bifunctional compounds containing an amino group ($–NH_2$) and a carboxyl group ($–COOH$). They are the building blocks of proteins and play vital roles in metabolism. The side chain, known as the **R group**, varies among amino acids and determines their chemical properties.

Amino acids can act as both acids and bases, making them **amphoteric**. They also exist in a special form called a **zwitterion**, where the amino group is protonated ($–NH_3^+$) and the carboxyl group is deprotonated ($–COO^-$), giving the molecule both positive and negative charges.

Fill in the blank: Amino acids exist as _____ at physiological pH, carrying both positive and negative charges.

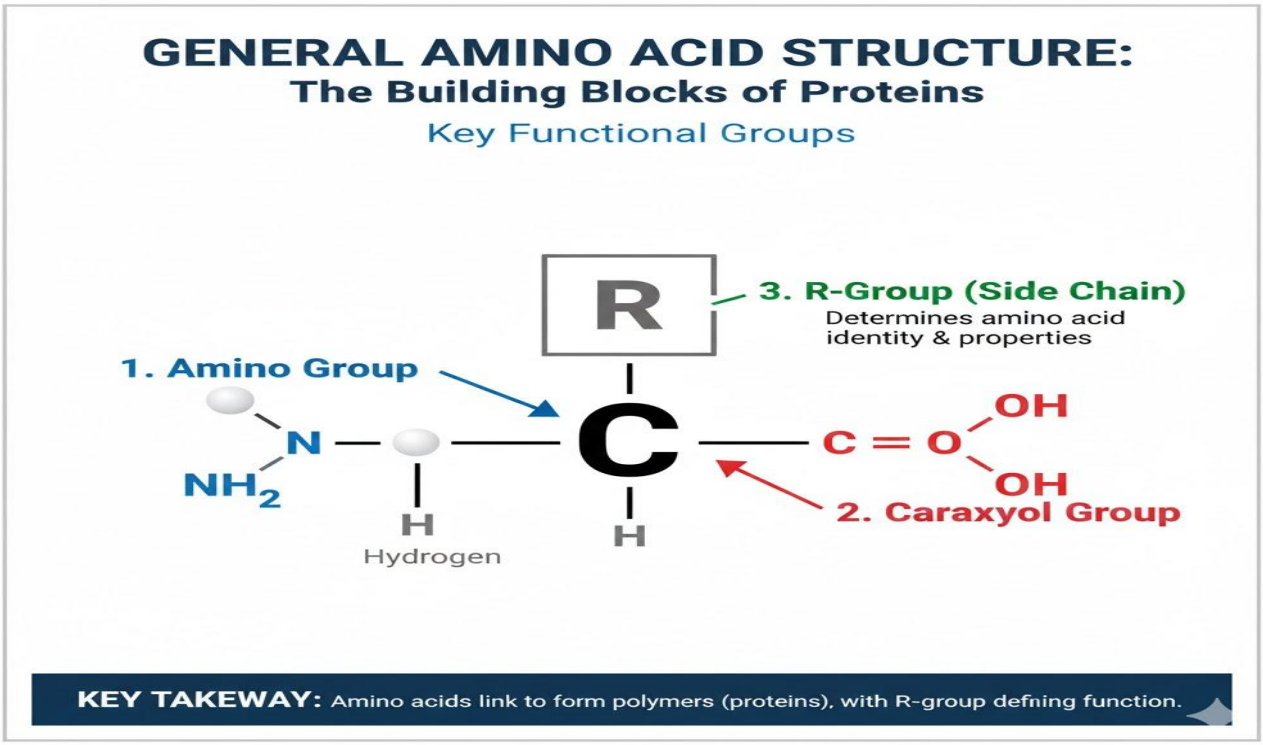


Figure 3.3 General structure of an amino acid

3.2.3 Esterification and hydrolysis reactions

Esters are compounds formed when a carboxylic acid reacts with an alcohol, producing an ester and water. This process is called **esterification**, and it is an example of a condensation reaction. Esters are known for their pleasant fragrances and are widely used in flavourings and perfumes.

The reverse process, **hydrolysis**, breaks down esters back into their parent alcohol and acid. Hydrolysis can occur under acidic or basic conditions, with base-catalysed hydrolysis often referred to as **saponification**, which is the basis of soap making.

Fill in the blank: The reaction between a carboxylic acid and an alcohol to form an ester is called _____.

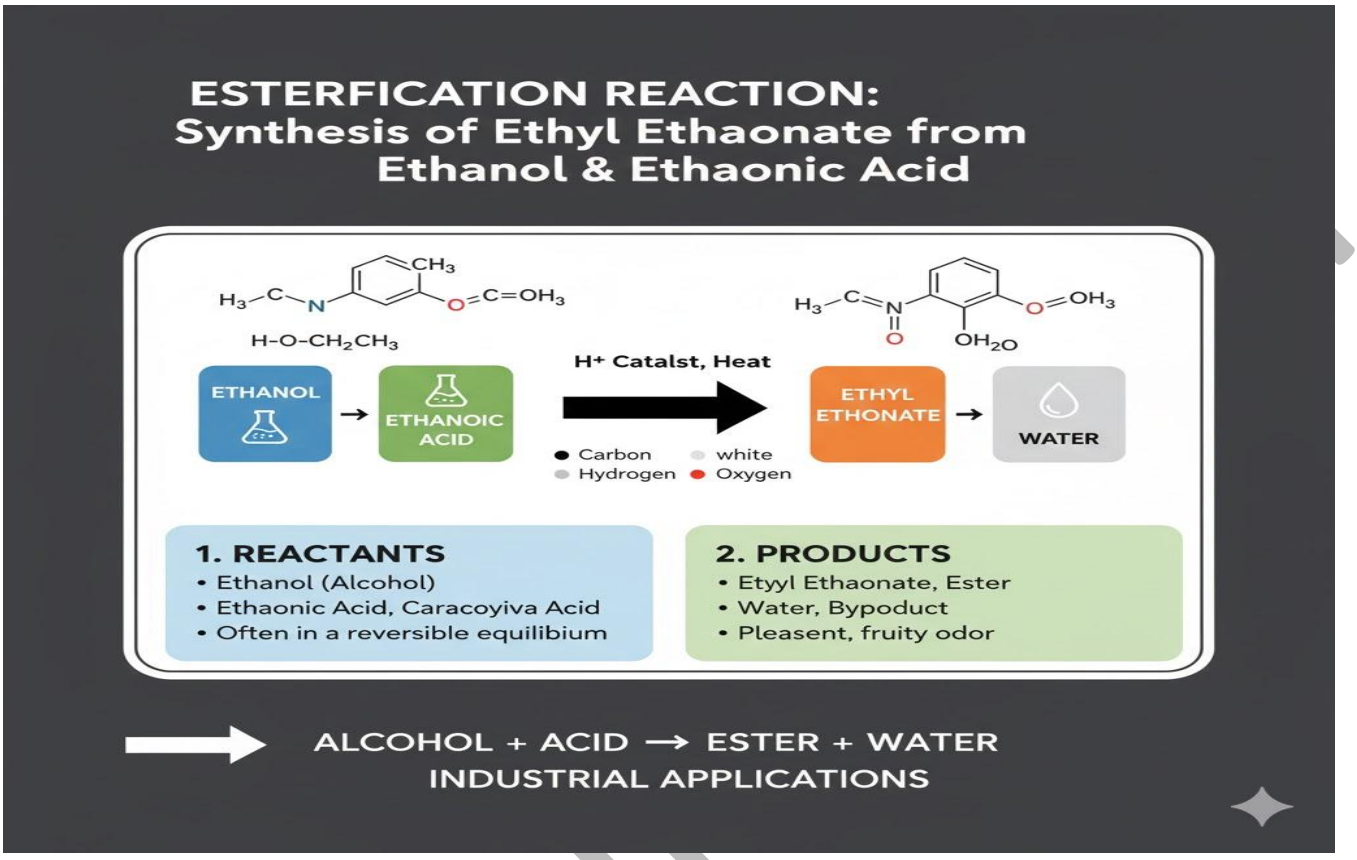


Figure 3.4 Esterification reaction between ethanol and ethanoic acid

Table 3.2 Common esters, their parent alcohol and acid, and uses

Ester	Parent alcohol	Parent acid	Uses
Ethyl ethanoate	Ethanol	Ethanoic acid	Solvent in paints and adhesives; flavouring agent
Methyl salicylate	Methanol	Salicylic acid	Used in liniments and ointments; flavouring and fragrance
Isoamyl acetate	Isoamyl alcohol	Acetic acid	Banana flavouring; fragrance industry
Propyl ethanoate	Propanol	Ethanoic acid	Pear flavouring; used in perfumes
Butyl butanoate	Butanol	Butanoic acid	Pineapple flavouring; fragrance and food industry

Pilot questions 3.2

What functional groups are present in hydroxy acids?
Give one example of a hydroxy acid and state its importance.
What two functional groups are present in amino acids?
What special form do amino acids exist in at physiological pH?
What is the name of the reaction that forms esters?
What is the reverse process of esterification called?

3.3 Reaction Mechanisms Of Bifunctional Compounds

3.3.1 Nucleophilic substitution mechanisms

Nucleophilic substitution is a reaction in which a **nucleophile** (a species that donates an electron pair) replaces a leaving group in a molecule. In bifunctional compounds, this mechanism is particularly important because the presence of two functional groups can influence reactivity.

For example, in amino acids, the amino group can act as a nucleophile, while in esters, the carbonyl carbon is susceptible to nucleophilic attack. The two main types of nucleophilic substitution are **SN1** (unimolecular, involving a carbocation intermediate) and **SN2** (bimolecular, involving a single-step mechanism).

Fill in the blank: In an SN2 reaction, the nucleophile attacks the substrate in a _____ step.

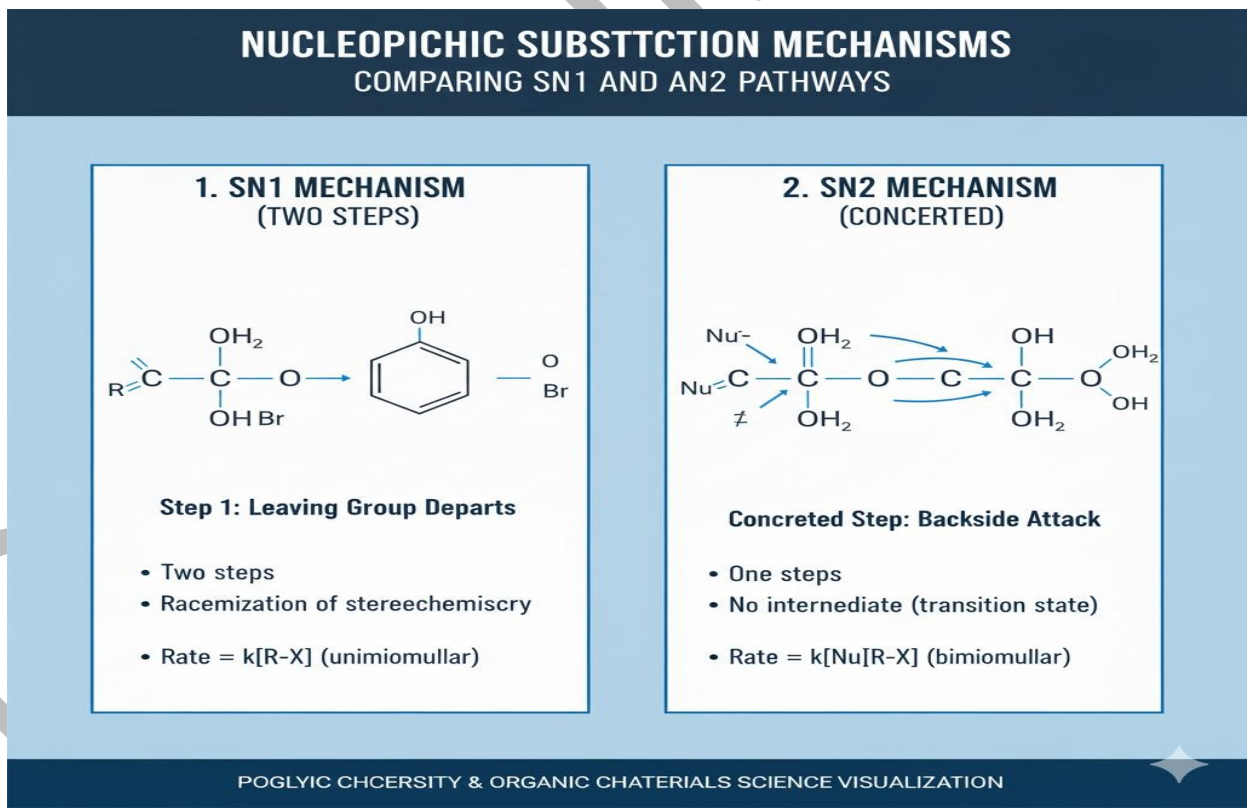


Figure 3.5 Nucleophilic substitution mechanisms (SN1 and SN2)

3.3.2 Elimination mechanisms

Elimination reactions involve the removal of atoms or groups from a molecule, resulting in the formation of a double bond. In bifunctional compounds, elimination can occur when one functional group facilitates the departure of another.

The two main types are **E1** (unimolecular elimination, involving a carbocation intermediate) and **E2** (bimolecular elimination, occurring in a single step). For example, hydroxy acids can undergo dehydration to form unsaturated acids.

Fill in the blank: The removal of atoms or groups to form a double bond is called _____.

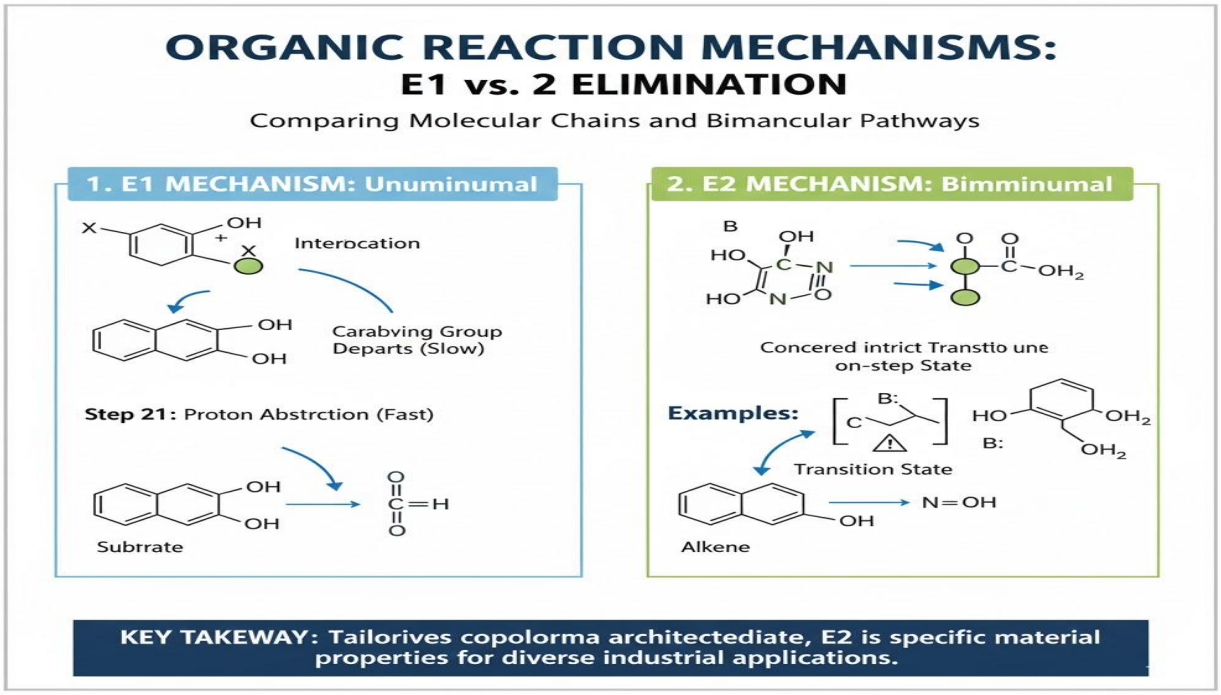


Figure 3.6 Elimination mechanisms (E1 and E2)

3.3.3 Addition mechanisms

Addition reactions occur when atoms or groups are added to a molecule, typically across a double bond. In bifunctional compounds, addition reactions are significant because they can modify both functional groups simultaneously or selectively.

For example, hydroxy acids can undergo addition reactions with halogens, while amino acids can participate in addition reactions during peptide bond formation. Addition reactions are often catalysed by acids or bases, depending on the substrate.

Fill in the blank: Addition reactions usually occur across a _____ bond.

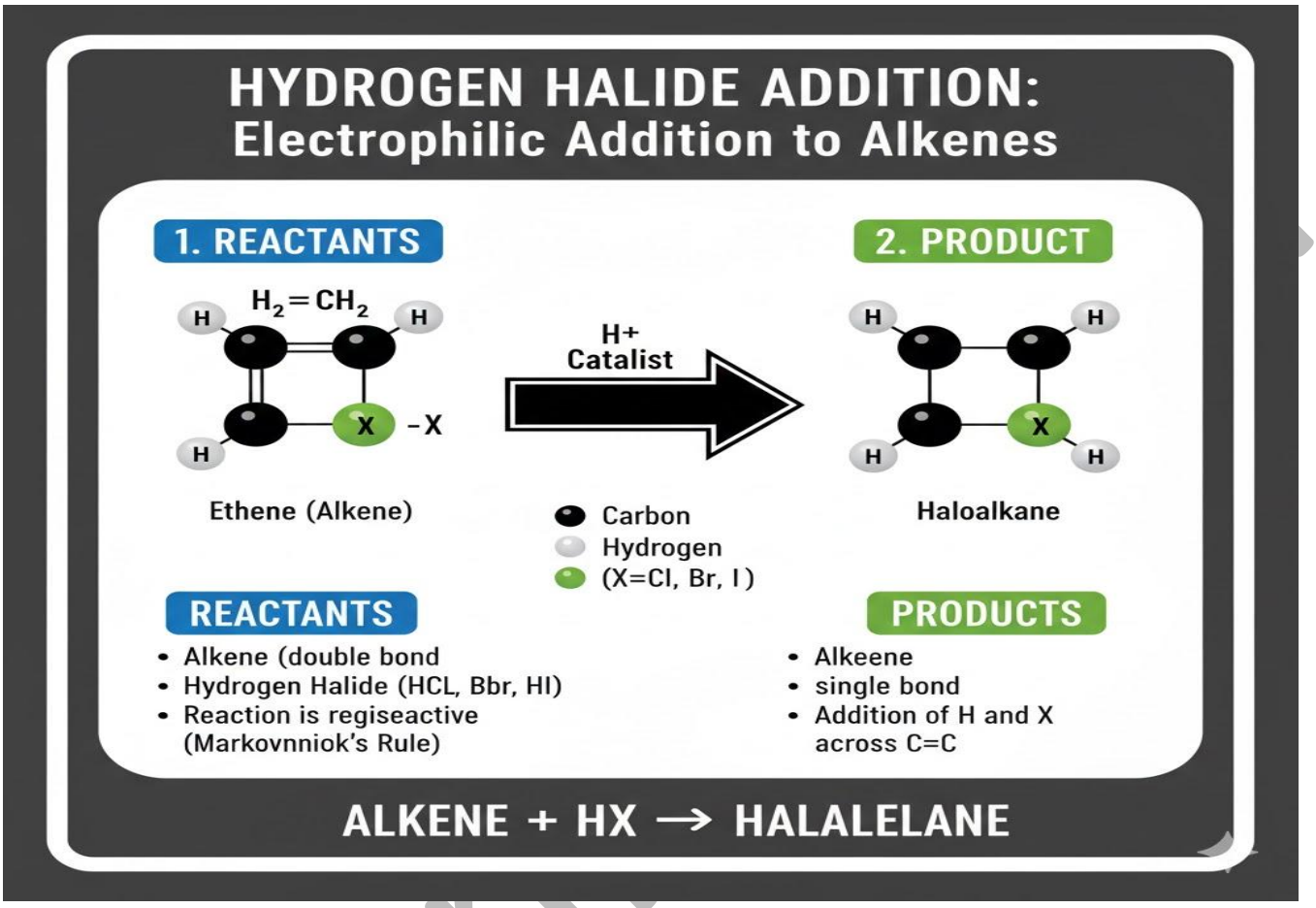


Figure 3.7 Addition mechanism across a double bond

Pilot questions 3.3

Define nucleophilic substitution.
Distinguish between SN1 and SN2 mechanisms.
What is formed during elimination reactions?
Name the two types of elimination mechanisms.
Across what type of bond do addition reactions usually occur?

3.4 Applications And Biological Relevance

3.4.1 Role of amino acids in proteins

Amino acids are bifunctional compounds containing both an amino group ($–NH_2$) and a carboxyl group (–COOH). Their dual functionality allows them to link together through peptide bonds, forming long chains that fold into proteins. Proteins are essential biomolecules that perform structural, catalytic, transport, and regulatory roles in living organisms.

For example, collagen provides strength to connective tissues, while enzymes such as amylase catalyse biochemical reactions. The specific sequence of amino acids determines the protein's structure and function.

Fill in the blank: Amino acids join together through _____ bonds to form proteins.

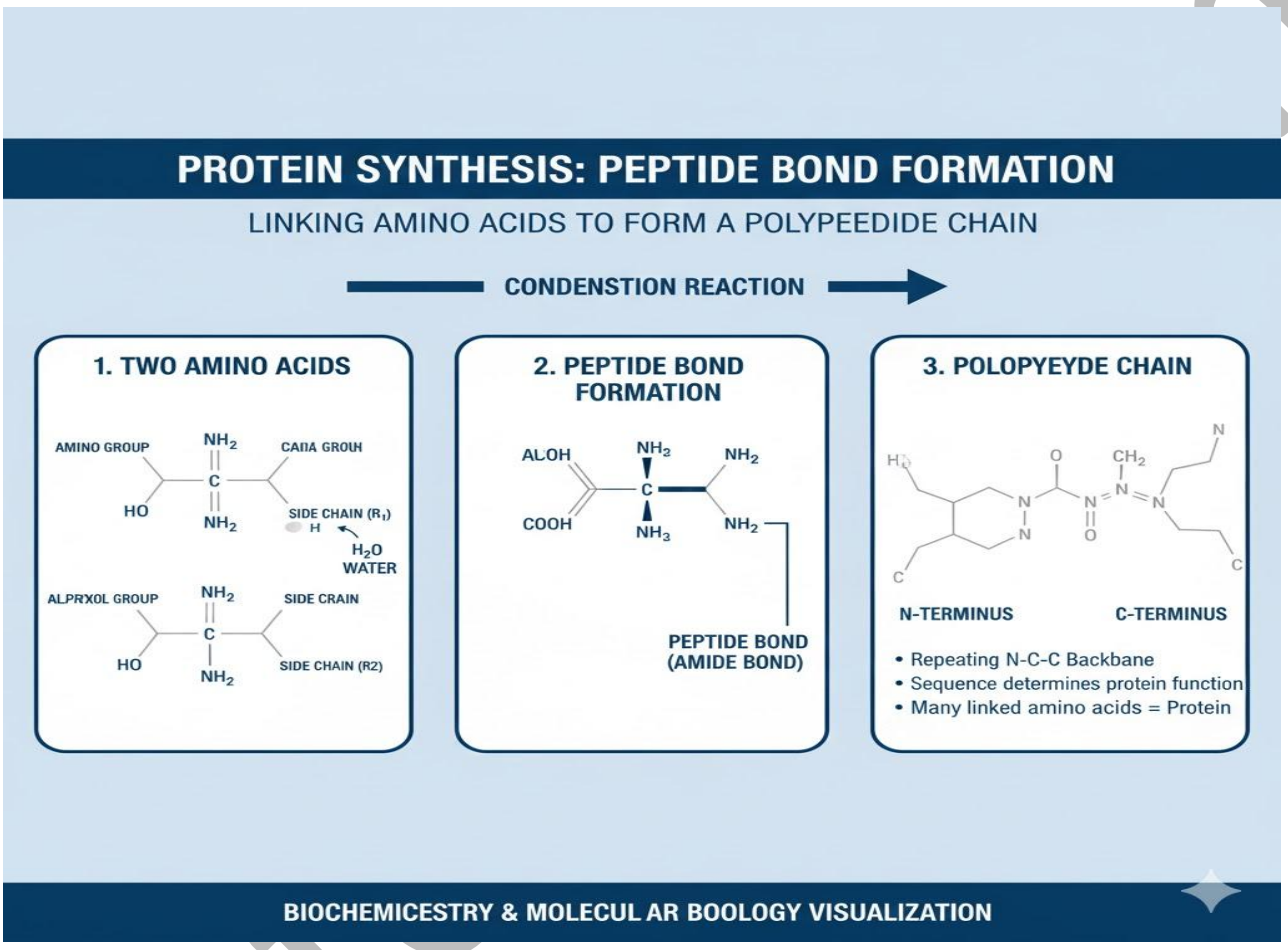


Figure 3.8 Role of amino acids in protein formation

3.4.2 Role of hydroxy acids in metabolism

Hydroxy acids are compounds containing both hydroxyl (–OH) and carboxyl (–COOH) groups. Their dual reactivity makes them central to metabolic pathways. For instance, lactic acid is produced during anaerobic respiration in muscles, while citric acid is a key intermediate in the citric acid cycle, which generates energy in cells.

Hydroxy acids can act as intermediates that connect different metabolic processes, ensuring efficient energy production and utilisation.

Fill in the blank: Citric acid is a hydroxy acid that plays a central role in the _____ cycle.

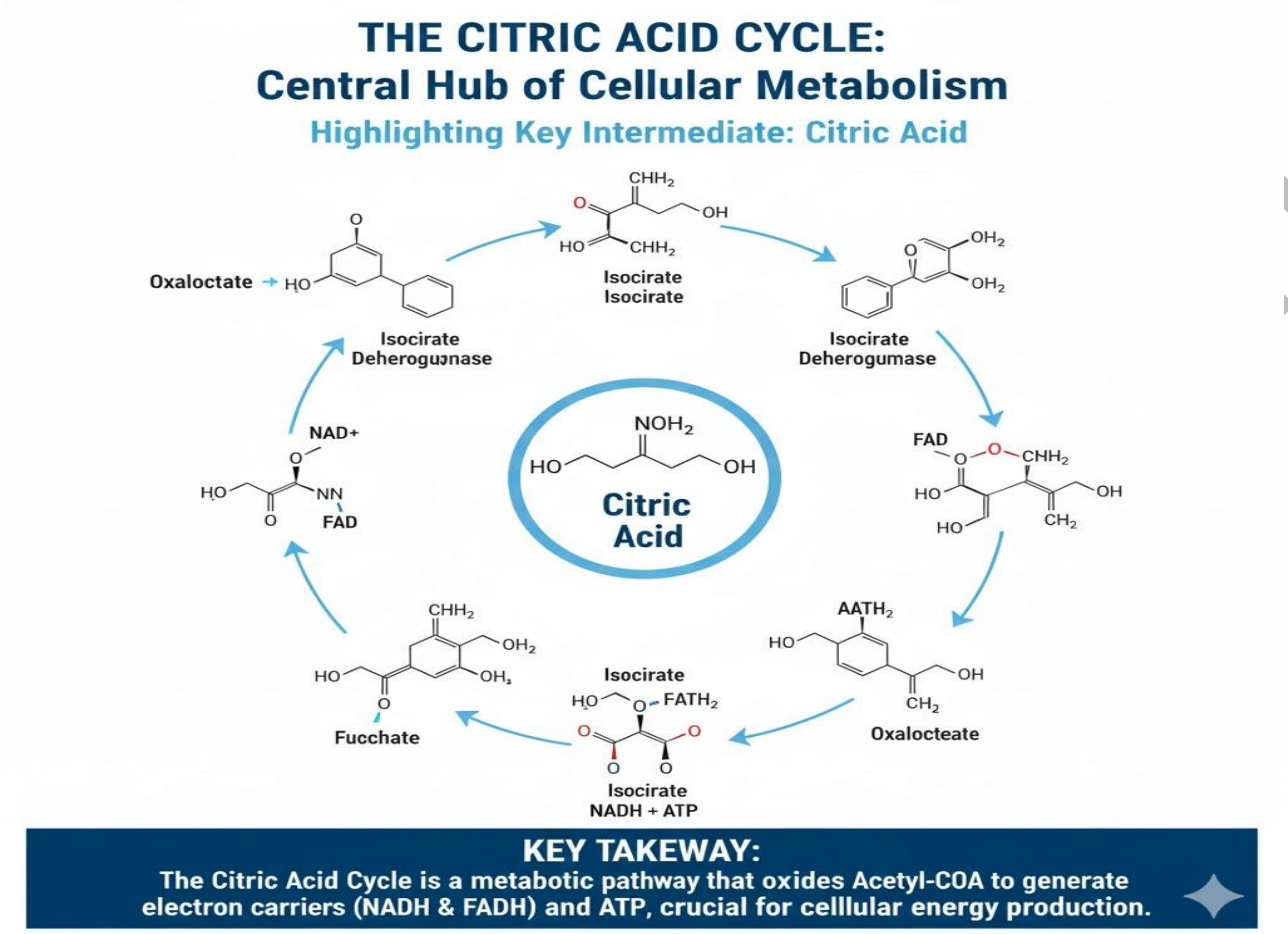


Figure 3.9 Role of citric acid in metabolism

3.4.3 Industrial and pharmaceutical applications

Bifunctional compounds are widely used in industry and medicine. **Esters** are employed in the manufacture of perfumes, flavourings, and solvents due to their pleasant aromas. **Amino acids** are used in nutritional supplements and as precursors for pharmaceuticals. **Hydroxy acids** are applied in cosmetics, particularly in skin treatments, because of their exfoliating properties.

In pharmaceuticals, bifunctional compounds often serve as building blocks for drug molecules, where their dual reactivity allows for targeted design and synthesis.

Fill in the blank: Esters are commonly used in the manufacture of _____ because of their pleasant aromas.

Pilot questions 3.4

What type of bond links amino acids together in proteins?
Give one example of a protein formed from amino acids.
Name one hydroxy acid involved in metabolism.

In which cycle does citric acid play a central role?
State one industrial use of esters.
Mention one pharmaceutical application of amino acids.

Series Summary

This Series has introduced you to bifunctional compounds, highlighting their unique dual reactivity and importance in both organic chemistry and biological systems. Starting off, we defined and classified bifunctional compounds, before moving on to alcohols, acids, and esters, where we explored hydroxy acids, amino acids, and esterification reactions. We then examined the mechanisms of nucleophilic substitution, elimination, and addition, showing how these reactions underpin the behaviour of bifunctional molecules. Finally, we considered their applications and biological relevance, including the role of amino acids in proteins, hydroxy acids in metabolism, and industrial uses of esters.

By completing this Series, you should now be able to define and classify bifunctional compounds, explain the structures and properties of hydroxy acids and amino acids, demonstrate esterification and hydrolysis, analyse reaction mechanisms, and evaluate their biological and industrial significance. These abilities directly align with the Series Learning Outcomes (SLOs), ensuring that you are well prepared to describe, apply, and assess the structures and mechanisms of bifunctional organic compounds with confidence.

Concept Check Questions [Series 3]

Objective questions

Define a bifunctional compound. (Linked to SLO 3.1)
Identify the two functional groups present in hydroxy acids. (Linked to SLO 3.2)
State the functional groups found in amino acids. (Linked to SLO 3.3)
Name the reaction between a carboxylic acid and an alcohol that produces an ester. (Linked to SLO 3.4)
Specify the type of bond formed when amino acids join to form proteins. (Linked to SLO 3.8)

Short-answer questions

6. Explain why amino acids are described as amphoteric. (Linked to SLO 3.3)
7. Describe one industrial use of esters. (Linked to SLO 3.10)
8. Give one example of a hydroxy acid and state its biological role. (Linked to SLO 3.9)
9. Distinguish between SN1 and SN2 nucleophilic substitution mechanisms. (Linked to SLO 3.5)
10. State one pharmaceutical application of amino acids. (Linked to SLO 3.10)

Long-answer questions

11. Analyse the structural features of hydroxy acids and amino acids, and explain how these

features influence their reactivity. (Linked to SLOs 3.2, 3.3)
12. Evaluate the importance of esterification and hydrolysis reactions in both biological and industrial contexts. (Linked to SLO 3.4, 3.10)
13. Explain the mechanisms of elimination and addition reactions in bifunctional compounds, giving examples of each. (Linked to SLOs 3.6, 3.7)
14. Assess the biological and industrial significance of bifunctional compounds, highlighting at least three distinct applications. (Linked to SLOs 3.8, 3.9, 3.10)

Answers to Concept Check Questions [Series 3]

Objective questions

Organic compounds containing two distinct functional groups.
Hydroxyl (–OH) and carboxyl (–COOH).
Amino ($–NH_2$) and carboxyl (–COOH).
Esterification.
Peptide bond.

Short-answer questions

6. Amino acids are amphoteric because they can act as both acids and bases.
7. Esters are used in perfumes and flavourings due to their pleasant aromas.
8. Citric acid; it plays a central role in the citric acid cycle.
9. SN1 involves a carbocation intermediate in two steps, while SN2 occurs in a single step with simultaneous attack and departure.
10. Amino acids are used in nutritional supplements and as precursors for drugs.

Long-answer questions

11. **Basic response:** Hydroxy acids contain hydroxyl and carboxyl groups, while amino acids contain amino and carboxyl groups. These dual groups allow them to undergo multiple reactions such as oxidation, esterification, and peptide bond formation.
Value-added response: Hydroxy acids act as intermediates in metabolism (e.g., citric acid in the citric acid cycle), while amino acids form proteins and exist as zwitterions at physiological pH, influencing solubility and reactivity.

Basic response: Esterification produces esters from acids and alcohols, while hydrolysis breaks esters back into their components.
Value-added response: In biology, esterification is important in lipid formation, while hydrolysis is crucial in digestion. Industrially, esterification is used in perfumes and flavourings, and hydrolysis (saponification) is used in soap production.

Basic response: Elimination reactions remove atoms to form double bonds, while addition reactions add atoms across double bonds.
Value-added response: Hydroxy acids can undergo dehydration (elimination) to form

unsaturated acids, while addition reactions such as halogenation modify double bonds. These mechanisms are central to synthetic organic chemistry and industrial processes.

Basic response: Bifunctional compounds are important in proteins, metabolism, and industrial uses such as perfumes.
Value-added response: Amino acids form proteins essential for life, hydroxy acids act as metabolic intermediates, and esters are used in pharmaceuticals, cosmetics, and flavourings. Their dual reactivity makes them versatile in both biological and industrial contexts.

Answers to Pilot Questions [Series 3]

Part 1 Introduction to bifunctional compounds

Organic compounds that contain two distinct functional groups.
Hydroxy acids and amino acids.
Amino group ($–NH_2$) and carboxyl group (–COOH).
They can undergo multiple reactions and serve as intermediates in synthesis and metabolism.
Perfumes and flavourings.

Part 2 Alcohols, acids, and esters as bifunctional compounds

Hydroxyl group (–OH) and carboxyl group (–COOH).
Lactic acid; produced in muscles during anaerobic respiration.
Amino group ($–NH_2$) and carboxyl group (–COOH).
Zwitterions.
Esterification.
Hydrolysis (or saponification under basic conditions).

Part 3 Reaction mechanisms of bifunctional compounds

A reaction in which a nucleophile replaces a leaving group.
SN1 involves a carbocation intermediate in two steps; SN2 occurs in a single step.
A double bond.
E1 and E2.
A double bond.

Part 4 Applications and biological relevance

Peptide bonds.

Collagen.
Citric acid.
Citric acid cycle.
Perfumes and flavourings.
Nutritional supplements and drug precursors.

Series 4: Stereochemistry and Named Organic Reactions

Part 1 Fundamentals of stereochemistry

4.1.1 Definition and scope of stereochemistry
4.1.2 Types of isomerism: structural vs stereoisomerism
4.1.3 Importance of stereochemistry in organic chemistry

Part 2 Chirality and stereoisomers

4.2.1 Concept of chirality and asymmetric carbon atoms
4.2.2 Enantiomers and diastereomers
4.2.3 Optical activity and measurement

Part 3 Conformational analysis and stereochemical effects

4.3.1 Conformations of alkanes and cycloalkanes
4.3.2 Steric hindrance and torsional strain
4.3.3 Stereoelectronic effects in reactions

Part 4 Selected named organic reactions

4.4.1 Aldol condensation
4.4.2 Cannizzaro reaction
4.4.3 Diels–Alder reaction
4.4.4 Friedel–Crafts reaction

Introduction

In the last Series, we explored bifunctional compounds and their reaction mechanisms, gaining insight into how molecules with two functional groups behave in both biological and industrial contexts. Building on that foundation, we now turn to **stereochemistry**, which examines the

three-dimensional arrangement of atoms in molecules, and to **named organic reactions**, which represent some of the most important transformations in synthetic chemistry. These topics are central to understanding how structure influences reactivity and how chemists design pathways to create useful compounds.

The aim of this Series is to equip you with the ability to explain stereochemical principles, analyse conformations and stereochemical effects, and apply knowledge of selected named reactions to practical and theoretical problems in organic chemistry.

We shall commence this Series by introducing the fundamentals of stereochemistry, including its scope and importance. Next, we will explore chirality and stereoisomers, focusing on enantiomers, diastereomers, and optical activity. Following that, we will move on to conformational analysis and stereochemical effects, examining how molecular shape and strain influence reactivity. Finally, we will wrap up by studying selected named organic reactions such as aldol condensation, Cannizzaro reaction, Diels–Alder reaction, and Friedel–Crafts reaction, thereby rounding off the Series with practical applications of stereochemical concepts.

Series Learning Outcomes

Upon completing this Series, you should be able to:

define stereochemistry and explain its scope and importance in organic chemistry,
distinguish between structural isomerism and stereoisomerism,
describe the concept of chirality and identify asymmetric carbon atoms,
differentiate between enantiomers and diastereomers,
demonstrate how optical activity is measured and interpreted,
analyse conformations of alkanes and cycloalkanes,
explain the effects of steric hindrance and torsional strain on molecular stability,
evaluate stereoelectronic effects in organic reactions,
describe the mechanism and applications of aldol condensation,
explain the Cannizzaro reaction and its significance,
demonstrate the steps of the Diels–Alder reaction, and
apply knowledge of the Friedel–Crafts reaction to practical examples in synthesis.

4.1 Fundamentals Of Stereochemistry

4.1.1 Definition and scope of stereochemistry

Stereochemistry is the branch of chemistry concerned with the three-dimensional arrangement of atoms in molecules and the effect of this arrangement on their chemical behaviour. It goes beyond simply knowing which atoms are connected, focusing instead on how they are oriented

in space. This spatial arrangement can dramatically influence the physical properties, reactivity, and biological activity of compounds.

For example, two molecules with the same molecular formula but different spatial arrangements may have entirely different smells, tastes, or medicinal effects. This makes stereochemistry a vital area of study in organic chemistry, pharmaceuticals, and biochemistry.

Fill in the blank: The branch of chemistry that studies the three-dimensional arrangement of atoms in molecules is called _____.

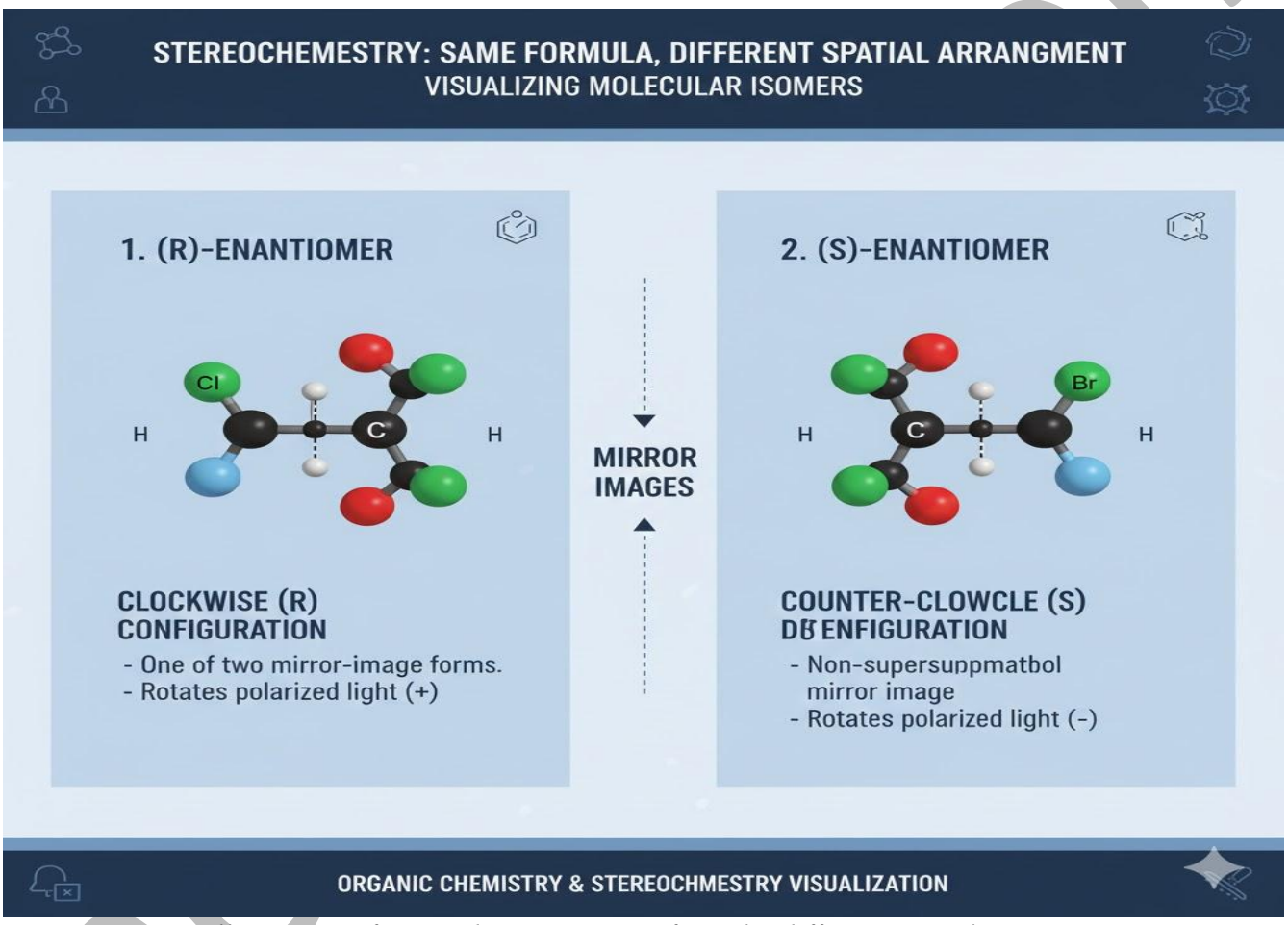


Figure 4.1 Illustration of stereochemistry: same formula, different spatial arrangement

4.1.2 Types of isomerism: structural vs stereoisomerism

Isomerism refers to the phenomenon where compounds have the same molecular formula but different arrangements of atoms. There are two broad types:

Structural isomerism occurs when atoms are connected in different orders, leading to variations such as chain isomers, position isomers, and functional group isomers.

Stereoisomerism occurs when atoms are connected in the same order but differ in their spatial arrangement. This includes **geometrical isomerism** (cis/trans) and **optical isomerism** (enantiomers).

Fill in the blank: Compounds with the same molecular formula but different spatial arrangements are called _____.

Table 4.1 Comparison of structural isomerism and stereoisomerism

Feature	Structural isomerism	Stereoisomerism
Definition	Compounds with the same molecular formula but different connectivity of atoms	Compounds with the same molecular formula and connectivity but different spatial arrangement
Types	Chain isomerism, position isomerism, functional group isomerism	Geometrical isomerism (cis/trans), optical isomerism (enantiomers, diastereomers)
Example 1	Butane (C_4H_{10}): n-butane and isobutane (different chain structures)	2-butene (C_4H_8): cis-2-butene and trans-2-butene (different spatial arrangement)
Example 2	Ethanol (C_2H_6O) and dimethyl ether (C_2H_6O): different functional groups	Lactic acid enantiomers: L-lactic acid and D-lactic acid (mirror images)
Key property	Differences in physical and chemical properties due to connectivity	Differences in optical activity or geometry, often with identical basic properties

4.1.3 Importance of stereochemistry in organic chemistry

Stereochemistry is crucial because many biological molecules are stereospecific. For instance, enzymes and receptors often recognise only one stereoisomer of a compound. This explains why one form of a drug may be therapeutic while another form may be inactive or even harmful.

In industrial chemistry, stereochemistry influences polymer properties, fragrance design, and food chemistry. In biochemistry, it explains phenomena such as the handedness of amino acids and sugars, which are essential for life.

Fill in the blank: The biological activity of a drug often depends on its _____ arrangement of atoms.

Pilot questions 4.1

Define stereochemistry.
Distinguish between structural isomerism and stereoisomerism.
Give one example of stereoisomerism.
Why is stereochemistry important in drug design?

State one industrial application of stereochemistry.

4.2 Chirality And Stereoisomers

4.2.1 Concept of chirality and asymmetric carbon atoms

Chirality refers to the property of a molecule that makes it non-superimposable on its mirror image, much like how your left and right hands are mirror images but cannot be perfectly aligned. In chemistry, chirality usually arises when a carbon atom is bonded to four different substituents. Such a carbon is called an **asymmetric carbon atom** or **chiral centre**.

Chiral molecules are important because their mirror images, known as **enantiomers**, can have very different biological activities. For example, one enantiomer of a drug may be therapeutic, while the other may be inactive or harmful.

Fill in the blank: A carbon atom bonded to four different substituents is called an _____.

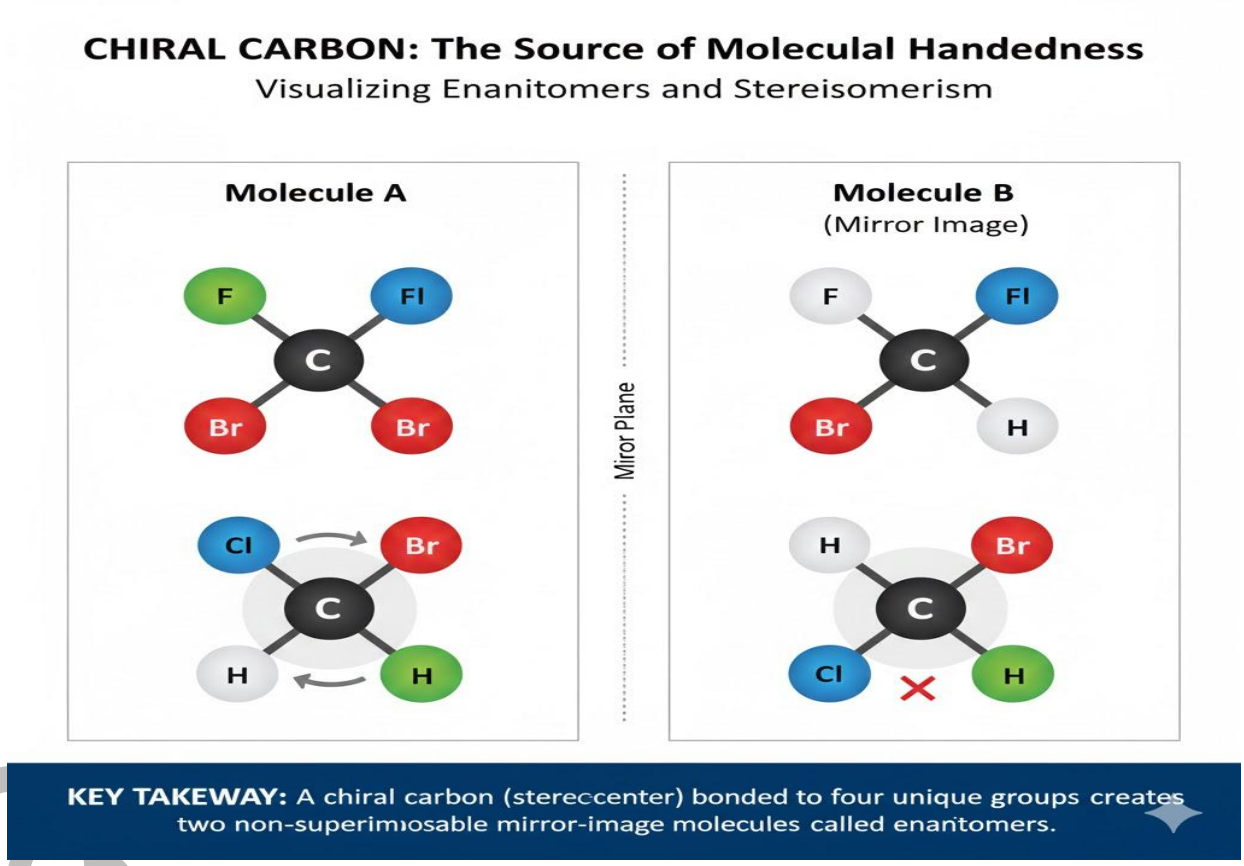


Figure 4.2 Illustration of chirality and asymmetric carbon atoms

4.2.2 Enantiomers and diastereomers

Enantiomers are stereoisomers that are non-superimposable mirror images of each other. They have identical physical properties except for the direction in which they rotate plane-polarised light and their interactions with other chiral environments.

Diastereomers, on the other hand, are stereoisomers that are not mirror images. They often differ in physical properties such as melting points, boiling points, and solubility, making them easier to separate than enantiomers.

Fill in the blank: Stereoisomers that are non-superimposable mirror images of each other are called _____.

4.2.3 Optical activity and measurement

Optical activity is the ability of chiral compounds to rotate the plane of polarised light. Enantiomers rotate light in equal magnitude but opposite directions: one is **dextrorotatory** (rotates light to the right, denoted as +), and the other is **laevorotatory** (rotates light to the left, denoted as –).

Optical activity is measured using a device called a **polarimeter**, which passes polarised light through a solution of the compound and records the angle of rotation. This property is crucial in distinguishing enantiomers and in determining the purity of chiral substances.

Fill in the blank: A compound that rotates plane-polarised light to the right is described as _____.

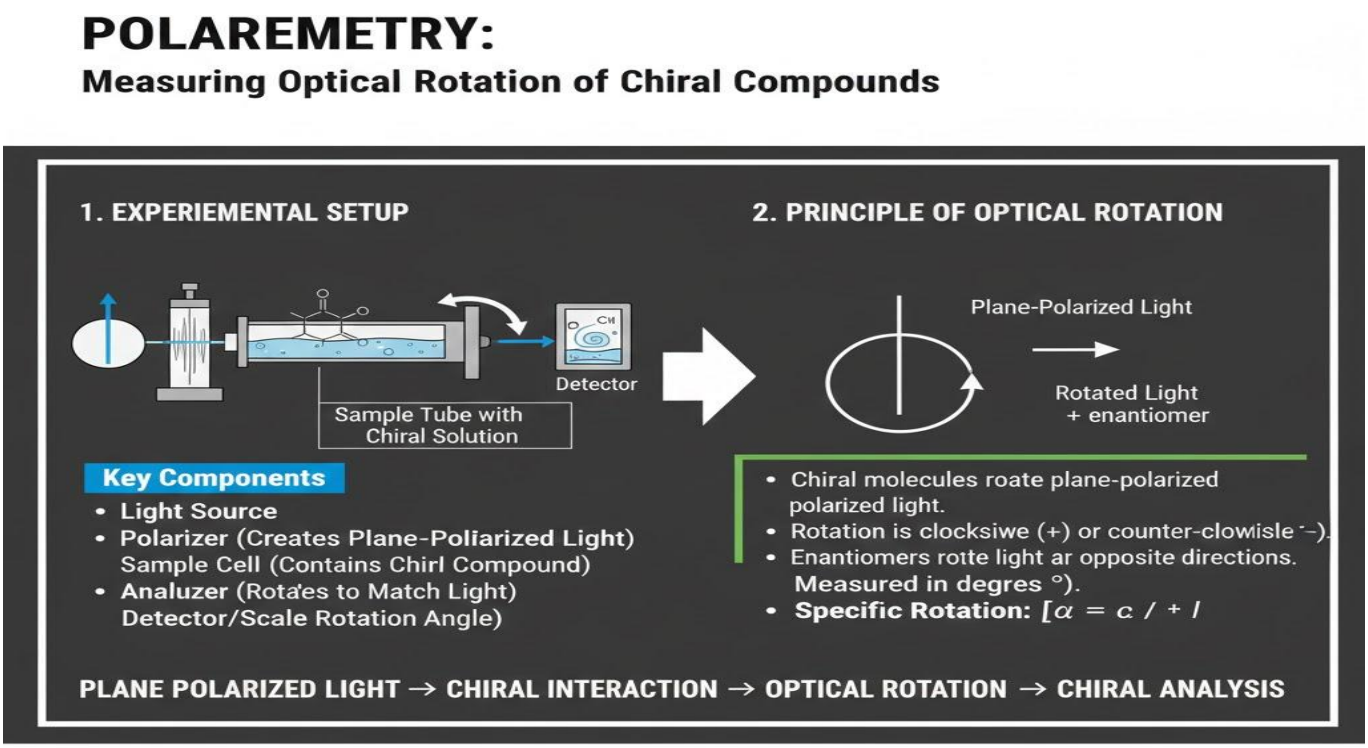


Figure 4.3 Measurement of optical activity using a polarimeter

Optical activity is a critical property in pharmaceutical chemistry because many drugs exist as **enantiomers**, which are mirror-image forms of the same molecule. Although enantiomers share the same chemical formula, their biological effects can differ dramatically.

For example, one enantiomer of a drug may bind effectively to a biological receptor and produce the desired therapeutic effect, while the other may be inactive or even harmful. A well-known case is **thalidomide**, where one enantiomer acted as a sedative, while the other caused severe birth defects.

Pharmaceutical companies therefore use **polarimetry** and other stereochemical techniques to measure and control optical activity during drug development. This ensures that only the beneficial enantiomer is present in the final medicine, improving safety and efficacy.

Pilot questions 4.2

What is chirality in molecules?
Define an asymmetric carbon atom.

Distinguish between enantiomers and diastereomers.
What property allows enantiomers to be distinguished using light?
Name the instrument used to measure optical activity.

4.3 Conformational Analysis And Stereochemical Effects

4.3.1 Conformations of alkanes and cycloalkanes

Conformational analysis is the study of the different spatial arrangements of atoms in a molecule that result from rotation around single bonds. These arrangements are called **conformations**, and they can influence the stability and reactivity of molecules.

In alkanes such as ethane and butane, rotation around the carbon–carbon single bond produces conformations like **staggered** (atoms are positioned as far apart as possible) and **eclipsed** (atoms are aligned, leading to repulsion). Staggered conformations are generally more stable due to reduced electron repulsion.

Cycloalkanes, such as cyclohexane, adopt conformations like the **chair** and **boat** forms. The chair conformation is more stable because it minimises torsional strain and steric hindrance.

Fill in the blank: The most stable conformation of cyclohexane is the _____ form.

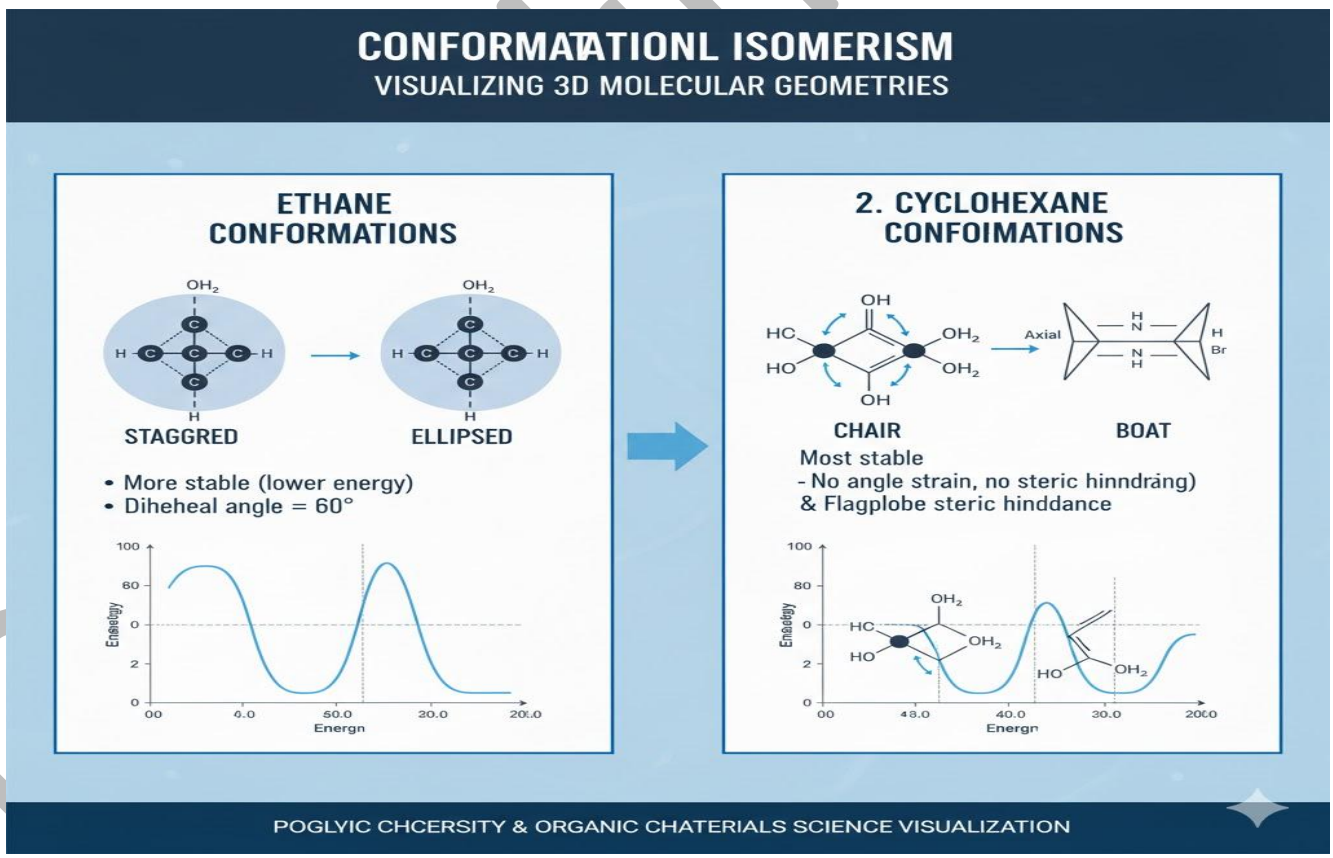


Figure 4.4 Conformations of alkanes and cycloalkanes

4.3.2 Steric hindrance and torsional strain

Steric hindrance occurs when atoms or groups are positioned too closely, causing repulsion that destabilises the molecule. This effect can influence reaction rates, as bulky groups may block access to reactive sites.

Torsional strain arises when bonds on adjacent atoms are eclipsed, leading to increased electron repulsion. Molecules tend to adopt conformations that minimise torsional strain, such as staggered arrangements.

Fill in the blank: Repulsion caused by atoms being too close together is known as _____.

4.3.3 Stereoelectronic effects in reactions

Stereoelectronic effects refer to the influence of orbital alignment and spatial arrangement on the stability and reactivity of molecules. These effects explain why certain conformations are favoured in reactions.

For example, in nucleophilic substitution reactions, the alignment of orbitals can determine whether the reaction proceeds via an SN1 or SN2 mechanism. Similarly, in elimination reactions, the anti-periplanar arrangement of bonds is often required for efficient removal of atoms.

Fill in the blank: The requirement for bonds to be anti-periplanar in elimination reactions is an example of a _____ effect.

Pilot questions 4.3

What is conformational analysis?
Name the most stable conformation of cyclohexane.
Define steric hindrance.
What is torsional strain?
Give one example of a stereoelectronic effect in organic reactions.

4.4 Selected Named Organic Reactions

4.4.1 Aldol condensation

Aldol condensation is a reaction in which an enolate ion, formed from an aldehyde or ketone, reacts with another carbonyl compound to produce a β-hydroxy aldehyde or ketone (called an aldol). This product can then undergo dehydration to form an α,β-unsaturated carbonyl compound.

This reaction is important in synthetic organic chemistry because it creates new carbon–carbon bonds, allowing chemists to build more complex molecules. It is widely used in the synthesis of pharmaceuticals, fragrances, and polymers.

Fill in the blank: The aldol condensation reaction is used to form new _____ bonds in organic synthesis.

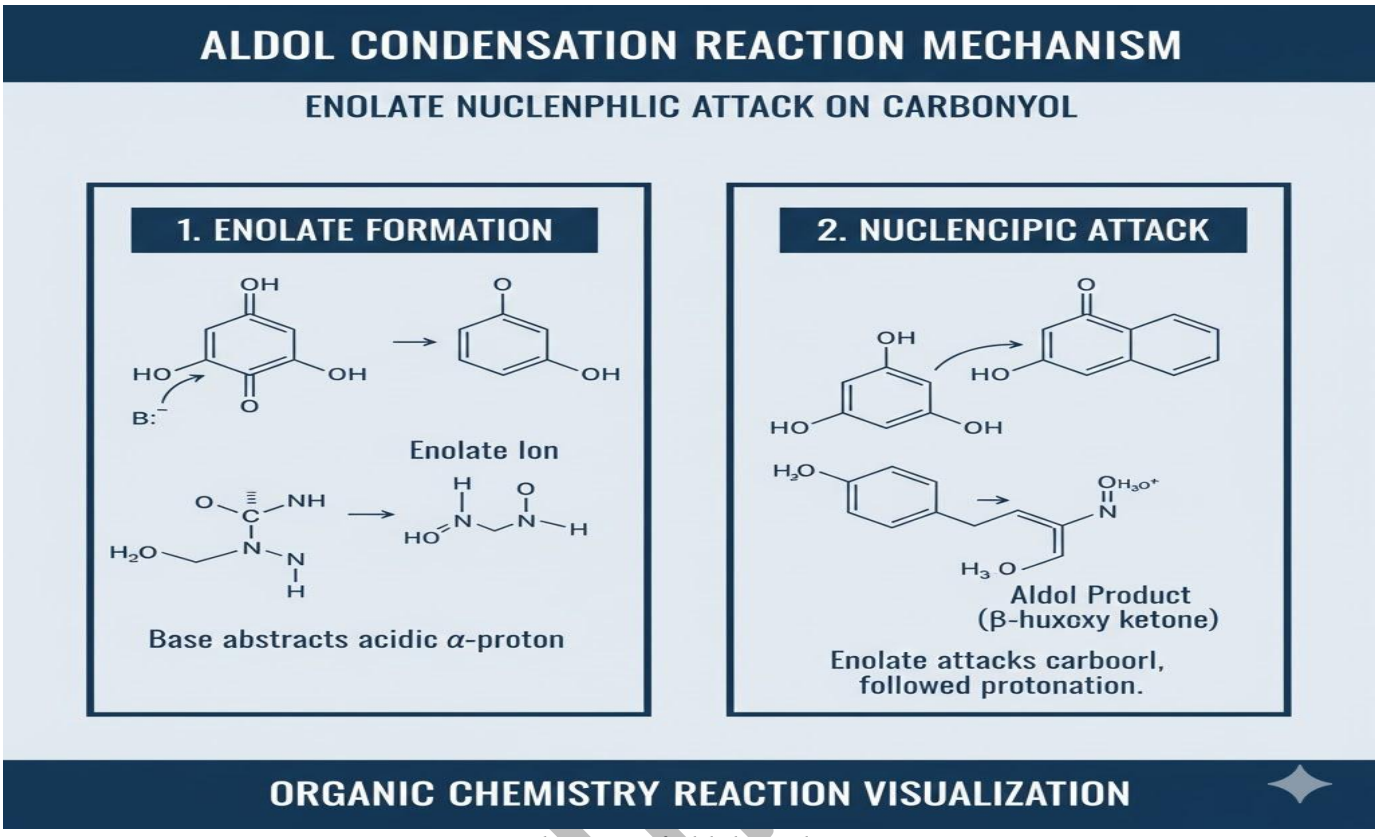


Figure 4.5 Mechanism of aldol condensation

4.4.2 Cannizzaro reaction

Cannizzaro reaction is a redox reaction that occurs when a non-enolisable aldehyde (one without α-hydrogen) is treated with a strong base. In this process, one molecule of the aldehyde is reduced to an alcohol, while another is oxidised to a carboxylate ion.

This reaction is significant because it demonstrates how aldehydes can undergo disproportionation in the absence of α-hydrogen atoms. It is also useful in producing alcohols and carboxylic acids from simple aldehydes.

Fill in the blank: In the Cannizzaro reaction, one aldehyde molecule is reduced to an alcohol while another is _____ to a carboxylate ion.

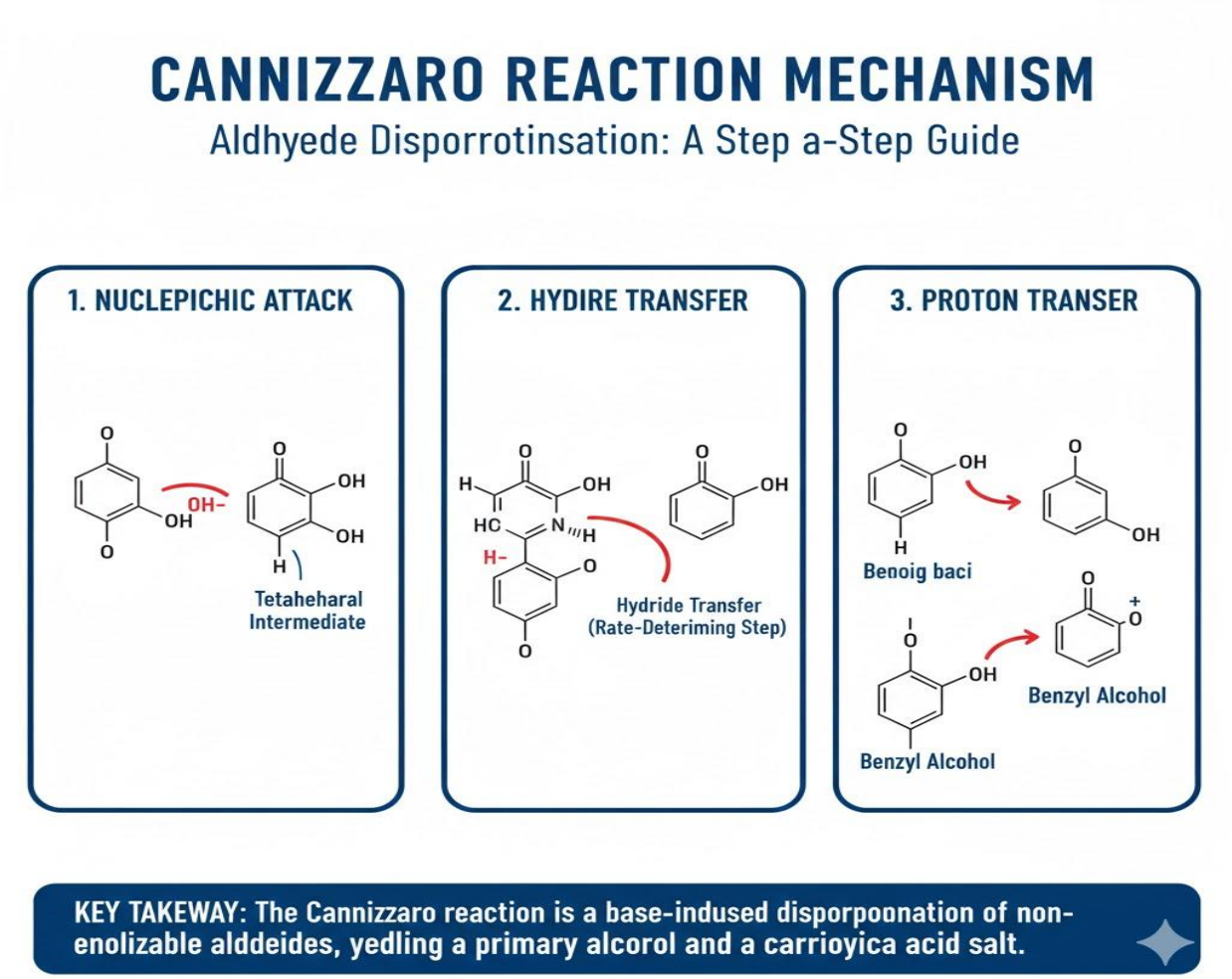


Figure 4.6 Cannizzaro reaction mechanism

4.4.3 Diels–Alder reaction

Diels–Alder reaction is a cycloaddition reaction between a conjugated diene and a dienophile (an alkene or alkyne), producing a six-membered ring. It is a concerted reaction, meaning all bond-making and bond-breaking occur simultaneously.

This reaction is highly valuable in synthetic chemistry because it allows the construction of cyclic compounds with high stereospecificity. It is widely used in the synthesis of natural products and complex organic molecules.

Fill in the blank: The Diels–Alder reaction involves a conjugated diene reacting with a _____ to form a six-membered ring.

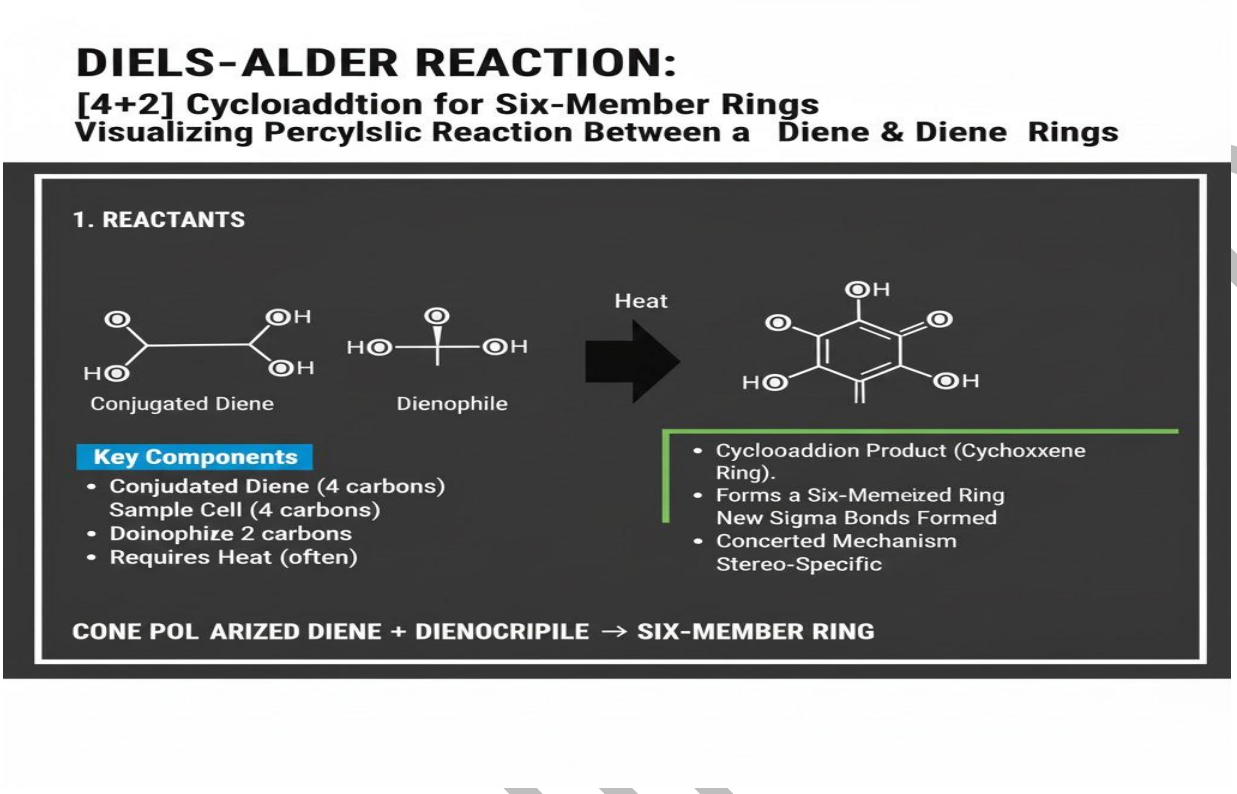


Figure 4.7 Diels–Alder reaction mechanism

4.4.4 Friedel–Crafts reaction

Friedel–Crafts reaction refers to two types of reactions: **alkylation** and **acylation** of aromatic compounds. Both reactions involve the introduction of substituents onto an aromatic ring using a Lewis acid catalyst such as aluminium chloride ($AlCl_3$).

Friedel–Crafts alkylation introduces an alkyl group onto the aromatic ring.
Friedel–Crafts acylation introduces an acyl group, producing aromatic ketones.

These reactions are widely used in the synthesis of aromatic compounds, including dyes, pharmaceuticals, and polymers.

Fill in the blank: Friedel–Crafts reactions require a _____ acid catalyst such as aluminium chloride.

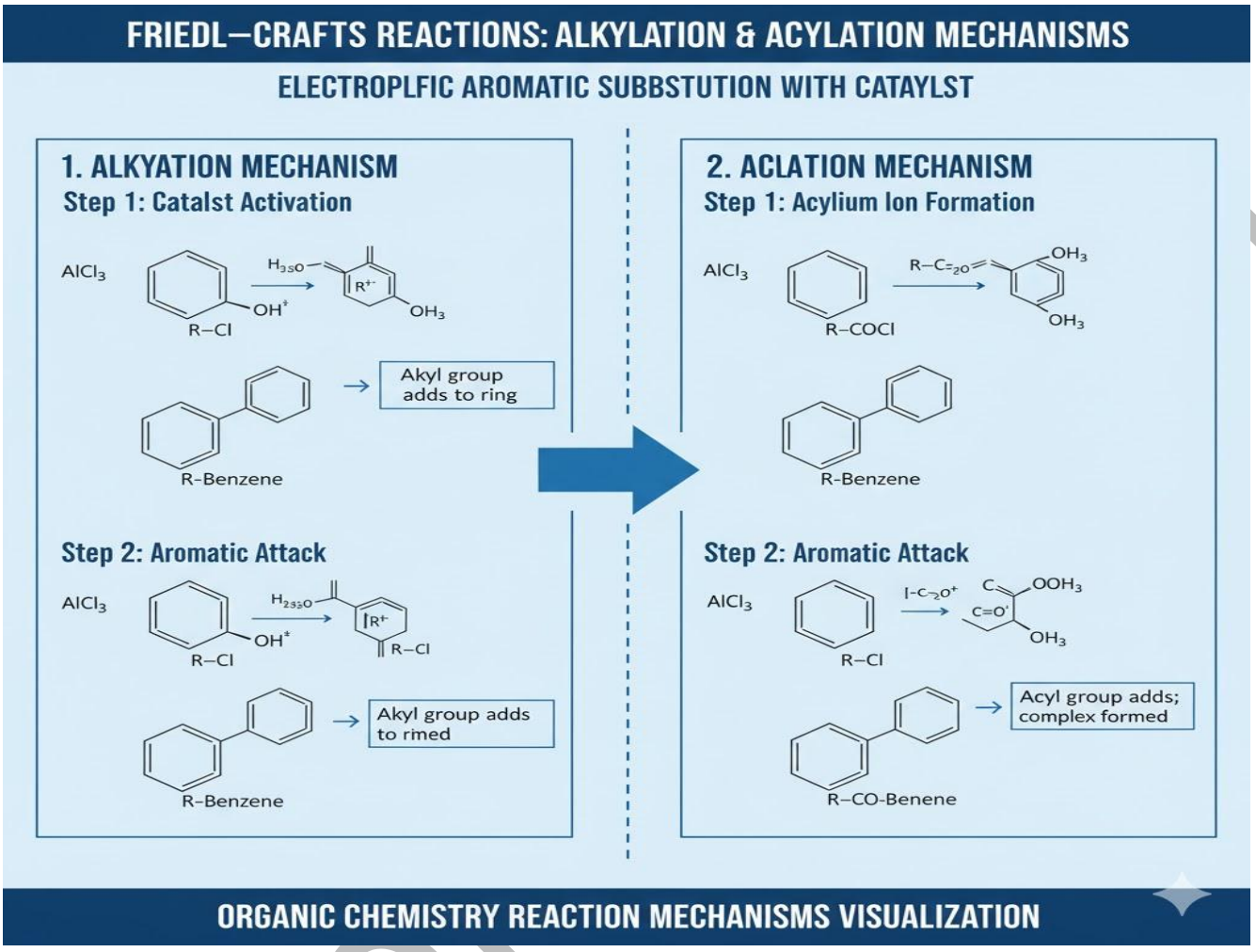


Figure 4.8 Friedel–Crafts alkylation and acylation mechanisms

Pilot questions 4.4

What type of bond is formed during aldol condensation?
What happens to aldehydes in the Cannizzaro reaction?
Which two reactants are required for the Diels–Alder reaction?
Name the catalyst used in Friedel–Crafts reactions.
State one industrial application of the Friedel–Crafts reaction.

Series Summary

This Series has focused on the principles of stereochemistry and key named reactions, highlighting their importance in understanding how molecular structure influences reactivity and biological activity. Starting off, we examined the fundamentals of stereochemistry, including its scope and the distinction between structural and stereoisomerism. We then explored chirality and stereoisomers, looking closely at asymmetric carbon atoms, enantiomers, diastereomers, and optical activity. Following that, we studied conformational analysis and stereochemical effects, considering how steric hindrance, torsional strain, and stereoelectronic factors shape molecular behaviour. Finally, we rounded off with selected named organic reactions such as aldol condensation, Cannizzaro reaction, Diels–Alder reaction, and Friedel–Crafts reaction, which demonstrate practical applications of stereochemical concepts in synthesis.

By completing this Series, you should now be able to define stereochemistry, distinguish between types of isomerism, describe chirality and optical activity, analyse conformations and stereochemical effects, and explain the mechanisms and applications of key named reactions. These abilities directly align with the Series Learning Outcomes (SLOs), equipping you with the knowledge and skills to confidently apply stereochemical principles and named reactions in both theoretical and practical contexts.

Concept Check Questions [Series 4]

Objective questions

Define stereochemistry. (Linked to SLO 4.1)
Identify the difference between structural isomerism and stereoisomerism. (Linked to SLO 4.2)
State what makes a carbon atom asymmetric. (Linked to SLO 4.3)
Name the stereoisomers that are non-superimposable mirror images. (Linked to SLO 4.4)
Specify the instrument used to measure optical activity. (Linked to SLO 4.5)
Identify the most stable conformation of cyclohexane. (Linked to SLO 4.6)
State the catalyst required for Friedel–Crafts reactions. (Linked to SLO 4.12)

Short-answer questions

8. Explain why chirality is important in drug design. (Linked to SLO 4.3)
9. Describe one difference between enantiomers and diastereomers. (Linked to SLO 4.4)
10. Give one example of torsional strain in alkanes. (Linked to SLO 4.7)
11. Explain the requirement for anti-periplanar geometry in elimination reactions. (Linked to SLO 4.8)
12. State one industrial application of the Friedel–Crafts reaction. (Linked to SLO 4.12)

Long-answer questions

13. Analyse the importance of conformational analysis in understanding molecular stability. (Linked to SLO 4.6, 4.7)
14. Evaluate the role of stereoelectronic effects in determining reaction pathways. (Linked to SLO 4.8)
15. Describe the mechanism and applications of aldol condensation. (Linked to SLO 4.9)
16. Explain the Cannizzaro reaction and its significance in organic chemistry. (Linked to SLO

4.10)
17. Demonstrate the steps of the Diels–Alder reaction and discuss its synthetic importance. (Linked to SLO 4.11)

Answers to Concept Check Questions [Series 4]

Objective questions

The study of the three-dimensional arrangement of atoms in molecules.
Structural isomerism differs in connectivity, stereoisomerism differs in spatial arrangement.
Bonding to four different substituents.
Enantiomers.
Polarimeter.
Chair conformation.
Lewis acid catalyst such as aluminium chloride ($AlCl_3$).

Short-answer questions

8. Chirality ensures that only one enantiomer may interact correctly with biological receptors.
9. Enantiomers are mirror images, diastereomers are not.
10. Eclipsed conformation of ethane.
11. Anti-periplanar geometry allows proper orbital overlap for elimination.
12. Used in the synthesis of dyes, pharmaceuticals, and polymers.

Long-answer questions

13. **Basic response:** Conformational analysis studies rotations around bonds and explains why certain conformations are more stable.
Value-added response: It helps predict reactivity, explains strain in molecules, and guides drug and polymer design.

Basic response: Stereoelectronic effects arise from orbital alignment influencing reaction pathways.
Value-added response: They explain selectivity in SN1/SN2 reactions, elimination geometry, and stabilisation in transition states.

Basic response: Aldol condensation involves enolate attacking a carbonyl to form β-hydroxy carbonyl compounds.
Value-added response: It is widely used in pharmaceuticals, fragrances, and polymer synthesis to build complex molecules.

Basic response: Cannizzaro reaction is a redox disproportionation of non-enolisable aldehydes.
Value-added response: It demonstrates aldehyde chemistry and is useful for producing alcohols and carboxylates industrially.

Basic response: Diels–Alder reaction is a cycloaddition between a conjugated diene and a dienophile forming a six-membered ring.

Value-added response: It is stereospecific, widely applied in natural product synthesis, and crucial for constructing cyclic frameworks.

Answers to Pilot Questions [Series 4]

Part 1 Fundamentals of stereochemistry

Stereochemistry.
Structural isomerism differs in connectivity, stereoisomerism differs in spatial arrangement.
Cis/trans isomerism.
Because only one stereoisomer may interact correctly with biological receptors.
Fragrance design and polymer chemistry.

Part 2 Chirality and stereoisomers

The property of a molecule being non-superimposable on its mirror image.
A carbon atom bonded to four different substituents.
Enantiomers are mirror images, diastereomers are not.
Optical activity.
Polarimeter.

Part 3 Conformational analysis and stereochemical effects

The study of different spatial arrangements of atoms due to rotation around single bonds.
Chair conformation.
Repulsion caused by atoms being too close together.
Increased electron repulsion when bonds are eclipsed.
Anti-periplanar geometry in elimination reactions.

Part 4 Selected named organic reactions

Carbon–carbon bonds.
One aldehyde is reduced to an alcohol while another is oxidised to a carboxylate ion.
A conjugated diene and a dienophile.

Lewis acid catalyst such as aluminium chloride ($AlCl_3$).
Synthesis of dyes, pharmaceuticals, and polymers.

Series 5: Alicyclic Carbon Compounds and Their Synthesis

Part 1 Introduction to alicyclic compounds

5.1.1 Definition and scope of alicyclic compounds
5.1.2 Distinction between aliphatic, aromatic, and alicyclic compounds
5.1.3 Importance of alicyclic compounds in organic chemistry

Part 2 Structure and properties of cycloalkanes

5.2.1 General formula and nomenclature of cycloalkanes
5.2.2 Conformations of cyclopropane, cyclobutane, and cyclohexane
5.2.3 Physical and chemical properties of cycloalkanes

Part 3 Reactions of alicyclic compounds

5.3.1 Substitution reactions in cycloalkanes
5.3.2 Addition reactions in cycloalkenes
5.3.3 Ring strain and its influence on reactivity

Part 4 Synthesis of alicyclic compounds

5.4.1 Laboratory methods of cycloalkane synthesis
5.4.2 Industrial synthesis and applications
5.4.3 Role of alicyclic compounds in pharmaceuticals and materials

Introduction

In the last Series, we explored stereochemistry and named organic reactions, focusing on how the three-dimensional arrangement of atoms influences reactivity and biological activity. Building on that foundation, we now turn our attention to **alicyclic compounds**, which occupy a unique position between aliphatic and aromatic systems. These compounds are not only structurally intriguing but also play a vital role in pharmaceuticals, materials science, and industrial

chemistry. Understanding their behaviour and methods of synthesis will deepen your grasp of organic chemistry and prepare you for more advanced applications.

The aim of this Series is to introduce you to the structure, properties, reactions, and synthesis of alicyclic compounds, equipping you with the knowledge and skills to analyse their behaviour and apply them in practical contexts.

We shall commence this Series by defining alicyclic compounds and distinguishing them from aliphatic and aromatic systems. Next, we will examine the structure and properties of cycloalkanes, including their conformations and reactivity. Following that, we will explore the reactions of alicyclic compounds, paying particular attention to substitution and addition processes as well as the role of ring strain. Finally, we will wrap up by studying methods of synthesis, both in the laboratory and industry, and consider their applications in pharmaceuticals and materials.

Series Learning Outcomes

Upon completing this Series, you should be able to:

- define alicyclic compounds and explain how they differ from aliphatic and aromatic compounds,
- describe the general formula and nomenclature of cycloalkanes,
- analyse the conformations of cyclopropane, cyclobutane, and cyclohexane,
- explain the physical and chemical properties of cycloalkanes,
- demonstrate how substitution reactions occur in cycloalkanes,
- illustrate addition reactions in cycloalkenes,
- evaluate the influence of ring strain on the reactivity of alicyclic compounds,
- describe laboratory methods for synthesising cycloalkanes,
- explain industrial synthesis routes and applications of alicyclic compounds, and
- apply knowledge of alicyclic compounds to examples in pharmaceuticals and materials science.

5.1 Introduction To Alicyclic Compounds

5.1.1 Definition and scope of alicyclic compounds

Alicyclic compounds are organic compounds that contain one or more carbon rings but are not aromatic. They combine features of both aliphatic and cyclic structures. Unlike aromatic compounds, alicyclic compounds do not have delocalised π-electrons across the ring. Instead, they behave more like alkanes, alkenes, or alkynes, depending on the type of bonds present in the ring.

These compounds are important because they form the backbone of many natural products, pharmaceuticals, and industrial chemicals. Their cyclic nature gives them unique properties compared to straight-chain compounds.

Fill in the blank: Organic compounds that contain carbon rings but are not aromatic are called _____.

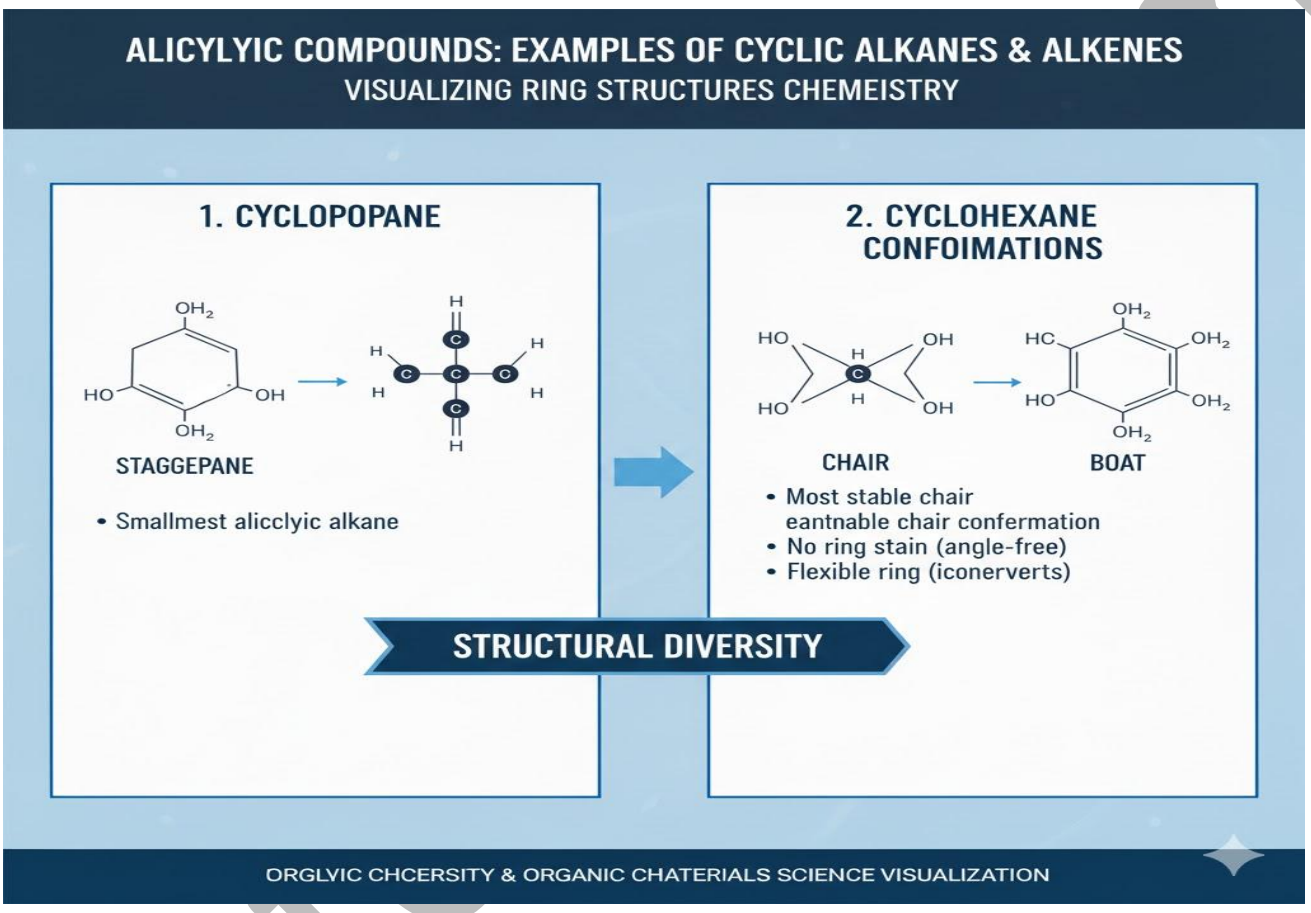


Figure 5.1 Examples of alicyclic compounds

5.1.2 Distinction between aliphatic, aromatic, and alicyclic compounds

Aliphatic compounds are open-chain hydrocarbons that may be saturated (alkanes) or unsaturated (alkenes, alkynes).
Aromatic compounds are cyclic hydrocarbons with delocalised π-electrons that follow Huckel's rule, such as benzene.
Alicyclic compounds are cyclic hydrocarbons that resemble aliphatic compounds in their bonding but lack aromaticity.

This distinction is crucial because it helps chemists predict reactivity and stability. For instance, aromatic compounds are unusually stable due to resonance, while alicyclic compounds may show strain depending on ring size.

Fill in the blank: Benzene is classified as an _____ compound because of its delocalised π-electrons.

Table 5.1 Comparison of aliphatic, aromatic, and alicyclic compounds

Feature	Aliphatic compounds	Aromatic compounds	Alicyclic compounds
Definition	Organic compounds with open-chain structures, which may be saturated or unsaturated	Cyclic compounds with delocalised π-electrons that follow Huckel's rule	Cyclic compounds that resemble aliphatic compounds but lack aromaticity
Bonding	Can contain single, double, or triple bonds	Conjugated π-system with resonance stabilisation	Single or multiple bonds, but no delocalised π-system
Examples	Ethane (C_2H_6), Propene (C_3H_6), Butyne (C_4H_6)	Benzene (C_6H_6), Naphthalene ($C_{10}H_8$), Toluene (C_7H_8)	Cyclopropane (C_3H_6), Cyclobutane (C_4H_8), Cyclohexane (C_6H_{12})
Key property	Reactivity depends on type of bond (alkane, alkene, alkyne)	High stability due to resonance, undergoes substitution rather than addition	Stability depends on ring size; smaller rings are strained and more reactive

5.1.3 Importance of alicyclic compounds in organic chemistry

Alicyclic compounds are widely studied because they occur naturally and have significant applications. Many natural products such as steroids, terpenes, and alkaloids contain alicyclic rings. In pharmaceuticals, cyclic structures often enhance biological activity and specificity. In industrial chemistry, alicyclic compounds are used in polymers, fuels, and agrochemicals.

Their importance lies in the balance between ring stability and reactivity. Smaller rings like cyclopropane are strained and highly reactive, while larger rings like cyclohexane adopt stable conformations.

Fill in the blank: Steroids and terpenes are examples of natural products that contain _____ rings.

Pilot questions 5.1

Define alicyclic compounds.
Distinguish between aliphatic, aromatic, and alicyclic compounds.
Give one example of an alicyclic compound.
Why are alicyclic compounds important in organic chemistry?
Name one natural product that contains alicyclic rings.

5.2 Structure And Properties Of Cycloalkanes

5.2.1 General formula and nomenclature of cycloalkanes

Cycloalkanes are saturated hydrocarbons in which carbon atoms are arranged in a ring structure. Their general formula is $\mathbf{C_nH_{2n}}$, which differs from the formula of alkanes (C_nH_{2n+2}) because the ring closes off two hydrogen atoms.

The nomenclature of cycloalkanes follows IUPAC rules. The prefix **"cyclo-"** is added before the name of the corresponding alkane. For example, cyclopropane (C_3H_6), cyclobutane (C_4H_8), and cyclohexane (C_6H_{12}). Substituents on the ring are named and numbered to give the lowest possible locants.

Fill in the blank: The general formula of cycloalkanes is _____.

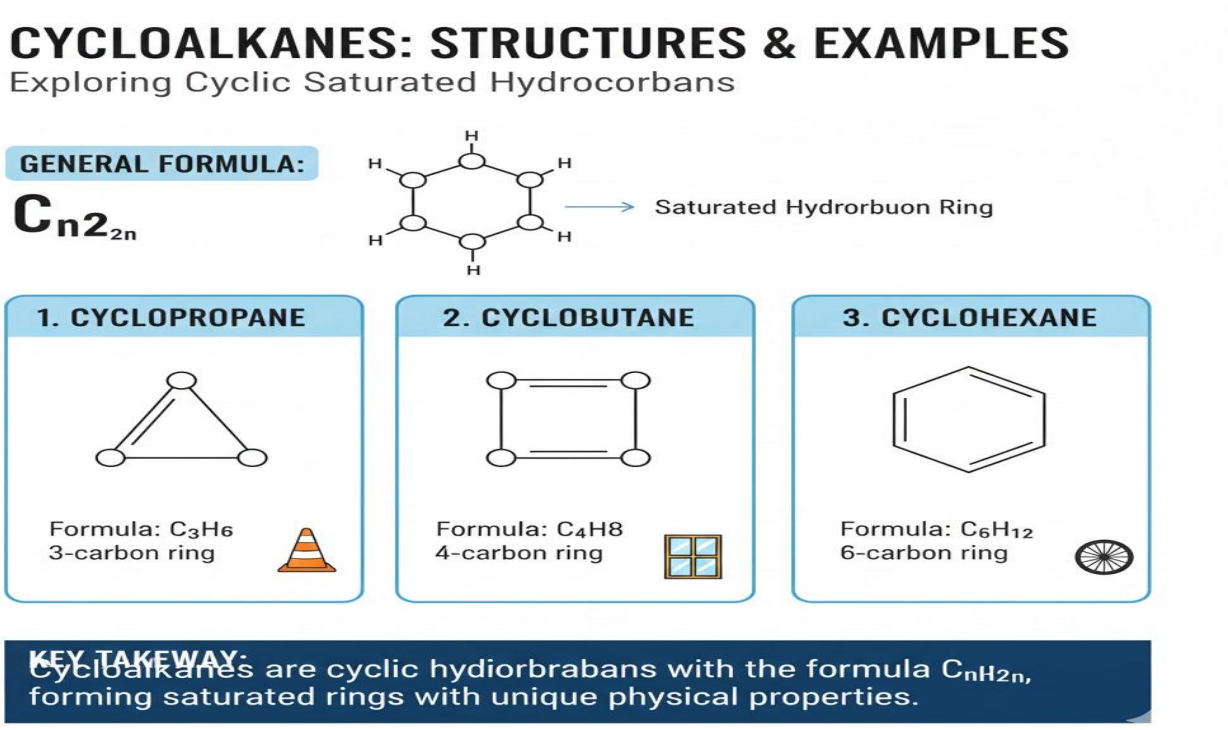


Figure 5.2 General formula and examples of cycloalkanes

5.2.2 Conformations of cyclopropane, cyclobutane, and cyclohexane

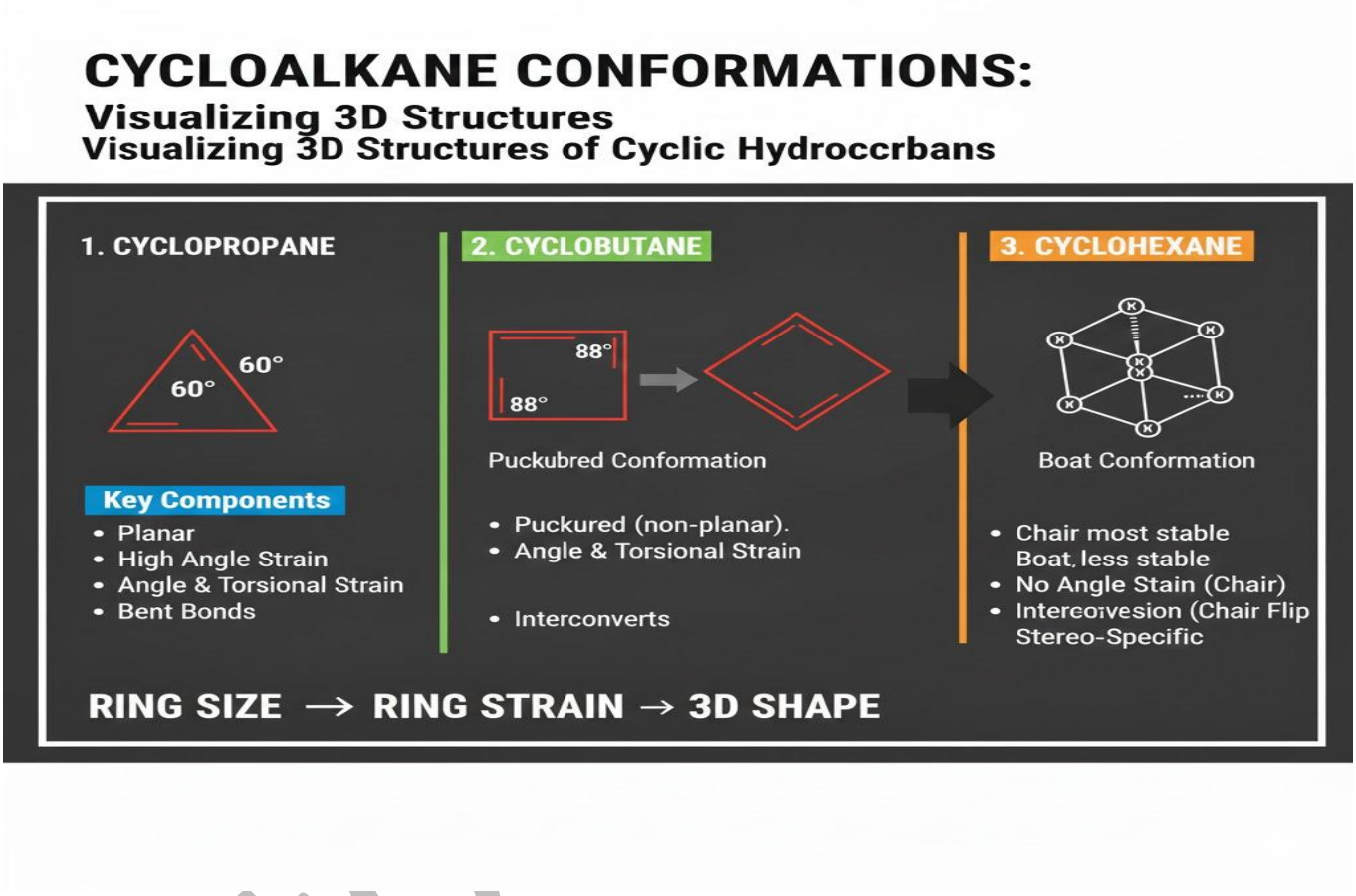
Cycloalkanes adopt different **conformations** to minimise strain.

Cyclopropane has significant **angle strain** because its bond angles are 60°, far from the ideal tetrahedral angle of 109.5°. This makes it highly reactive.

Cyclobutane has bond angles of about 90°, which also causes strain. To reduce torsional strain, cyclobutane adopts a slightly folded conformation.

Cyclohexane is the most stable cycloalkane. It adopts the **chair conformation**, which minimises both angle strain and torsional strain. The **boat conformation** is less stable due to steric hindrance.

Fill in the blank: The most stable conformation of cyclohexane is the _____ form.



Caption: Figure 5.3 Conformations of cyclopropane, cyclobutane, and cyclohexane

5.2.3 Physical and chemical properties of cycloalkanes

Cycloalkanes share many properties with alkanes but also show unique behaviour due to ring strain.

Physical properties: Cycloalkanes are generally non-polar, insoluble in water, and soluble in organic solvents. Their boiling points increase with molecular weight.

Chemical properties: Smaller rings such as cyclopropane and cyclobutane are more reactive due to strain, undergoing ring-opening reactions. Larger rings like cyclohexane are relatively stable and behave like alkanes in substitution and combustion reactions.

Fill in the blank: Smaller cycloalkanes such as cyclopropane are more reactive because of _____.

Table 5.2 Physical and chemical properties of cycloalkanes

Property type	Description	Examples and notes
Physical state	Most lower cycloalkanes are gases or liquids at room temperature	Cyclopropane (gas), Cyclohexane (liquid)
Polarity	Non-polar molecules, insoluble in water but soluble in organic solvents	Cyclohexane dissolves in benzene but not in water
Boiling point	Increases with molecular weight and ring size	Cyclopropane (–33 °C), Cyclohexane (81 °C)
Density	Slightly less dense than water	Cyclohexane density ≈ 0.78 g/cm³
Combustion	Burn with a clean flame, producing CO_2 and H_2O	Cyclohexane combustion yields carbon dioxide and water
Reactivity	Smaller rings are more reactive due to ring strain; larger rings are stable	Cyclopropane undergoes ring-opening; Cyclohexane is relatively inert
Substitution	Undergo halogen substitution reactions under UV light	Cyclohexane reacts with chlorine to form chlorocyclohexane
Addition	Cycloalkenes undergo addition reactions at the double bond	Cyclohexene hydrogenates to cyclohexane

Pilot questions 5.2

State the general formula of cycloalkanes.
Give the IUPAC name of C_6H_{12} in ring form.
Which cycloalkane has the greatest angle strain?
Name the most stable conformation of cyclohexane.
Why are smaller cycloalkanes more reactive than larger ones?

5.3 Reactions Of Alicyclic Compounds

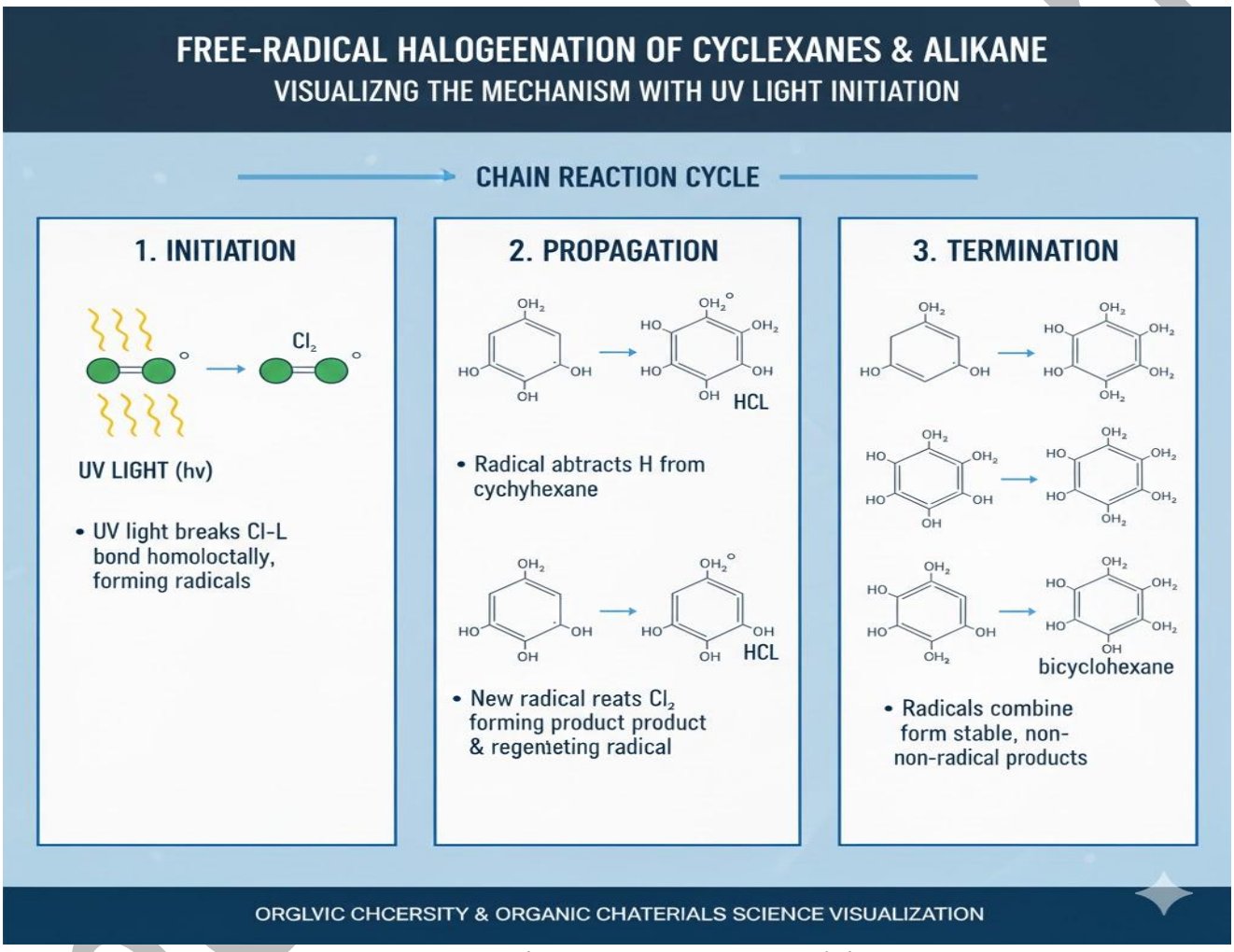
5.3.1 Substitution reactions in cycloalkanes

Substitution reactions are chemical processes in which one atom or group in a molecule is replaced by another. In cycloalkanes, substitution reactions often occur at the carbon–hydrogen

bonds, similar to alkanes. For example, halogenation of cyclohexane involves replacing a hydrogen atom with a halogen atom under the influence of light or heat.

These reactions are generally slower in cycloalkanes compared to open-chain alkanes because the ring structure restricts free rotation and accessibility of hydrogen atoms.

Fill in the blank: The replacement of a hydrogen atom in cyclohexane with a halogen atom is an example of _____.



Caption: Figure 5.4 Substitution reaction in cyclohexane

5.3.2 Addition reactions in cycloalkenes

Addition reactions occur when atoms or groups are added to a molecule without removing any existing atoms. Cycloalkenes, which contain double bonds within the ring, undergo addition reactions similar to alkenes. For instance, cyclohexene reacts with hydrogen in the presence of a catalyst to form cyclohexane.

Addition reactions are important because they reduce unsaturation and can convert reactive cycloalkenes into more stable cycloalkanes.

Fill in the blank: The reaction of cyclohexene with hydrogen to form cyclohexane is an example of _____.

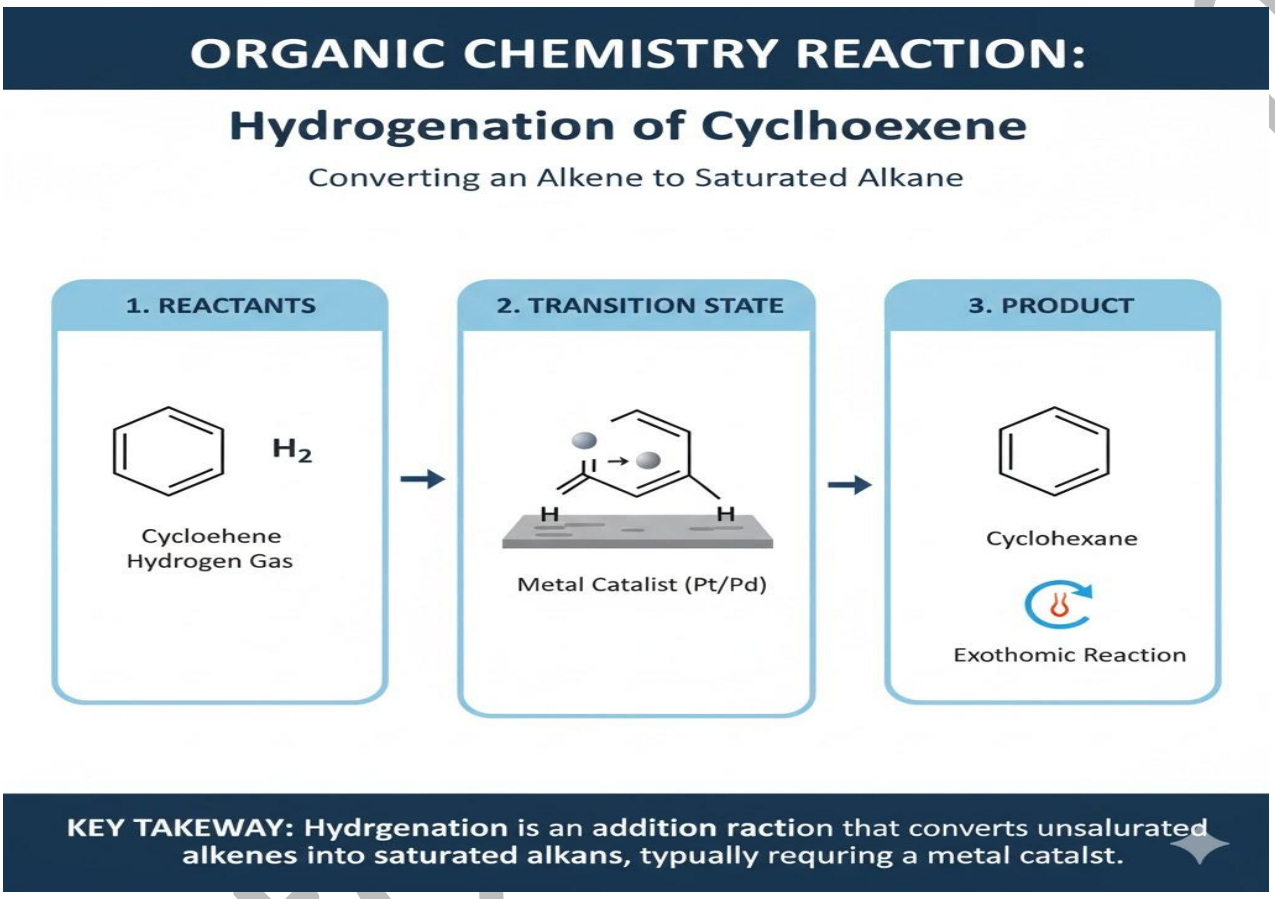


Figure 5.5 Addition reaction in cyclohexene

5.3.3 Ring strain and its influence on reactivity

Ring strain refers to the instability in cyclic compounds caused by deviation from ideal bond angles or torsional strain due to eclipsing interactions. Smaller rings such as cyclopropane and cyclobutane have high ring strain, making them more reactive. Larger rings like cyclohexane adopt stable conformations that minimise strain.

Ring strain explains why cyclopropane readily undergoes ring-opening reactions, while cyclohexane remains relatively inert under similar conditions.

Fill in the blank: Cyclopropane is highly reactive because of _____.

Pilot questions 5.3

What type of reaction replaces a hydrogen atom in cycloalkanes with another atom?
Give one example of an addition reaction in cycloalkenes.

Why are substitution reactions slower in cycloalkanes compared to alkanes?
Explain why cyclopropane is more reactive than cyclohexane.
State one industrial application of addition reactions in cycloalkenes.

5.4 Synthesis Of Alicyclic Compounds

5.4.1 Laboratory methods of cycloalkane synthesis

Cycloalkane synthesis in the laboratory involves preparing ring structures from simpler organic molecules. One common method is the **Wurtz reaction**, where dihalides undergo coupling in the presence of sodium metal to form cycloalkanes. Another method is **Dieckmann condensation**, which involves intramolecular ester condensation to produce cyclic β-keto esters that can be reduced to cycloalkanes.

These laboratory methods are valuable because they allow chemists to construct rings of varying sizes under controlled conditions. Smaller rings are often more difficult to synthesise due to ring strain, while medium-sized rings are more accessible.

Fill in the blank: The intramolecular ester condensation used to form cyclic β-keto esters is called _____.

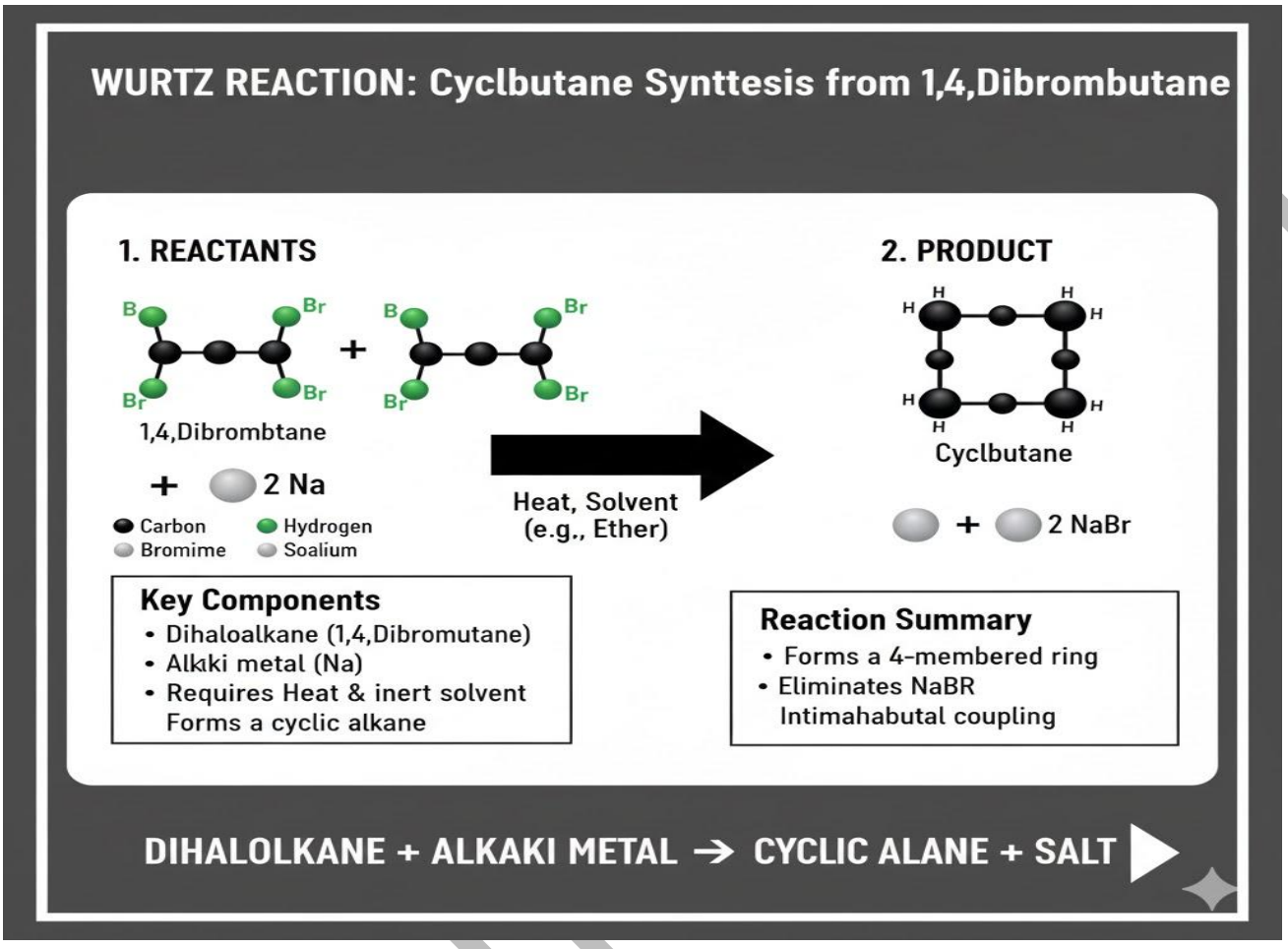


Figure 5.6 Laboratory synthesis of cyclobutane using the Wurtz reaction

5.4.2 Industrial synthesis and applications

In industry, alicyclic compounds are synthesised on a larger scale using catalytic processes. **Hydrogenation of aromatic compounds** is a key method, where benzene is hydrogenated to form cyclohexane. Cyclohexane is a major industrial chemical used in the production of nylon intermediates such as adipic acid and caprolactam.

Industrial synthesis focuses on efficiency, cost-effectiveness, and scalability. Catalysts such as nickel, platinum, or palladium are commonly employed to speed up reactions and improve yields.

Fill in the blank: Cyclohexane is produced industrially by hydrogenating _____.

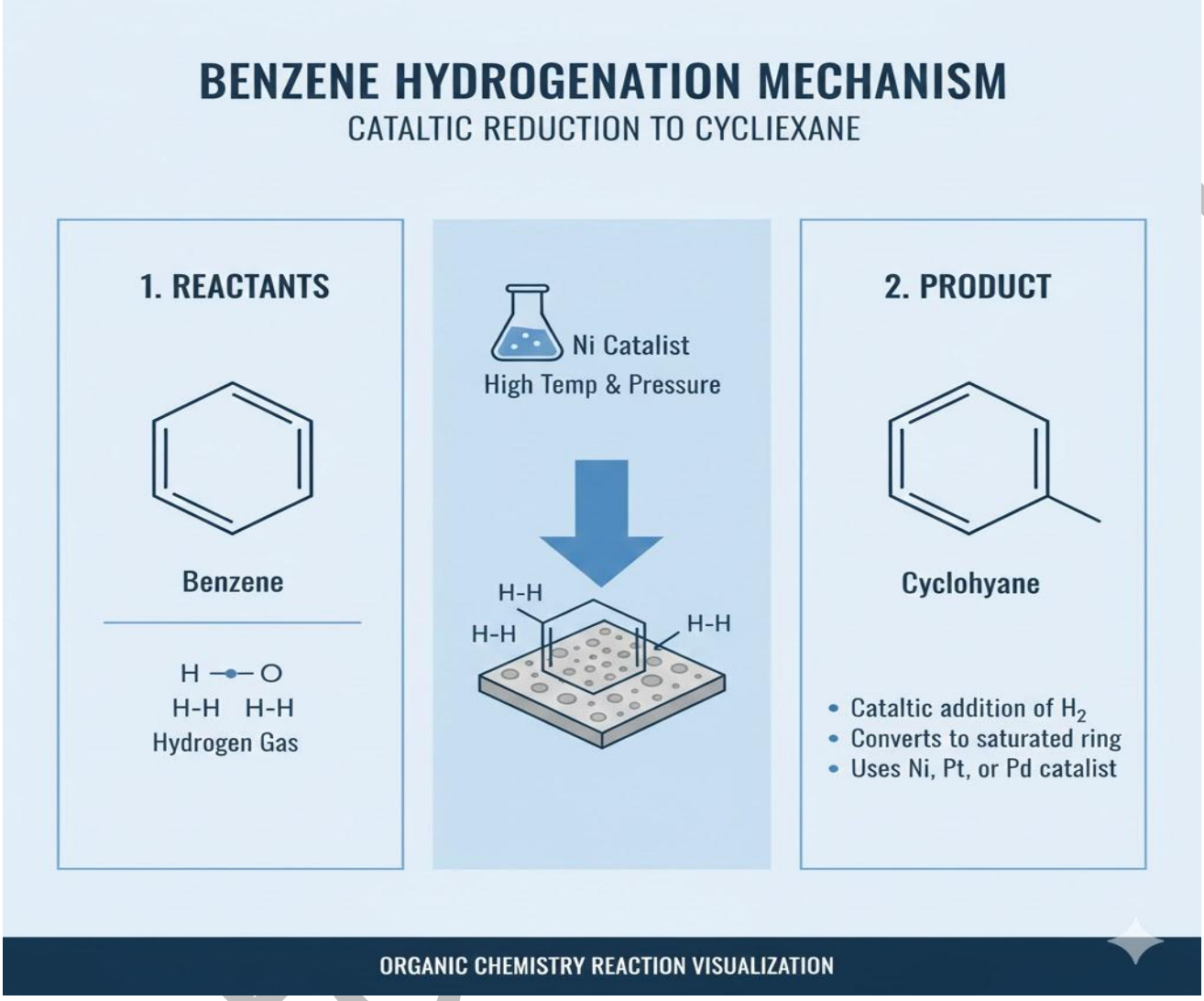


Figure 5.7 Industrial synthesis of cyclohexane

5.4.3 Role of alicyclic compounds in pharmaceuticals and materials

Alicyclic compounds play a crucial role in **pharmaceutical chemistry** and **materials science**. In pharmaceuticals, cyclic structures often enhance drug stability and specificity. For example, many steroid hormones are based on fused alicyclic rings. In materials science, cycloalkanes are used in the production of polymers, resins, and fuels.

The presence of cyclic structures often improves mechanical strength, chemical resistance, and biological activity. This makes alicyclic compounds indispensable in both natural and synthetic applications.

Fill in the blank: Steroid hormones are based on fused _____ rings.

Pilot questions 5.4

Name one laboratory method used to synthesise cycloalkanes.
What industrial process is used to produce cyclohexane?
Why are smaller rings more difficult to synthesise in the laboratory?
State one industrial application of cyclohexane.
Give one example of a pharmaceutical compound based on alicyclic rings.

Series Summary

This Series has introduced you to the fascinating world of alicyclic compounds, highlighting their structural features, properties, reactions, and methods of synthesis. Starting off, we defined alicyclic compounds and distinguished them from aliphatic and aromatic systems. We then examined the structure and properties of cycloalkanes, focusing on their general formula, nomenclature, and conformations such as the chair and boat forms of cyclohexane. Following that, we explored the reactions of alicyclic compounds, including substitution and addition processes, while emphasising the role of ring strain in determining reactivity. Finally, we rounded off with laboratory and industrial methods of synthesis, considering their applications in pharmaceuticals and materials science.

By completing this Series, you should now be able to define and describe alicyclic compounds, analyse their conformations and properties, explain their reactions, and apply knowledge of their synthesis in both laboratory and industrial contexts. These abilities directly align with the Series Learning Outcomes (SLOs), equipping you with the confidence to evaluate the behaviour of alicyclic compounds and appreciate their importance in organic chemistry and applied sciences.

Concept Check Questions [Series 5]

Objective questions

State the general formula of cycloalkanes. (Linked to SLO 5.2)
Identify the most stable conformation of cyclohexane. (Linked to SLO 5.3)
Define alicyclic compounds. (Linked to SLO 5.1)
Name the industrial process used to produce cyclohexane. (Linked to SLO 5.9)
Specify one natural product that contains fused alicyclic rings. (Linked to SLO 5.10)

Short-answer questions

6. Explain how alicyclic compounds differ from aromatic compounds. (Linked to SLO 5.1)
7. Describe one physical property of cycloalkanes. (Linked to SLO 5.4)
8. Give one example of a substitution reaction in cycloalkanes. (Linked to SLO 5.5)
9. Illustrate how hydrogenation converts cyclohexene into cyclohexane. (Linked to SLO 5.6)
10. Explain why smaller cycloalkanes are more reactive than larger ones. (Linked to SLO 5.7)

Long-answer questions
11. Analyse the conformations of cyclopropane, cyclobutane, and cyclohexane, highlighting their relative stability. (Linked to SLO 5.3)
12. Evaluate the influence of ring strain on the reactivity of alicyclic compounds. (Linked to SLO 5.7)
13. Describe one laboratory method for synthesising cycloalkanes and explain its significance. (Linked to SLO 5.8)
14. Discuss the industrial synthesis of cyclohexane and its applications. (Linked to SLO 5.9)
15. Demonstrate the role of alicyclic compounds in pharmaceuticals and materials science. (Linked to SLO 5.10)

Answers to Concept Check Questions [Series 5]

Objective questions

C_nH_{2n}
Chair conformation
Cyclic hydrocarbons that are non-aromatic but resemble aliphatic compounds in bonding.
Hydrogenation of benzene.
Steroids.

Short-answer questions
6. Aromatic compounds have delocalised π-electrons and follow Huckel's rule, while alicyclic compounds do not.
7. Cycloalkanes are non-polar, insoluble in water, and soluble in organic solvents.
8. Halogenation of cyclohexane under UV light.
9. Hydrogen adds across the double bond of cyclohexene to form cyclohexane.
10. Smaller rings have high angle strain, making them more reactive.

Long-answer questions
11. **Basic response:** Cyclopropane has high angle strain, cyclobutane has moderate strain, and cyclohexane is stable in chair form.
Value-added response: These conformations illustrate how bond angles and torsional strain affect reactivity, with cyclopropane prone to ring-opening and cyclohexane widely used as a stable industrial chemical.

Basic response: Ring strain increases reactivity by destabilising the molecule.
Value-added response: Ring strain explains why smaller rings undergo ring-opening reactions and why larger rings are stable, guiding synthetic strategies in organic chemistry.

Basic response: The Wurtz reaction couples dihalides to form cycloalkanes.
Value-added response: Laboratory methods like the Wurtz reaction and Dieckmann condensation are significant for constructing rings of varying sizes, especially in research and drug development.

Basic response: Cyclohexane is synthesised industrially by hydrogenating benzene.
Value-added response: This process is vital for producing nylon intermediates such as adipic acid and caprolactam, making cyclohexane a cornerstone of polymer and textile industries.

Basic response: Alicyclic compounds form the structural basis of steroids and other drugs.
Value-added response: Beyond pharmaceuticals, they enhance material properties such as strength and resistance in polymers, demonstrating their broad impact across science and industry.

Answers to Pilot Questions [Series 5]

Part 1 Introduction to alicyclic compounds

Alicyclic compounds are cyclic hydrocarbons that are non-aromatic but resemble aliphatic compounds in bonding.
Aliphatic compounds are open-chain hydrocarbons, aromatic compounds have delocalised π-electrons, and alicyclic compounds are cyclic but non-aromatic.
Cyclohexane.
They are important because they occur naturally in products such as steroids and terpenes and have wide applications in pharmaceuticals and industry.
Steroids.

Part 2 Structure and properties of cycloalkanes

C_nH_{2n}.
Cyclohexane.
Cyclopropane.
Chair conformation.
Because of high angle strain.

Part 3 Reactions of alicyclic compounds

Substitution reaction.
Hydrogenation of cyclohexene to cyclohexane.
Restricted rotation and reduced accessibility of hydrogen atoms.
Due to high ring strain.
Production of cycloalkanes used in fuels and polymers.

Part 4 Synthesis of alicyclic compounds

Wurtz reaction or Dieckmann condensation.
Hydrogenation of benzene.
Smaller rings have high ring strain, making them difficult to form.
Used in the production of nylon intermediates such as adipic acid and caprolactam.
Steroid hormones.