M.Sc. [Chemistry]
II - Semester
344 22

ORGANIC CHEMISTRY - II
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**INTRODUCTION**

Organic chemistry is the study of the structure, properties, composition, reactions, and preparation of carbon-containing compounds, which include not only hydrocarbons but also compounds with any number of other elements, including hydrogen (most compounds contain at least one carbon–hydrogen bond), nitrogen, oxygen, halogens, phosphorus, silicon, and sulfur. This branch of chemistry was originally limited to compounds produced by living organisms but has been broadened to include human-made substances such as plastics. The range of application of organic compounds is enormous and also includes, but is not limited to, pharmaceuticals, petrochemicals, food, explosives, paints, and cosmetics.

The great abundance of organic compounds, their fundamental role in the chemistry of life, and their structural diversity have made their study especially challenging and exciting. Organic chemistry is the largest area of specialization among the various fields of chemistry.

Before the nineteenth century, chemists generally believed that compounds obtained from living organisms were endowed with a vital force that distinguished them from inorganic compounds. According to the concept of vitalism, organic matter was endowed with a ‘vital force’. During the first half of the nineteenth century, some of the first systematic studies of organic compounds were reported. Around 1816 Michel Chevreul started a study of soaps made from various fats and alkalis. The latter half of the 19th century, however, witnessed systematic studies of organic compounds. In the early part of the 20th century, polymers and enzymes were shown to be large organic molecules, and petroleum was shown to be of biological origin.

This book, *Organic Chemistry - II*, is divided into four blocks, which are further subdivided into fourteen units. The first unit introduces the concept of elimination reactions while rules of Elimination reactions have been discussed in the following unit. The third unit deals with the concept of addition reaction. Addition to carbon-carbon multiple bond is focused on in the fourth unit while the fifth unit explains the addition to carbon-hetero multiple bond. Conformational analysis of acyclic and cyclic systems is discussed in the sixth unit while seventh unit deals with topotaxy and NMR distinction of organic compounds. Eighth units discusses carbenes and their reactions. And nitrenes have been explained in the following unit. Free radical reactions have been explained in the tenth unit while eleventh units focuses on fundamentals of photochemistry. Twelfth unit discusses photochemical reaction while thirteenth unit introduces you to pericyclic reactions. The last unit discusses chemotrophic reaction.

The book follows the self-instructional mode wherein each unit begins with an ‘Introduction’ to the topic. The ‘Objectives’ are then outlined before going on to the presentation of the detailed content in a simple and structured format. ‘Check Your Progress’ questions are provided at regular intervals to test the student’s understanding of the subject. ‘Answers to Check Your progress question’, a ‘Summary’, a list of ‘Key Words’ and a set of ‘Self-Assessment Questions and Exercises’ are provided at the end of each unit for effective recapitulation.
BLOCK - I

ELIMINATION AND ADDITION REACTION

UNIT 1  ELIMINATION REACTIONS

Structure
1.0 Introduction
1.1 Objectives
1.2 Elimination reactions
  1.2.1 The E, Mechanism
1.3 Answers to Check Your Progress Questions
1.4 Summary
1.5 Key Words
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1.0 INTRODUCTION

Elimination reaction is a type of organic chemical reactions in which a pair of atoms or groups of atoms are eliminated from a molecule, usually through the action of acids, bases, or metals and, in some cases, by heating to a high temperature. Organic compounds containing only single carbon-carbon bonds (saturated compounds) are transformed to compounds containing double or triple carbon-carbon bonds (unsaturated compounds) by the process of elimination reactions.

Elimination reactions are identified by the kind of atoms or groups of atoms eliminating from the molecule. The elimination of a hydrogen atom and a halogen atom, for example, is known as dehydrohalogenation; when both eliminating atoms are halogens, the reaction is known as dehalogenation. Similarly, the elimination of a water molecule, usually from an alcohol, is known as dehydration; when both eliminating atoms are hydrogen atoms, the reaction is known as dehydrogenation. On the basis of reaction kinetics, elimination reactions are classified as E₁ or E₂.

In an E₁ reaction, the reaction rate is proportional to the concentration of the substance to be transformed; in an E₂ reaction, the reaction rate is proportional to the concentrations of both the substrate and the eliminating agent.

In this unit, you will understand the process of elimination reactions. Further, you will understand the mechanism of E₁, E₂ and E₃,cB reactions.
1.1 OBJECTIVES

After going through this unit, you will be able to:
- Discuss the process of elimination reaction
- Explain the mechanism of E₁, E₂ and E₁cB reactions

1.2 ELIMINATION REACTIONS

In elimination reactions two substituents, from a pair of adjacent atoms in a molecule, are removed. As a consequence of the removal of atoms or groups from the adjacent atoms of molecule, unsaturation is introduced. The most common multiple bonds formed as a result of such reaction are

\[ \text{>C=O, >C≡N, >C=N—, >C=C—} \]

Commonly one of the two groups removed from the substrate in elimination reaction is an electrophile, usually a proton. The other group is generally a nucleophile which may be \( X^- \) (halide), \( \text{OH}^-, \text{RCOO}^- \) etc. The adjacent atoms of substrate molecule from which these groups are removed, are designated as \( \alpha^- \) and \( \beta^- \) atoms and the type of elimination is referred to as \( \beta^- \)-elimination. The elimination reactions in which two groups leave from the same atoms are less frequent and result in a highly reactive species having only six electrons in outer shell (cf. carbenes). In elimination reactions energy is released and this acts as the driving force for elimination reactions. For a conversion of \( sp^3 \) hybridized carbon to \( sp^2 \) carbon approx. 41 kcal/mole are released. Similarly conversion of \( sp^2 \) to \( sp^1 \) hybridized carbon results in a release of 23 kcal/mole.

\[
\begin{align*}
\text{CH}_3 & \quad \text{C} \quad \text{OH}^-
\end{align*}
\]

\[
\begin{align*}
\text{>C=O} & \quad + 41 \text{ kcal}
\end{align*}
\]

\[
\begin{align*}
\text{>C=C—} & \quad + 23 \text{ kcal}
\end{align*}
\]

Elimination reactions usually compete with nucleophilic substitution reactions at saturated carbon atoms (\( S_n \) reactions). By analogy to \( S_n \) reactions, in elimination also there are two extreme types of reactions. With nucleophile which are strong bases a concerted reaction involving a transition state results in bimolecular elimination designated as \( E_2 \). Another type involving ionization and formation of a carbocation which then loses a proton to result in elimination is designated as \( E_1 \) or unimolecular elimination. \( E_1 \) reactions follow first order kinetics whereas \( E_2 \) reactions follow second order kinetics. The two mechanisms are:

1. **\( E_1 \) mechanism**

2. **\( E_2 \) mechanism**
E$_2$ mechanism

$$
\text{H}_2\text{O} + \text{C}-\overset{\text{\textbullet}}{\text{\textbullet}}\text{R} \xrightarrow{\text{slow}} \left[ \text{H}_2\text{O} - \text{H} = \overset{\text{\textbullet}}{\text{\textbullet}}\text{R} - \overset{\text{\textbullet}}{\text{\textbullet}}\text{X} \right] \rightarrow \text{H}_2\text{O} + \overset{\text{\textbullet}}{\text{\textbullet}}\text{C} - \overset{\text{\textbullet}}{\text{\textbullet}}\text{X}
$$

Transition state

The E$_2$ reaction theoretically can involve the formation of a carbanion of the type $\overset{\text{\textbullet}}{\text{\textbullet}}\text{R} - \overset{\text{\textbullet}}{\text{\textbullet}}\text{X}$ but evidence has been obtained that such an intermediate is not formed in elimination reaction.

In E$_1$ reactions a carbocation is formed and the factors stabilizing carbocation will favour this type of elimination. In E$_2$ reactions a state has been suggested in which all the five atoms or groups involved must be in the same plane and the groups to be eliminated (H and X) must be trans with respect to each other. Hence it is also known as trans-elimination.

A special type of elimination reaction for explaining the formation of alkenes from alkyl halides through carbanion intermediate is known as E$_1$cB (Elimination 1st order conjugate base).

The reaction takes place around $sp^3$-$sp^3$ covalent bond with an $\alpha$-acidic hydrogen and a $\beta$-leaving group (like halide or tosyl etc.). A strong base abstracts the $\alpha$-proton forming carbanion. The electron pair of carbanion expels the leaving group forming a double bond.

When the carbanion-forming step is fast and deprotonation is reversible, the reaction is called (E$_1$cB), but when the first step is forming carbanion is slow and second step fast then the reaction is irreversible and is called E$_1$(cB)$_r$.

Some examples of elimination reactions are dehydration of alcohols, dehydrohalogenation of alkyl halides and dehydrogenation of alcohols etc.

**Structure and reactivity.** The nature of the substrate, solvent and the catalyst (usually a nucleophile) determine whether the reaction will proceed by E$_1$ or E$_2$ mechanism. It has also been observed that conditions favouring S$_1$1 reactions will lead to E$_1$ reactions as well. Similarly conditions favourable to S$_2$2 reactions also lead to E$_2$ reactions. The ratios of E$_1$ to S$_1$1 and E$_2$ to S$_2$2 reactions have been shown to be fairly constant for a given alkyl group, no matter what the departing group is. Unsymmetrical substrates generally give a mixture of olefins.

1.2.1 The E$_2$ Mechanism

$$
\text{H}_2\text{O} + \overset{\text{\textbullet}}{\text{\textbullet}}\text{CH}_3 \xrightarrow{\text{slow}} \left[ \text{H}_2\text{O} - \text{H} = \overset{\text{\textbullet}}{\text{\textbullet}}\text{CH}_3 - \overset{\text{\textbullet}}{\text{\textbullet}}\text{X} \right] \rightarrow \text{H}_2\text{O} + \overset{\text{\textbullet}}{\text{\textbullet}}\text{CH}_3 + \overset{\text{\textbullet}}{\text{\textbullet}}\text{X}
$$

Self-instructional Material
Elimination Reactions

The most common mechanism for dehydrohalogenation is the E₂ mechanism. It exhibits second-order kinetics, and both the alkyl halide and the base appear in the rate equation.

\[
\text{rate} = k[(\text{CH}_3)_2\text{CHBr}][\text{HO}^-]
\]

The reaction is concerted—all bonds are broken and formed in a single step.

E₂ reactions are regioselective and favor the formation of Zaitsev products.

**Factors Affecting the Rate of an E₂ Reaction**

There are close parallels between E₁ and S₂ mechanisms in how the identity of the base, the leaving group and the solvent affect the rate.

The base appears in the rate equation, so the rate of the E₂ reaction increases as the strength of the base increases.

E₂ reactions are generally run with strong, negatively charged bases like \(\text{OH}^-\) and \(\text{OR}^-\).

Polar aprotic solvents increase the rate of E₂ reactions.

There is a partial breaking of the bond to the leaving group in the transition state. So, the better the leaving group the faster the E₂ reaction.

Rate of reaction follows the order,

\[
\text{R–I} > \text{R–Br} > \text{R–Cl} > \text{R–F}
\]
The S$_2$ and E$_2$ mechanisms differ in how the R group affects the reaction rate.

As the number of R groups on the carbon with the leaving group increases, the rate of the E$_2$ reaction increases.

![Increasing rate of E2 reaction](image)

The increase in E$_2$ reaction rate with increasing alkyl substitution can be rationalized in terms of transition state stability.

In the transition state, the double bond is partially formed. Thus, the transition state for a more substituted alkene is lower in energy, reducing the activation energy for the reaction and making the reaction faster.

**Characteristics of an E$_2$ Reaction**

- **Kinetics**: Second order
- **Mechanism**: Single step
- **Identity of R group**: More substituted halides react faster
  - Rate: R$_2$CX $>$ R$_3$CHX $>$ RCH$_2$X
- **Strength of the base**: Stronger bases favor the reaction
- **Leaving group**: Better leaving group leads to faster reaction rates
- **Type of solvent**: Favored by polar aprotic solvents

E$_2$ reactions are stereoselective, resulting in the formation of trans-double bonds preferably.

![E2 reaction mechanism](image)

The E$_2$ reaction proceeds via a two-step mechanism: the bond to the leaving group breaks first before the π bond is formed. The slow step is unimolecular, involving only the alkyl halide.

It exhibits first-order kinetics,

\[
\text{rate} = k[\text{RCH}_2\text{Cl}]
\]
**Ei reactions also are regioselective and follow Zaitsev rule**

![Energy Profile for an Ei Reaction](image)

**Factors Affecting the Rate of an Ei Reaction**

The rate of an Ei reaction increases as the number of R groups on the carbon with the leaving group increases.

![Increasing rate of Ei reaction](image)

The strength of the base usually determines whether a reaction follows the Ei or E2 mechanism. Strong bases like OH⁻ and OR⁻ favor Ei reactions, whereas weaker bases like H₂O and ROH favor E2 reactions.

**Characteristics of an Ei Reaction**

- Kinetics: First order
- Mechanism: Two steps
Identity of R group – More substituted halides react faster
Rate: R$_3$CX > R$_2$CHX > RCH$_2$X

Strength of the base – Favored by weaker bases such as H$_2$O and ROH

Leaving group – Better leaving group leads to faster reaction rates.
Just as in $S_{N}1$ reactions, the rate determining step involves the C—X bond cleavage

Type of solvent – Favored by polar protic solvents, which can stabilize the ionic intermediates

$S_{N}1$ and $E_{1}$ Reactions

$S_{N}1$ and $E_{1}$ reactions have exactly the same first step—formation of a carbocation. They differ in what happens to the carbocation.

Since in both the reactions, the rate determining steps are the same, they cannot be individually controlled.

Because $E_{1}$ reactions are fast and strong nucleophiles are not competitive, only $S_{N}1$ or $E_{1}$ reactions are observed.

$S_{N}1$, $S_{N}2$, $E_{1}$ or $E_{2}$

3° Alkyl Halides
With strong bases: $E_{1}$ elimination occurs
With weak nucleophiles or bases: A mixture of products from $S_{N}1$ and $E_{1}$ reactions

1° Alkyl Halides
With strong nucleophiles: Substitution occurs by an $S_{N}2$ mechanism
With strong sterically hindered bases: Elimination occurs by an $E_{1}$ mechanism

2° Alkyl Halides
With strong bases and nucleophiles: A mixture of $S_{N}2$ and $E_{2}$ reaction products are formed
With strong sterically hindered bases: Elimination occurs by an $E_{2}$ mechanism
With weak nucleophiles or bases: A mixture of $S_{N}1$ and $E_{1}$ products results
**Elimination Reactions**

**NOTES**

**Stereochemistry of the E₂ Reaction**

The transition state of an E₂ reaction consists of four atoms from the substrate (one hydrogen atom, two carbon atoms, and the leaving group, X) aligned in a plane. There are two ways for the C—H and C—X bonds to be coplanar.

![Stereochemistry Diagram]

E₂ elimination occurs most often in the anti periplanar geometry. This arrangement allows the molecule to react in the lower energy staggered conformation, and allows the incoming base and leaving group to be further away from each other.

The anti periplanar geometry also allows direct interaction between the bonding electrons of C—H bond and the anti-bonding orbital of the C—X bond.

**E₂ Reactions in 6-Membered Rings**

The stereochemical requirement of an anti periplanar geometry in an E₂ reaction has important consequences for compounds containing six-membered rings.

**Chlorocyclohexane**

![Chlorocyclohexane Diagram]

For E₂ elimination, the C—Cl bond must be anti periplanar to the C—H bond on a β carbon, and this occurs only when the H and Cl atoms are both in the axial position. The requirement for trans-diaxial geometry means that elimination must occur from the less stable conformer.

**Dehydrohalogenation of cis-1-Chloro-2-methylycyclohexane**

![Dehydrohalogenation Diagram]

In this conformer two Hs are anti periplanar to the Cl.

In this conformer Cl is in an equatorial position and has no Hs periplanar to it.
The conformer with Cl in an axial orientation reacts to give two alkenes. The alkene that is more substituted is the major product.

Dehydrohalogenation of trans-1-Chloro-2-methylcyclohexane

In this conformer Cl is in an equatorial position and has no H or periplanar to it.

In this conformer one H and one CH₃ are anti periplanar to the Cl.

The conformer with Cl in an axial orientation has just one β-H atom. Only one product is formed, which is not what is predicted by the Zaitsev rule.

In conclusion with substituted cyclohexanes E₂ elimination should conclusion, cyclohexanes, occur with a trans diaxial arrangement of the leaving group and the β-H, and as a result of this requirement, the more substituted alkene is not necessarily the major product.

Stereospecificity in E₂ reactions

Diastereomeric starting compounds yield diastereomeric products after an E₂ reaction.
Elimination Reactions

NOTES

**E₂CB Reaction**

An elimination reaction that happens when a compound bearing a poor leaving group and an acidic hydrogen is treated with a base.

![Reaction Diagram]

**E₂CB stands for Elimination Unimolecular Conjugate Base.** The reaction is unimolecular from the conjugate base of the starting compound, which in turn is formed by deprotonation of the starting compound by a suitable base.

The electron withdrawing group (EWG) can be a carbonyl group (keto, aldehyde, ester), a nitro group, an electron deficient aromatic group etc. Dehydration of aldehydes is the most common E₂CB reaction.

**Check Your Progress**

1. What is dehydrohalogenation?
2. How is reaction rate determined in E₂ reactions?
3. What does E₂CB stand for?
4. Give some examples of elimination reactions.

### 1.3 ANSWERS TO CHECK YOUR PROGRESS QUESTION

1. The elimination of a hydrogen atom and a halogen atom, for example, is known as dehydrohalogenation.
2. In an E₂ reaction, the reaction rate is proportional to the concentration of the substance to be transformed.
3. Elimination Unimolecular Conjugate Base.
4. Some examples of elimination reactions are dehydration of alcohols, dehydrohalogenation of alkyl halides and dehydrogenation of alcohols etc.

1.4 SUMMARY

- In elimination reactions two substituents, from a pair of adjacent atoms in a molecule, are removed. As a consequence of the removal of atoms or groups from the adjacent atoms of molecule, unsaturation is introduced.
- $E_1$ reactions follow first order kinetics whereas $E_2$ reactions follow second order kinetics.
- In $E_1$ reactions a carbocation is formed and the factors stabilizing carbocation will favour this type of elimination. In $E_2$ reactions a state has been suggested in which all the five atoms or groups involved must be in the same plane and the groups to be eliminated (H and X) must be trans with respect to each other. Hence it is also known as trans-elimination.
- A special type of elimination reaction for explaining the formation of alkenes from alkyl halides through carbanion intermediate is known as $E_{\text{ac}}$ (Elimination 1st order conjugate base).
- Some examples of elimination reactions are dehydration of alcohols, dehydrohalogenation of alkyl halides and dehydrogenation of alcohols etc.

1.5 KEY WORDS

- **Elimination reaction**: Elimination reaction is a type of organic chemical reactions in which a pair of atoms or groups of atoms are eliminated from a molecule, usually through the action of acids, bases, or metals and, in some cases, by heating to a high temperature.
- **Saturated Compound**: Organic compounds containing only single carbon-carbon bonds.
- **Unsaturated compound**: Organic compounds containing double or triple carbon-carbon bonds

1.6 SELF ASSESSMENT QUESTIONS AND EXERCISE

**Short Answer Questions**

1. What is an elimination reaction? Explain with the help of an example.
2. What is the mechanism of $E_1$ reactions?
Elimination Reactions

NOTES

3. What is the mechanism of E₂ reactions?
4. What is the difference between S₈ and E₂ reactions?
5. Discuss the elimination reaction that happens when a compound bearing a poor leaving group and an acidic hydrogen is treated with base.

Long Answer Questions

1. Explain the formation of alkenes from alkyl halides through carbanion intermediate.
2. Discuss the factors affecting the rate of an E₁ reaction.
3. Discuss the factors affecting the rate of an E₂ reaction.
4. Analyze the reactant(s) and reaction conditions, then predict the structure of the major organic product and indicate the predominant mechanism of each reaction:

   I. \( \text{CH}_3\text{CH}_2\text{CH}_2\text{Br} \rightarrow \text{CH}_3\text{CH} (=\text{CH})\text{CH}_2\text{Br} \)

   II. \( \text{CH}_3\text{Br} \rightarrow \text{CH}_3\text{COH} \)

   III. \( \text{Cl} \rightarrow \text{CH}_3\text{CH}_2\text{OH} \)

1.7 FURTHER READINGS


UNIT 2  RULES OF ELIMINATION REACTIONS

Structure
2.0 Introduction
2.1 Objectives
2.2 Saytzeff’s Rule and Hofmann Rule
2.3 Pyrolytic cis Elimination
   2.3.1 Bredt’s Rule
2.4 Answers to Check Your Progress Questions
2.5 Summary
2.6 Key Words
2.7 Self Assessment Questions and Exercises
2.8 Further Readings

2.0 INTRODUCTION

Saytzeff’s rule (or Saytzeff’s rule, Saytzev’s rule) is an empirical rule for predicting the favored alkene product(s) in elimination reactions. While at the University of Kazan, Russian chemist Alexander Zaitsev studied a variety of different elimination reactions and observed a general trend in the resulting alkenes. Based on this trend, Zaitsev stated, “The alkene formed in greatest amount is the one that corresponds to removal of the hydrogen from the β-carbon having the fewest hydrogen substituents. More generally, Zaitsev’s rule predicts that in an elimination reaction, the most substituted product will be the most stable, and therefore the most favored. The rule makes no generalizations about the stereochemistry of the newly formed alkene, but only the regiochemistry of the elimination reaction. While effective at predicting the favored product for many elimination reactions, Zaitsev’s rule is subject to many exceptions.

Hofmann rule is an empirical rule used to predict regioselectivity of 1,2-elimination reactions occurring via E1cB mechanism. It states that, in a regioselective E1cB reaction, the major product is the less stable alkene, i.e., the alkene with the less highly substituted double bond.

You have studied about elimination reaction in the previous unit. In this unit, you will study the Saytzeff’s rule and the Hofmann rule to carryout elimination reactions.

2.1 OBJECTIVES

After going through this unit, you will be able to:

• Discuss Saytzeff’s rule
• Discuss Hofmann rule
2.2 Saytzeff’s Rule and Hofmann Rule

(1) Saytzeff rule (1875). According to this rule the neutral substrates (like alkyl halides) in elimination reaction predominantly yield the olefin bearing the larger number of alkyl groups around $\text{C}==\text{C}<$.

(2) Hofmann rule (1851). Charged substrates, like tetra-alkyl ammonium or trialkyl sulphonium salts, in elimination reaction yield predominantly the least substituted olefin or the olefin having the minimum of alkyl groups around the multiple bond.

These rules are illustrated by the examples given below:

\[
\text{C}_2\text{H}_5\text{CH}==\text{CHBr} \xrightarrow{\text{OH}^-}\text{C}_2\text{H}_5\text{CH}==\text{CH}_2 + \text{CH}_3\text{CH}==\text{CH}_2 \\
\text{(Saytzeff elimination)}
\]

\[
\text{C}_2\text{H}_5\text{CH}==\text{S(CH}_3\text{)}_2\xrightarrow{\text{OH}^-}\text{C}_2\text{H}_5\text{CH}==\text{CH}_2 + \text{CH}_3\text{CH}==\text{CH}_2 \\
\text{(Hofmann elimination)}
\]

Saytzeff elimination can be explained on the basis of the relative stabilities of the transition states leading to the formation of olefins. Hyperconjugation effect of the alkyl groups lowers the energy of the transition state in which larger number of such groups are present around carbon atoms involved and hence favours the predominant formation of olefin corresponding to this transition state.

The direction of Hofmann elimination is determined by the relative ease with which a proton can be lost from alternative carbon atoms. Presence of a charge in substrate influences the relative acidities of different protons and the most acidic proton is eliminated. Since an alkyl group produces an acid weakening inductive effect (+I effect), the olefin having lesser number of alkyl group around the double bond is formed predominantly.

As pointed earlier in unimolecular elimination reactions an intermediate carbocation is formed and therefore all the factors stabilizing such an intermediate will favour $E_1$ reactions. Hence $E_1$ reactions are favoured by (i) relative stabilities of the resulting carbocation, (ii) presence of larger number of alkyl groups causing $+I$ effect, (iii) steric effects, as crowding is reduced in the formation of a carbocation, and (iv) polar solvents which facilitate formation of intermediate ion.

The bimolecular elimination reactions are favoured by strongly electron attracting groups ($-I$ effect) in the substrate for the simple reason that they ease the removal of hydrogen from $\beta$-atom. So the effect is more pronounced if these groups are attached to $\beta$-atom. Presence of phenyl group at $\beta$-position also increases the rate of $E_2$ reaction by increasing the acidity of hydrogen and the stability of resulting olefin. Steric crowding at the reaction site also increases the rate of $E_2$ elimination, which is in contrast to $S_{\beta}2$ reactions. This may be because of two reasons—
firstly, with increase in alkyl substitution the number of hydrogens which may be attacked or eliminated increases and secondly the elimination reactions in general reduce the crowding in molecules by changing the bond angle from 109.5° in sp³ carbons to 120° in sp² carbons.

Change of attacking reagent does not alter the rate of E₁ reaction significantly but the rate of E₂ reaction increases with increase in the basicity of the reagent. Again the nature of departing group does not influence E₁ reaction whereas the rate of E₂ reaction increases in the following order for the departing halide group

\[ I > Br > Cl > F \]

Since both nucleophilic substitution and elimination reactions take place under similar conditions it is pertinent here to discuss these effects in terms of substitution versus elimination reactions. In general all features which tend to stabilize resultant olefin favour elimination over substitution reactions. **Thus relative stabilities of carbocations, steric factors, polar solvents etc., tend to favour elimination reactions. The increase in the strength of attacking base also favours elimination reactions. However, increase in the polarity of solvents favours substitution reactions whereas increase in the reaction temperature favours elimination because the energy of activation is high for elimination reactions.**

**Applications.** Eliminations result not only in the formation of >C≡C< and — C≡C — but also in the formations of >C=O, and — C≡N bonds. It is for this reasons that reactions like dehydration of alcohols, amides and oxidation of alcohols are also elimination reactions. Only some of these have been taken in examples explained ahead.

(1) Dehydrohalogenation of alkyl halides. Alkyl halides when treated with alcoholic KOH or NaOH undergo elimination of a molecule of hydrogen halide resulting in the formation of olefins. This elimination of hydrogen and halogen from the same molecule is known as dehydrohalogenation reaction.

\[
\text{Alkyl halide} \xrightarrow{\text{NaOH, } 4\text{K}} \xrightarrow{\text{H}_2\text{O, } 4\text{K}} \text{Olefins}
\]

Tertiary alkyl halides undergo the reaction most readily preferably by a E₁ mechanism. For other types of alkyl halides (secondary and primary) usually the E₂ mechanism is favoured. For example:

**E₁ mechanism**

\[
\text{CH}_3\text{CH}_2\text{Br} \xrightarrow{\text{SnCl}_2, } \text{HCl} \xrightarrow{\text{H}_2\text{O, } 4\text{K}} \text{CH}_3\text{CH}=\text{CH}_2 + \text{H}_2\text{O}
\]
Eliminating a halide ion, the alkyl halide gives a carbocation ion in the rate
determining slow step which then undergoes a fast elimination of a proton to give
olefin. A carbocation formed during the reaction may rearrange to give another
carbocation especially if a more stable carbocation can be formed by migration of
a hydrogen or alkyl group. This rearrangement will yield an olefin other than the
expected one.

E1 mechanism

\[
\text{KOH} \rightarrow \text{K}^+ + \text{OH}^- \\
\text{Br} \quad \text{now} \quad \text{Transition state} \quad \text{fast} \quad \text{H}_2\text{O} + \text{CH}_2\text{=CH}_2 + \text{Br}^-
\]

The mechanism involves the formation of a transition state in which nucleophile
\(\text{OH}^-\) or \(\text{OR}^-\) is abstracting a proton from alkyl halide and at the same time
bromine is leaving the molecule as a bromide ion.

The ease of elimination is similar for both \(E_1\) and \(E_2\) type of reactions. Thus for
a given halogen the rate of elimination increases in the order primary < secondary
< tertiary alkyl halide and for a given alkyl group the ease of elimination increases in
the order \(\text{Cl} < \text{Br} < \text{I}\). In cases where an alkyl halide may result in two types of
olefins the Saytzeff rule is generally observed.

It has also been observed that in unimolecular reaction the yield of olefin is low
and the substitution products are obtained in larger amounts whereas in a bimolecular
mechanism, elimination process is favoured over substitution.

(2) Dehydration of alcohol. The alcohols undergo elimination of a molecule of
water to give corresponding olefins under several different conditions. \(\text{H}_2\text{SO}_4\)
and \(\text{H}_3\text{PO}_4\) are commonly used for dehydration of alcohols (dehydration under
acidic conditions). If the vapours of alcohol are passed over heated alumina at a
temperature of about 400°C, the catalytic dehydration of alcohols takes place.
Other dehydrating agents which have been used frequently are \(\text{ZnCl}_2\) and \(\text{P}_2\text{O}_5\).
Dehydration with acids gives side products like ethers whereas catalytic
dehydration usually gives pure olefins. The ease of dehydration increases in the
order—primary > secondary > tertiary alcohols. The reactions are given below:

**Primary alcohol**

\[
\text{CH}_3\text{CH}_2\text{OH} \quad \xrightarrow{\text{AlCl}_3/\text{Al}_2\text{O}_3/400^\circ\text{C}} \quad \text{H}_2\text{C} = \text{CH}_2 + \text{H}_2\text{O}
\]

**Secondary alcohol**

\[
\text{CH}_3\text{CH} = \text{CH}_2 \quad \xrightarrow{\text{AlCl}_3/\text{Al}_2\text{O}_3/400^\circ\text{C}} \quad \text{H}_2\text{C} = \text{CHCH}_3 + \text{H}_2\text{O}
\]

**Isopropanol**

\[
\text{CH}_3\text{CH} = \text{CH}_2 \quad \xrightarrow{\text{H}_2\text{SO}_4/400^\circ\text{C}} \quad \text{H}_2\text{O}
\]
**Mechanism of dehydration.** When acids like H₂SO₄ or H₃PO₄ are used as dehydrating agents the mechanism is E₂. The alcohol by taking up a proton is converted to its conjugate acid (R·OH + H⁺ → RO⁻H₂) which then cleaves into H₂O and R⁺ (alkyl carbocation). This carbocation then eliminates a proton to yield olefins. Side reactions result in the formation of ethers also.

\[
\text{H}_2\text{SO}_4 \rightarrow \text{H}^+ + \text{HSO}_4^-
\]

**Side reactions**

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{OH} + \text{H}^+ & \rightarrow \text{CH}_3\text{CH}_2\text{O}^- + \text{SO}_2\text{H} \\
\text{CH}_3\text{CH}_2\text{OH} - \text{H}^+ & \rightarrow \text{CH}_3\text{CH}_2\text{OCH}_3
\end{align*}
\]

During dehydration in the presence of Al₂O₃, it is believed that alcohol is converted to some kind of aluminate ester which then decomposes to alkyl carboxylation. Alternatively the acidic impurities in alumina convert the alcohol to protonated alcohol and the dehydration proceeds by E₁ mechanism as above.

**Dehydrogenation of alcohols.** Dehydrogenation of alcohols to aldehydes and ketones may be considered as elimination reaction occurring by the loss of a molecule of hydrogen and resulting in the formation of carbon to oxygen double bond.
bond. The dehydrogenation can thus be carried out by using chromic acid (H$_2$CrO$_4$) or a mixture of Na$_2$CrO$_4$ with H$_2$SO$_4$. Alternatively when vapours of the alcohol are passed over freshly reduced copper heated to 300°, the primary alcohol are converted to aldehydes, secondary alcohols are converted to ketones, and a tertiary alcohol undergoes dehydration instead of dehydrogenation to form an olefin.

\[
\begin{align*}
\text{Pr. alcohol} & \quad \xrightarrow{\text{CuO (300°) or H$_2$CrO$_4$}} \quad \text{Aldehyde} \\
\text{Sec. alcohol} & \quad \xrightarrow{\text{CuO (300°) or H$_2$CrO$_4$}} \quad \text{Ketone}
\end{align*}
\]

The mechanism for chromic acid dehydrogenation in presence of a base like pyridine is:

\[
\begin{align*}
\text{CH}_3\text{CH(OH)} & \quad + \quad \text{OH}^-\text{Cr}_2\text{O}_7 \quad \xrightarrow{\text{H}_2\text{O}} \quad \text{CH}_3\text{C}==\text{O} \\
\text{Isopropyl alcohol} & \quad \text{Chromic} & \quad \text{Isopropyl chromate}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3\text{CH(OH)} & \quad \xrightarrow{\text{H}_2\text{O}} \quad \text{CH}_3\text{C}==\text{O} \\
\text{Ketene}
\end{align*}
\]

The chromic acid reacts with alcoholic group to form the corresponding ester. A base then abstracts a proton from this ester and the ester linkage breaks at oxygen to chromium bond to give carbonyl compounds.

When dehydrogenation is carried out in presence of a metal like copper, the reaction proceeds by a free radical elimination mechanism. Copper can absorb hydrogen with little change in the metal lattice and this hydrogen occupies holes in the crystal lattice of copper. That this hydrogen is not molecular hydrogen but is present in atomic (or radical) form has been supported by the strong reducing properties of such a copper crystal lattice. Absorbed hydrogen radicals are driven off in the form of molecular hydrogen by heating to a higher temperature. Thus the mechanism may be written as
Rules of Elimination Reactions

NOTES

(If one of the —R group is hydrogen the reaction will represent the dehydrogenation of primary alcohol to an aldehyde.)

The copper is able to break carbon-hydrogen and oxygen-hydrogen bonds by homolysis at high temperatures; it then adsorbs atomic hydrogen (or radicals) and finally gives them up as molecular hydrogen at high temperatures. The removal of hydrogen leaves an unpaired electron, each on carbon and oxygen which pairs up to give a double bond of carbonyl group. Reduced copper is more effective for dehydrogenation because it contains unpaired electrons which helps in the homolytic fission of C—H and O—H bonds.

2.3 PYROLYTIC CIS ELIMINATION

The E₁ mechanism (Elimination Internal/Intramolecular), also known as a thermal syn elimination or a pericyclic syn elimination, in organic chemistry is a special type of elimination reaction in which two vicinal substituents on an alkane framework leave simultaneously via a cyclic transition state to form an alkene in a syn elimination. This type of elimination is unique because it is thermally activated and does not require additional reagents unlike regular eliminations which require an acid or base, or would in many cases involve charged intermediates. This reaction mechanism is often found in pyrolysis.

General Features

Compounds that undergo elimination through cyclic transition states upon heating, with no other reagents present, are given the designation as E₁ reactions. Depending on the compound, elimination takes place through a four, five, or six-membered transition state.
The elimination must be syn and the atoms coplanar for four and five-membered transition states, but coplanarity is not required for six-membered transition states.

There is a substantial amount of evidence to support the existence of the Et mechanism such as:

1. The kinetics of the reactions were found to be first order
2. The use of free-radical inhibitors did not affect the rate of the reactions, indicating no free-radical mechanisms are involved
3. Isotope studies for the Cope elimination indicate the C-H and C-N bonds are partially broken in the transition state, this is also supported by computations that show bond lengthening in the transition state
4. Without the intervention of other mechanisms, the Et mechanism gives exclusively syn elimination products.

There are many factors that affect the product composition of Et reactions, but typically they follow Hofmann’s rule and lose a β-hydrogen from the least substituted position, giving the alkene that is less substituted (the opposite of Zaitsev’s rule). Some factors affecting product composition include steric effects, conjugation, and stability of the forming alkene.

For acyclic substrates, the Z-isomer is typically the minor product due to the destabilizing gauche interaction in the transition state, but the selectivity is not usually high.
The pyrolysis of N,N-dimethyl-2-phenylcyclohexylamine-N-oxide shows how conformational effects and the stability of the transition state affect product composition for cyclic substrates.

In the trans isomer, there are two cis-β-hydrogens that can eliminate. The major product is the alkene that is in conjugation with the phenyl ring, presumably due to the stabilizing effect on the transition state. In the cis isomer, there is only one cis-β-hydrogen that can eliminate, giving the nonconjugated regioisomer as the major product.

**Ester (Acetate) Pyrolysis**

The pyrolytic decomposition of esters is an example of a thermal syn elimination. When subjected to temperatures above 400 °C, esters containing β-hydrogens can eliminate a carboxylic acid through a 6-membered transition state, resulting in an alkene.

Isotopic labeling was used to confirm that syn elimination occurs during ester pyrolysis in the formation of stilbene.
**Routing of Elimination Reactions**

**NOTES**

**Sulfur Based**

**Sulfoxide Elimination**

β-hydroxy phenylsulfoxides were found to undergo thermal elimination through a 5-membered cyclic transition state, yielding β-keto esters and methyl ketones after tautomerization.

![Sulfoxide Elimination Diagram](image)

Allylic alcohols can be formed from β-hydroxy phenylsulfoxides that contain a β-hydrogen through an E1 mechanism, tending to give the β,γ-unsaturation.

![Allylic Alcohol Formation](image)

1,3-Dienes were found to be formed upon the treatment of an allylic alcohol with an aryl sulfide in the presence of triethylamine. Initially, a sulfinate ester is formed followed by a [2,3]-sigmatropic rearrangement to afford an allylic sulfoxide which undergoes thermal syn elimination to yield the 1,3-diene.

![1,3-Diene Formation](image)
Chugaev Elimination

The Chugaev elimination is the pyrolysis of a xanthate ester, resulting in an olefin. To form the xanthate ester, an alcohol reacts with carbon disulfide in the presence of a base, resulting in a metal xanthate which is trapped with an alkylating agent (typically methyl iodide). The olefin is formed through the thermal syn elimination of the β-hydrogen and xanthate ester. The reaction is irreversible because the resulting by-products, carbonyl sulfide and methanethiol, are very stable.

\[
\text{CH}_3\text{CH}_2\text{S}\text{CH}\text{CH}_3 + \text{NaOH} \rightarrow \text{CH}_3\text{CH}_2\text{S}\text{Na} + \text{CH}_3\text{CH}_2\text{CH}_2\text{O} + \text{H}_2\text{O}
\]

The Chugaev elimination is very similar to the ester pyrolysis, but requires significantly lower temperatures to achieve the elimination, thus making it valuable for rearrangement-prone substrates.

Burgess Dehydration Reaction

The dehydration of secondary and tertiary alcohols to yield an olefin through a sulfamate ester intermediate is called the Burgess dehydration reaction. The reaction conditions used are typically very mild, giving it some advantage over other dehydration methods for sensitive substrates. This reaction was used during the first total synthesis of taxol to install an exo-methylene group on the C ring.

First, the alcohol displaces the triethylamine on the Burgess reagent, forming the sulfamate ester intermediate. β-hydrogen abstraction and elimination of the sulfamate ester through a 6-membered cyclic transition state yields the alkene.
2.3.1 Bredt’s Rule

Bredt’s rule is an empirical observation in organic chemistry that states that a double bond cannot be placed at the bridgehead of a bridged ring system, unless the rings are large enough. The rule is named after Julius Bredt, who first discussed it in 1902 and codified it in 1924. It primarily relates to bridgeheads with carbon-carbon and carbon-nitrogen double bonds.

For example, two of the following isomers of norbornene violate Bredt’s rule, which makes them too unstable to prepare:

![Norbornene and Forbidden norbornene isomers]

Bredt’s rule is a consequence of the fact that having a double bond on a bridgehead would be equivalent to having a trans double bond on a ring, which is not stable for small rings (fewer than eight atoms) due to a combination of ring strain, and angle strain (nonplanar alkene). The p orbitals of the bridgehead atom and adjacent atoms are orthogonal and thus are not aligned properly for the formation of π bonds. Fawcett quantified the rule by defining $S$ as the number of non-bridgehead atoms in a ring system, and postulated that stability required $S \geq 9$ in bicyclic systems and $S \geq 11$ in tricyclic systems. There has been an active research program to seek compounds inconsistent with the rule, and for bicyclic systems a limit of $S \geq 7$ is now established with several such compounds having been prepared. The above norbornene system has $S \geq 5$ and so they are not preparable.

Bredt’s rule can be useful for predicting which isomer is obtained from an elimination reaction in a bridged ring system. It can also be applied to reaction mechanisms that go via carboxations and, to a lesser degree, via free radicals, because these intermediates, like carbon atoms involved in a double bond, prefer to have a planar geometry with 120° degree angles and sp² hybridization. The rule also allows the rationalisation of observations. For example, bicyclo[5.3.1]undecane-11-one-1-carboxylic acid undergoes decarboxylation on heating to 132°C, but the similar compound bicyclo[2.2.1]heptan-7-one-1-carboxylic acid remains stable beyond 500°C, despite both being β-keto acids with the carbonyl group on a one-carbon bridge and the carboxylate group on the bridgehead. The mechanism of decarboxylation involves an enolate intermediate, which is an $S \geq 9$ species in the former case and an $S \geq 5$ species in the latter, preventing the decarboxylation in the smaller ring system.

An anti-bredt molecule is one that is found to exist and be stable (within certain parameters) despite this rule. A recent (2006) example of such a molecule is 2-quinuclidonium tetrafluoroborate. Bridgehead double bonds can be found in
some natural products, discussed in a review by Mak, Pouwer and Williams, and an older review by Shea looked at bridgehead alkenes more generally.

Check Your Progress

1. What is dehydrohalogenation reaction?
2. What is E mechanism?
3. What is Bredt’s rule?

2.4 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Alkylic halides when treated with alcoholic KOH or NaOH undergo elimination of a molecule of hydrogen halide resulting in the formation of olefins. This elimination of hydrogen and halogen from the same molecule is known as dehydrohalogenation reaction.

2. The E mechanism, also known as a thermal syn elimination or a pericyclic syn elimination, in organic chemistry is a special type of elimination reaction in which two vicinal substituents on an alkane framework leave simultaneously via a cyclic transition state to form an alkene in a syn elimination.

3. Bredt’s rule is an empirical observation in organic chemistry that states that a double bond cannot be placed at the bridgehead of a bridged ring system, unless the rings are large enough.

2.5 SUMMARY

- According to Saytzeff’s rule the neutral substrates (like alkyl halides) in elimination reaction predominantly yield the olefin bearing the larger number of alkyl groups around \(-\text{C}==\text{C}-\).

- The direction of Hofmann elimination is determined by the relative ease with which a proton can be lost from alternative carbon atoms. Presence of a charge in substrate influences the relative acidities of different protons and the most acidic proton is eliminated. Since an alkly group produces an acid weakening inductive effect (+I effect), the olefin having lesser number of alkyl group around the double bond is formed predominantly.

- The relative stabilities of carboxocations, steric factors, polar solvents etc., tend to favour elimination reactions. The increase in the strength of attacking base also favours elimination reactions. However, increase in the polarity of solvents favours substitution reactions whereas increase in the reaction temperature favours elimination because the energy of activation is high for elimination reactions.
• The pyrolytic decomposition of esters is an example of a thermal syn elimination. When subjected to temperatures above 400 °C, esters containing β-hydrogens can eliminate a carboxylic acid through a 6-membered transition state, resulting in an alkene.

• Bredt’s rule is an empirical observation in organic chemistry that states that a double bond cannot be placed at the bridgehead of a bridged ring system, unless the rings are large enough. The rule is named after Julius Bredt, who first discussed it in 1902 and codified it in 1924. It primarily relates to bridgeheads with carbon-carbon and carbon-nitrogen double bonds.

2.6 KEY WORDS

• Saytzeff’s rule: It is an empirical rule for predicting the favored alkene product(s) in elimination reactions.

• Hofmann rule: It is an empirical rule used to predict regioselectivity of 1,2-elimination reactions occurring via E1cB mechanism. It states that, in a regioselective E1cB reaction, the major product is the less stable alkene, i.e., the alkene with the less highly substituted double bond.

2.7 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions
1. What are the rules of elimination reactions?
2. Differentiate between elimination reaction and substitution reaction.
3. How dehydrohalogenation take place in alkyl halides?
4. Discuss the dehydrogenation of alcohols.
5. Write a short note on Bredt’s rule.

Long Answer Questions
1. Discuss the Hofmann rule.
2. How does the pyrolysis take place in ester?
3. Analyze the sulfoxide elimination.
4. What is the end result of Chugaev elimination? Discuss in detail.

2.8 FURTHER READINGS


UNIT 3  ADDITION REACTION

NOTES

Structure
3.0  Introduction
3.1  Objectives
3.2  Addition Reaction
3.3  Stereochemistry of Additions
   3.3.1  Addition to Conjugated Systems
3.4  Answers to Check Your Progress Questions
3.5  Summary
3.6  Key Words
3.7  Self Assessment Questions and Exercises
3.8  Further Readings

3.0  INTRODUCTION

An addition reaction, in organic chemistry, is in its simplest terms an organic reaction where two or more molecules combine to form a larger one. Addition reactions are limited to chemical compounds that have multiple bonds, such as molecules with carbon–carbon double bonds (alkenes), or with triple bonds (alkynes). Molecules containing carbon—hetero double bonds like carbonyl (C=O) groups, or imine (C=N) groups, can undergo addition, as they too have double-bond character.

An addition reaction is the reverse of an elimination reaction. For instance, the hydration of an alkene to an alcohol is reversed by dehydration. There are two main types of polar addition reactions: electrophilic addition and nucleophilic addition. Two non-polar addition reactions exist as well, called free-radical addition and cycloadditions. Addition reactions are also encountered in polymerizations and called addition polymerization.

In the related addition-elimination reaction, an addition reaction is followed by an elimination reaction. In the majority of reactions it involves addition of nucleophiles to carbonyl compounds in what is called nucleophilic acyl substitution. Other addition-elimination reactions are the reaction of an aliphatic amine to an imine and an aromatic amine to a Schiff base in alkylamino-de-oxo-bisubstitution. The hydrolysis of nitriles to carboxylic acids is also a form of addition-elimination.

This unit discusses electrophilic, nucleophilic and free radical addition reactions. In the end of this unit, you will get an overview of regioselectivity and chemoselectivity in additions.
3.1 OBJECTIVES

After going through this unit, you will be able to:
- Discuss addition reactions
- Understand free radical, electrophilic, and nucleophilic addition reactions
- Get an overview of stereochemistry of additions

3.2 ADDITION REACTION

Compounds having unsaturation in the molecule have a tendency to add the attacking reagent molecule without eliminating any atom or group. Such reactions in which the attacking reagent adds to the substrate molecule are called addition reactions. In the process a triple bond may be converted to a double bond or single bond and a double bond is usually converted to single bond and the molecule acquires saturation. For each \( \pi \) bond of the molecule two \( \sigma \) bonds are formed and the hybridization state of carbon changes from \( sp \) to \( sp^2 \) and \( sp^2 \) to \( sp^3 \). Like substitution reactions, addition reactions can also be classified into categories depending on the type of reagent initiating this reaction and the molecularity of the reaction. Some examples are given below:

1. Free radical addition

Free-radical addition is an addition reaction in organic chemistry involving free radicals. The addition may occur between a radical and a non-radical, or between two radicals.

The basic steps with examples of the free-radical addition (also known as radical chain mechanism) are:
- **Initiation by a radical initiator**: A radical is created from a non-radical precursor
- **Chain propagation**: A radical reacts with a non-radical to produce a new radical species
- **Chain termination**: Two radicals react with each other to create a non-radical species

Free-radical reactions depend on a reagent having a (relatively) weak bond, allowing it to homolyse to form radicals (often with heat or light). Reagents without such a weak bond would likely proceed via a different mechanism. An example of an addition reaction involving aryl radicals is the Meerwein arylation.

**Addition of Mineral Acid to an Alkene**

To illustrate, consider the alkoxy radical-catalyzed, anti-Markovnikov reaction of hydrogen bromide to an alkene. In this reaction, a catalytic amount of organic
peroxide is needed to abstract the acidic proton from HBr and generate the bromine radical, however a full molar equivalent of alkene and acid is required for completion.

**NOTES**

Note that the radical will be on the more substituted carbon. Free-radical addition does not occur with the molecules HCl or HI. Both reactions are extremely endothermic and are not chemically favored.

\[
\text{Initiation:} \quad \text{R} + \text{Br} \rightarrow \text{R} - \text{H} + \text{Br}^-
\]

\[
\text{Termination:} \quad \text{Br}^- + \text{Br}^- \rightarrow \text{Br}^2-
\]

\[
\text{CH}_2=\text{CH} + \text{H}_2 \quad \text{Ni} \quad 140^\circ \rightarrow \quad \text{CH}_2=\text{CH}_2 \quad \text{H}_2\text{Ni} \quad 200^\circ \rightarrow \quad \text{CH}_3 - \text{CH}_3
\]

2. Electrophilic addition

In organic chemistry, an electrophilic addition reaction is an addition reaction where, in a chemical compound, a \( \pi \) bond is broken and two new \( \sigma \) bonds are formed. The substrate of an electrophilic addition reaction must have a double bond or triple bond.
The driving force for this reaction is the formation of an electrophile X* that forms a covalent bond with an electron-rich unsaturated C=C bond. The positive charge on X is transferred to the carbon-carbon bond, forming a carbocation during the formation of the C-X bond.

The overall reaction for electrophilic addition to ethylene.

In step 2 of an electrophilic addition, the positively charged intermediate combines with (Y) that is electron-rich and usually an anion to form the second covalent bond.

Step 2 is the same nucleophilic attack process found in an SN2 reaction. The exact nature of the electrophile and the nature of the positively charged intermediate are not always clear and depend on reactants and reaction conditions.

In all asymmetric addition reactions to carbon, regioselectivity is important and often determined by Markovnikov’s rule. Organoborane compounds give anti-Markovnikov additions. Electrophilic attack to an aromatic system results in electrophilic aromatic substitution rather than an addition reaction.

In Electrophilic addition the electrophile with the positive charge affects the formation of the total structure, which thus bears a positive charge as well, to make up for the new addition, which then results in the intermediate, bearing that positive charge. This intermediate is the key to understanding the electrophilic addition, which is due to the positive nature of the particles involved. If this is done, then the reactions can be understood by these additions as positively charged reactions. The positive charge bears result as the intermediate form otherwise known as the total structure of such an intermediate. The end product thus contains the complete structure, with the addition of Y, a nucleophile.

\[ \text{CH}_2=\text{CH}_2 + \text{Br}_2 \rightarrow \text{CH}_2\text{Br} \rightarrow \text{CH}_3\text{Br} \]

3. Nucleophilic addition

In organic chemistry, a nucleophilic addition reaction is an addition reaction where a chemical compound with an electron-deficient or electrophilic double or triple bond, a π bond, reacts with electron-rich reactant, termed a nucleophile, with
disappearance of the double bond and creation of two new single, or \( \sigma \), bonds. The reactions are involved in the biological synthesis of compounds in the metabolism of every living organism, and are used by chemists in academia and industries such as pharmaceuticals to prepare most new complex organic chemicals, and so are central to organic chemistry. Addition reactions require the presence of groups with multiple bonds in the electrophile (due to the fact that double bonds and even triple bonds can both lack electron rich sources); carbon–heteroatom multiple bonds as in carbonyls, imines, and nitriles, or carbon–carbon double or triple bonds. The lack of electron rich sources is due to the fact that these bonds are partially empty, even though they remain connected, since the region occupying the orbital is essentially dead. This electrophilic behavior is defined as empty space since everything inside is basically without any source of electricity except from outside the bond, since bonds tend to want to attract more to themselves (whether this be electric or non-electric can differ in most situations). The addition of the nucleophile means the continuous addition of a negative charge throughout the reaction, unless an electrophile also makes itself present to form a complete structure with no charge at all. The negative charge being continuous throughout the reaction until the formation of an intermediate, bearing the charge, thus is the addition reaction we have before us. Once this meets an electrophile, then the intermediate formed with the negative charge can thus be neutralized to form a complete structure via a type of bond.

\[
\text{CH}_3\text{C} \equiv \text{O} + \text{HCN} \rightarrow \text{CH}_3\text{C} \equiv \text{OH} \quad \text{(Acetonitrile)}
\]

In the first reaction a triple bond (sp carbon) is first converted to double bond (sp\(^2\) carbon) and then single bond (sp\(^3\) carbon) by the addition of four atoms of hydrogen. In the second reaction a \( \pi \) bond of sp\(^3\) hybridized carbon is converted to two \( \sigma \) bond of sp\(^3\) hybridized carbon by addition of two atoms of bromine. In the third reaction c = O adds up a molecule of HCN resulting in corresponding cyanohydrin. The \( \pi \) bond of sp\(^3\) carbon is changed to sp\(^2\) carbon \( \sigma \) bonds. In the last reaction a triple bond (carbon in sp state) is converted to a double bond (sp\(^2\) carbon) which then rearranges to give acetamide.

The addition reactions are the reactions of the double or triple bonds. In a >C=O or C=C– C the \( \pi \) electrons are most readily available. These \( \pi \) electrons will shield the molecule from nucleophilic reagents and therefore such molecules will be readily attacked by electrophilic reagents. Thus the addition to multiple carbon to carbon bonds is electrophilic addition reaction. In a >C=O or C=C– N, the \( \pi \) electron density is slightly shifted towards the more electronegative elements O and N, and at the approach of a reagent electronic shift results in complete transfer of this \( \pi \) electron pair to O or N (heteroatoms in general). Thus
carbon acquires a positive charge and the heteroatom a negative charge. Such carbon atoms will be preferentially attacked by nucleophilic reagents and therefore the additions to $\text{C}=$ O or $\text{C}=\text{N}$ groups are nucleophilic addition reactions. Further, a system having negatively charged oxygen is more stable than the positively charged carbon, hence the addition at carbon precedes the addition at oxygen.

**Check Your Progress**
1. What are the types of addition reaction?
2. In which addition reaction, the addition to multiple carbon to carbon bonds takes place?

### 3.3 STEREOCHEMISTRY OF ADDITIONS

In a carbon–carbon double bond, since the carbon atoms are $sp^2$ hybridized, all the six atoms (two carbon and four atoms attached to them) lie in one plane. During addition reactions, both the adding groups may come from the same side leading to syn-addition or from opposite side leading to anti-addition.

Let us take the case of 2-butene which exists as *cis*- and *trans*- isomers. Addition of bromine results in the formation of two asymmetric centres in the molecules. If *syn-* and *anti-* additions both take place randomly then the reaction is non-stereospecific. If the additions are only *syn-* or only *anti-* then we get one set of stereoisomers from *cis*-2-butene and a different set of stereoisomers from *trans*-2-butene. Such reactions are called stereospecific.

In actual practice, addition of bromine to *cis*-2-butene gives a *dl*-mixture while addition of bromine to *trans*-2-butene gives a meso compound suggesting that it is a stereospecific *anti*-addition

![Addition Reactions Diagram]

#### 3.3.1 Addition to Conjugated Systems

*Addition to conjugated dienes.* Although conjugated dienes are considered to be more stabilized, because of resonance, than simple olefins, yet they undergo electrophilic additions readily. However, in butadiene such a reaction with bromine results in two products, 3,4-dibromo-1-butene and 1,4-dibromo-2-butene as

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The addition of bromonium ion to butadiene gives an intermediate carboxation which is resonance stabilized. The carbocation (I) gives 1,2-addition resulting in 3,4-dibromo-1-butene and the carbocation (II) gives 1,4-addition resulting in 1,4-dibromo-2-butene. Lower temperature and non-polar solvents usually favour 1,2-additions whereas higher temperature and polar solvents favour 1,4-additions.

3.3.2 Regioselectivity and Chemoselectivity in Additions

Regioselectivity

In chemistry, regioselectivity is the preference of one direction of chemical bond making or breaking over all other possible directions. It can often apply to which of many possible positions a reagent will affect, such as which proton a strong base will abstract from an organic molecule, or where on a substituted benzene ring a further substituent will add.

A specific example is a halohydrin formation reaction with 2-propenylbenzene:

Because of the preference for the formation of one product over another, the reaction is selective. This reaction is regioselective because it selectively generates one constitutional isomer rather than the other.

Various examples of regioselectivity have been formulated as rules for certain classes of compounds under certain conditions, many of which are named. Among the first introduced to chemistry students are Markovnikov’s rule for the addition of protic acids to alkenes, and the Fürst-Plattner rule for the addition of nucleophiles to derivatives of cyclohexene, especially epoxide derivatives.
Regioselectivity in ring-closure reactions is subject to Baldwin’s rules. If there are two or more orientations that can be generated during a reaction, one of them is dominant (for example, Markovnikov/anti-Markovnikov addition across a double bond).

Regioselectivity can also be applied to specific reactions such as addition to pi ligands.

Selectivity also occurs in carbene insertions, for example in the Baeyer-Villiger reaction. In this reaction, an oxygen is regioselectively inserted near an adjacent carbonyl group. In ketones, this insertion is directed toward the carbon which is more highly substituted (i.e. according to Markovnikov’s rule). For example, in a study involving acetophenones, this oxygen was preferentially inserted between the carbonyl and the aromatic ring to give acetyl aromatic esters instead of methyl benzoates.

Addition of non-symmetrical reagent (i.e. A-B where A is not equal to B) to a non-symmetrical alkene (i.e. where the groups at each end of the double bond are different), then two isomeric products that are constitutional isomers can be obtained. For example, the reaction of HCl with propene gives 1-chloropropane and 2-chloropropane.

\[
\text{CH}_2=\text{CH}=	ext{CH}_2 + \text{HCl} \rightarrow \begin{cases} \text{CH}_3\text{CH}=(\text{CH})\text{Cl} & \text{(major)} \\
\text{CH}=(\text{CH})\text{CH}_2\text{Cl} & \text{(minor)} \end{cases}
\]

Normally, 2-chloropropane is the major product.

Since one product is favoured over the other, the reaction is said to be regioselective.

If 2-chloropropane were the only product then the reaction is said to be regiospecific.

Chemoselectivity

Chemoselectivity is the preferential outcome of a chemical reaction over a set of possible alternative reactions.

In another definition, chemoselectivity refers to the selective reactivity of one functional group in the presence of others; often this process in convoluted and protecting groups are on the molecular connectivity alone. Such predictions based on connectivity are generally considered plausible, but the physical outcome of the actual reaction is ultimately dependent on a number of factors that are practically impossible to predict to any useful accuracy (solvent, atomic orbitals, etc.).

Chemoselectivity can be difficult to predict, but observing selective outcomes in cases where many reactions are plausible, is common. Examples include the selective organic reduction of the greater relative chemoselectivity of sodium...
borohydride reduction versus lithium aluminium hydride reduction. In another example, the compound 4-methoxyacetophenone is oxidized by bleach at the ketone group at high pH (forming the carboxylic acid) and oxidized by EAS (to the aryl chloride) at low pH.

### Check Your Progress

3. What is non-stereospecific reaction?
4. What is more stabilized – Conjugated dienes or simple olefins?

### 3.4 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Free radical reaction, electrophilic reaction and nucleophilic reaction.
2. Electrophilic addition reaction.
3. If syn- and anti-additions both take place randomly then the reaction is non-stereospecific.
4. Conjugated dienes.

### 3.5 SUMMARY

- Compounds having unsaturation in the molecule have a tendency to add the attacking reagent molecule without eliminating any atom or group. Such reactions in which the attacking reagent adds to the substrate molecule are called addition reactions.
- Free-radical addition is an addition reaction in organic chemistry involving free radicals. The addition may occur between a radical and a non-radical, or between two radicals.
- In organic chemistry, an electrophilic addition reaction is an addition reaction where, in a chemical compound, a π bond is broken and two new σ bonds are formed. The substrate of an electrophilic addition reaction must have a double bond or triple bond.
- In organic chemistry, a nucleophilic addition reaction is an addition reaction where a chemical compound with an electron-deficient or electrophilic double or triple bond, a π bond, reacts with electron-rich reactant, termed a nucleophile, with disappearance of the double bond and creation of two new single, or σ, bonds.
- In chemistry, regioselectivity is the preference of one direction of chemical bond making or breaking over all other possible directions. It can often apply to which of many possible positions a reagent will affect, such as
which proton a strong base will abstract from an organic molecule, or where on a substituted benzene ring a further substituent will add.

- **Chemoselectivity** refers to the selective reactivity of one functional group in the presence of others; often this process in convoluted and protecting groups are on the molecular connectivity alone.

### 3.6 KEYWORDS

- **Addition reaction**: An addition reaction is in its simplest terms an organic reaction where two or more molecules combine to form a larger one. Addition reactions are limited to chemical compounds that have multiple bonds, such as molecules with carbon–carbon double bonds (alkenes), or with triple bonds (alkynes).

- **Electrophilic addition**: An electrophilic addition reaction is an addition reaction where, in a chemical compound, a π bond is broken and two new σ bonds are formed. The substrate of an electrophilic addition reaction must have a double bond or triple bond.

### 3.7 SELF ASSESSMENT QUESTIONS AND EXERCISES

**Short Answer Questions**

1. What is the mechanism of addition to conjugated dienes?
2. What do you understand by stereospecific anti-addition?
3. Discuss regioselectivity with the help of an example.
4. Discuss chemoselectivity with the help of an example.

**Long Answer Questions**

1. Explain free radical addition reaction with the help of an example.
2. What do you understand by electrophilic addition? Give examples.
3. Discuss the stereochemistry of addition reactions.
4. Write a brief note on addition reactions.

### 3.8 FURTHER READINGS


**BLOCK - II**

**ADDITION TO MULTIPLE BOND AND CONFORMATIONAL ANALYSIS**

**UNIT 4  ADDITION TO CARBON-CARBON MULTIPLE BOND**

**Structure**
- 4.0 Introduction
- 4.1 Objectives
- 4.2 Addition to Carbon-Carbon Multiple Bond
  - 4.2.1 Michael Reaction
  - 4.2.2 Gilman Reagent
  - 4.2.3 Diels-Alder Reaction
- 4.3 Answers to Check Your Progress Questions
- 4.4 Summary
- 4.5 Key Words
- 4.6 Self Assessment Questions and Exercises
- 4.7 Further Readings

**4.0  INTRODUCTION**

A carbon–carbon bond is a covalent bond between two carbon atoms. The most common form is the single bond: a bond composed of two electrons, one from each of the two atoms. The carbon–carbon single bond is a sigma bond and is formed between one hybridized orbital from each of the carbon atoms. In ethane, the orbitals are sp3-hybridized orbitals, but single bonds formed between carbon atoms with other hybridizations do occur (For example, sp2 to sp3). In fact, the carbon atoms in the single bond need not be of the same hybridization. Carbon atoms can also form double bonds in compounds called alkenes or triple bonds in compounds called alkynes. A double bond is formed with an sp2-hybridized orbital and a p-orbital that is not involved in the hybridization. A triple bond is formed with an sp-hybridized orbital and two p-orbitals from each atom. The use of the p-orbitals forms a pi bond.

Carbon–carbon bond-forming reactions are organic reactions in which a new carbon–carbon bond is formed. They are important in the production of many man-made chemicals such as pharmaceuticals and plastics. Some examples of reactions which form carbon–carbon bonds are aldol reactions, Diels–Alder reaction, and the addition of a Grignard reagent to a carbonyl group, a Heck
reaction, a Michael reaction and a Wittig reaction.

The directed synthesis of desired three-dimensional structures for tertiary carbons was largely solved during the late 20th century, but the same ability to direct quaternary carbon synthesis did not start to emerge until the first decade of the 21st century. One of the most general and useful reactions of alkenes and acetylenes for synthetic purposes is the addition of electrophilic reagents.

In this Unit, you will learn about reactions in which reagents add to carbon-carbon multiple bonds.

4.1 OBJECTIVES

After going through this unit, you will be able to:

- Discuss electrophilic addition at carbon-carbon multiple bonds
- Understand addition of halogens and hypohalous acids to olefins
- Discuss the mechanism of Michael addition
- Describe the structure of Gilman reagent
- Know about Diels-Alder Reaction

4.2 ADDITION TO CARBON-CARBON MULTIPLE BOND

The electrophilic addition reactions are observed in alkenes, alkynes and conjugated systems and essentially mean the addition of a molecule to the double bond. Thus if a reagent breaks up to give a negative and a positive ion each one of these are added to double bond. Why the reaction is then known as an electrophilic addition although both the electrophile and the nucleophile are adding to the same double bond? The answer to this lies in the fact that the addition reaction is initiated by the attack of electrophile on the multiple bond which is slow and is the rate determining step and this is followed by the addition of nucleophile which is a fast reaction. In all addition reactions, \( \sigma \) bonds are converted to \( \sigma^* \) bonds or the hybridization state of carbon changes from \( sp^3 \) to \( sp^2 \) or \( sp^3 \) and from \( sp^2 \) to \( sp^3 \). The examples of such reactions are hydration and hydrogenation of olefins, additions of halogens and halogen acids to olefins and ozonolysis.

In electrophilic addition reactions an electrophile approaches the double or triple bond and in the first step forms a covalent bond with one of the carbon by converting \( \pi \) bond into a pair of \( \sigma \) bonds, resulting in the formation of a carbocation which then takes up a nucleophile to result in addition product. Thus:

\[
\text{Olefin} \quad + \quad \text{Electrophile} \quad \rightarrow \quad \text{Carbocation}
\]
Addition to Carbon-Carbon
Multiple Bond

Alternatively, the $E^-$ can also be the positive end of a dipolar reagent. Thus for bromination following mechanism may be written:

\[
\begin{align*}
&\text{C} = \text{C}^- + X^- \xrightarrow{\text{Fast}} \text{C} = \text{C}^- \\
&\text{Addition product}
\end{align*}
\]

(iii) A cation of the type II is possible because of the lone pairs of electrons at bromine which may be co-ordinated with electron deficient carbon. It has been suggested that electrophile first interacts with 2 electrons to form a $\pi$ complex which later changes to a $\sigma$ complex or carbocation, exemplified as follows:

\[
\begin{align*}
&\text{C} = \text{C}^- + E^+ \xrightarrow{\text{Fast}} \text{C} = \text{C}^- + X^- \\
&\text{n-Complex} \\
&\xrightarrow{S_N} \text{C} = \text{C}^- + X^- \xrightarrow{\text{Fast}} \text{Product}
\end{align*}
\]

The $\pi$ complex or the three membered ring cation is roughly on one side of the double bond and therefore the attack of nucleophile must occur from the other side of the double bond. Thus the two groups are added on opposite sides of the double bond—such additions are known as **trans-additions**. On the other hand if the two groups are added on the same side of the double bond such additions are known as **cis-additions**. Most electrophilic additions are trans additions. Thus stereochemistry of addition reactions yields useful information about the mechanism of these reactions.

**Structure and Reactivity**

Two carbon atoms are involved in double bond formation. Which one of these is chosen for electrophilic addition? In symmetrical olefins these two carbon atoms are identical in character and therefore addition of electrophile at either of these will yield the same product but in unsymmetrical olefins like propylene the two carbon atoms involved in double bond are not identical and hence the addition of electrophile to each one of these respectively should result in two isomeric products. Since the addition of electrophile to double or triple bond gives a carbocation it is logical to expect that carbocation having greater stability will predominate. *So the electromeric shift of electrons and addition of electrophile will take place in such a manner so as to form the more stable carbocation.* The has been dealt at length under Markownikoff’s rule later in this section.

An electrophile attacks at the site rich in electrons so all the structural features which tend to increase electron density at the double or triple bond will increase the rate of reactions. *Thus electron donating substituents (+I effect) will increase...*
the rate of reaction whereas electron withdrawing substituents (−I effect) will decrease it. Structural features increasing the stability of carbocation tend to speed up the reaction. The polar solvents, likewise, markedly increase the reaction rate. The order of reactivity of double bonds to electrophilic additions in some of the common compounds is given below in increasing order which may be understood in terms of inductive effects.

\[
\begin{align*}
\text{CH}_2=\text{CH} & \quad \text{Acrylic acid} & \quad \text{CH}_3=\text{CH}_2 & \quad \text{Ethene} & \quad \text{CH}_2=\text{CH}_2 & \quad \text{Propene} \\
\text{CH}_3\text{C}==\text{CH}_2 & \quad 2\text{-Methylpropene} & \quad \text{CH}_3\text{C}==\text{CH}_2 & \quad 2\text{-Methyl-1-butene} & \quad \text{CH}_3\text{C}==\text{CH}_3 & \quad 3,3\text{-Dimethyl-1-butene}
\end{align*}
\]

**Applications**

(i) **Addition of Halogens and hypohalous acids to olefins.** When a halogen molecule or hypohalous acid reacts with olefin the α bond is polarised by electroneric shift. The positively polarised halogen attacks and combines with the carbon carrying the pair of electrons after electrons rearrangements. A cyclic halonium ion is formed which prevents cis-addition of OH⁻. Then the completion of addition occurs by a trans combination of a bromide or hydroxide ion. The mechanism of addition of hypochlorous acid may briefly be illustrated as

\[
\text{HOCl} + \text{Cl}^- \rightarrow \text{Cl}^+ + \text{HO}^{-}
\]

In the reaction with bromine it is the bromonium ion (Br⁺) which is the attacking species rather than bromide ion because the latter is more stable than former by virtue of its stable electronic configuration. As already mentioned the attack of Br⁺ or OH⁻ on the carbocation takes place from the side other than the one occupied by Br⁻ or Cl⁻ resulting in trans-addition. In simple aliphatic compounds the trans-addition has no significance because the product can easily change to cis-form by simple rotation along the carbon to carbon bond but it becomes important if the geometry of the molecule prevents this free rotation as in cyclic compounds.

This ionic mechanism is supported by the fact that the reaction rate is accelerated as the polarity of solvent is increased. If the reaction is carried out in presence of a number of anions like CO₃⁻, NO₂⁻, RO⁻ etc. then these are also incorporated in some of the substrate molecules. Thus:

\[
\begin{align*}
\text{CH}_2=\text{CH}_2 + \text{Br}_2 & \rightarrow \text{Br}^- + \text{Br}^- + \text{CH}_2=\text{CH}_2 & (4.1) \\
\text{Br}^- & \rightarrow \text{Br}^- + \text{CH}_2=\text{CH}_2 + \text{H}_2 & (4.2)
\end{align*}
\]
These products (4.2) to (4.4) are not the products of substitution of (4.1) but are formed as a result of competition between various anions for reaction with carboxation intermediate.

(ii) Addition of halogen acids to olefins. The addition of halogen acid (HX) to olefins may be shown as follows:

\[
\begin{align*}
\text{(I)} & \quad \text{C} = \text{C} + 3\text{H_2} \quad \text{Fast} \quad \text{C} = \text{C} + 3\text{H}^+ \\
\text{Slow} & \quad \text{C} = \text{C} + 3\text{H}^+ \\
\text{(II)} & \quad \text{X} + \text{C} = \text{C} \quad \text{H}^+ \quad \text{C} = \text{C} + 3\text{H}^+ \\
\end{align*}
\]

n-Complex

The addition of halogen acids to olefins is first order in olefin and indefinite (or third) order in halogen acid. The purpose of the other HX molecules is to polarise a HX molecule and to remove halide ion as shown in (I) and (II). Combination of a proton with π electrons gives a π complex which polarizes the π electrons pair by electromeric shift and combines with this pair to give a σ complex. The addition of halide ion then completes the addition.

When the olefin is asymmetric, the addition of halogen acid (HX) or hypohalous acid (HOX) can theoretically result in two possible products. Thus:

\[
\begin{align*}
\text{R} = \text{CH}_2 \text{CH}_2 + \text{H}^+ \quad & \rightarrow \quad \text{R} + \text{CH}_2 = \text{CH}_2 \\
& \quad \quad \text{(Observed)} \\
\text{R} = \text{CH}_2 \text{CH}_2 + \text{H}^+ \quad & \rightarrow \quad \text{R} + \text{CH}_2 = \text{CH}_2 - \text{X} \\
& \quad \quad \text{(Not observed)} \\
\end{align*}
\]

But in such reactions it is the first type which predominates. To explain this Markovnikov in 1869 gave a generalization which is known as Markovnikov’s rule. According to this rule “the negative part of the addendum (reagent which is adding) goes to the carbon atom, constituting the double bond, which is poorer in hydrogen.”

Obviously in such cases the direction of polarization of bond by electromeric shift is determined by the inductive effect (+I effect) of the alkyl group and thus it polarizes in such a manner that the electron pair shifts to carbon which is farthest
from the allyl substituent. Also the predominant direction will depend upon the formation of carboxation intermediate of greater stability. Thus out of the two carboxations which may be formed in above reaction

\[
\begin{align*}
R-\overset{\text{I}}{\text{CH}}-\overset{\text{OH}}{\text{CH}}_3 & \quad R-\overset{\text{II}}{\text{CH}}_2-\overset{\text{CH}}{\text{OH}}_2 \\
\text{Acrylic acid} & \\
\end{align*}
\]

the (I) will be more stable as it is a secondary carboxation whereas (II) is a primary carboxation. Thus the stability of carboxation is the basis of familiar Markovnikov’s rule. However, this rule is only applicable in ionic additions to hydrocarbons having only one multiple linkage. Exceptions to Markovnikov’s rule are encountered in cases where factors other than hyperconjugation or inductive effect influence the relative stabilities of the two carboxations derived from one olefin. Thus addition of HBr to olefinic acids like acrylic acid proceeds as follows:

\[
\begin{align*}
\text{CH}_3\overset{\text{O}}{\text{CH}}_2\overset{\text{I}}{\text{Br}} & \quad \stackrel{\text{H}^+}{\text{Br}^-} \quad \text{CH}_3\overset{\text{O}}{\text{CH}}_2\overset{\text{II}}{\text{OH}}_2 \\
\text{Acrylic acid} & \\
\end{align*}
\]

In acrylic acid both –I effect of — COOH group and –M effect (mesomeric effect) favours the formation of intermediate carboxation (III) and thus anti-Markovnikov addition takes place. Similarly in trifluoromethyl ethylene the –I effect of three fluorine atoms causes the formation of carboxation (IV) and again anti-Markovnikov addition occurs

\[
\begin{align*}
\text{\overset{\text{III}}{\text{C}}-\overset{\text{OH}}{\text{CH}}_3-\overset{\text{F}}{\text{CH}}_2 & \quad \overset{\text{H}^+}{\text{Br}^-} \quad \text{\overset{\text{IV}}{\text{C}}-\overset{\text{OH}}{\text{CH}}_2-\overset{\text{F}}{\text{CH}}_2-\overset{\text{Br}}{\text{CH}}_2} \\
\text{Trifluoromethyl ethylene} & \\
\end{align*}
\]

Anti-Markovnikov addition of HBr to olefins is also observed if peroxides or elemental oxygen are present in the reaction mixture. This is known as Kharasch effect or peroxide effect. Kharasch and Mayo in 1933 found that the presence of peroxide results in the free radical addition reaction. The peroxides decompose to give free radicals which in turn abstracts hydrogen from halogen acids to give bromine free radicals. These radicals induce homolytic fission of electron pair and the bromine radical then combines with carbon atom of high electron availability. The intermediate free radical, so formed, is stabilised by the formation of bridged bromine radical, and this finally abstracts a hydrogen from HBr to give addition product.
The reaction proceeds through a free radical mechanism can be shown by adding inhibitors, like hydroquinone which combines with free radicals, and thus decrease the rate of reaction. The free radical addition is favoured by non-polar solvents. However addition of hydrogen chloride and hydrogen iodide to olefins is not effected by peroxides.

(ii) **Hydroboration of olefins.** Reaction of diborane (B\(_2\)H\(_6\)) with an olefinic double bond to produce alkylboranes is termed as **hydroboration** (H.C. Brown). In the reaction diborane behaves as if it were its non-existent monomer borane (BH\(_3\)).

\[ \text{Olefin} \rightarrow \text{Alkyloborane} \rightarrow \text{Di(alkyl)borane} \rightarrow \text{Tri(alkyl)borane} \]

The addition of diborane is an electrophilic attack by diborane on \(\pi\) electrons of olefins in accordance with Markownikoff’s rule.

Due to the formation of a four centered transition state both hydrogen and boron become linked to the same side of the double bond leading to a cis addition.

\[ \text{Olefin} + \text{Borane hydride} \rightarrow \text{Transition state} \rightarrow \text{Alkyloborane} \]

Hydroboration is an important synthetic method because alkyl-boranes can be transformed into a number of useful products.
(iv) **Hydration of olefins.** Addition of a molecule of water to olefins is known as hydration reaction. Hydration of olefins in acidic media results in the formation of alcohols. The mechanism for hydration is the electrophilic addition at $\text{C} $ <- C <

$$
\text{H} + \text{H} \\
\text{O}_\text{water} \\
\text{H}_2\text{O}
$$

Initially, a proton adds up at double bond to form a $\pi$ complex which then changes to $\sigma$ complex or intermediate carbocation. This then adds a molecule of water followed with the elimination of a proton to yield alcohols. Dilute acid used is the source of proton.

(v) **Ozonoysis.** Addition of ozone to olefinic linkage resulting in the formation of ozonide, which on subsequent hydrogenation gives carbonyl compounds, is known as ozonoysis. The reaction follows the electrophilic addition reaction mechanism.

\[ \text{C} + \text{O}_3 \rightarrow \text{C} = \text{O} \]  
\[ \text{Ozone} \]
\[ \text{Ozoxide} \]
\[ \text{C} = \text{O} \]  
\[ \text{O} \]  
\[ \text{O-ozonide} \]

Ozone may be represented as a resonance hybrid of structures $O-O-O$ and $O-O-O$. Such a polar molecule causes the electromeric shift of $\pi$ electron pair and combines through its positive pole with carbon bearing the electron pair and later the negative pole also combines with the positive centre of resultant carbocation to yield the ozonide. The ozonide by a series of rearrangement steps yields iso-ozonide. The iso-ozonide is cleaved by hydrogenation or hydrolysis to $>\text{C} = \text{O}$ compounds.

Ozonoysis is used to locate the position of double bonds in olefins.

### 4.2.1 Michael Reaction

The Michael reaction or Michael addition is the nucleophilic addition of a carbamion or another nucleophile to an $\alpha, \beta$-unsaturated carbonyl compound. It belongs to the larger class of conjugate additions. This is one of the most useful methods for the mild formation of $\text{C} - \text{C}$ bonds. Many asymmetric variants exist.
In this scheme the R and R’ substituents on the nucleophile (a Michael donor) are electron-withdrawing groups such as acyl and cyano making the methylene hydrogen acidic forming the carbanion on reaction with base B. The substituent on the activated alkene, also called a Michael acceptor, is usually a ketone making it an enone, but it can also be a nitro group.

**Definition**

As originally defined by Arthur Michael, the reaction is the addition of an enolate of a ketone or aldehyde to an α,β-unsaturated carbonyl compound at the β carbon. A newer definition, proposed by Kohler, is the 1,4-addition of a doubly stabilized carbon nucleophile to an α,β-unsaturated carbonyl compound. Some examples of nucleophiles include beta-ketoesters, malonates, and beta-cyanoesters. The resulting product contains a highly useful 1,5-dioxygenated pattern.

Classical examples of the Michael reaction are the reaction between diethyl malonate (Michael donor) and diethyl fumarate (Michael acceptor), that of mesityl oxide and diethyl malonate, that of diethyl malonate and methyl crotonate, that of 2-nitropropane and methyl acrylate, that of ethyl phenylacetoacetate and acrylonitrile and that of nitropropane and methyl vinyl ketone.

The Michael addition is an important atom-economical method for diastereoselective and enantioselective C–C bond formation. A classical tandem sequence of Michael and aldol additions is the Robinson annulation.

**Mechanism**

In the reaction mechanism, there is 1 (with R an alkoxy group) as the nucleophile:

![Diagram of Michael addition mechanism](image)

Deprotonation of 1 by base leads to carbanion 2 stabilized by its electron-withdrawing groups. Structures 2A to 2C are three resonance structures that can be drawn for this species, two of which have enolate ions. This nucleophile reacts with the electrophilic alkene 3 to form 4 in a conjugate addition reaction. Proton abstraction from protonated base (or solvent) by the enolate 4 to 5 is the final step.

The course of the reaction is dominated by orbital, rather than electrostatic, considerations. The HOMO of stabilized enolates has a large coefficient on the
central carbon atom while the LUMO of many alpha, beta unsaturated carbonyl compounds has a large coefficient on the beta carbon. Thus, both reactants can be considered soft. These polarized frontier orbitals are of similar energy, and react efficiently to form a new carbon–carbon bond.

Like the aldol addition, the Michael reaction may proceed via an enol, silyl enol ether in the Mukaiyama-Michael addition, or more usually, enolate nucleophile. In the latter case, the stabilized carbonyl compound is deprotonated with a strong base (hard enolization) or with a Lewis acid and a weak base (soft enolization). The resulting enolate attacks the activated olefin with 1,4-regioselectivity, forming a carbon–carbon bond. This also transfers the enolate to the electrophile. Since the electrophile is much less acidic than the nucleophile, rapid proton transfer usually transfers the enolate back to the nucleophile if the product is enolizable; however, one may take advantage of the new locus of nucleophilicity if a suitable electrophile is pendant. Depending on the relative acidities of the nucleophile and product, the reaction may be catalytic in base. In most cases, the reaction is irreversible at low temperature.

4.2.2 Gilman Reagent

A Gilman reagent is a lithium and copper (diorganocopper) reagent compound, R₅CuLi, where R is an alkyl or aryl. These reagents are useful because, unlike related Grignard reagents and organolithium reagents, they react with organic halides to replace the halide group with an R group (the Corey-House reaction). Such displacement reactions allow for the synthesis of complex products from simple building blocks.

\[
\begin{align*}
\text{R} & \rightarrow \text{Cu} \oplus \text{Li} \\
\text{R} & \rightarrow \text{Li} \\
\text{R} \rightarrow \text{Cu} + \text{R} \rightarrow \text{Li} + \\
\end{align*}
\]

**Fig. 4.1 General structure of a Gilman reagent**

Generalized chemical reaction showing Gilman reagent reacting with organic halide to form products and showing Cu(III) reaction intermediate

These reagents were discovered by Henry Gilman and coworkers. Lithium dimethylcopper (CH₃)₂CuLi can be prepared by adding copper(I) iodide to methyl lithium in tetrahydrofuran at –78 °C. In the reaction depicted below, the Gilman reagent is a methyliating reagent reacting with an alkyne in a conjugate addition, and the negative charge is trapped in a nucleophilic acyl substitution with the ester group forming a cyclic enone.
Structure
Lithium dimethylcuprate exists as a dimer in diethyl ether forming an 8-membered ring. Similarly, lithium diphenylcuprate crystallizes as a dimeric etherate, $\text{[Li(OEt$_2$)$_2$]}(\text{CuPh$_2$})_2$.

![Structure of Lithium dimethyl cuprate](image)

*Fig. 4.2 Structure of Lithium dimethyl cuprate*

If the Li$^+$ ions are complexed with the crown ether 12-crown-4, the resulting diorganocuprate anions adopt a linear coordination geometry at copper.

![Linear coordinate Geometry at copper](image)

*Fig. 4.3 Linear coordinate Geometry at copper*

Mixed Cuprates
More useful generally than the Gilman reagents are the so-called mixed cuprates with the formula $[\text{RCuX}]^-$ and $[\text{R}_2\text{CuX}]^-$, such compounds are often prepared by the addition of the organolithium reagent to copper(I) halides and cyanide. These mixed cuprates are more stable and more readily purified. One problem addressed by mixed cuprates is the economical use of the alkyl group. Thus, in some applications, the mixed cuprate has the formula $\text{Li}([\text{Cu}(\text{2-thienyl})(\text{KCN})\text{R}])$ is prepared by combining thienyllithium and cuprous cyanide followed by the organic group to be transferred. In this higher order mixed cuprate, both the cyanide and thienyl groups do not transfer, only the R group does.

Conjugate Addition of Gilman Reagents
Gilman reagents (lithium dialkylcuprates) can be used to carry out nucleophilic addition upon $\alpha,\beta$ unsaturated carbonyl compounds, adding an alkyl group to the $\beta$-carbon. This is a useful reaction for organic synthesis.
4.2.3 Diels-Alder Reaction

The Diels-Alder reaction is a conjugate addition reaction of a conjugated diene to an alkene (the dienophile) to produce a cyclohexene. The simplest example is the reaction of 1,3-butadiene with ethene to form cyclohexene:

\[
\begin{align*}
\text{CH}_2=CH-CH=CH_2 & \quad \text{+} \quad \text{CH}_2=CH_2 \\
\text{Butadiene} & \quad \text{+} \quad \text{Ethene} \\
\text{Cyclohexene} & \quad \text{+} \quad \text{Heat}
\end{align*}
\]

The analogous reaction of 1,3-butadiene with ethyne to form 1,4-cyclohexadiene is also known:

\[
\begin{align*}
\text{CH}_2=CH-CH=CH_2 & \quad \text{+} \quad \text{HC}≡\text{CH} \\
\text{Butadiene} & \quad \text{+} \quad \text{Acetylene} \\
\text{1,4-Cyclohexadiene} & \quad \text{+} \quad \text{Heat}
\end{align*}
\]

Since the reaction forms a cyclic product, via a cyclic transition state, it can also be described as a "cycloaddition". The reaction is a concerted process:

\[
\begin{align*}
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H}
\end{align*}
\]

Due to the high degree of regio- and stereoselectivity (due to the concerted mechanism), the Diels-Alder reaction is a very powerful reaction and is widely used in synthetic organic chemistry. The reaction usually thermodynamically favourable due to the conversion of 2 \(\pi\)-bonds into 2 new stronger \(\sigma\)-bonds. The two reactions shown above require harsh reaction conditions, but the normal Diels-Alder reaction is favoured by electron withdrawing groups on the electrophilic dienophile and by electron donating groups on the nucleophilic diene.
Some common examples of the components are shown below:

Check Your Progress
1. What are the examples of electrophilic addition reactions?
2. What is the effect of electron donating substituents on the rate of reactions?
3. What is peroxide effect?
4. What is used to locate the position of double bonds in olefins?

4.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS
1. The examples are hydration and hydrogenation of olefins, additions of halogens and halogen acids to olefins and ozonolysis.
2. Electron donating substituents will increase the rate of reaction whereas electron withdrawing substituents will decrease it.
3. Anti-Markovnikov addition of HBr to olefins is also observed if peroxides or elemental oxygen are present in the reaction mixture. This is known as kharasch effect or peroxide effect.
4. Ozonolysis.

4.4 SUMMARY
- The electrophilic addition reactions are observed in alkenes, alkynes and conjugated systems and essentially mean the addition of a molecule to the double bond. Thus if a reagent breaks up to give a negative and a positive ion each one of these are added to double bond.
- When a halogen molecule or hypohalous acid reacts with olefin the bond is polarised by electromeric shift. The positively polarised halogen attacks and combines with the carbon carrying the pair of electrons after electromeric shift. A cyclic halonium ion is formed which prevents cis-addition of OH. Then the completion of addition occurs by a trans combination of a bromide or hydroxide ion.
- Markovnikov in 1869 gave a generalization which is known as Markovnikov’s rule. According to this rule “the negative part of the
addendum (reagent which is adding) goes to the carbon atom, constituting the double bond, which is poorer in hydrogen.”

- Anti-Markovnikov addition of HBr to olefins is also observed if peroxides or elemental oxygen are present in the reaction mixture. This is known as kharasch effect or peroxide effect.
- Reaction of diborane (B₂H₆) with an olefinic double bond to produce alkylboranes is termed as Hydroboration (H.C. Brown). In the reaction diborane behaves as if it were its non-existent monomer borane (BH₃).
- Addition of a molecule of water to olefins is known as hydration reaction. Hydration of olefins in acidic media results in the formation of alcohols.
- Addition of ozone to olefinic linkage resulting in the formation of ozonide, which on subsequent hydrogenation gives carbonyl compounds, is known as ozonolysis.
- The Michael reaction or Michael addition is the nucleophilic addition of a carbanion or another nucleophile to an α,β-unsaturated carbonyl compound. It belongs to the larger class of conjugate additions. This is one of the most useful methods for the mild formation of C–C bonds.
- A Gilman reagent is a lithium and copper (diorganocopper) reagent compound, R₂CuLi, where R is an alkyl or aryl. These reagents are useful because, unlike related Grignard reagents and organolithium reagents, they react with organic halides to replace the halide group with an R group (the Corey-House reaction).
- The Diels-Alder reaction is a conjugate addition reaction of a conjugated diene to an alkene (the dienophile) to produce a cyclohexene.

4.5 KEY WORDS

- **Carbon–carbon bond**: A carbon–carbon bond is a covalent bond between two carbon atoms.
- **Electrophilic addition**: The electrophilic addition reactions are observed in alkenes, alkynes and conjugated systems and essentially mean the addition of a molecule to the double bond.

4.6 SELF ASSESSMENT QUESTIONS AND EXERCISES

**Short Answer Questions**

1. Why the reaction is known as an electrophilic addition when both the electrophile and the nucleophile are adding to the same double bond?

2. What is the difference between trans-additions and cis-additions?
3. Discuss the addition of halogens to olefins.
4. What is Michael reaction?
5. What do you understand by conjugate addition of Gilman reagents?

**Long Answer Questions**

1. Discuss the mechanism of addition of (a) HI (b) Br₂, and (c) HOCl to propene.
2. Discuss the mechanism and predict the products from the reaction of bromine with propene dissolved in methanol containing lithium chloride.
3. State and illustrate ‘Markownikoff’s rule’ and ‘peroxide effect’ taking example of the addition of HBr to propene.
4. Discuss the examples of Diels-Alder reaction.
5. Discuss the mechanism of Michael reaction.
6. Give the electronic mechanism of the following:
   (a) Hydroboration of olefins
   (b) Hydration of olefins
   (c) Ozonolysis

**4.7 FURTHER READINGS**


UNIT 5  ADDITION TO CARBON-HETERO MULTIPLE BOND

NOTES

Structure

5.0 Introduction
5.1 Objectives
5.2 Addition to Carbon-Hetero Multiple Bond
5.3 Answers to Check Your Progress Questions
5.4 Summary
5.5 Key Words
5.6 Self Assessment Questions and Exercises
5.7 Further Readings

5.0 INTRODUCTION

Nucleophilic addition reactions of nucleophiles with electrophilic double or triple bond (π bonds) create a new carbon center with two additional single, or σ, bonds. Addition of a nucleophile to carbon–heteroatom double or triple bonds such as >C=O or -C≡N show great variety. These types of bonds are polar (have a large difference in electronegativity between the two atoms); consequently, their carbon atoms carries a partial positive charge. This makes the molecule an electrophile, and the carbon atom the electrophilic center; this atom is the primary target for the nucleophile. Chemists have developed a geometric system to describe the approach of the nucleophile to the electrophilic center, using two angles, the Bürgi-Dunitz and the Flippin-Lodge angles after scientists that first studied and described them.

In this unit, you will study about addition to carbon-hetero multiple bond.

5.1 OBJECTIVES

After going through this unit, you will be able to:

• Understand addition to carbon-hetero multiple bond
• Know about various condensation reactions and their mechanism

5.2 ADDITION TO CARBON-HETERO MULTIPLE BOND

Unlike the carbon to carbon multiple bonds, the carbon to oxygen double bonds are highly polarized because of greater electronegativity of oxygen atom. The π electrons are shifted towards oxygen atom by simple electromeric effect at the
requirement of the attacking reagent. The carbon thus acquires a positive charge and becomes more susceptible to attack by electron rich nucleophiles. On the other hand, oxygen is attacked by electron deficient electrophiles completing the addition reaction. The product wherever possible undergoes elimination of water molecules to result in the double bond (see condensation reactions) formation.

\[
\text{Nucleophile} \quad \overset{\cdot}{\text{C}}\overset{\cdot}{\text{O}} \quad \overset{\cdot}{\text{X}}^{-} \quad \overset{\cdot}{\text{C}}\overset{\cdot}{\text{O}} \quad \overset{\cdot}{\text{X}} \quad \overset{\cdot}{\text{H}}^{+} \quad \overset{\cdot}{\text{C}}\overset{\cdot}{\text{O}} \quad \overset{\cdot}{\text{X}}^{+}
\]

The above scheme shows a simple nucleophilic addition of a nucleophile X to > C=O groups. At the approach of X- the \(\pi\) electrons are shifted towards oxygen by electroneric shift. The nucleophile combines with the positively charged carbon to yield anion which then takes up a proton or electrophile at oxygen to give the end product.

**Structure and reactivity.** Since the nucleophilic addition involves the addition of nucleophile to positively charged carbon, the reactivity of this carbon depends on the magnitude of this charge. The order of reactivity of some carbonyl compounds decreases in the order given below:

\[
\overset{\cdot}{\text{H}} \overset{\cdot}{\text{C}}\overset{\cdot}{\text{O}} \quad \overset{\cdot}{\text{H}} \overset{\cdot}{\text{C}}\overset{\cdot}{\text{O}} \quad \overset{\cdot}{\text{R}} \overset{\cdot}{\text{C}}\overset{\cdot}{\text{O}} \quad \overset{\cdot}{\text{R'}} \overset{\cdot}{\text{C}}\overset{\cdot}{\text{O}} \quad \overset{\cdot}{\text{R}} \overset{\cdot}{\text{C}}\overset{\cdot}{\text{O}} \quad \overset{\cdot}{\text{R}}
\]

Formaldehyde | Aldehyde | Ketones | Ethers | Amides | k-type

The electron donating groups (with +I effect) reduce the reactivity of the positively charged carbon in the above examples which is reflected in the order shown above. The resonance effect due to lone pair at adjacent hetero atoms as in amide etc., also contribute to decreased reactivity. The presence of bulky groups also decrease the reactivity of the positively charged carbon due to crowding around the carbon. On the other hand, electron withdrawing group (with –I effect) tend to increase its reactivity. Thus chloral (CCl, CHO) because of the –I effect due to three chlorine atoms is highly susceptible to nucleophilic additions—so much so that it can react with a very weak nucleophile like water to form a stable compound chloral hydrate.
Thus percentage hydration gives a complete idea regarding the reactivity of the >C＝O group. The percentage hydration of some compounds is as follows:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Hydration %</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCHO</td>
<td>99</td>
</tr>
<tr>
<td>CH₃CHO</td>
<td>58</td>
</tr>
<tr>
<td>CH₃COCH₃</td>
<td>0</td>
</tr>
</tbody>
</table>

Polar solvents, acids and bases catalyze nucleophilic addition reactions.

**Applications**

1. **Addition of HCN and NaHSO₃ (sodium bisulphite) to carbonyl group.** The addition of HCN and NaHSO₃ to >C＝O group is a simple nucleophilic addition. HCN combines with >C＝O group in the presence of basic catalysts to give corresponding cyano-hydrin. The base helps in dissociating HCN to H⁺ and CN⁻ ions. At the approach of CN⁻ the π electrons undergo electromeric shift towards oxygen. The cyanide ion then combines with carbon of the >C＝O group to give an anion (I) which then combines with an electrophile H⁺ to give cyano-hydrin.

\[
\text{HCN} \rightarrow H^+ + CN^- \\
\text{R-C-H} + \text{CN}^- \rightarrow \text{R-O-H} \quad \text{OH} \\
\]

Addition of sodium bisulphite to carbonyl group occurs in the absence of acids or bases because sodium bisulphite readily ionizes to give bisulphite anion nucleophile which then adds to carbon of carbonyl group resulting in anion (I). The (I) then rearranges by migration of a hydrogen from —SO₂H group to negatively charged oxygen to give anion (II) which then combines with sodium ion to give bisulphite addition product.

\[
\text{NaHSO}_3 \rightarrow \text{Na}^+ + \text{HSO}_3^- \\
\text{R-C-R' \rightarrow HSO}_3^- o_{\text{slow}} \rightarrow \text{R-OH} \rightarrow \text{R-C-R' \rightarrow SO}_2H \quad \text{SO}_2^\text{O} \quad \text{SO}_2\text{Na} \\
\]

2. **Addition of ammonia and amine derivatives to carbonyl group.** Ammonia and its derivatives like R—NH₂ (amines), NH₂OH (hydroxylamine), NH₂CO.NH₂ (semicarbazide), and NH₂.NH₂ (hydrazine) etc., add to carbonyl group by a nucleophilic addition mechanism. The addition is catalyzed by acids and also by bases. The following general mechanism may be written for these reactions.
Amine derivatives act as nucleophiles because of the presence of the lone pair of electrons at nitrogen. At the approach of these reagents, a electron pair is shifted to oxygen by electromeric effect and the lone pair of nitrogen co-ordinates with electron deficient carbon to give a dipolar intermediate. This then rearranges by migration of proton from nitrogen to oxygen carrying the negative charge. Finally the addition is followed by elimination of a molecule of water to result in a carbon to nitrogen double bond.

The reaction of ammonia is different with different carbonyl compounds. Thus formaldehyde with ammonia gives hexamethylene tetramine \((\text{CH}_2)_6\text{N}_4\); acetaldehyde and other aldehydes give aldehyde ammonia \(R\text{CH}(\text{OH})\text{NH}_2\); whereas ketones usually undergo condensation reaction to give complex products.

Products of some of these reactions like oximes, phenyl hydrazones, semicarbazides etc. are useful derivatives of carbonyl compounds helpful in their identifications.

(3) **Hydride transfer reaction.** Reductions of carbonyl compounds by \(\text{LiAIH}_4\) (lithium aluminium hydride) or \(\text{NaBH}_4\) (sodium borohydride) are in essence nucleophilic additions of a hydride ion to the carbon atom. \(\text{LiAIH}_4\) dissociates to give \(\text{AIH}_3\), which acts as a carrier of hydride ion. The reduction of ketones and esters may be represented as given below:

\[
\begin{align*}
\text{Ketone} & & \text{Aldehyde} \\
R\text{C} = \text{O} & \rightarrow & R\text{CH} \rightarrow R\text{C} \rightarrow R\text{CH}
\end{align*}
\]

These reagents react with hydroxylic solvents so the reduction is carried out in either ether or tetrahydrofuran (THF). The reaction is specific for the reduction of aldehydes, ketones, acids and esters to alcohols.

(4) **Aldol condensation.** When aldehydes and ketones having \(\alpha\)-hydrogen atoms are treated with alkali, they undergo self-addition between two molecules to form a \(\beta\)-hydroxy aldehyde or \(\beta\)-hydroxy ketone (known as aldols). This addition is usually followed by elimination of a water molecule resulting in overall condensation reaction. The reaction is therefore known as **Aldol condensation reaction.** Essentially this is a nucleophilic addition of a carbanion, generated by the abstraction of a proton from \(\alpha\)-position of an aldehyde or ketone by a base, to the carbonyl

\[
\begin{align*}
\text{Formaldehyde} & & \text{Aldol} \\
1\text{C} = \text{O} & \rightarrow & \text{RCHCH}_2\text{OH}
\end{align*}
\]
group. The reaction can occur between two or more molecules of same or different aldehyde or ketone, and between one or more molecules each of an aldehyde and a ketone. Also an aldehyde or ketone having no α-hydrogen atom may condense with another aldehyde or ketone having α-hydrogen atoms. Some examples are given below to illustrate this point.

(i) CH₃CHO + CH₃CHO \rightarrow CH₃CHO + CH₃CHO

Araldehyde (2 mol) \[\text{[4-hydroxy butyraldehyde (Aldol)]]

(ii) CH₃COCH₃ + CH₃COCH₃ \rightarrow CH₃CH₂COCH₃

Acetone \[\text{(4-hydroxy-4-methyl-2-pentanone)}

(iii) CH₃CHO + CH₃COCH₃ \rightarrow CH₃CH₂COCH₃

Araldehyde \[\text{Acetone} \rightarrow \text{4-hydroxy-2-pentanone}

(iv) CH₃CHO + CH₃CH₂CHO \rightarrow CH₃CH₂CHO

Araldehyde \[\text{Propionaldehyde \[\text{α-Methyl-4-hydroxy butyraldehyde]}\]

As seen in the above examples, in crossed aldol condensations the carbonyl group of aldehydes is more reactive than carbonyl group of ketones. Thus the aldol formation involves carbonyl group of aldehyde and α-hydrogen of ketone. Similarly when condensation is between two aldehydes the α-hydrogen comes from aldehyde having bigger alkyl group.

Reaction between two molecules of an aldehyde, not having α-hydrogen atoms, in presence of alkali, results in Cannizzaro’s reaction. Thus formaldehyde reacts with NaOH to form a mixture of methyl alcohol and sodium formate.

Generally accepted mechanism for aldol condensation may be written as below:

(i) \text{NaOH} \rightarrow \text{Na}^+ + \text{OH}^-

\begin{align*}
\text{OH}^- + \text{CH₃CHO} & \rightarrow \text{CH₃CH₂CO} + \text{H} \\
\text{Carbonylation (i)}
\end{align*}

(ii) \text{R} \rightarrow \text{R} + \text{CH₃CHO} \rightarrow \text{R} + \text{CH₃CHO} \rightarrow \text{R} + \text{CH₃CHO} + \text{OH}^-

\begin{align*}
\text{Aldol}
\end{align*}
In the first step the alkali gives OH⁻ ions which abstracts a proton from the π-position of the carbonyl group to form a carbanion (I). This carbanion attacks the carbonyl group of other molecule causing electromeric shift of π electrons and adds to the electron deficient carbon of the carbonyl group giving anion (II). This anion then takes up a proton from water to form aldol. Usually the aldol undergoes dehydration reaction (elimination of a molecule of water) to form α,β-unsaturated aldehyde or ketone in presence of acids and bases.

However the reaction does not stop here because the aldol is still having a free carbonyl group. It can add another molecule of aldehyde or ketone having α-hydrogen atoms to give a more complex aldol. Thus

\[
\begin{align*}
  &\text{OH} \\
  &\text{R—CH—CH₂ CHO + CH₂ CHO} \xrightarrow{\text{OH}} \text{R—CH—CH—CH₂ CHO} \\
  &\xrightarrow{-\text{H₂O}} \\
  &\text{R—CH—CH—CHO} + \text{CH₂ CHO} \xrightarrow{\text{OH}} \text{R—CH—CH—CH₂ CHO} \\
  &\xrightarrow{-\text{H₂O}} \\
  &\text{R—CH—CH—CHO + CH₂ CHO} \xrightarrow{\text{OH}} \text{R—CH—CH—CH—CHO}
\end{align*}
\]

Condensation Reactions

The term condensation has been used to describe a wide variety of organic reactions resulting in the lengthening of the carbon skeleton of the molecule. However it may be defined as a reaction (through functional groups) between two or more molecules of the same or different compounds resulting in the formation of new carbon to carbon bonds with or without the elimination of simple molecules like water, alcohol, metallic halides etc. However, the term condensation has been used rather loosely in organic chemistry and often includes the formation of other bonds besides carbon to carbon.

There can be two types of condensation reactions:

1. **Intramolecular Condensation.** When the two functional groups of the same molecule react to eliminate a simple molecule the reaction is known as Intramolecular condensation for example, formation of a γ-lactone from γ-hydroxybutyric acid.

\[
\begin{align*}
  &\text{O—H} \xrightarrow{\Delta} \text{HO} \\
  &\text{CH₂—CH₂—CH₂—C=O} \xrightarrow{\Delta} \text{CH₂—CH₂—CH₂—C=O} \\
  &\gamma\text{-hydroxybutyric acid} \xrightarrow{\Delta} \gamma\text{-butyrolactone}
\end{align*}
\]

2. **Intermolecular Condensation.** The condensation reaction between two molecules of the same or different compounds is known as Intermolecular condensation. Thus two molecules of acetaldehyde condense in presence of sodium hydroxide to give aldol.
The reaction is called aldol condensation.

A large number of intermolecular condensation reactions are observed between similar or different carbonyl compounds. Important reactions of this class are Aldol condensation, Claisen condensation, Benzoin condensation and Perkin reaction.

(i) Claisen Condensation

\[
\text{CH}_3\text{CHO} + \text{HCH}_2\text{CHO} \rightarrow \text{H}_2 \text{Na} \rightarrow \text{CH}_3\text{CH}(\text{OH})\text{CH}_2\text{CHO}
\]

Claisen (1887) observed that when esters having hydrogens at \(\alpha\)-carbon atoms are treated with sodium alkoxides, they are transformed to \(\beta\)-keto esters. Such condensations between two molecules of esters having \(\alpha\)-hydrogen atoms in the presence of a base, resulting in the formation of a compound having reactive methylene group, are known as Claisen condensation reactions. The following mechanism has been suggested for the reaction:

(a) Reaction of sodium with ethyl alcohol gives ethoxide ion which acts as a base:

\[
2\text{C}_2\text{H}_5\text{OH} + 2\text{Na} \rightarrow 2\text{C}_2\text{H}_5\text{ONa} + \text{H}_2
\]

\[
\text{C}_2\text{H}_5\text{ONa} \rightarrow \text{C}_2\text{H}_5\text{O}^- + \text{Na}^+
\]

(b) The ethoxide ion, so formed, abstracts a proton form the \(\alpha\)-carbon of the esters like ethyl acetate to give a carbanion

\[
\text{H}_3\text{C} \equiv \text{CH} + \text{H}_3\text{C} \equiv \text{CO} \text{CH}_2\text{OH} \rightarrow \text{CH}_3\text{CH} \equiv \text{CO} \text{CH}_2\text{OH} \rightarrow \text{CH}_3\text{CH} \equiv \text{CO} \text{CH}_2\text{Oh}
\]

(c) This carbanion induces the electromeric shift in the carbonyl group of the other ester molecule. As a result of this shift, the carbon atom of carbonyl group acquires a positive charge and the carbanion combines with it to give an anion.

\[
\text{CH}_3\text{CH} \equiv \text{CO} \text{CH}_2\text{OH} \rightarrow \text{CH}_3\text{CH} \equiv \text{CO} \text{CH}_2\text{O}^{-}
\]

(d) As the attacking reagent, i.e., carbanion is removed by addition, the electron pair which has shifted to oxygen because of electromeric effect, reverts back to form a double bond and the ethoxide ion is expelled with its pair of electrons.
Ethyl acetoacetate

On acidification with acetic acid it is converted to a tautomeric mixture of the two forms of ethyl acetoacetate

![Keto form](image)

![Enol form](image)

Claissen condensation can be carried out between different esters also when a mixture of different products is obtained. The reaction may also be extended to the condensations between esters and carbonyl compounds like ketones etc. Thus:

![Ethyl acetoacetate](image)

Methyl ethyl ketone

\[ \text{CH}_2=CHC_2H_4 + \text{H}_2\text{C}==\text{CHC}_2H_5 \rightarrow \text{NaC}_2\text{H}_2\text{O} \rightarrow \text{CH}_2=\text{CHC}_2\text{H}_4 \text{C}_2\text{H}_5 \]

(ii) Benzoin condensation

Aromatic aldehydes like benzaldehyde, furfural etc., when treated with ethanolic potassium cyanide and refluxed, undergo dimerization to form keto-alcohols. Since benzaldehyde forms benzoin by condensation of its two molecules, the reaction is known as benzoin condensation. Furfural, on benzoin condensation, forms furoin.

\[ 2\text{C}_8\text{H}_6\text{CHO} \overset{\text{KCN}}{\rightarrow} \text{C}_8\text{H}_6\text{C}==\text{CH(OH)}\text{C}_6\text{H}_5 \]

Benzaldehyde

Furfural

\[ \text{CHO} \]

Furoin

Nitro and hydroxy benzaldehydes and cinnamaldehyde do not undergo benzoin condensation, while halo- and \( p \)-dimethylamino benzaldehydes give only poor yields of benzoins. Though anisaldehyde is unreactive towards self-condensation, it, however, forms 4-methoxy benzoin in 70 per cent yield, when condensed with benzaldehyde:

\[ \text{CHO} + \text{CHO} \overset{\text{KCN}}{\rightarrow} \text{CHO} \]

Aminobenzaldehyde

4-Methoxy benzoin

Relatively only a few examples of benzoin type of condensation are known in aliphatic compounds. When there are \( \alpha \)-hydrogen atoms, the aldol condensation
proceeds in the presence of basic cyanide in forming analogous compounds, R.CO.CHOH.R., known as acyloins, which are usually prepared by the condensation of esters in an inert medium in the presence of metallic sodium. Sodium salts of enediols on subsequent hydrolysis form acyloins.

**Mechanism**

Lapworth was the first to point out that the reaction is not a simple aldol type condensation, as it is not catalysed by ordinary bases but rather specifically by alkali cyanides. He proposed that the first step in the benzoin condensation is the addition of cyanide ion to the aldehyde, followed by proton transfer to form cyanohydrin. Since the cyanohydrin contains hydrogen at-α carbon to the cyanide group, it can undergo base catalysed addition to the carbonyl group of a second aldehyde molecule. Cyanohydrin of benzoin thus formed then loses a molecule of HCN to form benzoin.

\[
\begin{align*}
  &\text{C}_2\text{H}_4\text{O}_2H \xrightarrow{\text{NaCN}} \text{C}_2\text{H}_4\text{OH} + \text{HCN} \\
  &\text{C}_2\text{H}_4\text{OH} + \text{C}_2\text{H}_4\text{OH} \xrightarrow{\text{H}^+} \text{C}_2\text{H}_4\text{OH} + \text{C}_2\text{H}_4\text{H}_2
\end{align*}
\]

The carbanion intermediate is resonance stabilised and is formed preferentially from the cyanohydrin.

Applications

Benzoin condensation is used for the preparation of keto-alcohols of the aromatic series of the type of benzoin. It is also used as the first step in the preparation of benzil and benzoic acid from benzaldehyde.

\[
\begin{align*}
  2\text{C}_2\text{H}_4\text{O}_2H &\xrightarrow{\text{EN}} \text{C}_2\text{H}_5\text{C}_6\text{H}_4\text{CHOH}\text{C}_2\text{H}_5 \\
  \text{C}_2\text{H}_5\text{C}_6\text{H}_4\text{CHOH}\text{C}_2\text{H}_5 &\xrightarrow{\text{H}^+} \text{C}_2\text{H}_5\text{C}_6\text{H}_4\text{COH}
\end{align*}
\]
**(iii) Perkin Reaction**

In 1867 W.H. Perkin observed that when aromatic aldehydes are heated with the anhydride of an aliphatic acid in the presence of the sodium salt of the same acid, an \( \alpha, \beta \) unsaturated acid is formed. The reaction is known as **Perkin reaction** and is shown mainly by aromatic aldehydes. For example benzaldehyde, when heated with acetic anhydride in the presence of sodium acetate, forms cinnamic acid.

\[
\text{C}_6\text{H}_5\text{CHO} + \text{(CH}_2\text{CO})_2\text{O} \xrightarrow{\text{CH}_3\text{COONa}} \text{170-175°C} \quad \text{C}_6\text{H}_5\text{CH}==\text{CHCOOH} + 2\text{CH}_3\text{COOH}
\]

Similarly

\[
\text{C}_6\text{H}_5\text{CHO} + \text{(CH}_2\text{CH}_2\text{CO})_2\text{O} \xrightarrow{\text{CH}_3\text{CH},\text{CH}_2\text{COONa}} \text{C}_6\text{H}_5\text{CH}==\text{C.COOH} \quad \text{α-Methyl cinnamic acid}
\]

\[+ \text{2CH}_3\text{CH}_2\text{COOH}\]

Substituted benzaldehydes also undergo Perkin reaction and it has been noticed that substituents affect the yields of substituted cinnamic acids. The electron-withdrawing substituents increase the yield of the substituted cinnamic acids, while electron-releasing groups decrease it. Table 5.1 illustrates the point.

**Table 5.1**

<table>
<thead>
<tr>
<th>Substituent</th>
<th>Yield %</th>
<th>Substituent</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>45-50</td>
<td>4-Chloro</td>
<td>71</td>
</tr>
<tr>
<td>2-Chloro</td>
<td>63</td>
<td>3-Chloro</td>
<td>75</td>
</tr>
<tr>
<td>3-Chloro</td>
<td>52</td>
<td>4-Chloro</td>
<td>75</td>
</tr>
<tr>
<td>2-Nitro</td>
<td>2-Nitro</td>
<td>3-Nitro</td>
<td>2-Nitro</td>
</tr>
</tbody>
</table>

Salicylaldehyde, phthalic anhydride and furfural also undergo Perkin reaction.

1. \[
\text{CH}_3\text{CO} + \text{(CH}_2\text{CO})_2\text{O} \xrightarrow{\text{CH}_3\text{COONa}} \text{360°} \quad \text{CH}_3\text{CO} + \text{2CH}_3\text{COOH}
\]

2. \[
\text{Phthalic anhydride} + \text{(CH}_2\text{CO}_2\text{O} \xrightarrow{\text{CH}_3\text{COOK}} \text{150-200°} \quad \text{C}_6\text{H}_5\text{CH}==\text{CHCOOH} + 2\text{CH}_3\text{COOH}
\]
Mechanism

Perkin believed that it is an aldol type addition of anhydride to aromatic aldehydes, whereas Fittig argued that it is the carboxylate anion that adds to aldehydes. However, the present view is that carboxylate anion abstracts a proton from the α-carbon of the anhydride forming a carbanion I. This carbanion undergoes nucleophilic addition at carbonyl carbon of the aldehyde. The anion (II) so formed takes up a proton to form a hydroxy compound (III), which first undergoes dehydration in the presence of anhydride and then in the presence of acid, hydrolyses to form an α, β-unsaturated acid.

(i) \( \text{CH}_2\text{COONa} \xrightarrow{\text{H}^+} \text{CH}_2\text{COO}^- \)

\[ \xrightarrow{\text{NaCH}_2\text{COO} + \text{H}^+ \text{CH}_2\text{C}=\text{O} \xrightarrow{\text{H}^+} \text{CH}_2\text{COOH} + \text{CH}_2\text{C}^- \]

(ii) \( \text{C}_6\text{H}_5\text{CHO} + \text{CH}_2\text{COO}^- \xrightarrow{\text{H}^+} \text{C}_6\text{H}_5\text{COO}^-\text{CO.CH}_3 \)

\[ \xrightarrow{\text{H}^+ \text{(then CH}_2\text{COOH)}} \text{C}_6\text{H}_5\text{CH}^-\text{COO}^-\text{CO.CH}_3 \]

(iii) \( \text{C}_6\text{H}_5\text{CHO} + \text{H}_2\text{O} \xrightarrow{\text{H}_2\text{O}} \text{C}_6\text{H}_5\text{CH}^-\text{COO}^-\text{CO.CH}_3 \)

\[ \xrightarrow{\text{H}_2\text{O}} \text{C}_6\text{H}_5\text{CH}^-\text{COO}^-\text{CO.CH}_3 \]

Applications

Perkin reaction is not only useful in the synthesis of α,β-unsaturated acids like cinnamic acid, but is also employed for the synthesis of coumarin used in perfumery.
Knoevenagel Condensation

The Knoevenagel condensation reaction is an organic reaction named after Emil Knoevenagel. It is a modification of the aldol condensation. A Knoevenagel condensation is a nucleophilic addition of an active hydrogen compound to a carbonyl group followed by a dehydration reaction in which a molecule of water is eliminated (hence condensation). The product is often an α,β-unsaturated ketone (a conjugated enone).

\[
\begin{align*}
\text{R} & \quad \text{R} \\
\text{O} & \quad -\text{H}_2\text{O}
\end{align*}
\]

In this reaction the carbonyl group is an aldehyde or a ketone. The catalyst is usually a weakly basic amine. The active hydrogen component has the form

- \(Z-\text{CH}_2-Z\) or \(Z-\text{CHR}_2-Z\) for instance diethyl malonate, Meldrum’s acid, ethyl acetoacetate or malonic acid, or cyanoacetic acid.
- \(Z-\text{CHR}R_2\) for instance nitromethane.

where \(Z\) is an electron withdrawing functional group. \(Z\) must be powerful enough to facilitate deprotonation to the enolate ion even with a mild base. Using a strong base in this reaction would induce self-condensation of the aldehyde or ketone. The Hantzsch pyridine synthesis, the Gewald reaction and the Feist–Benary furan synthesis all contain a Knoevenagel reaction step. The reaction also led to the discovery of CS gas.

Mannich Reaction

The Mannich reaction is an organic reaction which consists of an amino alkylation of an acidic proton placed next to a carbonyl functional group by formaldehyde and a primary or secondary amine or ammonia. The final product is a β-amino-carbonyl compound also known as a Mannich base. Reactions between aldimines and \(\alpha\)-methylen carbonyls are also considered Mannich reactions because these imines form between amines and aldehydes. The reaction is named after chemist Carl Mannich.

\[
\begin{align*}
\text{R} & \quad \text{R} \\
\text{N} & \quad \text{H} \\
\text{H} & \quad -\text{H}_2\text{O}
\end{align*}
\]

The Mannich reaction is an example of nucleophilic addition of an amine to a carbonyl group followed by dehydration to the Schiff base. The Schiff base is an electrophile which reacts in the second step in an electrophilic addition with a compound containing an acidic proton (which is, or had become an enol). The Mannich reaction is also considered a condensation reaction.
In the Mannich reaction, primary or secondary amines or ammonia, are employed for the activation of formaldehyde. Tertiary amines lack an N–H proton to form the intermediate enamine. α-CH-acidic compounds (nucleophiles) include carbonyl compounds, nitriles, acetylenes, aliphatic nitro compounds, α-alkyl-pyridines or imines. It is also possible to use activated phenyl groups and electron-rich heterocycles such as furan, pyrrole, and thiophene. Indole is a particularly active substrate; the reaction provides gramine derivatives.

**Reaction Mechanism**

The mechanism of the Mannich reaction starts with the formation of an iminium ion from the amine and the formaldehyde.

The compound with the carbonyl functional group (in this case a ketone) can tautomerize to the enol form, after which it can attack the iminium ion.

**Dieckmann Condensation**

Dieckmann condensation is the intramolecular chemical reaction of diesters with base to give β-keto esters. It is named after the German chemist Walter Dieckmann (1869–1925). The equivalent intermolecular reaction is the Claisen condensation.
Reaction Mechanism

Deprotonation of an ester at the α-position generates an enolate ion which then undergoes a 5-exo-trig nucleophilic attack to give a cyclic enol. Protonation with a Bronsted-Lowry acid (H₂O⁺ for example) re-forms the β-keto ester.

Due to the steric stability of five- and six-membered rings, these structures will preferentially be formed. 1,6 diesters will form five-membered cyclic β-keto esters, while 1,7 diesters will form six-membered β-keto esters.

Darzens Reaction

The Darzens reaction (also known as the Darzens condensation or glycidic ester condensation) is the chemical reaction of a ketone or aldehyde with an α-haloester in the presence of a base to form an α,β-epoxy ester, also called a "glycidic ester". This reaction was discovered by the organic chemist Auguste George Darzens in 1904.

Reaction Mechanism

The reaction process begins when a strong base is used to form a carbanion at the halogenated position. Because of the ester, this carbanion is a resonance-stabilized enolate, which makes it relatively easy to form. This nucleophilic structure attacks another carbonyl component, forming a new carbon–carbon bond. These first two steps are similar to a base-catalyzed aldol reaction. The oxygen anion in this aldol-like product then does an intramolecular S_N₂ attack on the formerly-nucleophilic halide-bearing position, displacing the halide to form an epoxide. This reaction sequence is thus a condensation reaction since there is a net loss of HCl when the two reactant molecules join.
The primary role of the ester is to enable the initial deprotonation to occur, and other carbonyl functional groups can be used instead. If the starting material is an α-halo amide, the product is an α,β-epoxy amide. If an α-halo ketone is used, the product is an α,β-epoxy ketone. Any sufficiently strong base can be used for the initial deprotonation. However, if the starting material is an ester, the alkoxide corresponding to the ester side-chain is commonly chosen in order to prevent complications due to potential acyl exchange side reactions.

**Wittig Reaction**

The Wittig reaction or Wittig olefination is a chemical reaction of an aldehyde or ketone with a triphenyl phosphonium ylide (often called a Wittig reagent) to give an alkene and triphenylphosphine oxide.

\[
\begin{align*}
&\text{R}^1\backslash\text{O} - \text{R}^2\backslash\text{O} + \text{Ph}_3\text{P}^+ \rightarrow \text{R}^3\backslash\text{O} - \text{R}^4\backslash\text{O} + \text{Ph}_3\text{P}^+\text{O} \\
&\text{R}^1\backslash\text{O} - \text{R}^2\backslash\text{O} \quad \text{C} - \text{C} - \text{R}^3\backslash\text{O} - \text{R}^4\backslash\text{O} \quad \text{Ph}_3\text{P}^+\text{O}
\end{align*}
\]

The Wittig reaction was discovered in 1954 by Georg Wittig, for which he was awarded the Nobel Prize in Chemistry in 1979. It is widely used in organic synthesis for the preparation of alkenes. It should not be confused with the Wittig rearrangement.

Wittig reactions are most commonly used to couple aldehydes and ketones to singly-substituted triphenylphosphonium ylides. For the reaction with aldehydes, the double bond geometry is readily predicted based on the nature of the ylide. With unstabilised ylides (R^1 = alkyl) this results in (Z)-alkene product with moderate to high selectivity. With stabilized ylides (R^1 = ester or ketone), the (E)-alkene is formed with high selectivity. The (E)/(Z) selectivity is often poor with semistabilized ylides (R^1 = aryl).

To obtain the (E)-alkene for unstabilized ylides, the Schlosser modification of the Wittig reaction can be used. Alternatively, the Julia olefination and its variants also provide the (E)-alkene selectively. Ordinarily, the Horner-Wadsworth-Emmons reaction provides the (E)-enoate (α,β-unsaturated ester), just as the Wittig reaction does. To obtain the (Z)-enoate, the Still-Gennari modification of the Horner-Wadsworth-Emmons reaction can be used.

**Reformatsky Reaction**

The Reformatsky reaction (sometimes spelled Reformatskii reaction) is an organic reaction which condenses aldehydes or ketones, with α-halo esters, using a metallic zinc to form β-hydroxy-esters.
The organozinc reagent, also called a ‘Reformatsky enolate’, is prepared by treating an alpha-halo ester with zinc dust. Reformatsky enolates are less reactive than lithium enolates or Grignard reagents and hence nucleophilic addition to the ester group does not occur. The reaction was discovered by Sergey Nikolaevich Reformatsky.

**Reaction Mechanism**

Zinc metal is inserted into the carbon-halogen bond of the α-haloester by oxidative addition 1. This compound dimerizes and rearranges to form two zinc enolates 2. The oxygen on an aldehyde or ketone coordinates to the zinc to form the six-member chair like transition state 3. A rearrangement occurs in which zinc switches to the aldehyde or ketone oxygen and a carbon-carbon bond is formed 4. Acid workup 5,6 removes zinc to yield zinc(II) salts and a β-hydroxy-ester 7.

**Grignard Reaction**

The Grignard reaction is an organometallic chemical reaction in which alkyl, vinyl, or aryl-magnesium halides (Grignard reagents) add to a carbonyl group in an aldehyde or ketone. This reaction is an important tool for the formation of carbon-carbon bonds. The reaction of an organic halide with magnesium is not a Grignard reaction, but provides a Grignard reagent.

Grignard reactions and reagents were discovered by and are named after the French chemist François Auguste Victor Grignard (University of Nancy, France), who published it in 1900 and was awarded the 1912 Nobel Prize in Chemistry for this work. Grignard reagents are similar to organolithium reagents because both...
are strong nucleophiles that can form new carbon–carbon bonds. The nucleophilicity increases if the alkyl substituent is replaced by an amido group. These amido magnesium halides are called Hauser bases.

**Reaction Mechanism**

The Grignard reagent functions as a nucleophile, attacking the electrophilic carbon atom that is present within the polar bond of a carbonyl group. The addition of the Grignard reagent to the carbonyl typically proceeds through a six-membered ring transition state.

However, with hindered Grignard reagents, the reaction may proceed by single-electron transfer. Similar pathways are assumed for other reactions of Grignard reagents, for example, in the formation of carbon–phosphorus, carbon–tin, carbon–silicon, carbon–boron and other carbon–heteroatom bonds.

---

**Check Your Progress**

1. What is Aldol condensation?
2. What is a condensation reaction?
3. What are the types of condensation reaction?
4. Define Perkin reaction?

---

**5.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS**

1. When aldehydes and ketones having α-hydrogen atoms are treated with alkali, they undergo self-addition between two molecules to form a β-hydroxy aldehyde or β-hydroxy ketone (known as aldols). This addition is usually followed by elimination of a water molecule resulting in overall condensation reaction. The reaction is therefore known as Aldol condensation reaction.

2. A reaction (through functional groups) between two or more molecules of the same or different compounds resulting in the formation of new carbon to carbon bonds with or without the elimination of simple molecules like water, alcohol, metallic halides etc. is known as condensation reaction.

3. There can be two types of condensation reactions: Intramolecular Condensation and Intermolecular Condensation.
4. In 1867 W.H. Perkin observed that when aromatic aldehydes are heated with the anhydride of an aliphatic acid in the presence of the sodium salt of the same acid, an α, β, unsaturated acid is formed. The reaction is known as Perkin reaction and is shown mainly by aromatic aldehydes.

5.4 SUMMARY

- Unlike the carbon to carbon multiple bonds, the carbon to oxygen double bonds are highly polarized because of greater electronegativity of oxygen atom.
- Polar solvents, acids and bases catalyze nucleophilic addition reactions.
- Amine derivatives act as nucleophiles because of the presence of the lone pair of electrons at nitrogen.
- The reaction of ammonia is different with different carbonyl compounds.
- Products of some of these reactions like oximes, phenyl hydrazones, semicarbazides etc. are useful derivatives of carbonyl compounds helpful in their identifications.
- When aldehydes and ketones having α-hydrogen atoms are treated with alkali, they undergo self-addition between two molecules to form a β-hydroxy aldehyde or β-hydroxy ketone (known as aldols). This addition is usually followed by elimination of a water molecule resulting in overall condensation reaction. The reaction is therefore known as Aldol condensation reaction.
- Reaction between two molecules of an aldehyde, not having α-hydrogen atoms, in presence of alkali, results in Cannizzaro’s reaction. Thus formaldehyde reacts with NaOH to form a mixture of methyl alcohol and sodium formate.
- A reaction (through functional groups) between two or more molecules of the same or different compounds resulting in the formation of new carbon to carbon bonds with or without the elimination of simple molecules like water, alcohol, metallic halides etc. is known as condensation reaction.
- There can be two types of condensation reactions: Intramolecular Condensation and Intermolecular Condensation.
- Claisen (1887) observed that when esters having hydrogens at α-carbon atoms are treated with sodium alkoxides, they are transformed to β-keto esters. Such condensations between two molecules of esters having α-hydrogen atoms in the presence of a base, resulting in the formation of a compound having reactive methylene group, are known as Claisen condensation reactions.
- Aromatic aldehydes like benzaldehyde, furfural etc., when treated with ethanolic potassium cyanide and refluxed, undergo dimerization to form...
keto-alcohols. Since benzaldehyde forms benzoin by condensation of its two molecules, the reaction is known as benzoin condensation.

- In 1867 W.H. Perkin observed that when aromatic aldehydes are heated with the anhydride of an aliphatic acid in the presence of the sodium salt of the same acid, an α,β unsaturated acid is formed. The reaction is known as Perkin reaction and is shown mainly by aromatic aldehydes.

- A Knoevenagel condensation is a nucleophilic addition of an active hydrogen compound to a carbonyl group followed by a dehydration reaction in which a molecule of water is eliminated (hence condensation). The product is often an α,β-unsaturated ketone (a conjugated enone).

- The Mannich reaction is an organic reaction which consists of an amino alkylation of an acidic proton placed next to a carbonyl functional group by formaldehyde and a primary or secondary amine or ammonia. The final product is a β-amino-carbonyl compound also known as a Mannich base. Reactions between aldmines and α-methylene carboxyls are also considered Mannich reactions because these imines form between amines and aldehydes. The reaction is named after chemist Carl Mannich.

### 5.5 KEY WORDS

- **Nucleophilic addition**: Nucleophilic addition reactions of nucleophiles with electrophilic double or triple bond (π bonds) create a new carbon center with two additional single, or σ, bonds.

- **Condensation**: The term condensation has been used to describe a wide variety of organic reactions resulting in the lengthening of the carbon skeleton of the molecule. However it may be defined as a reaction (through functional groups) between two or more molecules of the same or different compounds resulting in the formation of new carbon to carbon bonds with or without the elimination of simple molecules like water, alcohol, metallic halides etc.

### 5.6 SELF ASSESSMENT QUESTIONS AND EXERCISES

**Short Answer Questions**

1. Write the mechanism of Aldol condensation.
2. What is a condensation reaction? Describe its types.
3. Give the mechanism of Claisen condensation.
4. What is the mechanism of benzoin condensation?
5. What is the mechanism of Perkin reaction?
6. What do you understand by Knoevenagel condensation?
Long Answer Questions

1. Explain additions at carbon to oxygen double bonds.
2. Describe the electronic mechanism of addition of HCN and NaHSO₃ (sodium bisulphite) to carbonyl group.
3. Describe the electronic mechanism of addition of ammonia and amine derivatives to carbonyl group.
4. Discuss the reductions of carbonyl compounds by lithium aluminium hydride or sodium borohydride.
5. Illustrate the concept of Aldol condensation with the help of some examples.
6. Discuss the applications of benzoin condensation.

5.7 FURTHER READINGS


UNIT 6 CONFORMATIONAL ANALYSIS OF ACYCLIC AND CYCLIC SYSTEMS

Structure
- 6.0 Introduction
- 6.1 Objectives
- 6.2 Conformational analysis of Acyclic and Cyclic Systems
  - 6.2.1 Fused and Bridged Cyclic Systems
- 6.3 Answers to Check Your Progress Questions
- 6.4 Summary
- 6.5 Key Words
- 6.6 Self Assessment Questions and Exercises
- 6.7 Further Readings

6.0 INTRODUCTION

The different spatial arrangements that a molecule can adopt due to rotation about the internal \( \sigma \) bonds are called conformations. Structures that only differ based on these rotations are conformational isomers or conformers. The study of the energy changes that occur during these rotations is called conformational analysis. An understanding of the forces at work and the energy associated with these processes is important because the structure of a molecule can have a significant influence on the molecular properties, including dictating the outcome of a reaction. Although the ideas are developed for the simplest functional groups, the alkanes, the same principles can be expanded and applied to other functional groups.

This unit introduces you to the concept of conformations in organic chemistry. You will be studying about conformational analysis of cyclic and acyclic systems.

6.1 OBJECTIVES

After going through this unit, you will be able to:
- Understand the concept of conformations
- Know about Baeyer’s strain theory
- Discuss Sachse-Mohr Theory
6.2 CONFORMATIONAL ANALYSIS OF ACYCLIC AND CYCLIC SYSTEMS

Conformations of Alkanes

The sigma bond joining the two carbon atoms in ethane is symmetrical about the nuclear axis. This symmetry of the bond permits free rotation of the two carbon atoms with respect to each other, along the bond axis without breaking the bond. Since the two carbon atoms are having tetrahedral arrangement and the valency angles are 109.5°, the free rotation of carbons on their axis gives rise to various arrangements of relative position of the hydrogens attached to these carbon atoms. All such arrangements of the atoms in a molecular structure, in space, which are possible because of the concept of free rotation around a single \( \sigma \) (sigma) bond are known as Conformations of the molecule. Since conformations are obtained on rotation around a bond, they are sometimes also called rotamers. It can also be said that conformations are different arrangement of atoms that can be converted into one another by rotation about a single bond. The study of the preferred conformation in a molecule and relating their physical and chemical properties to their preferred conformation is known as Conformational analysis.

Methane has only one carbon atom and so only one spatial arrangement is possible whereas ethane could be represented as shown in the form of saw-horse drawings:

![Saw-horse drawings](image)

1. Ellipted form
2. Staggered form
3. Intermediate form

In the above representation the dark-black lines are supposed to be below the plane of paper and the dotted lines to be above the plane of paper.

In the spatial arrangement (1) shown, the hydrogen atoms of one carbon atom lie exactly opposite or parallel to those of the other and the arrangement is known as Ellipted form. In (2) the hydrogen atoms of one carbon lie exactly in the middle of the position occupied by the hydrogens of the other carbon atom. This arrangement is known as Staggered form. Any other arrangement which will be in between these two extreme positions of hydrogens is shown in (3). A better way to represent these forms is to use Newman projection formulae as shown. In writing Newman projection formulae the molecule is viewed from the top along the C—C bond. The top carbon atom is shown as a dot and bottom carbon atom as a circle with three hydrogen attached to each one of them.
Conformational analysis of Acyclic and Cycle Systems

NOTES

Obviously, there will be a slight difference in the energy of each of these forms, though they will be having identical chemical and physical properties. In the eclipsed form hydrogen atoms are placed opposite to each other resulting in crowding of the molecule and therefore repulsive forces will be greater. The eclipsed form is of high energy, and thus will be unfavoured. The crowding and repulsive forces will be slightly less in intermediate form hence its energy will be lower than eclipsed form. In staggered form the hydrogen atoms are far apart from each other and the repulsive forces will be minimum. Consequently this form will be the favoured one and of lowest energy. The curve in Figure 6.1 shows the change in the energy of the molecule as the carbon atoms are rotated on their axis.

Any point in the above curve for ethane refers to some conformation of ethane molecule. The ones at the trough of the curve are of minimum energy known as staggered conformations while those at the crest are of maximum energy called eclipsed conformations. The energy difference between the staggered and eclipsed form in ethane is small, i.e., only 3 kcal/mole and so these forms are easily interconvertible but under normal conditions most of the ethane molecules exist in staggered form, i.e., the form of least interaction amongst hydrogen.

Fig. 6.1. Energy of Various Conformations of Ethane.
In case of 1,2-dibromoethane the important conformations are:

The dipole moment of staggered or anti-form will be zero as the two C-Br bonds are antiparallel to each other while gauche form will have finite dipole moment and the eclipsed or syn form will have maximum dipole moment. Actual dipole moment of 1,2-dibromoethane is 1 Debye under normal conditions indicating that staggered and gauche conformations are in equilibrium and the equilibrium constant changes with temperature as the population of gauche form increases.

**Conformations of Propane**

For propane the important conformations are given below:

There is only one H—CH₃ interaction which raises the energy difference between staggered and eclipsed conformation to about 3.3 kcal/mole. Under normal conditions most of the propane molecules exist in staggered conformation.

**Conformations of n-Butane**

The important conformations for butane are

Figure 6.2 represents the potential energy as a function of angle of rotation for n-butane.
Fig. 6.2. Energy of Various Conformations of Butane.

Study of the above diagram for the energy of various conformations of \( n \)-butane indicates that eclipsed form V representing the eclipsing of two bulky methyl groups is the conformation of highest energy while the staggered form III in which the methyl groups are maximum distance apart (i.e., 180°) is the conformation of least energy and hence most stable. In addition, another maxima, lower than the one for eclipsed conformation represents the eclipsing of the methyl groups with the hydrogens II.

There is yet another trough, higher in energy than the one for staggered conformation, representing gauche conformation I and IV in which the methyl groups are at 60° to one another.

The energy barrier between the highest crest (corresponding to eclipsed form) and the lowest trough (corresponding to staggered form is approximately 6.0 kcal/mole, while the energy difference between the second crest (representing interaction of two methyl groups with two hydrogen) and the lowest trough is about 3.6 kcal/mole.

The gauche form (the trough higher than the one representing staggered form) differs from the staggered form by about 0.8 kcal/mole.

Thus \( n \)-butane has three stable conformations, two gauche or skew (I and IV in Figure 6.2) which are mirror images of each other and one staggered conformation (III) which is most stable.

These different conformations corresponding to different energy are called conformational isomers or conformers. Conformations III and I or III and IV are not mirror images of each other and hence are conformational diastereoisomers.
Relative Stability of Cycloalkanes and Baeyer’s Strain Theory

The properties of cycloalkanes are determined by the size of ring. Thus 3- or 4-membered rings are difficult to prepare while 5- or 6-membered ring compounds are prepared easily. Similarly 3- or 4-membered rings are more reactive and tend to undergo addition reactions rather than substitution reactions.

From an examination of the stability of cycloalkanes it is clear that the stability increases with the size of ring up to cyclopentane and from cyclohexane onwards all cycloalkanes are quite stable. The relative stability of cycloalkanes was explained by Adolf von Baeyer in a theory known as Baeyer’s strain theory, first postulated in 1885.

According to Le Bel and van’t Hoff, the four valencies of carbon atom are directed towards the corners of a regular tetrahedron and hence the angle between any two valencies is 109°28’. Therefore Baeyer argued if carbon atoms unite to form a closed chain, the valency angles are distorted from their natural directions and a strain is set up in the molecule depending on the extent of distortion of normal valency angles. The greater the strain, the greater is the instability of the ring. It was also assumed that various ring systems are planar.

On the basis of the above concept of Baeyer’s strain theory a number of phenomenon were explained. For example it explained the relatively greater stability of saturated aliphatic hydrocarbons—as in these compounds there is no distortion from normal valency angle and therefore there is no strain in the molecule. One the other hand unsaturated compounds having double or triple bonds are under considerable strain because of distortion of valency angle (in fact the valency angle is reduced to zero) therefore they are unstable.

Baeyer’s strain theory has also been applied to the problem of relative stability of cycloalkanes. In cyclopropane, the carbon atoms lie at the corners of an equilateral triangle. The bonds joining these carbon atoms are, thus, at an angle of 60°, and the distortion of each bond is 1/2 (109°28’ – 60°) = 24°44’. This distortion sets up strain in the molecule called Baeyer strain and therefore cyclopropane is relatively unstable. Similarly the values of distortion of valency angle in different cycloalkanes may be obtained and is given below:

<table>
<thead>
<tr>
<th>Double bond</th>
<th>Cyclopropane</th>
<th>Cyclobutane</th>
<th>Cyclopentane</th>
<th>Cyclohexane</th>
<th>Cycloheptane</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+54°44’</td>
<td>+9°32’</td>
<td>+0°54’</td>
<td>–5°16’</td>
<td>–9°33’</td>
</tr>
</tbody>
</table>

According to strain theory, the strain is proportional to the distortion of normal valency angle. Thus from the values given above it follows that cyclopentane is under least strain and should therefore be most stable. In the other systems the molecules are under strain and therefore tend to open up to relieve the strain by forming saturated compounds. Since the instability is directly proportional to the strain, it is clear from the above data that cyclopentane is more stable than cyclobutane which in turn is more stable than cyclopropane. The compounds having double bonds are the least stable of all. These theoretical deductions have been fully confirmed by experiments.
Additional evidence in favour of Baeyer’s strain theory is provided in the formation of lactones from \( \gamma \)- and \( \delta \)-hydroxyacids as the resulting rings are 5- and 6-membered with nominal strain. Similarly only \( \gamma \)- and \( \delta \)-amino acids form lactams readily, the ring size being 5- and 6- having minimum strain. Another example is the ready formation of 5- and 6-membered ring anhydride when 1,4- and 1,5-dicarboxylic acids are heated.

**Limitations of Baeyer’s Strain Theory.** However, Baeyer’s theory has failed to explain many known facts. Some of these are given below:

1. On the basis of distortion strain cyclohexane should be somewhat unstable which is against the known facts.
2. Data on the heat of combustion of various cycloalkanes suggests that rings larger than cyclopentane or cyclohexane are stable. In fact, they are equal in stability to the corresponding alkanes, whereas according to this theory higher rings should be considerably strained and therefore unstable.
3. Cycloalkanes with rings of 10, 15, 17 or more carbon atoms have been prepared and found to be stable.
4. It cannot explain the ease with which carbon-carbon double bonds are formed.

**Sachse-Mohr Theory of Strainless Rings**

Baeyer had assumed that the carbon atoms of ring lie in the same plane and his strain theory was able to explain satisfactorily the reactivity or stability of rings containing up to five carbon atoms. In order to explain the anomalous stability of larger rings, Sachse in 1890 suggested that *rings with six or more carbon atoms are not planar but are puckered*. Since the carbon atoms lie in different planes the normal valency angle is retained and the rings are known as strainless rings. According to him cyclohexane exists in two strainless forms—non-rigid ‘boat’ or trough form and rigid ‘chair’ form. These are also referred to as different conformations of cyclohexane. The chair form of cyclohexane is more stable than the boat form and under normal conditions most cyclohexane molecules exist in the chair form. It is not possible to isolate these forms because the energy of interconversion of these forms is only 5.6 kcal/mole. Such non-planar strain-free rings (puckered rings) are also possible for higher cycloalkanes.

The theory was further elaborated by Mohr in 1918 who emphasized the predominance of chair form and applied the theory of strainless rings to fused ring systems like decalin. The *cis*- and *trans*-forms of decalin were isolated by Huckel in 1925. Mohr assigned boat and chair forms to two cyclohexane rings fused in
cis and trans decalinS respectively. However Hassel in 1946 suggested that both in cis and trans decalins the two rings are in chair form—the only difference being in the mode of combination of the two rings.

**Coulson and Moffit’s Concept**

A covalent bond between two atoms is formed by the overlap of atomic orbitals of the atoms involved. The greater the extent of overlapping the stronger is the bond formed. In cycloalkanes the carbon atoms are in \textit{sp}^3 hybridised state and the bond angles (C—C—C angle) should be 109.5°. Theoretically the C—C bond angle in cyclopropane should be 60° and it cannot be 109.5°. Therefore the carbon atoms in cyclopropane cannot be located as in the case of ordinary carbon-carbon bond but are placed in such a manner that only a partial overlap of \textit{sp}^3 hybrid orbital occurs—so that the C—C—C valency angle is distorted only slightly (in fact to approx. 105°) and H—C—H angle is increased from normal 109.5° to 114°. In short the \textit{sp}^3 hybrid orbitals overlap at an angle to form so called ‘bent’ or ‘banana’ bonds. As the extent of overlapping in appreciably less the carbon-carbon bond in cyclopropane is much weaker than the carbon-carbon bond in aliphatic saturated compounds.

Similarly, in cyclobutane the molecule has bent bonds but the decrease in overlapping is much less than in cyclopropane. It is therefore more stable than cyclopropane.

Thus according to Coulson and Moffit’s concept the decrease in the stability of a ring compound is due to relatively poor overlapping of atomic orbitals in the formation of carbon-carbon bonds in cyclopropane and cyclobutane.
Conformational Analysis of Alkyclic Compounds

Study of the preferred conformation of a compound and correlating it with the physical and chemical properties of the preferred conformation of the compounds is known as Conformational Analysis. In simple alkyclic compounds, due to distortion of valency angle (Baeyer’s strain), the molecule tends to take up non-planar configuration forming strainless rings. Apart from Baeyer’s strain there exist other types of strain in the molecule. Thus in cyclopropane every hydrogen atom is almost in contact with the neighbouring hydrogen atoms thus producing strain due to mutual repulsion of three pairs of hydrogen atoms. This strain associated with partial or complete eclipsing of neighbouring atoms is called eclipsing strain.

In cyclobutane apart from Baeyer’s angle strain and eclipsing strain due to mutual repulsion of four pairs of eclipsing hydrogen atoms, there is an additional strain due to non-bonded interactions (bond-opposition strain) between first and fourth carbon atoms which are only 2.2 Å away from each other. The theoretical value of all these strains together is much greater than the experimental value of strains determined thermodynamically. Therefore it is suggested that one of the carbon atoms of cyclobutane is twisted out of plane to reduce the actual strain in the molecule. This strain which twists one or more atoms of the ring out of plane is termed as torsional strain or Pitzer strain.

Similarly in cyclopentane, though the Baeyer’s angle strain is very small yet the molecule acquires strainless ‘envelope’ type conformation which is flexible. This is due to the large Pitzer torsional strain because of mutual repulsion of five pairs of eclipsing hydrogen and bond-opposition strain for non-bonded carbon atoms. It is obvious that by acquiring puckered state more stability is achieved due to staggering of hydrogen atoms than is lost through increasing angle strain.

The individual carbon atoms of the ring move up and down to the average plane of the ring in a manner which results in continuous change in the out of plane carbon giving it a wave like appearance.

Conformation of Cyclohexane

Sachse in 1890 suggested that cyclohexane ring exists in two nonplanar forms i.e. boat and chair conformations. The energy difference between the two forms was found to be only 5.6 kcal/mole by Pitzer. This energy barrier is too small to prevent their interconversion. Therefore it is not possible to resolve them.

By electron diffraction studies Hassel in 1943 demonstrated that at room temperature most of the molecules of cyclohexane exist in chair conformation. This was to be expected as the boat form has greater energy content. In the chair form all the C—H bonds on adjacent carbon atoms are in skew position while in
the boat form only four of them are in skew position and two in _eclipsed_ position. These _eclipsed_ interactions are responsible for higher energy of the boat form. Bowsprit–flagpole interactions (_f-f_) and _eclipsed_ interactions (_x-x_, _y-y_) are shown here in boat form:

However, in the chair conformation all the twelve hydrogens are not equivalent. If a line is drawn through the centre of the cyclohexane chair then it will be found that six _C—H_ bonds are parallel to this line and six _C—H_ bonds are directed outwards away from this line, as shown in the figure below. The former are known as _axial_ (a) bonds while latter are known as _equatorial_ (e) bonds. It should be noted that all bond angles are 109.5° and the _axial_ bonds on adjacent atoms, though parallel to the line drawn through centre, are directed in opposite direction, i.e., upwards and downwards. The chair conformation is sufficiently flexible to turn itself upside down so that all bonds which were _axial_ originally become _equatorial_ and _vice versa_.

![Interconversion of the two chair forms of cyclohexane](image)

*Interconversion of the two chair forms of cyclohexane
(a = axial bond; e = equatorial bond)*

The potential energy curve of cyclohexane as a function of conformations of cyclohexane is shown in Figure 6.3.

![Potential Energy Curve](image)

*Fig. 6.3. Interconversion of Conformations of Cyclohexane.*

As can be seen the chair form is the most stable one. It is due to the fact that there is neither the angle strain nor the bond opposition or _eclipsing_ strain. If the chair form is to be converted to boat form, some _angular_ distortion is required because several bonds have to be rotated and the molecule passes through the
highest energy state corresponding to half-chair form (i.e. an energy barrier of approximately 10 kcal/mole), then through skew boat form and finally acquires the boat form.

The energy difference between the chair and boat form is high enough so that these conformations are capable of existing but not high enough to prevent their interconversion at room temperature. Hence they are not separable.

In the boat form also there is no angle strain but there is bond opposition or eclipsing strain of four pairs of hydrogen of bottom carbon atoms and also strain due to interaction of pairs of hydrogen at the top carbon atoms known as **bowspirit flagpole** interaction.

As a result almost 99.9% of cyclohexane molecules exist in chair conformation under normal conditions. However, there are some molecules in which cyclohexane ring exists in boat form. For example [2.2.2] Bicyclooctane must exist in boat form due to structural requirement.

Similarly, trans-1,3-di-t-butylcyclo-hexane exists in boat form because if this molecule takes up chair conformation there would be very high interaction between axial t-butyl group and axial hydrogen atoms.

**Monosubstituted Cyclohexanes**

As pointed out earlier most molecules in cyclohexane exist in chair conformation. In the chair conformation of cyclohexane each and every carbon has two kinds of bonds, those parallel to an axis drawn through the ring pointing in upward and downward direction on alternate carbon atoms known as ‘axial’ or ‘a’ bonds and those pointing sideways (one on each carbon) known as equatorial or ‘e’ bond (Barton, Hassel and Pitzer (1953) nomenclature).

It has been found that any group other than hydrogen in axial position interacts with other axial hydrogen atoms (non-bonded repulsions) on the third carbon atom as shown here (axial-axial interaction).
The interactions are minimum when the substituent group is in equatorial position. Thus the energy of the conformation having a substituent in equatorial position is much lower than the conformation having the same group in axial position.

If we consider methylocyclohexane, theoretically two isomeric chair forms are possible—one in which the methyl substituent is in equatorial position and the other in which the methyl substituent is in axial position. The situation is further complicated because of the fact that equatorially substituted chair conformation can readily converts itself into a flexible form and then to another chair conformation in which the same substituent now becomes axial.

![Interconversion of chair conformation of methylocyclohexane via flexible boat form](image)

The axial conformer has two interactions (axial-axial) with non-bonded hydrogen (as in gauche form of butane). No such interactions are there in equatorial conformer and the energy difference between the two forms is around 1.8 kcal/mole. Hence about 95% of the molecules in methylocyclohexane exist in equatorial conformation at room temperature but can be frozen out as distinct separate entities at −78°C.

If there are more than one substituents then that chair conformation is the preferred form which has maximum number of equatorial substituents. These stability trends of substituted cyclohexanes can actually be verified by the study of acidities of the alicyclic dicarboxylic acids.

Transannular Strain. The higher heats of combustion of medium size (8 to 13 membered) alicyclic compounds and the difficulties in their formation is attributed to a non-classical transannular strain. In these alicyclic compounds hydrogens situated on the opposite sides of the ring are very close and their mutual repulsion leads to transannular interaction strain. This strain may lead to change in the bond angles and may also result in a number of unusual reactions where a positive carbocation centre (formed during the reaction) may migrate to another carbon atom which may be remote along the carbon chain but close in space to it.

Disubstituted Cyclohexanes

In the chair form of cyclohexane the substituents prefer to occupy the less sterically hindered equatorial position. In di- or poly- substituted cyclohexanes all the substituents may or may not occupy equatorial position in every isomer but that isomer is usually more stable in which all or most substituents occupy equatorial positions.

1. 4-Dimethyl cyclohexane exists in two stereoisomeric forms cis- and trans- each of which can have two conformations
Conformational analysis of Acyclic and Cycle Systems

\[
\begin{array}{c|cc}
\text{cis-isomer} & \text{trans-isomer} \\
\hline
\text{cis- (e,a)} & \text{cis- (a,e)} & \text{trans- (e,e)} & \text{trans- (a,a)} \\
\text{Strain Energy} & 1.8 \text{kcal} & 1.8 \text{kcal} & 0 \text{kcal} & 3.6 \text{kcal} \\
\end{array}
\]

The order of their stability is: \( \text{trans- (e,e)} > \text{cis- (e,a)} = \text{cis- (a,e)} > \text{trans- (a,a)} \)

1. 3-Dimethylcyclohexane. Its stereoisomers and conformations are

\[
\begin{array}{c|cc}
\text{cis-isomer} & \text{trans-isomer} \\
\hline
\text{cis- (e,e)} & \text{cis- (a,a)} & \text{trans- (e,a)} & \text{trans- (a,e)} \\
\text{Strain Energy} & 0 \text{kcal} & > 3.6 \text{kcal} & 1.8 \text{kcal} & 1.8 \text{kcal} \\
\end{array}
\]

The order of their stability is: \( \text{cis- (e,e)} > \text{trans- (e,a)} > \text{trans- (a,a)} > \text{cis- (a,a)} \)

1. 2-Dimethylcyclohexane. Stereoisomers and conformations are

\[
\begin{array}{c|cc}
\text{cis-isomer} & \text{trans-isomer} \\
\hline
\text{cis- (e,a)} & \text{cis- (a,e)} & \text{trans- (e,e)} & \text{trans- (a,a)} \\
\text{Strain Energy} & 1.8 \text{kcal} & 1.8 \text{kcal} & 0 \text{kcal} & 3.6 \text{kcal} \\
\end{array}
\]

The order of their stability is: \( \text{trans- (e,e)} > \text{cis- (e,a)} > \text{cis- (a,e)} > \text{trans- (a,a)} \)

The conformational energy (or strain energy) of a conformation is the energy difference between molecules with a substituent in axial and equatorial positions.

In case the two substituents are different, then the conformation in which the group with higher conformational energy occupies the equatorial position is generally more stable. It may be noted that conformational energy is not dependent simply on the size but effective volume and presence of charge also play an important role in deciding it.
6.2.1 Fused and Bridged Byclic Systems

Compounds with two rings fused together are known as bicycles. Bicyclic systems can be either fused or bridged bicyclic. Fused rings share two adjacent carbon atoms while the bridged rings share two non-adjacent carbon atoms (called the bridgehead carbons) with one or more carbon atoms between them. In this section, you will study about mainly decalins.

Decalins are examples of fused ring systems. In fused ring systems, two rings share an edge. Decalins contain ten carbons total, but the ten carbons are divided into two rings, each of which is six carbons around.

The IUPAC name of decalin is bicyclo[4.4.0]decane (the numbers 4, 4, 0 represent the number of carbon atoms in each ring besides the bridgehead carbons). Decalin is also known as decahydronaphthalene as it is a saturated analog of naphtalene and can be prepared from it by hydrogenation in a fused state in the presence of a catalyst. The synthesis lead to the formation of two stereoisomers of decalin. One, where both the hydrogens at the bridgehead carbons are ‘cis’ to each other and the other, where both the hydrgens are ‘trans’ to each other.

Decalins are examples of fused ring systems. In fused ring systems, two rings share an edge. Decalins contain ten carbons total, but the ten carbons are divided into two rings, each of which is six carbons around.

There are two possible isomers of decalin: cis and trans. The easiest way to distinguish the two isomers is to look for the two hydrogens on the shared edge between the two rings. Those two hydrogens are found on the same face of the cis decalin.
The two hydrogens along the junction are seen on the opposite faces in trans-decalin.

### Check Your Progress

1. What is conformational analysis?
2. What are conformers?
3. How the properties of cycloalkanes are determined?
4. What is the relation between strain and distortion of normal valency angle?

### 6.3 Answers to Check Your Progress Questions

1. The study of the preferred conformation in a molecule and relating their physical and chemical properties to their preferred conformation is known as conformational analysis.
2. Different conformations corresponding to different energy are called conformational isomers or conformers.
3. The properties of cycloalkanes are determined by the size of ring.
4. According to strain theory, the strain is proportional to the distortion of normal valency angle.

### 6.4 Summary

- All such arrangements of the atoms in a molecular structure, in space, which are possible because of the concept of free rotation around a single $\sigma$ (sigma) bond are known as Conformations of the molecule.
- Since conformations are obtained on rotation around a bond, they are sometimes also called rotamers. It can also be said that conformations are different arrangement of atoms that can be converted into one another by rotation about a single bond.
• The study of the preferred conformation in a molecule and relating their physical and chemical properties to their preferred conformation is known as Conformational analysis.

• Methane has only one carbon atom and so only one spatial arrangement is possible.

• Energy of various conformations of n-butane indicates that eclipsed form V representing the eclipsing of two bulky methyl groups is the conformation of highest energy while the staggered form III in which the methyl groups are maximum distance apart (i.e., 180°) is the conformation of least energy and hence most stable. In addition, another maxima, lower than the one for eclipsed conformation represents the eclipsing of the methyl groups with the hydrogens II.

• n-butane has three stable conformations, two gauche or skew which are mirror images of each other and one staggered conformation which is most stable.

• The properties of cycloalkanes are determined by the size of ring. Thus 3- or 4-membered rings are difficult to prepare while 5- or 6-membered ring compounds are prepared easily. Similarly 3- or 4-membered rings are more reactive and tend to undergo addition reactions rather than substitution reactions.

• In order to explain the anomalous stability of larger rings, Sachse in 1890 suggested that rings with six or more carbon atoms are not planar but are puckered. Since the carbon atoms lie in different planes the normal valency angle is retained and the rings are known as strainless rings.

• In simple alicyclic compounds, due to distortion of valency angle (Baeyer’s strain), the molecule tends to take up non-planar configuration forming strainless rings. Apart from Baeyer’s strain there exist other types of strain in the molecule. Thus in cyclopropane every hydrogen atom is almost in contact with the neighbouring hydrogen atoms thus producing strain due to mutual repulsion of three pairs of hydrogen atoms. This strain associated with partial or complete eclipsing of neighbouring atoms is called eclipsing strain.

6.5  KEY WORDS

• Conformations: The different spatial arrangements that a molecule can adopt due to rotation about the internal 6 bonds are called conformations.

• Conformational analysis: Structures that only differ based on these rotations are conformational isomers or conformers. The study of the energy changes that occur during these rotations is called conformational analysis.
6.6 SELF ASSESSMENT QUESTIONS AND EXERCISES

NOTES

Short Answer Questions
1. What do you understand by conformational analysis?
2. Draw cis-decalin and trans-decalin using a wedge/dash picture.
3. What are the limitations of Baeyer’s strain theory?
4. Discuss relative stability of cycloalkanes and Baeyer’s strain theory.

Long Answer Questions
1. What are conformations? Illustrate your answer with examples.
2. Discuss the conformations of n-butane.
3. Write short notes on:
   (a) Boat and chair form
   (b) Eclipsed and staggered form
   (c) Axial and equatorial bonds
   (d) Transannular strain
   (e) Pitzer strain
4. Draw all the stereoisomers and conformers of 1,2, 1,3 and 1,4-disubstituted cyclohexanes and arrange them in the order of their decreasing stability.
5. Discuss Sachse-Mohr theory of strainless rings.

6.7 FURTHER READINGS

UNIT 7  TOPICITY AND NMR
DISTINCTION OF
ORGANIC COMPOUNDS

Structure
7.0 Introduction
7.1 Objectives
7.2 Topicity and Prostereoisomerism
7.3 Topicity of Ligands and Faces
    7.3.1 Homotopic Ligands and Faces
    7.3.2 Heterotopic Ligands and Faces
7.4 NMR Distinction of Organic Compounds
7.5 Answers to Check Your Progress Questions
7.6 Summary
7.7 Key Words
7.8 Self Assessment Questions and Exercises
7.9 Further Readings

7.0 INTRODUCTION

The subfield of stereochemistry is the branch of chemistry that’s concerned with
the three-dimensional or spatial orientation of compounds. Under the umbrella of
stereochemistry, topicity seeks to define the specific relationship between atoms
or groups of atoms (substituents) that are bonded to a molecule. It’s very similar
to how you define the relatives in your family based on their position in the family
tree. The topicity of two or more substituents is classified as one of four different
relationships. The four possible relationships are called homotopic, heterotopic,
enantiotopic, and diastereotopic.

In this unit, you will study about topicity of organic compounds.

7.1 OBJECTIVES

After going through this unit, you will be able to:

- Understand the concept of topicity
- Discuss topicity of ligands and faces
7.2 **TOPICITY AND PROSTEREOISOMERISM**

**Topicity**

In stereochemistry, topicity is the stereochemical relationship between substituents and the structure to which they are attached. Depending on the relationship, such groups can be heterotopic, homotopic, enantiotopic, or diastereotopic.

**Prochirality**

In stereochemistry, prochiral molecules are those that can be converted from achiral to chiral in a single step. An achiral species which can be converted to a chiral in two steps is called proprochiral.

Molecules which display chirality are called chiral for example, (S)-(+-)lactic acid is chiral. Chirality is associated with this type of molecules is known as centre of chirality and chiral centre at C₂ carbon. Some other type of chirality also presents in molecules which do not have chiral centres, but they show chirality due to disymmetrisation of axis and plane.

![Fig. 7.1 Chiral and Prochiral Molecule](image)

In propionic acid (2), replacement of H₅A or H₅B by the OH gives a (S)-(+-)-lactic acid (1) or (R)-(+-)-lactic acid. The protons H₅A and H₅B of the propionic acid are the hetero (different) topic (place). The molecule 2 is prochiral means this can be converted to chiral compound 1 by replacing its ligands (H₅A or H₅B) by the different ligands (OH). The carbon C₂ is called as parochiral centre.

The term chirality in stereoisomerism should similarly be replaced by the term prochirality in prostereoisomerism. It would mean that if two homomorphic ligands at a prochiral centre (or axis or plane) be made different, a chiral centre (or axis or plane) would result. Just as a stereogenic centre may not necessarily be a chiral centre, a prostereogenic centre may not necessarily be a prochiral centre, i.e., a centre may be prostereogenic without being prochiral.
Fig. 7.2 Prochiral Centre in Propionic Acid

Substitution is one of the common ways to interconverting the organic molecules. The lactic acid in principle can be synthesized by the addition of methylmagnesium bromide to carbonyl of the glyoxylic acid (may be necessary to protect acid group as ester). If the attack of the Grignard reagent on the front face of the carbonyl gives a (S)-lactic acid and attack on the rear face gives (R)-lactic acid. Thus, the carbonyl group in glyoxylic acid also prochiral and present as two heterotopic faces.

Fig. 7.3 Attack of Grignard Reagent to Front and Rear Faces of Carbonyl Group of the Glyoxylic Acid

7.3 TOPICITY OF LIGANDS AND FACES

A ligand cannot itself be called homotopic or heterotopic; in order to use this terminology, a comparison with other homomorphic ligand or ligands present either in the same molecule (internal comparison) or in a different molecule (external comparison) is necessary.
### 7.3.1 Homotopic Ligands and Faces

Some of the apparently identical ligands are not equivalent towards enzyme or in their NMR signals.

How will we decide whether the nuclei (ligand) are equivalent?

There are two criteria-

(i) Substitution criterion and (ii) Symmetry criterion.

Similarly addition and symmetry criterion serve to test the equivalency of faces.

#### Substitution and Addition Criterion

Two homomorphic (homo means same and morph means form) ligands are homotopic if the replacement of first one and then the other by different ligand leads to the same structure. Two hydrogen atoms of the methylene bromide (7) are homotopic because replacement of either by chlorine gives the same CHBr₂Cl (8).

![Homotopic Ligands in Methylene Bromide](image1)

**Fig. 7.4 Homotopic Ligands in Methylene Bromide**

The three hydrogen atoms in acetic acid (9) are homotopic because replacement of any one of them by fluorine gives one and same fluoroacetic acid (10).

![Homotopic Ligands in Acetic Acid](image2)

**Fig. 7.5 Homotopic Ligands in Acetic Acid**

Methine hydrogen atoms in (R)-tartaric acid (11) are homotopic because replacement of either of them for example, by deuterium gives the same (2R, 3R)-tartaric-2-d acid (12).
7.3.2 Heterotopic Ligands and Faces

There are two kinds:

1. Enantiotopic
   - related through symmetry plane, \( \sigma \)
   - substitution gives enantiomers

   \[
   \begin{align*}
   \text{H} & \quad \text{H} \quad \rightarrow \quad \text{D} & \quad \text{H} \\
   \text{X} & \quad \text{Y} & \quad \rightarrow \quad \text{X} & \quad \text{Y} \quad \quad \text{and} \\
   \text{D} & \quad \text{H} & \quad \rightarrow \quad \text{D} & \quad \text{H} \\
   \text{X} & \quad \text{Y} & \quad \rightarrow \quad \text{X} & \quad \text{Y} \quad \quad \text{and} \\
   \text{H} & \quad \text{D} & \quad \rightarrow \quad \text{H} & \quad \text{D}
   \end{align*}
   \]

2. Diastereotopic
   - not related by symmetry
   - substitution gives diastereomers

   \[
   \begin{align*}
   \text{H} & \quad \text{Y} & \quad \rightarrow \quad \text{D} & \quad \text{Y} \\
   \text{X} & \quad \text{Y} & \quad \rightarrow \quad \text{X} & \quad \text{Y} \quad \quad \text{and} \\
   \text{H} & \quad \text{Y} & \quad \rightarrow \quad \text{D} & \quad \text{Y} \\
   \text{X} & \quad \text{Y} & \quad \rightarrow \quad \text{X} & \quad \text{Y} \quad \quad \text{and} \\
   \text{H} & \quad \text{D} & \quad \rightarrow \quad \text{H} & \quad \text{D}
   \end{align*}
   \]

Examples

- Substitution leads in one step from an achiral to a chiral compound

\[
\begin{align*}
\text{H} & \quad \text{H} \quad \rightarrow \quad \text{D} \quad \text{H} \\
\text{H} & \quad \text{D} \quad \rightarrow \quad \text{H} \quad \text{D}
\end{align*}
\]
H atoms are enantiotopic

- Creation of a new C*

Atereochemically distinct, but not in a mirror-image fashion.

**Diastereotopic ligands in 'H NMR spectra**

**Diastereotopic H-atoms**

- H couples to each H differently
- H signal is a doublet of doublets (two lines overlap in the center).

**Diastereotopic Me-groups**

- each CH$_3$ couples to H differently
- CH$_3$ signals are a doublet each (two lines overlap in the center)
Heterotopic Faces

There are two kinds:

1. Enantiotopic
   - related through symmetry plane,
   - addition gives enantiomers

2. Diastereotopic
   - not related by symmetry
   - addition gives diastereomers

7.4 NMR DISTINCTION OF ORGANIC COMPOUNDS

Schematic representation of NMR spectra of some organic compounds are given below with peak assignments which are self-explanatory.

1. Benzene
   - Six aromatic protons
   - Peaks at 2.3 ppm

2. Toluene
   - Five aromatic protons
   - Three proton
   - Peaks at 2.9 and 7.7 ppm
3. **Ethyl benzene**  

![Diagram of ethyl benzene](image)

4. **Isopropyl bromide**  

![Diagram of isopropyl bromide](image)

5. **1,1,2-Tribromoethane**  

![Diagram of 1,1,2-tribromoethane](image)

6. **Acetaldehyde**  

![Diagram of acetaldehyde](image)
7. Acetic acid

![Diagram of Acetic Acid]

8. Ethyl acetate

![Diagram of Ethyl Acetate]

9. Methyl propionate

![Diagram of Methyl Propionate]

10. Acetophenone

![Diagram of Acetophenone]

Check Your Progress

1. What are chiral molecules?
2. What are homotopic ligands?
3. What are the two kinds of heterotopic faces?
7.5 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Molecules which display chirality are called chiral. For example, (S)-(+)-lactic acid is chiral.

2. Two homomorphic (homos means same and morph means form) ligands are homotopic if the replacement of first one and then the other by different ligand leads to the same structure.

3. Enantiotopic and diastereotopic.

7.6 SUMMARY

- Under the umbrella of stereochemistry, topicality seeks to define the specific relationship between atoms or groups of atoms (substituents) that are bonded to a molecule.
- Topicality is the stereochemical relationship between substituents and the structure to which they are attached. Depending on the relationship, such groups can be heterotopic, homotopic, enantiotopic, or diastereotopic.
- In stereochemistry, prochiral molecules are those that can be converted from achiral to chiral in a single step. An achiral species which can be converted to a chiral in two steps is called proprochiral.
- A ligand cannot itself be called homotopic or heterotopic; in order to use this terminology, a comparison with other homomorphic ligand or ligands present either in the same molecule (internal comparison) or in a different molecule (external comparison) is necessary.

7.7 KEY WORDS

- **Topicality**: Topicality is the stereochemical relationship between substituents and the structure to which they are attached. Depending on the relationship, such groups can be heterotopic, homotopic, enantiotopic, or diastereotopic.
- **Prochirality**: In stereochemistry, prochiral molecules are those that can be converted from achiral to chiral in a single step. An achiral species which can be converted to a chiral in two steps is called proprochiral.

7.8 SELF ASSESSMENT QUESTIONS AND EXERCISES

**Short Answer Questions**

1. Write a short note topicality.
2. What do you understand by prochirality?
3. Examine the attack of Grignard reagent to front and rear faces of carbonyl group of the glyoxylic acid.

**Long Answer Questions**

1. Discuss homotopic ligands and faces.
2. Discuss heterotopic ligands and faces.
3. Discuss NMR spectrum organic compounds.

### 7.9 FURTHER READINGS


BLOCK - III
REACTION INTERMEDIATES

UNIT 8  CARBENES

Structure
8.0 Introduction
8.1 Objectives
8.2 Carbenes
8.3 Answers to Check Your Progress Questions
8.4 Summary
8.5 Key Words
8.6 Self Assessment Questions and Exercises
8.7 Further Readings

8.0  INTRODUCTION

Carbene, any member of a class of highly reactive molecules containing divalent carbon atoms - that is, carbon atoms that utilize only two of the four bonds they are capable of forming with other atoms. Occurring usually as transient intermediates during chemical reactions, they are important chiefly for what they reveal about chemical reactions and molecular structure. In addition, some chemical compounds, particularly those in which the molecules contain carbon atoms arranged in small rings, can best be prepared by the use of carbenes.

A carlene is a neutral molecule which contains a carbon atom with an electron valency of 6 (two bonds and two nonbonding electrons). They are a very reactive type of compound, often too reactive to be observed. There are two forms of carbenes:

Triplet carbenes - have two unpaired electrons, one in an 'sp2' orbital, one in a 'p' orbital.

Singlet carbenes - have a lone pair in a nonbonding 'sp2' orbital, and an empty 'p' orbital.

The two types of car bene are different, not only in their structure and electron distribution but also in reactivity.

This unit gives you an overview of carbenes and reactions with carbenes.
8.1 OBJECTIVES

After going through this unit, you will be able to:
- Understand the structure and generation of carbenes
- Know about addition and insertion reactions of carbenes
- Discuss rearrangement reaction

8.2 CARBENES

In chemistry, a carbene is a molecule containing a neutral carbon atom with a valence of two and two unshared valence electrons. The general formula is \( \text{R-} \text{(C=)} \text{-R} \) or \( \text{R=C} \): where the R represent substituents or hydrogen atoms.

The term “carbene” may also refer to the specific compound \( \text{H,C} \); also called methylene, the parent hydride from which all other carbene compounds are formally derived. Carbenes are classified as either singlets or triplets, depending upon their electronic structure. Most carbenes are very short lived, although persistent carbenes are known. One well-studied carbene is dichlorocarbene \( \text{Cl}_2\text{C} \), which can be generated in situ from chloroform and a strong base.

![Fig. 8.1 Methylene, the Simplest Carbene](image)

**Structures and Bondings**

The two classes of carbenes are singlet and triplet carbenes. Singlet carbenes are spin-paired. In the language of valence bond theory, the molecule adopts an \( \text{sp}^2 \) hybrid structure. Triplet carbenes have two unpaired electrons. Most carbenes have a nonlinear triplet ground state, except for those with nitrogen, oxygen, or sulfur atoms, and halides directly bonded to the divalent carbon.

Carbenes are called singlet or triplet depending on the electronic spins they possess. Triplet carbenes are paramagnetic and may be observed by electron spin resonance spectroscopy if they persist long enough. The total spin of singlet carbenes is zero while that of triplet carbenes is one. Bond angles are 125°–140° for triplet methylene and 102° for singlet methylene (as determined by EPR). Triplet carbenes are generally stable in the gaseous state, while singlet carbenes occur more often in aqueous media.

For simple hydrocarbons, triplet carbenes usually have energies 8 kcal/mol (33 kJ/mol) lower than singlet carbenes, thus, in general, triplet is the more stable
state (the ground state) and singlet is the excited state species. Substituents that can donate electron pairs may stabilize the singlet state by delocalizing the pair into an empty p orbital. If the energy of the singlet state is sufficiently reduced it will actually become the ground state. No viable strategies exist for triplet stabilization. The carbene called 9-fluorenylidene has been shown to be a rapidly equilibrating mixture of singlet and triplet states with an approximately 1.1 kcal/mol (4.6 kJ/mol) energy difference. It is, however, debatable whether diaryl carbene such as the fluorene carbene are true carbenes because the electrons can delocalize to such an extent that they become in fact biradicals. In silico experiments suggest that triplet carbenes can be thermodynamically stabilized with electropositive heteroatoms such as in silyl and siloxy carbene, especially trifluorosilyl carbene.

![Fig. 8.2 Singlet and Triplet Carbenes](image)

**Reactivity**

Singlet and triplet carbenes exhibit divergent reactivity. Singlet carbenes generally participate in chelotropic reactions as either electrophiles or nucleophiles. Singlet carbenes with unfilled p-orbital should be electrophilic. Triplet carbenes can be considered to be biradicals, and participate in stepwise radical additions. Triplet carbenes have to go through an intermediate with two unpaired electrons whereas singlet carbene can react in a single concerted step.

Due to these two modes of reactivity, reactions of singlet methylene are stereospecific whereas those of triplet methylene are stereoselective. This difference can be used to probe the nature of a carbene. For example, the reaction of methylene generated from photolysis of diazomethane with cis-2-butene or with trans-2-butene each give a single diastereomer of the 1,2-dimethyleclop propane product: *cis* from *cis* and *trans* from *trans*, which proves that the methylene is a singlet. If the methylene were a triplet, one would not expect the product to depend upon the starting alkene geometry, but rather a nearly identical mixture in each case.

Reactivity of a particular carbene depends on the substituent groups. Their reactivity can be affected by metals. Some of the reactions carbenes can do are insertions into C-H bonds, skeletal rearrangements, and additions to double bonds. Carbenes can be classified as nucleophile, electrophilic, or ambiphilic. For example, if a substituent is able to donate a pair of electrons, most likely carbene will not be electrophilic. Alkyl carbenes insert much more selectively than methylene, which does not differentiate between primary, secondary, and tertiary C-H bonds.
Cyclopropanation

Carbenes add to double bonds to form cyclopropanes. A concerted mechanism is available for singlet carbenes. Triplet carbenes do not retain stereochemistry in the product molecule. Addition reactions are commonly very fast and exothermic. The slow step in most instances is generation of carbene. A well-known reagent employed for alkene-to-cyclopropane reactions is Simmons-Smith reagent. This reagent is a system of copper, zinc, and iodine, where the active reagent is believed to be iodomethylzinc iodide. Reagent is complexed by hydroxy groups such that addition commonly happens syn to such group.

C—H insertion

Insertions are another common type of carbene reactions. The carbene basically interposes itself into an existing bond. The order of preference is commonly: 1. X—H bonds where X is not carbon 2. C—H bond 3. C–C bond. Insertions may or may not occur in single step.

Intramolecular insertion reactions present new synthetic solutions. Generally, rigid structures favor such insertions to happen. When an intramolecular insertion is possible, no intermolecular insertions are seen. In flexible structures, five-membered ring formation is preferred to six-membered ring formation. Both inter- and intramolecular insertions are amendable to asymmetric induction by choosing chiral ligands on metal centers.
Alkylidene carbenes are alluring in that they offer formation of cyclopentene moieties. To generate an alkylidene carbene a ketone can be exposed to trimethylsilyldiazomethane.

**Generation of Carbenes**

- A method that is broadly applicable to organic synthesis is induced elimination of halides from gem-dihalides employing organolithium reagents. It remains uncertain if under these conditions free carbenes are formed or metal-carbene complex. Nevertheless, these metallocarbenes (or carbenoids) give the expected organic products.

  \[ R_2CB_r + BuLi \rightarrow R_2CLi(Br) + BuBr \]

  \[ R_2CLi(Br) \rightarrow R_2C + LiBr \]

- For cyclopropanations, zinc is employed in the Simmons–Smith reaction. In a specialized but instructive case, alpha-halohgmercury compounds can be isolated and separately thermolyzed. For example, the “Seyferth reagent” releases CCl₄ upon heating.

  \[ C_2H_5HgCCl_2 \rightarrow CCl_4 + C_2H_5HgCl \]

- Most commonly, carbenes are generated from diazoalkanes, via photolytic, thermal, or transition metal-catalyzed routes. Catalysts typically feature rhodium and copper. The Bamford-Stevens reaction gives carbenes in aprotic solvents and carbenium ions in protic solvents.

- Base-induced elimination HX from haloforms (CHX₃) under phase-transfer conditions.

- Photolysis of diazirines and epoxides can also be employed. Diazirines are cyclic forms of diazoalkanes. The strain of the small ring makes
photoexcitation easy. Photolysis of epoxides gives carbonyl compounds as side products. With asymmetric epoxides, two different carbonyl compounds can potentially form. The nature of substituents usually favors formation of one over the other. One of the C-O bonds will have a greater double bond character and thus will be stronger and less likely to break. Resonance structures can be drawn to determine which part will contribute more to the formation of carbonyl. When one substituent is alkyl and another aryl, the aryl-substituted carbon is usually released as a carbene fragment.

- Carbenes are intermediates in the Wolff rearrangement.

**Wolff Rearrangement**

\[
\begin{align*}
\text{Ph} & \quad \text{Ph} \\
\text{N}_2 & \quad \text{Ph} \\
\text{Ph} & \quad \text{Ph}
\end{align*}
\]

**Check Your Progress**

1. What are the forms of carbenes?
2. Name the simplest carbene.
3. Triplet carbenes have how many unpaired electrons?
8.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

NOTES

1. There are two forms of carbone: singlet and triplet.
3. Triplet carbenes - have two unpaired electrons, one in an ‘sp2’ orbital, one in a ‘p’ orbital.

8.4 SUMMARY

- In chemistry, a carbone is a molecule containing a neutral carbon atom with a valence of two and two unshared valence electrons. The general formula is R-(C)=R’ or R=C: where the R represent substituents or hydrogen atoms.
- There are two forms of carbone: Triplet carbenes - have two unpaired electrons, one in an ‘sp’ orbital, one in a ‘p’ orbital. Singlet carbenes - have a lone pair in a nonbonding ‘sp’ orbital, and an empty ‘p’ orbital.
- Carbenes are called singlet or triplet depending on the electronic spins they possess. Triplet carbenes are paramagnetic and may be observed by electron spin resonance spectroscopy if they persist long enough.
- Singlet and triplet carbenes exhibit divergent reactivity. Singlet carbenes generally participate in chelotropic reactions as either electrophiles or nucleophiles. Singlet carbenes with unfilled p-orbital should be electrophile. Triplet carbenes can be considered to be diradicals, and participate in stepwise radical additions. Triplet carbenes have to go through an intermediate with two unpaired electrons whereas singlet carbene can react in a single concerted step.
- Insertions are another common type of carbone reactions. The carbene basically interposes itself into an existing bond. The order of preference is commonly: 1. X–H bonds where X is not carbon 2. C–H bond 3. C–C bond.
- Carbenes are intermediates in the Wolff rearrangement.

8.5 KEY WORDS

- **Carbene**: Carbene, any member of a class of highly reactive molecules containing divalent carbon atoms—that is, carbon atoms that utilize only two of the four bonds they are capable of forming with other atoms.
- **Addition**: In addition, some chemical compounds, particularly those in which the molecules contain carbon atoms arranged in small rings, can best be prepared by the use of carbenes.
8.6 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions
1. What are carbenes?
2. Discuss the structure of carbenes.
3. Discuss the generation of carbenes.

Long Answer Questions
1. Explain carbone addition to alkenes.
2. Discuss C-H insertion.
3. Illustrate the mechanism of Wolff rearrangement.

8.7 FURTHER READINGS


UNIT 9  NITRENE

NOTES

9.0  INTRODUCTION

The element nitrogen is essential to life. Considerable attention is thus paid to the development of synthetic methods for its introduction into molecules. Nitrenes, long regarded as highly reactive but poorly selective species, have recently emerged as useful tools for the formation of C-N bonds.

In chemistry, a nitrene (R−N) is the nitrogen analogue of a carbene. The nitrogen atom has only 6 valence electrons and is therefore considered an electrophile. A nitrene is a reactive intermediate and is involved in many chemical reactions. The simplest nitrene, HN, is also called imidogen.

Generic name for HN: and substitution derivatives thereof, containing an electrically neutral univalent nitrogen atom with four non-bonding electrons. Two of these are paired; the other two may have parallel spins (triplet state) or antiparallel spins (singlet state). The name is the strict analogue of carbene and, as a generic name, it is preferred to a number of alternatives proposed (“imene”, “imine radical”, “azeine”, “azylene”, “azacarbenes”, “imin”, “imidogen”).

This unit gives you an overview of nitrenes and reactions with nitrenes.

9.1  OBJECTIVES

After going through this unit, you will be able to:

- Understand the structure and generation of nitrenes
- Know about insertion reactions of carbenes
- Discuss rearrangement reactions
9.2 NITRENES

In chemistry, a nitrene (R–N=) is the nitrogen analogue of a carbene. The nitrogen atom has only 6 valence electrons and is therefore considered an electrophile. A nitrene is a reactive intermediate and is involved in many chemical reactions. The simplest nitrene, HN, is also called imidogen.

\[ R-N= \]

**Fig. 9.1 The Generic Structure of a Nitrene Group**

**Electron Configuration**

In the most simple nitrene, the linear imidogen (:N–H), two of the 6 available electrons form a covalent bond with hydrogen, two others create a free electron pair and the two remaining electrons occupy two degenerate p orbitals. Consistent with Hund’s rule the low energy form of imidogen is a triplet with one electron in each of the p orbitals and the high energy form is the singlet state with an electron pair filling one p orbital and the other one vacant.

As with carbenes, a strong correlation exists between the spin density on the nitrogen atom which can be calculated in silico and the zero-field splitting parameter D which can be derived experimentally from electron spin resonance. Small nitrenes such as NH or CF₃N have D values around 1.8 cm⁻¹ with spin densities close to a maximum value of 2. At the lower end of the scale are molecules with low D (< 0.4) values and spin density of 1.2 to 1.4 such as 9-anthrylnitrene and 9-phenanthrylnitrene.

**Structure and Hybridization**

Nitrenes are nitrogen analogous of carbenes. The nitrogen atom possess only six valence electrons; in nitrenes the triplet state is lower in energy than the single state.

Because nitrenes are so reactive, they are not isolated. Instead, they are formed as reactive intermediates during a reaction. There are two common ways to generate nitrenes:

- From azides by thermolysis or photolysis, with expulsion of nitrogen gas. This method is analogous to the formation of carbenes from diazo compounds.
- From isocyanates, with expulsion of carbon monoxide. This method is analogous to the formation of carbenes from ketenes.
Generation
From 1, 1 elimination

NOTES
From azides

Reactions
Nitrene reactions include:

- **Nitrene C–H Insertion.** A nitrene can easily insert into a carbon to hydrogen covalent bond yielding an amine or amid. A singlet nitrene reacts with retention of configuration. In one study a nitrene, formed by oxidation of a carbamate with potassium persulfate, gives an insertion reaction into the palladium to nitrogen bond of the reaction product of palladium(II) acetate with 2-phenylpyridine to methyl N-(2-pyridylphenyl)carbamate in a cascade reaction:

A nitrene intermediate is suspected in this C–H insertion involving an oxime, acetic anhydride leading to an isoindole:
Nitrene Cycloaddition. With alkenes, nitrenes react to form aziridines, very often with nitrenoid precursors such as nosyl- or tosyl-substituted [N-(phenylsulfonyl)iminophenylidinane (PhI=NNs or PhI=NTs respectively)] but the reaction is known to work directly with the sulfonamide in presence of a transition metal based catalyst such as copper, palladium, or gold:

In most cases, however, [N-(p-nitrophensulfonyl)iminophenylidinane (PhI=NNs) is prepared separately as follows:

Nitrene transfer takes place next:
In this particular reaction both the cis-stilbene illustrated and the trans form (not depicted) result in the same trans-aziridine product, suggesting a two-step reaction mechanism. The energy difference between triplet and singlet nitrenes can be very small in some cases, allowing interconversion at room temperature. Triplet nitrenes are thermodynamically more stable but react stepwise allowing free rotation and thus producing a mixture of stereochemistry.

### 9.3 Hoffmann and Beckmann Rearrangement Reactions

Hofmann and Beckmann rearrangement reactions are given below as examples of rearrangement with nitrogen as migration terminus:

**Hofmann Rearrangement**

\[
R-C\stackrel{O}{\text{NH}_2} \xrightarrow{\text{HOFb}} \text{N} = \text{C} = \text{O} \xrightarrow{\text{H}_2\text{O}} R-\text{NH}_2
\]

*Acid anhydride  
Base*  
*Acid anhydride  
Base*

**Beckman Rearrangement**

\[
R\xrightarrow{\text{R}} C=\text{N} \xrightarrow{\text{PCl}_3 \text{ or H}_2\text{SO}_4} \text{OH} \xrightarrow{\text{N} = \text{C} = \text{O} \xrightarrow{\text{H}_2\text{O}} R-\text{NH} \xrightarrow{\text{R}} ^{\text{R}} \]

*Ketene  
Substituted amide*  
*Ketone  
Substituted amide*

In Hofmann rearrangement elimination takes place to give a nitrene intermediate (I) which then by migration of the group R with its pair of electrons to the electron deficient nitrogen atom gives an isocyanate. Addition of water followed with the elimination of CO₂ gives the amine with one less carbon atom.

In the Beckmann rearrangement the oxime is converted to its O-ester (—OH group is converted to ester group). This group is then eliminated and the resulting ion carries a positive charge at nitrogen which then neutralizes its charge by inducing the migration of a group with its electron pair to it. Finally addition of a OH⁻ ion or H₂O completes the rearrangement.
Beckmann rearrangement is also intramolecular rearrangement. The most interesting feature of this rearrangement is that it is always the *trans*-alkyl group which migrates preferentially regardless of electron donating abilities or nucleophilicity of migrating group.

### 9.3.1 Curtius Rearrangement and Schmidt Reaction

#### Curtius Rearrangement

The Curtius rearrangement (or Curtius reaction or Curtius degradation), first defined by Theodor Curtius in 1885, is the thermal decomposition of an acyl azide to an isocyanate with loss of nitrogen gas. The isocyanate then undergoes attack by a variety of nucleophiles such as water, alcohols and amines, to yield a primary amine, carbamate or urea derivative respectively.

**Preparation of Acyl Azide**

The acyl azide is usually made from the reaction of acid chlorides or anydrides with sodium azide or trimethylsilyl azide. Acyl azides are also obtained from treating acylhydrazines with nitrous acid. Alternatively, the acyl azide can be formed by the direct reaction of a carboxylic acid with diphenylphosphoryl azide (DPPA).
Reaction Mechanism

It was believed that the Curtius rearrangement was a two-step process, with the loss of nitrogen gas forming an acyl nitrene, followed by migration of the R-group to give the isocyanate. However, recent research has indicated that the thermal decomposition is a concerted process, with both steps happening together, due to the absence of any nitrene insertion or addition byproducts observed or isolated in the reaction. Thermodynamic calculations also support a concerted mechanism.

The migration occurs with full retention of configuration at the R-group. The migratory aptitude of the R-group is roughly tertiary > secondary > primary. The isocyanate formed can then be hydrolyzed to give a primary amine, or undergo nucleophilic attack with alcohols and amines to form carbamates and urea derivatives respectively.

Schmidt Reaction

The Schmidt reaction is an organic reaction in which an azide reacts with a carbonyl group to give an amine or amide, with expulsion of nitrogen. It is named after Karl Friedrich Schmidt (1887–1971), who first reported it in 1924 by successfully converting benzophenone and hydrazoic acid to benzanilide. Surprisingly, the intramolecular reaction wasn’t reported until 1991 but has become important in the synthesis of natural products.
The reaction is effective with carboxylic acids to give amines (above), and with ketones to give amides (below).

**Reaction Mechanism**

The carboxylic acid Schmidt reaction starts with acylium ion 1 obtained from protonation and loss of water. Reaction with hydrazoic acid forms the protonated azido ketone 2, which goes through a rearrangement reaction with the alkyl group R, migrating over the C-N bond with expulsion of nitrogen. The protonated isocyanate is attacked by water forming carbamate 4, which after deprotonation loses carbon dioxide to the amine.

The reaction is related to the Curtius rearrangement except that in this reaction the azide is protonated and hence with different intermediates.

In the reaction mechanism for the ketone Schmidt reaction, the carbonyl group is activated by protonation for nucleophilic addition by the azide, forming intermediate 3, which loses water in an elimination reaction to temporary imine 4, over which one of the alkyl groups migrates from carbon to nitrogen with loss of nitrogen. A similar migration is found in the Beckmann rearrangement. Attack by water and proton loss converts 5 to 7, which is a tautomer of the final amide.
Nitrones

NOTES

Schmidt Reaction Mechanism Amide Formation

Migration of Carbon to an Electron Deficient Heteroatom

Check Your Progress

1. What is imidogen?
2. The nitrogen atom possesses how many valence electrons?
3. Which reaction is the thermal decomposition of an acyl azide to an isocyanate with loss of nitrogen gas?

9.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. The simplest nitrene, HN, is also imidogen.
2. The nitrogen atom possesses only six valence electrons.
3. Curtius rearrangement.
9.4 SUMMARY

- Nitrenes are nitrogen analogous of carbenes. The nitrogen atom possess only six valence electrons; in nitrenes the triplet state is lower in energy than the single state.

- There are two common ways to generate nitrenes: From azides by thermolysis or photolysis, with expulsion of nitrogen gas. This method is analogous to the formation of carbenes from diazo compounds. And from isocyanates, with expulsion of carbon monoxide. This method is analogous to the formation of carbenes from ketenes.

- In Hofmann rearrangement elimination takes place to give a nitrene intermediate (I) which then by migration of the group R with its pair of electrons to the electron deficient nitrogen atom gives an isocyanate. Addition of water followed with the elimination of CO₂ gives the amine with one less carbon atom.

- Beckmann rearrangement is also intramolecular rearrangement. The most interesting feature of this rearrangement is that it is always the trans-alkyl group which migrates preferentially regardless of electron donating abilities or nucleophilicity of migrating group.

- The Curtius rearrangement (or Curtius reaction or Curtius degradation), first defined by Theodor Curtius in 1885, is the thermal decomposition of an acyl azide to an isocyanate with loss of nitrogen gas. The isocyanate then undergoes attack by a variety of nucleophiles such as water, alcohols and amines, to yield a primary amine, carbamate or urea derivative respectively.

- The Schmidt reaction is an organic reaction in which an azide reacts with a carbonyl group to give an amine or amide, with expulsion of nitrogen. It is named after Karl Friedrich Schmidt (1887–1971), who first reported it in 1924 by successfully converting benzophenone and hydrazoic acid to benzanilide. Surprisingly, the intramolecular reaction wasn’t reported until 1991 but has become important in the synthesis of natural products.

9.5 KEY WORDS

- Nitrene: A nitrene (R–N) is the nitrogen analogue of a carbene. The nitrogen atom has only 6 valence electrons and is therefore considered an electrophile. A nitrene is a reactive intermediate and is involved in many chemical reactions.

- Schmidt Reaction: The Schmidt reaction is an organic reaction in which an azide reacts with a carbonyl group to give an amine or amide, with expulsion of nitrogen.
9.6 SELF ASSESSMENT QUESTIONS AND EXERCISES

NOTES

Short Answer Questions
1. What are nitrenes?
2. Discuss the structure of nitrenes.
3. Discuss the generation of nitrenes.

Long Answer Questions
1. Discuss Nitrene C–H insertion.
2. Explain Nitrene cycloaddition.
3. Illustrate the rearrangement with nitrogen as migration terminus.

9.7 FURTHER READINGS


UNIT 10 FREE RADICAL REACTIONS

Structure
10.0 Introduction
10.1 Objectives
10.2 Free Radical Reactions
  10.2.1 Depiction in Chemical Reactions
  10.2.2 Formation
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10.3 Polymerization, Substitution, Addition and Rearrangements Reactions
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10.0 INTRODUCTION

Radical, also called Free Radical, in chemistry, molecule that contains at least one unpaired electron. Most molecules contain even numbers of electrons, and the covalent chemical bonds holding the atoms together within a molecule normally consist of pairs of electrons jointly shared by the atoms linked by the bond. Most radicals may be considered to have arisen by cleavage of normal electron-pair bonds, every cleavage having produced two separate entities, each of which contains a single, unpaired electron from the broken bond (in addition to all the rest of the normal, paired electrons of the atoms).

Radicals are important in combustion, atmospheric chemistry, polymerization, plasma chemistry, biochemistry, and many other chemical processes. A large fraction of natural products is generated by radical-generating enzymes. In living organisms, the radicals superoxide and nitric oxide and their reaction products regulate many processes, such as control of vascular tone and thus blood pressure. They also play a key role in the intermediary metabolism of various biological compounds. Such radicals can even be messengers in a process dubbed redox signaling. A radical may be trapped within a solvent cage or be otherwise bound. Radical chain reactions are an important part in organic chemistry both as radical substitution and radical addition reactions. Radical addition chain reactions, for instance, may be found in radical polymerization.
Free Radical Reactions

In this unit, you will learn about free radicals and the reactions involving free radicals like polymerization, substitution, addition and rearrangement.

### 10.1 OBJECTIVES

After going through this unit, you will be able to:

- Get an overview of free radicals
- Discuss the mechanism of free radical reactions

### 10.2 FREE RADICAL REACTIONS

In chemistry, a radical is an atom, molecule, or ion that has an unpaired valence electron. With some exceptions, these unpaired electrons make radicals highly chemically reactive. Many radicals spontaneously dimerize. Most organic radicals have short lifetimes. A notable example of a radical is the hydroxyl radical (HO•), a molecule that has one unpaired electron on the oxygen atom. Two other examples are triplet oxygen and triplet carbene (CH•) which have two unpaired electrons.

Radicals may be generated in a number of ways, but typical methods involve redox reactions. Ionizing radiation, heat, electrical discharges, and electrolysis are known to produce radicals. Radicals are intermediates in many chemical reactions, more so than is apparent from the balanced equations. Radicals are important in combustion, atmospheric chemistry, polymerization, plasma chemistry, biochemistry, and many other chemical processes. A large fraction of natural products is generated by radical-generating enzymes. In living organisms, the radicals superoxide and nitric oxide and their reaction products regulate many processes, such as control of vascular tone and thus blood pressure. They also play a key role in the intermediary metabolism of various biological compounds. Such radicals can even be messengers in a process dubbed redox signaling. A radical may be trapped within a solvent cage or be otherwise bound.

#### 10.2.1 Depiction in Chemical Reactions

In chemical equations, radicals are frequently denoted by a dot placed immediately to the right of the atomic symbol or molecular formula as follows:

\[
\text{Cl}_2 \xrightarrow{\text{UV}} 2\text{Cl}^-
\]

Radical reaction mechanisms use single-headed arrows to depict the movement of single electrons:

The homolytic cleavage of the breaking bond is drawn with a ‘fish-hook’ arrow to distinguish from the usual movement of two electrons depicted by a
standard curly arrow. The second electron of the breaking bond also moves to pair up with the attacking radical electron; this is not explicitly indicated in this case. Radicals also take part in radical addition and radical substitution as reactive intermediates. Chain reactions involving radicals can usually be divided into three distinct processes. These are initiation, propagation, and termination.

- **Initiation** reactions are those that result in a net increase in the number of radicals. They may involve the formation of radicals from stable species as in Reaction 1 above or they may involve reactions of radicals with stable species to form more radicals.

- **Propagation** reactions are those reactions involving radicals in which the total number of radicals remains the same.

- **Termination** reactions are those reactions resulting in a net decrease in the number of radicals. Typically two radicals combine to form a more stable species, for example: \(2\text{Cl}^* \rightarrow \text{Cl}_2\)

### 10.2.2 Formation

**Homolysis**

Radicals can form by breaking of covalent bonds by homolysis. The homolytic bond dissociation energies, usually abbreviated as “\(\Delta H^\ddagger\)” are a measure of bond strength. Splitting \(\text{H}_2\) into \(2\text{H}^*\), for example, requires a \(\Delta H^\ddagger\) of +435 kJ\(\text{mol}^{-1}\), while splitting \(\text{Cl}_2\) into \(2\text{Cl}^*\) requires a \(\Delta H^\ddagger\) of +243 kJ\(\text{mol}^{-1}\). For weak bonds, homolysis can be induced thermally. Strong bonds require high energy photons or even flames to induce homolysis.

**From other radicals**

Radicals or charged species add to non-radicals to give new radicals. This process is the basis of the radical chain reaction. Being prevalent and a diradical, \(\text{O}_2\) reacts with many organic compounds to generate radicals together with the hydroperoxide radical. This process is related to rancidification of unsaturated fats.

**One electron redox**

Radicals may also be formed by single-electron oxidation or reduction of an atom or molecule. These redox reactions occur in electrochemical cells and in ionization chambers of mass spectrometers.

### 10.2.3 Persistence and Stability

Although radicals are generally short-lived due to their reactivity, there are long-lived radicals. These are categorized as follows:

**Stable radicals**

The prime example of a stable radical is molecular dioxygen (\(\text{O}_2\)). Another common example is nitric oxide (\(\text{NO}\)). Organic radicals can be long lived if they occur in a
conjugated π system, such as the radical derived from α-tocopherol (vitamin E). There are also hundreds of examples of thietyl radicals, which show low reactivity and remarkable thermodynamic stability with only a very limited extent of π resonance stabilization.

**Persistent radicals**

Persistent radical compounds are those whose longevity is due to steric crowding around the radical center, which makes it physically difficult for the radical to react with another molecule. Examples of these include Gomberg’s triphenylmethyl radical, Fremy’s salt (Potassium nitrosodisulfonate, (KSO₂)₂NO●), aminoxyls, (general formula R₂NO●) such as TEMPO, TEMPOL, nitroyl nitroxides, and azephenylgens and radicals derived from PTM (perchlorophenylmethyl radical) and TTM (tris(2,4,6-trichlorophenyl)methyl radical). Persistent radicals are generated in great quantity during combustion, and “may be responsible for the oxidative stress resulting in cardiopulmonary disease and probably cancer that has been attributed to exposure to airborne fine particles”.

Gomberg’s free radical can be generated by following reaction in lab -

\[(\text{Ph})_3\text{C}-\text{Cl} + \text{Ag} \rightarrow (\text{Ph})_3\text{C●} + \text{AgCl}\]

The reason for persistivity of free radicals is either the delocalisation of unpaired electron (e.g. triphenylmethyl radical) or the unavailability of unpaired electron to other species due to the screening of neighbouring atoms/groups (for example, tri-tert-butylphenoxyl radical).

**Diradicals**

Diradicals are molecules containing two radical centers. Multiple radical centers can exist in a molecule. Atmospheric oxygen naturally exists as a diradical in its ground state as triplet oxygen. The low reactivity of atmospheric oxygen is due to its diradical state. Non-radical states of dioxygen are actually less stable than the diradical. The relative stability of the oxygen diradical is primarily due to the spin-forbidden nature of the triplet-singlet transition required for it to grab electrons, i.e., “oxidize”. The diradical state of oxygen also results in its paramagnetic character, which is demonstrated by its attraction to an external magnet. Diradicals can also occur in metal-oxo complexes, lending themselves for studies of spin forbidden reactions in transition metal chemistry. Carbenes in their triplet state can be viewed as diradicals centred on the same atom, while these are usually highly reactive persistent carbenes are known, with N-heterocyclic carbenes being the most common example.

**10.2.4 Reactivity**

Radical alkyl intermediates are stabilized by similar physical processes to carbocations: as a general rule, the more substituted the radical center is, the more stable it is. This directs their reactions. Thus, formation of a tertiary radical (R₃C●)
is favored over secondary (R₂H₂C•), which is favored over primary (RH₂C•). Likewise, radicals next to functional groups such as carbonyl, nitrile, and ether are more stable than tertiary alkyl radicals. Radicals attack double bonds. However, unlike similar ions, such radical reactions are not as much directed by electrostatic interactions. For example, the reactivity of nucleophilic ions with α,β-unsaturated compounds (C=O–C=C=O) is directed by the electron-withdrawing effect of the oxygen, resulting in a partial positive charge on the carbonyl carbon. There are two reactions that are observed in the ionic case: the carbonyl is attacked in a direct addition to carbonyl, or the vinyl is attacked in conjugate addition, and in either case, the charge on the nucleophile is taken by the oxygen. Radicals add rapidly to the double bond, and the resulting radical carbonyl is relatively stable; it can couple with another molecule or be oxidized. Nonetheless, the electrophilic/nucleophilic character of radicals has been shown in a variety of instances. One example is the alternating tendency of the copolymerization of maleic anhydride (electrophile) and styrene (slightly nucleophilic).

In intramolecular reactions, precise control can be achieved despite the extreme reactivity of radicals. In general, radicals attack the closest reactive site the most readily. Therefore, when there is a choice, a preference for five-membered rings is observed; four-membered rings are too strained, and collisions with carbons six or more atoms away in the chain are infrequent.

Triplet carbenes and nitrenes, which are diradicals, have distinctive chemistry.

<table>
<thead>
<tr>
<th>Check Your Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. What are propagation reactions?</td>
</tr>
<tr>
<td>2. What are the processes involved in chain reactions involving radicals?</td>
</tr>
</tbody>
</table>

### 10.3 POLYMERIZATION, SUBSTITUTION, ADDITION AND REAPRANGEMENT REACTIONS

**Polymerisation Reactions**

The combination of simple molecules repeatedly two or more times in some regular manner so that they combine to form a larger or long chain molecule is known as polymerisation. The simple molecules which combine together are called, monomers and the products are known as dimer (only two monomer units), trimer (only three monomer units), or polymer (many monomer units). Carothers in 1931 defined polymerization as intermolecular combinations that are functionally capable of proceeding indefinitely. Starting from a monomer M formation of the polymer may be shown as:
Free Radical Reactions

\[ \text{M} \xrightarrow{+M} \text{Dimer} \xrightarrow{+M} \text{Trimer} \xrightarrow{+M} \text{Polymer} \]

Similarly starting from two different monomers M and M', the polymerisation may be shown as:

\[ \text{M} + \text{M'} \xrightarrow{+M} \text{Dimer} \xrightarrow{+M} \text{M'} + \text{M} \xrightarrow{+M} \text{Trimer} \xrightarrow{+M} \text{Polymer} \]

In these cases dimer is the compound having two repetitive monomer units, trimer having three, and polymer having many such repetitive units. A polymer which is formed from more than one monomer is often referred to as a copolymer of these co-monomers.

A vast majority of natural products like proteins, starch, rubber cellulose etc., are all polymers and are called natural polymers. The attempts to imitate these natural polymers have resulted in an exhaustive and systematic study of the process of polymerisation and a large number of new synthetic polymers like plastics, nylon, terylene have been developed by purely synthetic methods. The monomers for these synthetic polymers are mostly obtained from petroleum and are called petrochemicals.

Polymerisation reactions are divided into two groups:
1. Condensation polymerisation
2. Addition polymerisation.

In condensation polymerisation the basic monomer units combine through a condensation reaction by elimination of simple molecules (water, ammonia etc.) to give a product, generally of high molecular weight. Nylon and terylene are condensation polymers. Nylon is a polyamide formed by condensation of adipic acid with hexamethylene diamine accompanied with the elimination of water molecules.

\[ \text{HOOC}-(\text{CH}_2)_5\text{COOH} + \text{H}_2\text{N}-(\text{CH}_2)_6\text{NH}_2 \xrightarrow{\text{Formation of amide linkages}} \text{HOOC}-(\text{CH}_2)_5\text{NH}-(\text{CH}_2)_6\text{COOH} \]

Nylon (Polyamide)

Terylene is a polyester formed by the condensation of terephthalic acid with ethylene glycol accompanied with the elimination of water molecules.

\[ n\text{HO.CH}_2\text{CH}_2\text{OH} + n\text{HOOC}-(\text{CH}_2)_4\text{COOH} \xrightarrow{\text{Formation of ester linkages}} \text{HO}-(\text{OC}-(\text{CH}_2)_4\text{O})_n-(\text{OC}-(\text{CH}_2)_4\text{COOH}) \]

Terylene (Polyester)
In addition polymerization, the monomer units combine together to give a new product having the same empirical formula but a higher molecular weight. There is no liberation of simple small molecules like water during addition polymerisation. The monomers for addition polymerisation are mainly unsaturated compounds. For example, ethylene polymerises to give polyethylene or polythene—a plastic; and vinyl chloride polymerises to give polyvinyl chloride or P.V.C.

\[ n\text{CH}_2=\text{CH} \longrightarrow \text{[CH}_2-\text{CH}_2]_n \quad \text{(Polyethylene)} \]

\[ n\text{CH}_2=\text{CH} \longrightarrow \text{[CH}_2\text{CH}_2]_n \quad \text{(Polyvinyl chloride)} \]

The addition polymerisation may be initiated by anionic, cationic or free radical reagents. Such a reagent is known as an initiator and this determines the type and course of polymerisation reaction. The three different types of mechanisms for addition polymerisation are given below:

**Free radical mechanism**

1. **Initiation**

   \[ I \quad \text{(Initiator)} \longrightarrow I^- \quad \text{(Free radical)} \]

   \[ I^- + \text{CH}_2=\text{CH}_2 \longrightarrow \text{I}^-\text{CH}_2-\text{CH}_2 \quad \text{(New free radical)} \]

2. **Propagation**

   \[ \text{I}^-\text{CH}_2-\text{CH}_2 + \text{CH}_2=\text{CH}_2 \longrightarrow \text{I}^-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2 \quad \text{and so on} \]

3. **Termination**

   \[ 2 \quad \text{I}^-\text{CH}_2-\text{CH}_2-\text{I}^-\text{CH}_2 \longrightarrow \text{I}^-\text{CH}_2-\text{CH}_2-\text{I}^-\text{CH}_2 \quad \text{etc.} \]

**Anionic mechanism**

1. **Initiation**

   \[ I^- \longrightarrow \text{X}^- \quad \text{(Anion)} \]

   \[ \text{X}^- + \text{CH}_2=\text{CH}_2 \longrightarrow \text{X}^-\text{CH}_2-\text{CH}_2 \quad \text{(A new anion)} \]

2. **Propagation**

   \[ \text{X}^-\text{CH}_2-\text{CH}_2 + \text{CH}_2=\text{CH}_2 \longrightarrow \text{X}^-\text{CH}_2-\text{CH}_2-\text{CH}_2 \text{ and so on.} \]

3. **Termination**

   \[ \text{X}^-\text{CH}_2-\text{CH}_2-\text{I}^-\text{CH}_2 \quad \text{H}^+ \text{or a cation} \quad \text{X}^-\text{CH}_2-\text{CH}_2-\text{CH}_2 \text{Polymer} \]
Cationic mechanism

1. Initiation

\[ \text{I} \rightarrow \text{E}^+ \]  
\[ \text{E}^+ + \text{CH}_2=\text{CH}_2 \rightarrow \text{E} \rightarrow \text{CH}_3-\text{CH}_2^- \]  
(Cation)

\[ \text{E}^- + \text{CH}_2=\text{CH}_2 \rightarrow \text{E} \rightarrow \text{CH}_3-\text{CH}_2^- \]  
(A new cation)

2. Propagation

\[ \text{E} \rightarrow \text{CH}_3-\text{CH}_2^- + \text{CH}_2=\text{CH}_2 \rightarrow \text{E} \rightarrow \text{CH}_3-\text{CH}_2^- \rightarrow \text{CH}_3 \]  
and so on.

3. Termination

\[ \text{E} \rightarrow \text{CH}_3-\text{CH}_2^- + \text{E} \rightarrow \text{E} \rightarrow \text{CH}_3-\text{CH}_2^- \rightarrow \text{CH}_3 \]  
\[ \text{X}_{(n \text{ monomer})} \rightarrow \text{E} \rightarrow \text{CH}_3-\text{CH}_2^- \rightarrow \text{CH}_3 \text{X}_{(n \text{ monomer})} \]  
(Polymer)

Distinction Between Condensation and Polymerisation

1. Most common feature of the polymerisation reactions is that these are reversible reactions. Thus polymers by simple chemical operations may be converted back to monomers. Condensation reactions may or may not be reversible.

2. The polymers generally have very high molecular weights (except simple dimer, trimer etc.) whereas condensation products have comparatively lower molecular weights.

3. The condensation reaction may take place between same or different molecules or different types of groups whereas polymerisation occurs between similar monomers except in case of condensation polymerisation.

4. The molecular weight of polymers is a simple multiple of monomer molecular weight except in condensation polymerisation. The condensation products are formed by elimination of simple molecules and hence their molecular weights do not bear any multiple relationship with starting material.

5. Condensation reactions generally proceed through the formation of new carbon to carbon bonds between the condensing molecules whereas it is not necessary in polymerisation reactions. Thus simple polymers of many compounds like aldehydes involve only formation of bonds between carbon and oxygen. Thus formaldehyde gives:

\[ 3\text{HCHO} \quad \rightarrow \quad \text{CH}_2=\text{CH}_2 + \quad \n\text{HCHO} \quad \rightarrow \quad \text{CH}_2\text{O}_n \]

Formaldehyde

6. Generally condensation refers to those reactions in which the resultant product is made up of a smaller number of reacting molecules but if the number of reacting molecules is large it is called condensation polymerisation.
10.3.1 Substitution Reaction—Free Radical Substitution

Substitution reactions initiated by free radicals are known as free radical substitution reactions. A mechanism for such a general reaction $A - B + C - D \rightarrow A - C + B - D$ may be written as:

(i) Initiation $\cdot A - B \rightarrow A \cdot + B$ (Homolysis)
(ii) Reaction $C - D + A \cdot \rightarrow C - A + \cdot D$ (Propagation)
(iii) Termination $\cdot B + \cdot D \rightarrow B - D$

or $\cdot D + \cdot D \rightarrow D - D$

The initiation step is generally induced by heat or light depending on the molecule to be broken homolytically. Peroxides, peracids, azo compounds etc., are the most common source of free radicals. The halogen molecules and ketones give free radicals by absorbing energy from light. In the second step, the step of actual reaction, a free radical on reacting with a molecule $C - D$ generates a new radical $\cdot D$. This step is also referred to as propagation step. Finally all free radical reactions terminate by combination of free radicals or by disproportionation. Actually there may be a very large number of propagation steps in between initiation and termination of free radical reactions.

Free radical reactions are characterized by the three important features (i) They are unaffected by the polar substances like acids, bases or polar solvents, (ii) They are initiated and accelerated by a free radical source, and (iii) They are inhibited by substances that scavenge free radicals e.g. $O_2$, benzoquinone etc.

The important free radical substitutions illustrated here are halogenation of alkanes; and arylation of aromatic compounds by diazonium salts (Gomberg reaction).

Reactivity and structure. The reactivity of a substrate to free radical substitution has been studied with hydrogen as a departing group and the chlorine radical as attacking or abstracting reagent. Normally for different types of hydrogen the rate of substitution increases in the order primary $<$ secondary $<$ tertiary.

The preferred position of substitution in alkyl radicals attached to aromatic ring is the $\alpha$-hydrogen because the resulting radical, after removal of hydrogen, can acquire stability by delocalizing this electron over the entire ring. The positions next to electron withdrawing groups like $\cdot COOH$, $\cdot CN$ etc. are generally not attacked by free radicals. This may appear rather strange because radical reactions are not influenced by electron density distribution in substrate but since the combination of free radical with an electron of the molecule requires sufficient electron density at the centre, hence the effect. Solvents usually have no effect on such reactions. If the reaction takes place with optically active reactants the products are racemic because of planar configuration of free radical.
Applications

(i) Halogenation of alkanes
Chlorination of methane is induced by light and is a free radical substitution reaction. The mechanism for the reaction may be explained as follows:

In the initiation step a molecule of halogen (chlorine in this reaction) by absorption of energy from sunlight, gives two chlorine free radicals by homolysis.

In the propagation step, this radical then abstracts a proton from hydrocarbon (methane) to give a methyl free radical and HCl molecule. This methyl free radical then cleaves a chlorine molecule by homolysis to form methyl chloride and chlorine free radical which may again start the propagation step till all methane and chlorine is used up, giving CH₃Cl₂, CHCl₃ and CCl₄. The reaction terminates when two free radicals combine to give a neutral molecule.

Initiation
\[ \text{Cl}_2 \xrightarrow{\text{by light}} 2\text{Cl}^- \]

Propagation
\[
\begin{align*}
\text{Cl}^- + \text{CH}_4 & \rightarrow \text{CH}_3 + \text{HCl} \\
\text{CH}_3 + \text{Cl}_2 & \rightarrow \text{CH}_3\text{Cl} + \text{Cl}^- \\
\text{CH}_2 + \text{Cl}^- & \rightarrow \text{CH}_3\text{Cl} \\
2\text{CH}_3^- & \rightarrow \text{CH}_3 - \text{CH}_3 
\end{align*}
\]

Termination

Allylic and benzylic bromination. Bromination with N-bromosuccinimide (NBs) used to introduce bromine adjacent to olefinic, aromatic and carbonyl groups (Wohl–Ziegler bromination) is also a free radical substitution reaction.

\[
\begin{align*}
\text{C}_6\text{H}_5\text{CH}_3 & \xrightarrow{\text{min}} \text{C}_6\text{H}_5\text{CH} = \text{CH} - \text{Br} \\
\text{CH}_2 = \text{CH} - \text{CH}_3 & \xrightarrow{\text{min}} \text{CH} = \text{CH} - \text{CH}_2 - \text{Br} \\
\text{CH} = \text{C} & \xrightarrow{\text{Min}} \text{CH} = \text{CHCOOH} \\
\text{CH} = \text{C} - \text{NBr} & \xrightarrow{\text{Min}} \text{BrCH} = \text{C} - \text{CH} = \text{CHCOOH} \\
\end{align*}
\]

The reaction is favored at low concentrations of Br₂. The low energy of allylic C−H bond helps in homolysis to form a resonance stabilized radical.

(ii) Oxidation of hydrocarbons by oxygen
The photosensitized air oxidation of many organic compounds is a free radical substitution reaction initiated by oxygen in presence of initiators. The reaction proceeds as:

Initiation
\[ \text{R} - \text{H} \xrightarrow{\text{O}_2} \text{R} = \text{O}_2 + \text{I} - \text{H} \]

Propagation
\[
\begin{align*}
\text{RO}_2^- + \text{R} - \text{H} & \rightarrow \text{R} - \text{O} - \text{O} - \text{H} + \text{R}^- \\
\text{R}^- + \text{O}_2 & \rightarrow \text{R} - \text{O}_2^- 
\end{align*}
\]
**Termination** \[ \text{RO}_2^- + \text{R}^- \rightarrow \text{R} - \text{O} - \text{O} - \text{R} \text{ etc.} \]

**(iii) Arylation of aromatic compounds (Gomberg reaction)**

The reaction of benzene diazonium halide with benzene gives diphenyl by a free radical substitution reaction.

\[
\text{C}_6\text{H}_4\text{H} + \text{C}_6\text{H}_5\text{N}_2\text{X} \xrightarrow{\text{Alkali}} \text{C}_6\text{H}_4\text{H} \rightarrow \text{C}_6\text{H}_5\text{H} \text{ (Diphenyl)}
\]

The mechanism of the reaction is as follows:

**Initiation** \[ \text{C}_6\text{H}_4\text{H} \rightarrow \text{N} = \text{N} \rightarrow \text{X} \]

**Propagation**

\[ \text{C}_6\text{H}_4\text{H} \rightarrow \text{C}_6\text{H}_5\text{H} \]

**Termination** \[ \text{C}_6\text{H}_5\text{H} \rightarrow \text{C}_6\text{H}_5^- + \text{X} \]

**10.3.2 Free-Radical Addition**

Free-radical addition is an addition reaction in organic chemistry involving free radicals. The addition may occur between a radical and a non-radical, or between two radicals.

The basic steps with examples of the free-radical addition (also known as radical chain mechanism) are:

- Initiation by a radical initiator: A radical is created from a non-radical precursor.
- Chain propagation: A radical reacts with a non-radical to produce a new radical species
- Chain termination: Two radicals react with each other to create a non-radical species

Free-radical reactions depend on a reagent having a (relatively) weak bond, allowing it to homolyse to form radicals (often with heat or light). Reagents without such a weak bond would likely proceed via a different mechanism. An example of an addition reaction involving aryl radicals is the Meerwein arylation.
10.4 BARTON, SANDMEYER, ULLMANN, PSCHORR AND HUNSDIECKER REACTIONS

NOTES

Barton Reaction

The Barton reaction, also known as the Barton nitrite ester reaction, is a photochemical reaction that involves the photolysis of an alkyl nitrite to form a \( \delta \)-nitroso alcohol.

The Barton reaction involves a homolytic RO-NO cleavage, followed by \( \delta \)-hydrogen abstraction, free radical recombination, and tautomerization to form an oxime. Selectivity for the \( \delta \)-hydrogen is a result of the conformation of the 6-membered radical intermediate. Often, the site of hydrogen atom abstraction can be easily predicted. This allows the regio- and stereo-selective introduction of functionality into complicated molecules with high yield.

Reaction Mechanism

The Barton reaction commences with a photochemically induced cleavage of the nitrite O-N bond, typically using a high pressure mercury lamp. This produces an alkoxyl radical which immediately abstracts a hydrogen atom from the \( \delta \)-carbon. In the absence of other radical sources or other proximal reactive groups, the alkyl radical recombines with the nitrosyl radical. The resultant nitroso compounds undergoes tautomerization to the isolated oxime product.

![Barton Reaction Mechanism](image)

The carbon centered radical can be intercepted by other radical sources such as iodine or acrylonitrile. The first instance results in the \( \delta \)-hydrogen being replaced with iodine, then subsequent cyclization to a tetrahydrofuran by an SN2 reaction. The second example results in a chain elongation product with the oxime formed 2 carbon units further from the oxygen than normal.

Sandmeyer Reaction

The Sandmeyer reaction is a chemical reaction used to synthesize aryl halides from aryl diazonium salts using copper salts as reagents or catalysts. It is an example of a radical-nucleophilic aromatic substitution. The Sandmeyer reaction provides a method through which one can perform unique transformations on benzene, such as halogenation, cyanation, trifluoromethylation, and hydroxylation.
Reaction Mechanism

Formation of the nitrosonium ion

Formation of the benzenediazonium ion

Sandmeyer Reaction

Ullmann Reaction
The Ullmann reaction or Ullmann coupling is a coupling reaction between aryl halides and copper. The reaction is named after Fritz Ullmann.

\[
2 \text{Ar-X} + \text{Cu} \rightarrow \text{Ar-Ar} \quad X = \text{I, Br}
\]
Ullmann-type reaction is the copper-promoted conversion of aryl halides to aryl ethers, aryl thioethers, and aryl amines. Ullmann-type reactions are comparable to Buchwald-Hartwig reactions.

**NOTES**

In the case of Ullmann-type reactions (aminations, etherifications, etc. of aryl halides), the reaction involves copper(I) alkoxide or copper(I) amides. The copper(I) reagent can be generated in situ from the aryl halide and copper metal. Even copper(II) sources are effective. A number of innovations have been developed with regards to copper reagents.

These copper(I) compounds subsequently react with the aryl halide in a net metathesis reaction:

- \( \text{Ar}^-\text{X} + \text{RO}^-\text{Cu} \rightarrow \text{Ar}^-\text{OR} + \text{CuX} \)
- \( \text{Ar}^-\text{X} + \text{RSCu} \rightarrow \text{Ar}^-\text{SR} + \text{CuX} \)
- \( \text{Ar}^-\text{X} + 2 \text{RNHCu} \rightarrow \text{Ar}^-\text{NHR} + \text{CuX} \)

In the case of C-N coupling, kinetic studies implicate oxidative addition reaction followed by reductive elimination.

**Pschorr Cyclization**

The Pschorr cyclization is a name reaction in organic chemistry, which was named after its discoverer, the German chemist Robert Pschorr (1868-1930). It describes the intramolecular substitution of aromatic compounds via aryldiazonium salts as intermediates and is catalyzed by copper. The reaction is a variant of the Gomberg-Bachmann reaction. The following reaction scheme shows the Pschorr cyclization for the example of phenanthrene.

**Reaction Mechanism**

In the course of the Pschorr cyclization, a diazotization of the starting compound occurs, so that an aryldiazonium salt is formed as intermediate. For this, sodium nitrite is added to hydrochloric acid to obtain nitrous acid. The nitrous acid is protonated and reacts with another equivalent of nitrous acid to the intermediate 1 which is later used for the diazotization of the aromatic amine:
The intermediate 1 reacts in the following way with the starting compound:

Intermediate 1 replaces a hydrogen atom from the amino group of the starting compound. A nitroso group is introduced as new substituent, producing under the release of nitrous acid intermediate 2. Intermediate 2 then reacts via a tautomerism and dehydration to the aryl diazonium cation 3.

Nitrogen is then cleaved from the aryl diazonium cation 3 by the use of the copper catalyst. The aryl radical thus formed reacts via ring closure to the intermediate stage 4. Finally, rearomatization takes place using again the copper catalyst and phenanthrene is formed.

**Hunsdiecker Reaction**

The Hunsdiecker reaction (also called the Borodin reaction or the Hunsdiecker–Borodin reaction) is a name reaction in organic chemistry whereby silver salts of carboxylic acids react with a halogen to produce an organic halide. It is an example of both a decarboxylation and a halogenation reaction as the product has one fewer carbon atoms than the starting material (lost as carbon dioxide) and a halogen...
atom is introduced its place. The reaction was first demonstrated by Alexander Borodin in his 1861 reports of the preparation of methyl bromide from silver acetate. Shortly after, the approach was applied to the degradation of fatty acids in the laboratory of Adolf Lieben. However, it is named for Cläre Hunsdiecker and her husband Heinz Hunsdiecker, whose work in the 1930s developed it into a general method. Several reviews have been published, and a catalytic approach has been developed.

Reaction Mechanism

The reaction mechanism of the Hunsdiecker reaction is believed to involve organic radical intermediates. The silver salt of the carboxylic acid 1 will quickly react with bromine to form acyl hypohalite intermediate 2. Formation of the diradical pair 3 allows for radical decarboxylation to form the diradical pair 4, which will quickly recombine to form the desired organic halide 5. The trend in the yield of the resulting halide is primary > secondary > tertiary.

Check Your Progress

3. How Carothers defined polymerization?
4. What is the Sandmeyer reaction?

10.5 ANSWERS TO CHECK YOUR PROGRESS QUESTION

1. Propagation reactions are those reactions involving radicals in which the total number of radicals remains the same.
2. Chain reactions involving radicals can usually be divided into three distinct processes. These are initiation, propagation, and termination.
3. Carothers in 1931 defined polymerization as intermolecular combinations that are functionally capable of proceeding indefinitely.
4. The Sandmeyer reaction is a chemical reaction used to synthesize aryl halides from aryl diazonium salts using copper salts as reagents or catalysts. It is an example of a radical-nucleophilic aromatic substitution.
10.6 SUMMARY

- A radical is an atom, molecule, or ion that has an unpaired valence electron. With some exceptions, these unpaired electrons make radicals highly chemically reactive. Many radicals spontaneously dimerize. Most organic radicals have short lifetimes.
- Radicals or charged species add to non-radicals to give new radicals. This process is the basis of the radical chain reaction. Being prevalent and a diradical, \( \text{O}_2 \) reacts with many organic compounds to generate radicals together with the hydroperoxide radical. This process is related to nacidification of unsaturated fats.
- Although radicals are generally short-lived due to their reactivity, there are long-lived radicals. These are categorized as follows: Stable radicals, Persistent radicals and Diradicals.
- Radical alkyl intermediates are stabilized by similar physical processes to carbocations: as a general rule, the more substituted the radical center is, the more stable it is. This directs their reactions. Thus, formation of a tertiary radical \( (R,C\bullet) \) is favored over secondary \( (R,HC\bullet) \), which is favored over primary \( (RH,C\bullet) \). Likewise, radicals next to functional groups such as carbonyl, nitrile, and ether are more stable than tertiary alkyl radicals.
- Radical chain reactions play an important part in organic chemistry both as radical substitution and radical addition reactions. Radical addition chain reactions, for instance, may be found in radical polymerization.
- Free-radical addition is an addition reaction in organic chemistry involving free radicals. The addition may occur between a radical and a non-radical, or between two radicals.
- The important free radical substitutions are halogenation of alkanes; and arylation of aromatic compounds by diazonium salts (Gomberg reaction).
- The combination of simple molecules repeatedly two or more times in some regular manner so that they combine to form a larger or long chain molecule is known as polymerisation.

10.7 KEY WORDS

- **Free radicals**: Radical, also called Free Radical, in chemistry, molecule that contains at least one unpaired electron.
- **Polymerization**: The combination of simple molecules repeatedly two or more times in some regular manner so that they combine to form a larger or long chain molecule is known as polymerisation.
10.8 SELF ASSESSMENT QUESTIONS AND EXERCISES

NOTES

Short Answer Questions

1. What are free radicals? Discuss.
2. How are free radicals formed?
3. What do you understand by the stability of free radicals?
4. What are the main reactions involving free radicals? Discuss.
5. What is the difference between condensation and polymerization?
6. Discuss the mechanism involved in oxidation of hydrocarbons by oxygen.

Long Answer Questions

1. Illustrate the mechanism of free radical polymerization.
2. Explain the applications of free radical substitution reaction.
3. Explain in brief addition of free radicals.
4. Discuss the reaction mechanism of Hunsdiecker reaction.
5. Write a short note on the following reaction:
   (a) Barton
   (b) Gomberg
   (c) Sandmayer
   (d) Ullmann
   (e) Pschorr

10.9 FURTHER READINGS

UNIT 11 FUNDAMENTALS OF PHOTOCHEMISTRY

11.0 INTRODUCTION

Photochemistry is the branch of chemistry concerned with the chemical effects of light. Generally, this term is used to describe a chemical reaction caused by absorption of ultraviolet (wavelength from 100 to 400 nm), visible light (400–750 nm) or infrared radiation (750–2500 nm).

In nature, photochemistry is of immense importance as it is the basis of photosynthesis, vision, and the formation of vitamin D with sunlight. Photochemical reactions proceed differently than temperature-driven reactions. Photochemical paths access high energy intermediates that cannot be generated thermally, thereby overcoming large activation barriers in a short period of time, and allowing reactions otherwise inaccessible by thermal processes. Photochemistry is also destructive.

This unit discusses the concept of photochemistry in detail. You will learn about principles, processes and mechanism of photochemistry.

11.1 OBJECTIVES

After going through this unit, you will be able to:

- Learn the principles of photochemistry
- Understand organic photochemistry
- Discuss photochemical processes
- Explain mechanism of energy absorption
11.2 FUNDAMENTALS OF PHOTOCHEMISTRY - PRINCIPLES

The study of chemical reactions, isomerizations and physical behavior that may occur under the influence of visible and/or ultraviolet light is called Photochemistry. Two fundamental principles are the foundation for understanding photochemical transformations:

- **The first law of photochemistry, the Grotthuss-Draper law**, states that light must be absorbed by a compound in order for a photochemical reaction to take place.

- **The second law of photochemistry, the Stark-Einstein law**, states that for each photon of light absorbed by a chemical system, only one molecule is activated for subsequent reaction. This “photoequivalence law” was derived by Albert Einstein during his development of the quantum (photon) theory of light.

In the case of photochemical reactions, light provides the activation energy. Simplistically, light is one mechanism for providing the activation energy required for many reactions. If laser light is employed, it is possible to selectively excite a molecule so as to produce a desired electronic and vibrational state. Equally, the emission from a particular state may be selectively monitored, providing a measure of the population of that state. If the chemical system is at low pressure, this enables scientists to observe the energy distribution of the products of a chemical reaction before the differences in energy have been smeared out and averaged by repeated collisions.

The absorption of a photon of light by a reactant molecule may also permit a reaction to occur not just by bringing the molecule to the necessary activation energy, but also by changing the symmetry of the molecule’s electronic configuration, enabling an otherwise inaccessible reaction path, as described by the Woodward–Hoffmann selection rules. A 2+2 cycloaddition reaction is one example of a pericyclic reaction that can be analyzed using these rules or by the related frontier molecular orbital theory.

Some photochemical reactions are several orders of magnitude faster than thermal reactions; reactions as fast as 10–9 seconds and associated processes as fast as 10–15 seconds are often observed.

The photon can be absorbed directly by the reactant or by a photosensitizer, which absorbs the photon and transfers the energy to the reactant. The opposite process is called quenching when a photoexcited state is deactivated by a chemical reagent.
Most photochemical transformations occur through a series of simple steps known as primary photochemical processes. One common example of these processes is the excited state proton transfer.

### 11.2.1 Organic Photochemistry

The study of organic chemical reactions which occur by the action of light is included in the Organic Photochemistry. The energy associated with infrared radiations is only sufficient to cause rotational and vibrational excitations of the molecules while the energy associated with ultraviolet and visible radiations is capable of causing electronic excitations in the molecules which may result in a chemical reaction. For a reaction to take place reacting molecule must be supplied the required activation energy. In case of photochemical reactions this activation energy is obtained from ultraviolet or visible radiations. Most common example of a photochemical reaction is the process of photosynthesis in plants, whereby carbon dioxide and water combine in the presence of sunlight to produce carbohydrates.

**Photochemical Processes**

Photochemical reactions generally consist of two processes:

(a) **Primary process.** In which the ultraviolet or visible light is absorbed by the reactants to produce excited state. According to **Einstein law of photochemical equivalence** the quantum yield of the primary processes in the photochemical reactions should be 1.0 as absorption of light by molecules is quantised and each molecule will absorb only one quantum of energy.

\[
\text{Quantum yield (} \Phi \text{)} = \frac{\text{No. of molecules reacting or formed in unit time}}{\text{No. of quanta absorbed in unit time}}.
\]

In most photochemical reactions the quantum yield is less than 1.0 because of the decay of some light energy in processes like fluorescence, phosphorescence etc. but in some photochemical reactions which proceed as chain reactions the quantum yield may have a very high value due to secondary processes.

(b) **Secondary process.** The activated product of primary process may further undergo several types of chemical reactions namely isomerization, dimerization, rearrangement as well as addition, substitution and elimination reactions.

Sometimes the activated product (after absorption of light) itself does not undergo any reaction but transfers its energy to another molecule (called **acceptor**) which then undergoes a chemical reaction. Such reactions are called **photonsensitised reactions** and the energy transfer from donor to acceptor is referred to as **sensitisation.**

**Mechanism of Energy Absorption and Excited States**

In molecular spectroscopy, a Jablonski diagram is a diagram that illustrates the electronic states of a molecule and the transitions between them. The states are
arranged vertically by energy and grouped horizontally by spin multiplicity. Nonradiative transitions are indicated by squiggly arrows and radiative transitions by straight arrows. The vibrational ground states of each electronic state are indicated with thick lines, the higher vibrational states with thinner lines. The diagram is named after the Polish physicist Aleksander Jablonski.

In a typical organic molecule the electrons are usually paired in the ground state and occupy bonding $\sigma$, $\pi$ or $n$ (non-bonding) orbitals while $\sigma^*$ and $\pi^*$ antibonding orbitals are vacant. Absorption of radiation of correct energy may result in $\sigma \rightarrow \sigma^*$, $\pi \rightarrow \pi^*$, $\pi \rightarrow \pi^*$ absorption. Of these only $n \rightarrow \sigma^*$ and $\pi \rightarrow \pi^*$ absorptions occur in proper ultraviolet or visible region and are of significance in photochemistry.

On absorption of radiation of proper energy one of the electron from a pair is excited to next available vacant antibonding orbital without spin inversion. This excited state where the electron spin remains paired is called excited singlet state ($S_1$). This electronic excitation is generally followed by spin inversion of excited electron giving rise to a new excited state with two unpaired electrons which is called excited triplet state ($T_1$). The excited triplet state is generally more stable than the corresponding singlet state because of less interelectronic repulsion but direct excitation of the ground state ($S_0$) to a triplet state ($T_1$) is not possible and hence $T_1$ is always formed via $S_1$. This $S_1$ to $T_1$ change is a slow process but if $S_1$ is sufficiently long lived (as in carbonyl compounds) then $S_1$ to $T_1$ change known as intersystem crossing may occur efficiently.

However, a molecule may also be excited to higher states such as upper excited singlet state ($S_2$) or ($S_3$) etc. The lifetime of upper excited singlet state is very small (usually $10^{-11}$ sec.) and they decay to lowest excited singlet state ($S_1$) by internal conversion process. $S_1$ state has an average life of approximately $10^{-8}$ sec. and may undergo several processes:

(i) Revert to ground state ($S_0$) by emitting a photon; the process known as **fluorescence**;
(ii) Reverting to $S_0$ by radiationless emissions;
(iii) $S_1$ may decay to a $T_1$; or
(iv) $S_1$ may undergo a chemical reaction.

$AT_1$ state cannot be converted back to $S_1$ due to higher energy of $S_1$ but it may undergo several processes, for example,

(i) Radiationless decay to $S_0$;
(ii) Revert to ground state ($S_0$) emitting a photon; the process known as **phosphorescence**;
(iii) $T_1$ may undergo chemical reaction.
Fig. 11.1 Jolanski Diagram Possible Excitation and Loss of Excitation Energy

As is clear from the above figure $S_2$ and $T_1$ states have different energy contents and electronic configurations. Therefore they are expected to exhibit different chemical and photochemical reactions as can be seen in the photochemistry of olefins discussed in the next unit.

Check Your Progress

1. A chemical reaction that occurs as a consequence of light absorption is called what?
2. What is known as dissociation of molecule to form free radicals on absorption of light?
3. Excited state formed initially by absorption of radiation by a molecule is generally which state?

11.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Photochemical reaction.
2. Primary process.
3. Singlet state.

11.4 SUMMARY

- The study of chemical reactions, isomerizations and physical behavior that may occur under the influence of visible and/or ultraviolet light is called Photochemistry.
• Most common example of a photochemical reaction is the process of photosynthesis in plants, whereby carbon dioxide and water combine in the presence of sunlight to produce carbohydrates.

• According to Einstein law of photochemical equivalence the quantum yield of the primary processes in the photochemical reactions should be 1.0 as absorption of light by molecules is quantised and each molecule will absorb only one quantum of energy.

• Most photochemical transformations occur through a series of simple steps known as primary photochemical processes. One common example of these processes is the excited state proton transfer.

• On absorption of radiation of proper energy one of the electron from a pair is excited to next available vacant antibonding orbital without spin inversion. This excited state where the electron spin remains paired is called excited singlet state (S\(_1\)). This electronic excitation is generally followed by spin inversion of excited electron giving rise to a new excited state with two unpaired electrons which is called excited triplet state (T\(_1\))\(^1\).

• The triplet state is generally more stable than the corresponding singlet state because of less interelectronic repulsion but direct excitation of the ground state (S\(_0\)) to a triplet state (T\(_1\)) is not possible and hence T\(_1\) is always formed via S1. This S\(_1\) to T\(_1\) change is a slow process but if S\(_1\) is sufficiently long lived (as in carbonyl compounds) then S\(_1\) to T\(_1\) change known as intersystem crossing may occur efficiently.

11.5 KEY WORDS

• Photochemistry: The study of chemical reactions, isomerizations and physical behavior that may occur under the influence of visible and/or ultraviolet light is called Photochemistry.

• Singlet state: Excited state formed initially by absorption of radiation by a molecule.

11.6 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. Discuss the principles of photochemistry.
2. What processes are included in photochemical reactions?
3. Write a short note on quantum efficiency.
4. What do you understand by sensitisation?
5. What is quenching?
Long Answer Questions

1. What are photochemical processes? Explain with examples.
2. How does a triplet state differ from singlet state? Explain by taking a suitable example.
3. Explain the following terms in brief:
   (a) Excited singlet state
   (b) Intersystem crossing
   (c) Internal conversion
   (d) Photosensitizer
4. Reactions of singlet and triplet excited state of same molecule may be different. Explain giving one example.
5. Draw Jablonski diagram and explain its mechanism.

11.7 FURTHER READINGS

UNIT 12 PHOTOCHEMICAL REACTION

12.0 INTRODUCTION

Photochemical reaction, a chemical reaction initiated by the absorption of energy in the form of light. The consequence of molecules’ absorbing light is the creation of transient excited states whose chemical and physical properties differ greatly from the original molecules. These new chemical species can fall apart, change to new structures, combine with each other or other molecules, or transfer electrons, hydrogen atoms, protons, or their electronic excitation energy to other molecules. Excited states are stronger acids and stronger reductants than the original ground states.

It is this last property that is crucial in the most important of all photochemical processes, photosynthesis, upon which almost all life on Earth depends. Through photosynthesis, plants convert the energy of sunlight into stored chemical energy by forming carbohydrates from atmospheric carbon dioxide and water and releasing molecular oxygen as a byproduct.

Photochemical reactions and the properties of excited states are also critical in many commercial processes and devices. Photography and xerography are both based upon photochemical processes, while the manufacture of semiconductor chips or the preparation of masks for printing newspapers relies on UV light to destroy molecules in selected regions of polymer masks.

In chemistry isomerization (also isomerisation) is the process by which one molecule is transformed into another molecule which has exactly the same atoms, but the atoms have a different arrangement, for example, A-B-C → B-A-C (these related molecules are known as isomers. In some molecules and under some conditions, isomerization occurs spontaneously. Many isomers are roughly equal in bond energy, and so exist in roughly equal amounts, provided that they can

Structure
12.0 Introduction
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interconvert somewhat freely; that is, the energy barrier between the two isomers is not too high. When the isomerization occurs intramolecularly it is considered a rearrangement reaction.

This unit discusses photochemical reactions and their mechanisms.

### 12.1 Objectives

After going through this unit, you will be able to:

- Understand the mechanism of photochemical reactions
- Know about Norrish type I and II reactions
- Discuss the photochemistry of olefins

### 12.2 Photochemical Reaction

**Photochemical Elimination Reactions—Norrish Type I Reactions**

Photochemical reactions of ketones resulting in the cleavage of carbon-carbon bond (α-C—C bond) adjacent to carbonyl group followed by elimination are referred to as *Norrish type I* reactions. The bond dissociation energy of α-carbon-carbon bond in carbonyl compounds is comparatively low and photoexcitation of carbonyl compounds generally results in the homolytic fission of the α-carbon-carbon bond.

The most studied example is that of acetone. Irradiation of acetone in vapour or liquid phase with radiation of 280 nm results in $n \rightarrow \pi^*$ excited singlet state ($S_1$) of acetone. At room temperature most of the excited singlet state molecules undergo intersystem crossing to excited triplet state ($T_1$). The $T_1$ then undergoes cleavage at α-carbon-carbon bond yielding a methyl and an acetyl radical.

$$\text{(CH}_3\text{CO)} \quad \text{by} \quad \text{CH}_3C=O \quad \text{Triplet state} \quad \text{Acetyl radical} \quad \text{Methyl radical}$$

At room temperature the two acetyl radicals combine to form biacetyl

$$2 \text{CH}_3C=O \quad \quad \text{Biacetyl}$$

The other products obtained are methane, acetaldehyde and hexane-2,5-dione which may be formed as follows:

$$\begin{align*}
\text{CH}_3C=O & \quad + \quad \text{CH}_3\text{COCH}_3 \\
\text{Acetyl radical} & \quad \quad \text{Acetone} \quad \quad \text{Acetaldehyde} \quad \quad \text{Acetonyl radical} \\
\text{-CH}_3 & \quad + \quad \text{CH}_3\text{COCH}_3 \\
\text{Methyl radical} & \quad \quad \text{Methane} \quad \quad \text{Acetonyl radical}
\end{align*}$$

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**Photochemical Reaction**

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**NOTES**

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**Self-Instructional Material**

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\[ 2 \text{CH}_3\text{CO.CH}_3 \rightarrow \text{CH}_3\text{CO.CH}_2\text{CH}_2\text{CO.CH}_3 \]

Acetyl radical \hspace{1cm} Hexane-2,5-dione

At higher temperatures (>100°C) there is less intersystem crossing and thus the important species taking part in Norrish type I reaction is excited singlet state which results in decarbonylation of acetyl radical to produce methyl radical. These methyl radicals then combine to form ethane.

\[
\text{CH}_3\text{CO} \rightarrow \text{CH}_3\text{CHO} \rightarrow \text{CH}_3\text{C} + \text{CH}_4
\]

Singlet excited state \hspace{1cm} Acetyl radical \hspace{1cm} Methyl radical

\[
\text{CH}_3 \rightarrow \text{CH} + \text{CO}
\]

Carbon monoxide

\[
2 \cdot \text{CH}_3 \rightarrow \text{CH}_2\text{CH}_3
\]

Ethane

In unsymmetrical ketones, the homolytic fission of \(\alpha\)-carbon-carbon bond, in the excited state occurs in a way so as to produce the more stable of the two possible free radicals. Thus methyl ethyl ketone and methyl isopropyl ketone undergo photodecomposition as below:

\[
\text{CH}_3\text{C(O)CH}_2\text{CH}_3 \rightarrow \text{CH}_3\text{COCH}_2\text{CH}_3 \rightarrow \text{CH}_3\text{C} + \text{CH}_3\text{CH}_2
\]

Methyl ethyl ketone \hspace{1cm} Excited state \hspace{1cm} Acetyl radical

\[
\text{CH}_3\text{COCH}(\text{CH}_3)_2 \rightarrow \text{CH}_3\text{COOCH}(\text{CH}_3)_2 \rightarrow \text{CH}_3\text{C} + \text{CH}_3\text{CH}_2\text{CH}_3
\]

Methyl isopropyl ketone

Photolysis of dibenzyl ketone in Norrish type I reaction forms dibenzyl and carbon monoxide.

\[
(C_6\text{H}_5\text{CH}_2)_2\text{CO} \rightarrow [(C_6\text{H}_5\text{CH}_2)_2\text{CO}]^* \rightarrow \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2 + \text{C}_6\text{H}_5\text{CH}_2\text{C}
\]

Benzyl radical \hspace{1cm} Benzyl (aryl methyl) radical

\[
\text{C}_6\text{H}_5\text{CH}_2\text{C} \rightarrow \text{C}_6\text{H}_5\text{CH}_2 + \text{CO}
\]

Carbon monoxide

\[
2\text{C}_6\text{H}_5\text{CH}_2 \rightarrow \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{C}
\]

Dibenzyl

Some other interesting examples of Norrish type I reaction are photolytic decarboxylation of cyclopentanone and other cyclic ketones.
or alternatively the initial biradical formed may undergo a hydrogen transfer reactions forming ketone or unsaturated aldehyde.

Norrish Type II Reactions
In ketones where the carbon chain is large and has a hydrogen at α-position the photochemical reaction results in the formation of an alkene and a ketone and is known as Norrish type II reaction.

On absorption of ultraviolet radiation hexane-2-one undergoes $\pi \rightarrow \pi^*$ as well as $\pi \rightarrow \pi^*$ excitation forming a singlet state which by intersystem crossing changes to triplet state.
This triplet state is involved in intramolecular hydrogen abstraction from \( \gamma \)-carbon probably forming a six membered cyclic transition state. The latter then changes to an alken and enolic form of ketone by homolysis of \( \beta \)-carbon-carbon bond of original ketone. Spectroscopic evidence suggests that disappearance of the starting ketone occurs at almost the same rate as the appearance of enolic form of end product ketone. The intermediate transition state (I) formed by \( \gamma \)-hydrogen abstraction by oxygen atom is a biradical and may lead to ring closure forming a by-product.

In case all the \( \gamma \)-hydrogens are replaced by deuterium, the reaction proceeds readily forming alkene and ketone. It appears that there is some kind of an equilibrium between excited state of starting ketone and the biradical (I) though it requires more energy to break O—D bond. Hence the reaction proceeds smoothly only in forward direction.

Sometimes Norrish type II reaction may be accompanied by a Norrish type I reaction, as has been observed in case of irradiation of 2-pentanone

Norrish Type I

\[
\text{CH}_3\text{COCH}_2\text{CH}_2\text{CH}_3 \xrightarrow{hv} [\text{CH}_3\text{CO} + \text{CH}_3\text{H}_2\text{CH}_3] \rightarrow (\text{CH}_3\text{CH}_2\text{CH}_2\text{H}) + \text{CH}_3\text{COCH}_2\text{H}
\]

Norrish Type II

\[
\text{CH}_3\text{COCH}_2\text{CH}_2\text{CH}_3 \xrightarrow{hv} [\text{CH}_3\text{H}_2\text{O} + \text{CH}_3\text{CH}_2\text{CH}_3] \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{H} + \text{CH}_3\text{CH}_2\text{COCH}_2\text{H}
\]
**Photoaddition of Alkene to Carbonyl Compounds Paterno Büchi Reaction**

When a carbonyl compound and alkene mixture is irradiated with light of suitable wavelength, they undergo photocycloaddition to form oxetanes. The reaction is commonly referred to as **Paterno Büchi** reaction. The reaction occurs when the mixture is irradiated with radiations absorbed by carbonyl compound rather than by radiations absorbed by alkynes. This suggests that the reaction is initiated by $n \rightarrow \pi^*$ transition. However in conjugated ketones both $n \rightarrow \pi^*$ as well as $\pi \rightarrow \pi^*$ excited states may participate in the reaction.

![Reaction Mechanism](image)

In cases where there is a possibility of formation of two different oxetanes (for example with an unsymmetrical alkene) then one of these is a major product (about 90%) and other one is a minor product.

**Mechanism of the Paterno Büchi reaction may be summarised as follows:**

1. **Singlet state**
   - Ketone $\rightarrow$ Singlet state $\rightarrow$ Intramolecular cyclization $\rightarrow$ Triplet state

2. **Triplet state**
   - Minor product (10%)

3. **Major product (90%)**
   - Unsymmetrical alkene

*Self-instructional Material*

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Photochemical Reaction

Notes

The olefin used in the reaction is unsymmetrical which leads to formation of two different oxetanes. Preferential formation of major product shows that the intermediate is a biradical and the addition occurs in a manner so as to form the most stable biradical intermediate (i.e. a 3° radical rather than 1° radical).

Evidence for the involvement of triplet excited state follows from the similarities with the photoreduction reaction of the ketone. Any carbonyl compound which is inert towards photoreduction does not show photocycloaddition reaction also. Since a triplet state is involved in photoreduction, it therefore follows that same must be involved in photocycloaddition also.

The reaction does not appear to be a concerted one but involves formation of a biradical as the irradiation of benzophenone with either cis- or trans- butene-2 gives the same mixture of both isomeric oxetanes. Had it been a concerted reaction different products would have resulted in each case?

Paterno-Büchi reaction fails to occur with conjugated dienes whose triplet excitation energy is less than that of ketone but occurs with acetylenes.

Photochemistry of α,β-Unsaturated Ketones

In α,β-unsaturated ketones due to conjugation the energy gap between \( \pi \) and \( \pi^* \) is much less as compared to a saturated ketone. Consequently \( \pi \rightarrow \pi^* \) transition occur at much longer wavelength. Ultraviolet absorption spectra of a common \( \alpha,\beta \)-unsaturated ketone show two absorption maxima — one around 220 nm (for \( \pi \rightarrow \pi^* \)) and other around 310 nm (for \( n \rightarrow \pi^* \)). Irradiation of such a ketone may result in any of these transitions but excited state has more of \( \pi \rightarrow \pi^* \) character than \( n \rightarrow \pi^* \) triplet character which undergoes either photocycloaddition or olefin addition at the double bond of α,β-unsaturated ketone.

Photodimerization of cyclic α,β-unsaturated ketone like cyclopentenone yields two different dimers in almost equal amounts — one in which two units are joined head to head (I) and the other in which two units are joined head to tail (II).

\[
\text{Cyclopentenone} \quad \begin{array}{c} \text{(I)} \\ \text{(II)} \end{array}
\]

Similarly cyclohexenone also gives two major products

Photocycloaddition of alkenes to cyclic α,β-unsaturated ketones generally involves the initial formation of a carbon-carbon bond between the α-carbon of α,β-unsaturated ketone and the olefin giving a biradical which then cyclizes.
12.3 PHOTOCHEMISTRY OF OLEFINS

Photochemistry of Olefins—Isomerization and Dimerization

Irradiation of olefins with proper ultraviolet radiations causes $\pi \rightarrow \pi^*$ transition with no change in multiplicity resulting in a singlet excited state, the transition being symmetry allowed. This excited singlet state may undergo isomerization or may change to triplet excited state by intersystem crossing which then undergoes isomerization easily as the triplet excited state possesses a lower energy barrier to rotation around the double bond.

Photoisomerization of stilbene is perhaps the most understood case. When either cis- or trans- stilbene is irradiated with 210 nm radiation a mixture containing 93% cis- and 70% trans- isomer of stilbene is formed. Absorption of radiation by either isomer forms excited singlet state which by intersystem crossing changes to respective triplet state leading to photoisomerization by interconversion or via a common excited triplet state as shown below:

- $\text{cis-Stilbene} \rightarrow \text{trans-Stilbene}$
- $\text{trans-Stilbene} \rightarrow \text{cis-Stilbene}$
- $\text{Trans Stilbene} \rightarrow \text{cis-Stilbene}$

**Check Your Progress**

1. Photolysis of acetone at room temperature to yield biacetyl and other products is what of reaction?
2. Hexane-2-one undergoes photolysis to form propene and acetone. The reaction is an example of which reaction?
3. Photolysis of dibenzyl ketone to form dibenzyl and CO is a reaction known as?
Photoisomerization of stilbene can be sensitized by a sensitizer like benzophenone. Thus when either cis- or trans-stilbene mixed with benzophenone is irradiated with a radiation of 366 nm (a wavelength at which stilbene does not show any absorption), first an excited singlet state of benzophenone is formed which by inter-system crossing changes to excited triplet state. This excited triplet state of benzophenone acts as a donor toward either cis- or trans-stilbene and energy transfer from excited triplet state of donor to either cis- or trans-stilbene (acceptor) forms the corresponding excited triplet state of stilbene regenerating benzophenone in the ground state. Photoisomerization then occurs either through interconversion of excited triplet state of stilbene or via a common triplet intermediate as shown below:

\[
\begin{align*}
C_6H_5COC_6H_5 & \xrightarrow{h\nu} [C_6H_5COC_6H_5]^T_c \\
\text{Benzophenone} & \quad + \\
& \quad \text{cis-Stilbene or trans-Stilbene}
\end{align*}
\]

\[
\text{cis-Stilbene + trans-Stilbene} \xrightarrow{99\%} \quad \text{[C}_6\text{H}_5\text{CH} \rightleftharpoons \text{CHC}_6\text{H}_5\text{]}^{T_c} + \quad \text{C}_6\text{H}_5\text{COC}_6\text{H}_5 (\text{Ground state})
\]

Direct irradiation of butadiene with radiation of 217 nm yields cycllobutene and bicyclo[1.1.0] butane as a result of valence isomerization.

\[
\begin{align*}
\text{Butadiene} & \xrightarrow{h\nu} \quad \boxed{\text{Bicyclo[1.1.0]butane}} + \quad \boxed{\text{Cycllobutene}}
\end{align*}
\]

As butadiene exists in solution as a mixture of 95% trans- and 5% cis-conformers, the irradiation causes \( \pi \rightarrow \pi^* \) transition or from \( \psi_2 \) to \( \psi_3 \) resulting in increased bonding between \( \text{C}_1 \) and \( \text{C}_2 \). The conformational character of butadienes is thus retained in the excited singlet state \( (S_1) \). Due to large energy difference between excited singlet state \( (S_1) \) and the excited triplet state \( (T_1) \) of butadiene the inter-system crossing is not efficient and (\( S_1 \)) of cis- and trans-butadienes isomerizes to cycllobutene and bicyclobutane respectively as shown below:

\[
\begin{align*}
\text{Butadiene} & \xrightarrow{h\nu} \quad \boxed{\text{Bicyclo[1.1.0]butane}} \quad (S_1) \\
\text{trans-Butadiene} & \xrightarrow{h\nu} \quad \boxed{\text{Cycllobutene}} \\
\text{cis-Butadiene} & \xrightarrow{h\nu} \quad \boxed{\text{Bicyclo[1.1.0]butane}} \quad (S_1)
\end{align*}
\]

However irradiation of butadiene in presence of sensitizer benzophenone (or biacetyl) with radiation of 366 nm results in dimerization to various products.

\[
\begin{align*}
\text{Benzophenone} & \xrightarrow{h\nu} \quad \boxed{\text{Butadiene}} + \quad \boxed{\text{Butadiene}} + \quad \boxed{\text{Butadiene}}
\end{align*}
\]
On absorption of radiation benzophenone changes to \( S_1 \) and then \( T_1 \) state. The \( T_1 \) states of butadiene are of lower energy than those of benzophenone. Therefore energy transfer from donor (\( T_1 \) of benzophenone) to acceptor takes place efficiently forming \( T_1 \) states of butadienes. It is these excited triplet states of butadiene which then add another molecule of butadiene (\( S_0 \)) to form various dimers.

\[
\text{C}_6\text{H}_5\text{COC}_2\text{H}_5 \quad \xrightarrow{\text{hv}} \quad \left[\text{C}_6\text{H}_5\text{COC}_2\text{H}_5\right]^{T_1} \quad \rightarrow \quad \left[\text{C}_6\text{H}_5\text{COC}_2\text{H}_5\right]^{T_1}
\]

[pseudo-butadiene]

Various other olefins undergo dimerization reaction in presence of a photosensitizer to yield an addition product via the formation of an excited triplet state. Thus norbornene undergoes dimerization in the presence of photosensitizer acetone on irradiation with radiation of 280 nm.

[pseudo-norbornene]

Similarly the photosensitized dimerization of isoprene in the presence of sensitizer benzophenone results in a typical cycloaddition to form a number of products having 4, 6 or 8 membered rings.
1,3-Cyclohexadiene when irradiated with radiation causing $\pi \rightarrow \pi^*$ transition results in formation of 1,3,5-hexatriene.

\[
\text{hv} \rightarrow \text{CH}_2=\text{CH} \equiv \text{CH} \equiv \text{CH} \equiv \text{CH}_2
\]

However, in the presence of benzophenone as photosensitizer, the absorption of proper radiation excites benzophenone to $S_1$ state which changes to $T_1$ by intersystem crossing. It is this $T_1$ excited state of benzophenone which acts as a donor for acceptor 1,3-cyclohexadiene which is excited to triplet state and undergoes dimerization to give cycloaddition products.

\[
\begin{array}{c}
\text{hv} \quad \text{Benzophenone} \\
\text{1,3-Cyclohexadiene} \\
\text{1,3,5-Hexatriene}
\end{array}
\]

**Photochemistry of Carbonyl Compounds—Photoreduction and Photoelimination Reactions**

Amongst a wide variety of organic compounds by far the most studied and understood are the photochemical reactions of carbonyl compounds.

Photoreduction of benzophenone to benzinoninocool occurs when a solution of benzophenone and isopropyl alcohol is irradiated with radiation of 345 nm. Isopropyl alcohol does not absorb at this wavelength and absorption of radiation by benzophenone causes $n \rightarrow \pi^*$ transition

\[
2\text{C}_6\text{H}_5\text{COCH}_3 + (\text{CH}_3)\text{CHOH} \xrightarrow{\text{hv}} \text{OH} \quad \text{OH} \quad \begin{array}{c}
\text{Benzophenone} \\
\text{Isopropyl alcohol}
\end{array} \rightarrow \begin{array}{c}
\text{C}_6\text{H}_5\text{COOH} + \text{CH}_3\text{CHO} \\
\text{Benzoin} \quad \text{Acetone}
\end{array}
\]

Initial light absorption produces $S_1$ state which then undergoes rapid *intersystem crossing* to give $T_1$ states.

\[
\begin{array}{ccc}
\text{hv} & \text{hv} & \text{hv} \\
\text{(C}_6\text{H}_5\text{)CO} & \text{hv} & \text{(C}_6\text{H}_5\text{)CO} \\
\text{Inter} & \text{Inter} & \text{Inter} \\
\text{system} & \text{system} & \text{system} \\
\text{crossing} & \text{crossing} & \text{crossing}
\end{array} \rightarrow \begin{array}{c}
\text{hv} \\
\text{(C}_6\text{H}_5\text{)CO} \quad \text{C} \equiv \text{O}_1 \text{ }^1 \mathrm{I} \\
\text{Intersystem} \\
\text{crossing}
\end{array}
\]

The $T_1$ triplet state has a structure resembling alkoxy radical and abstracts $\alpha$-hydrogen of isopropyl alcohol forming two radicals I and II.

\[
\begin{array}{ccc}
\text{hv} & \text{hv} & \text{hv} \\
\text{(C}_6\text{H}_5\text{)CO} & \text{hv} & \text{(C}_6\text{H}_5\text{)CO} \\
\text{Inter} & \text{Inter} & \text{Inter} \\
\text{system} & \text{system} & \text{system} \\
\text{crossing} & \text{crossing} & \text{crossing}
\end{array} \rightarrow \begin{array}{c}
\text{hv} \\
\text{(C}_6\text{H}_5\text{)CO} \quad \text{C} \equiv \text{O}_1 \text{ }^1 \mathrm{I} \\
\text{Intersystem} \\
\text{crossing}
\end{array}
\]

The $T_1$ triplet state has a structure resembling alkoxy radical and abstracts $\alpha$-hydrogen of isopropyl alcohol forming two radicals I and II.

\[
\begin{array}{ccc}
\text{hv} & \text{hv} & \text{hv} \\
\text{(C}_6\text{H}_5\text{)CO} & \text{hv} & \text{(C}_6\text{H}_5\text{)CO} \\
\text{Inter} & \text{Inter} & \text{Inter} \\
\text{system} & \text{system} & \text{system} \\
\text{crossing} & \text{crossing} & \text{crossing}
\end{array} \rightarrow \begin{array}{c}
\text{hv} \\
\text{(C}_6\text{H}_5\text{)CO} \quad \text{C} \equiv \text{O}_1 \text{ }^1 \mathrm{I} \\
\text{Intersystem} \\
\text{crossing}
\end{array}
\]

The $T_1$ triplet state has a structure resembling alkoxy radical and abstracts $\alpha$-hydrogen of isopropyl alcohol forming two radicals I and II.

\[
\begin{array}{ccc}
\text{hv} & \text{hv} & \text{hv} \\
\text{(C}_6\text{H}_5\text{)CO} & \text{hv} & \text{(C}_6\text{H}_5\text{)CO} \\
\text{Inter} & \text{Inter} & \text{Inter} \\
\text{system} & \text{system} & \text{system} \\
\text{crossing} & \text{crossing} & \text{crossing}
\end{array} \rightarrow \begin{array}{c}
\text{hv} \\
\text{(C}_6\text{H}_5\text{)CO} \quad \text{C} \equiv \text{O}_1 \text{ }^1 \mathrm{I} \\
\text{Intersystem} \\
\text{crossing}
\end{array}
\]

Combination of two units of II gives benzinoninocool

\[
\begin{array}{c}
\text{hv} \\
\text{(C}_6\text{H}_5\text{)CO} \quad \text{C} \equiv \text{O}_1 \text{ }^1 \mathrm{I} \\
\text{Intersystem} \\
\text{crossing}
\end{array}
\]

\[
2 \text{C}_6\text{H}_5\text{CO} \xrightarrow{\text{hv}} \text{C}_6\text{H}_5\text{CO} + \text{CH}_3\text{CHO} + \text{CH}_3\text{CH}_2\text{CHO}
\]

\[
\text{Benzoin} \quad \text{Acetone}
\]
The quantum yield for the formation of benzpinacol is approximately 1, hence the second molecule of I is not formed by abstraction of another quantum of light but is formed by reaction between benzophenone and radical obtained from isopropyl alcohol after hydrogen abstraction (II).

\[(\text{CH}_3)_2\text{C}^-\text{OH} + (\text{C}_6\text{H}_5)\text{CO} \rightarrow (\text{C}_6\text{H}_5)\text{C}^-\text{OH} + (\text{CH}_3)\text{CO}\]

The reaction is a general one and can be observed in case of large number of aliphatic as well as aromatic ketones and \(\alpha\)-ketoesters in presence of wide varieties of solvents such as toluene, cyclohexane, methanol etc.

\[
\text{CH}_3\text{COCH}_3 + \text{CH}_3\text{CHOHCH}_3 \xrightarrow{\text{hv}} (\text{CH}_3)_2\text{C}^- \quad (\text{CH}_3)_2\text{CO} + \text{C}_6\text{H}_5\text{CH}_3 \xrightarrow{\text{hv}} (\text{C}_6\text{H}_5)\text{C}^- + \text{C}_6\text{H}_5\text{CH}_2
\]

Benzophenone Toluene

Benzyl radical

In the above reaction dibenzyl and benzyl diphenyl carbinol are also formed probably due to following side reactions:

\[
(\text{C}_6\text{H}_5)\text{C}^- \text{OH} + \text{C}_6\text{H}_5\text{CH}_3 \xrightarrow{\text{hv}} (\text{C}_6\text{H}_5)\text{C}^-\text{OH} + \text{C}_6\text{H}_5\text{CH}_2
\]

Benzyl radical Benzyl diphenyl carbinol

Evidence for the participation of \(T_1\) state rather than \(S_0\) state in benzpinacol formation comes from the quenching studies. Naphthalene is a known quencher which deactivates the excited states. Irradiation of benzoquinone and isopropyl alcohol mixture mixed with small amounts of naphthalene appreciably reduces the quantum yield. This can only happen if excited benzophenone molecule transfers its energy to naphthalene and returns to the ground state. Obviously such an energy transfer is not possible with short lived \(S_1\) state but only in \(T_1\) states which has sufficient long life to collide with naphthalene (which is in low concentration) resulting in energy transfer.

12.3.1 Di-pi Methane Rearrangement

Cross-Conjugated Derivatives

Derivatives of 2,5-cyclohexadiene are common in nature, and their photochemical transformations posed a challenge to early researchers. Some reactions of 4,4-diphenyl-2,5-cyclohexadiene are presented in the following diagram. Although 2,3-diphenylphenol was a product from irradiation in aqueous dioxane, it is actually formed from 6,6-diphenylbicyclo[3.1.0]hex-3-ene-2-one, the initial rearrangement product. It should be noted that a similar bicyclo[3.1.0]hexane isomer was formed by irradiation of 4,4-diphenyl-2-cyclohexenones.
These photochemical rearrangements occur by way of triplet excited states, which are conveniently depicted as diradicals. Bond reorganization may take place in the triplets, which eventually intersystem cross to singlet species. Charge separation in these states may then lead to rearrangement to a stable product.

The photo-isomerization shown above is one example of a general family of reactions known as di-π-methane rearrangements, other examples of which are illustrated in the following diagram. These transformations are often photo-sensitized, indicating they proceed by way of triplet excited states. As the name suggests, substrates exhibiting this rearrangement are comprised of two π-functions separated by a saturated (sp²-hybrid) carbon atom (designated by a red dot in the illustration). In the event, a 1,2-shift of one ene-group, followed by a bond formation between the terminal sites of the remaining π-function leads to a vinylcyclopropane product. One of the unsaturated functions may be a carbonyl or imine group.
A photo-isomerization of this kind was used by H. Zimmerman (Wisconsin) to prepare the novel self-replicating diene semibullvalene from barrelene.

Conjugated Derivatives

Derivatives of 6,6-disubstituted 2,4-cyclohexadienones are also photochemically reactive. Some examples are given in the following diagram. Electroyclic ring opening to an unsaturated ketene is the favored transformation. Since nucleophilic compounds such as water, alcohols and amines add rapidly to ketenes, the resulting carboxylic acid or derivative is the final isolated product. If no nucleophilic reactants are present, the conjugated ketene diene will recylize to the starting compound. Slower reactions leading to phenolic products may then occur. In the last (bottom) example, additional methyl substituents reduce the reactivity of the trans-ketene intermediate, so that only strongly nucleophilic amines are able to trap it. The ketene is removed by light induced isomerization and cyclization. As in the previous dienones, a triplet excited state undergoes decay to polar singlets that are thought to decompose in the manner depicted in the gray-shaded area.

Check Your Progress

4. Photoirradiation of cyclic α,β-unsaturated ketones results in what process?
5. Direct irradiation of butadiene with radiation of 217 nm yields what as a result of valence isomerization?
12.4 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

<table>
<thead>
<tr>
<th>NOTES</th>
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</thead>
<tbody>
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<td>1. Norrish type I reaction.</td>
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<tr>
<td>2. Norrish type II reaction.</td>
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<tr>
<td>3. Norrish type I reaction.</td>
</tr>
<tr>
<td>4. Photodimerization.</td>
</tr>
<tr>
<td>5. Cyclobutene and bicyclo[1.1.0] butane.</td>
</tr>
</tbody>
</table>

12.5 SUMMARY

- Photochemical reactions of ketones resulting in the cleavage of carbon-carbon bond (α-C—C bond) adjacent to carbonyl group followed by elimination are referred to as Norrish type I reactions.
- In ketones where the carbon chain is large and has a hydrogen at α-position the photochemical reaction results in the formation of an alkene and a ketone and is known as Norrish type II reaction.
- When a carbonyl compound and alkene mixture is irradiated with light of suitable wavelength, they undergo photocycloaddition to form oxetanes. The reaction is commonly referred to as Paterno-Büchi reaction.
- Paterno-Büchi reaction fails to occur with conjugated dienes whose triplet excitation energy is less than that of ketone but occurs with acetylenes.
- Photodimerization of cyclic α,β-unsaturated ketone like cyclopentenone yields two different dimers in almost equal amounts — one in which two units are joined head to head and the other in which two units are joined head to tail.
- Photoisomerization of stilbene can be sensitized by a sensitizer like benzophenone. Thus when either cis- or trans- stilbene mixed with benzophenone is irradiated with a radiation of 366 nm (a wavelength at which stilbene does not show any absorption), first an excited singlet state of benzophenone is formed which by intersystem crossing changes to excited triplet state.

12.6 KEY WORDS

- **Photochemical reaction**: A chemical reaction initiated by the absorption of energy in the form of light. The consequence of molecules’ absorbing light is the creation of transient excited states whose chemical and physical properties differ greatly from the original molecules.
• **Isomerization**: It is the process by which one molecule is transformed into another molecule which has exactly the same atoms, but the atoms have a different arrangement.

### 12.7 SELF ASSESSMENT QUESTIONS AND EXERCISES

**Short Answer Questions**

1. What are photochemical reactions? Give examples.
2. Discuss the photochemistry of olefins.
3. What are cross-conjugated derivatives?
4. What are conjugated derivatives?

**Long Answer Questions**

1. Write short notes on
   a) Norrish type I reactions
   b) Norrish type II reactions
   c) Paterno Büchi reactions
   d) Photosensitized reactions
2. Explain with the help of suitable examples
   a) Photo reduction
   b) Photoisomerization
   c) Photodimerization
   d) Photoelimination
3. Write a brief note on photochemistry of α,β-unsaturated carbonyl compounds.
4. Illustrate the mechanism of photochemical addition of carbonyl compounds of alkenes.

### 12.8 FURTHER READINGS


**NOTES**


UNIT 13 PERICYCLIC REACTIONS

Structure
13.0 Introduction
13.1 Objectives
13.2 Pericyclic Reactions
13.3 Answers to Check Your Progress Questions
13.4 Summary
13.5 Key Words
13.6 Self Assessment Questions and Exercises
13.7 Further Readings

CASE 13.0 INTRODUCTION

In organic chemistry, a pericyclic reaction is a type of organic reaction wherein the transition state of the molecule has a cyclic geometry, the reaction progresses in a concerted fashion, and the bond orbitals involved in the reaction overlap in a continuous cycle at the transition state. Pericyclic reactions stand in contrast to linear reactions, encompassing most organic transformations and proceeding through an acyclic transition state, on the one hand and concerted reactions, which proceed through a doubly cyclic, concerted transition state on the other hand. Pericyclic reactions are usually rearrangement or addition reactions. The major classes of pericyclic reactions are electrocyclic reaction, cycloaddition (and cycloreversion), sigmatropic reaction, group transfer reaction, ene reaction, chelotropic reaction, and dyotropic reaction. Ene reactions and chelotropic reactions are often classified as group transfer reactions and cycloadditions/reversions, respectively, while dyotropic reactions and group transfer reactions (if ene reactions are excluded) are rarely encountered.

This unit discusses the pericyclic reaction and its major classes.

CASE 13.1 OBJECTIVES

After going through this unit, you will be able to:

- Analyze pericyclic reactions
- Discuss Woodward-Hoffmann rules
- Understand frontier molecular orbital theory

CASE 13.2 PERICYCLIC REACTIONS

A large number of reactions of olefinic compounds are known which do not involve ionic or free radical intermediates and are initiated by heat or light. Apparently.....
solvents and catalysts do not affect these reactions. Such reactions in which bonds are broken and made in a single concerted step through a cyclic transition state were termed as *pericyclic reactions* by Woodward and Hoffmann in 1965. Most of these reactions are highly stereospecific, so much so that initiation of reaction by heat or light gives products with different stereochemical nature.

Pericyclic reactions include some of the most important reactions in organic chemistry which were poorly understood till recently and were called ‘no-mechanism reactions’. Diels-Alder reaction and Claisen reaction can be cited here as examples of pericyclic reactions. These reactions are divided into following four classes:

(i) **Electrocyclic Reactions**

In organic chemistry, an electrocyclic reaction is a type of pericyclic rearrangement where the net result is one pi bond being converted into one sigma bond or vice versa. These reactions are usually categorized by the following criteria:

- Reactions can be either photochemical or thermal.
- Reactions can be either ring-opening or ring-closing (electrocyclization).
- Depending on the type of reaction (photochemical or thermal) and the number of pi electrons, the reaction can happen through either a conrotatory or disrotatory mechanism.
- The type of rotation determines whether the cis or trans isomer of the product will be formed.

(ii) **Cycloaddition Reactions: Diels–Alder Reaction**

A cycloaddition is a chemical reaction, in which “two or more unsaturated molecules (or parts of the same molecule) combine with the formation of a cyclic adduct in which there is a net reduction of the bond multiplicity.” The resulting reaction is a cyclization reaction. Many but not all cycloadditions are concerted and thus pericyclic. Nonconcerted cycloadditions are not pericyclic. As a class of addition reaction, cycloadditions permit carbon–carbon bond formation without the use of a nucleophile or electrophile.

The Diels-Alder reaction is perhaps the most important and commonly taught cycloaddition reaction. Formally it is a [4+2] cycloaddition reaction and exists in a huge range of forms, including the inverse electron-demand Diels–Alder reaction, Hexadehydro Diels–Alder reaction and the related alkyne trimerization. The reaction can also be run in reverse in the retro-Diels–Alder reaction.
(iii) Sigmatropic Reactions

A sigmatropic reaction in organic chemistry is a pericyclic reaction wherein the net result is one \( \pi \)-bond is changed to another \( \pi \)-bond in an uncatalyzed intramolecular process. The name sigmatropic is the result of a compounding of the long-established sigma designation from single carbon–carbon bonds and the Greek word tropos, meaning turn. In this type of rearrangement reaction, a substituent moves from one part of a \( \pi \)-bonded system to another part in an intramolecular reaction with simultaneous rearrangement of the \( \pi \) system. True sigmatropic reactions are usually uncatalyzed, although Lewis acid catalysis is possible. Sigmatropic reactions often have transition-metal catalysts that form intermediates in analogous reactions. The most well-known of the sigmatropic rearrangements are the [3,3] Cope rearrangement, Claisen rearrangement, Carroll rearrangement and the Fischer indole synthesis.

(a) Cope reaction

(b) Claisen reaction

(c) Cheletropic reaction

Conservation of Molecular Orbital Symmetry Principle

Woodward and Hoffmann (1965) in order to explain pericyclic reactions, suggested that all concerted reactions occur with conservation of molecular orbital symmetry. This is known as conservation of molecular orbital symmetry principle.

A concerted reaction is one in which bond breaking and bond formation occur synchronously without the formation of an intermediate. According to this principle
if the molecular orbital symmetry characteristics of the reactants and products are same, a concerted reaction will occur readily. Thus by observing the symmetry characteristics of the molecular orbitals of reactants and products it can be predicted whether a particular reaction is allowed or not. If the occupied molecular orbitals of the reactants can be converted to the occupied molecular orbitals of the products, the reaction is said to be symmetry allowed, if not it is said to be symmetry-forbidden.

Two other methods, namely Frontier Molecular Orbital (FMO) method (Fukui and Pearson, 1971) and Möbius-Huckel Perturbation molecular orbital (PMO) method (Dewar and Zimmermann, 1971) have been developed to explain the pericyclic reactions.

The basic principle involved in pericyclic reactions is that orbitals of reactants interact to form a transition state which then changes to orbitals of the products. If the transition state is of relatively low energy then the reaction will be favoured.

Participating bond electrons in such reactions may be present in sigma σ or pi (π) bonding orbitals. These bonding orbitals are characterised by a node and phase sign (+ or −).

In the conversion of cyclobutene to butadiene the constituents of the bonding orbital, which breaks, must rotate to convert into the bonding orbitals of butadiene. Either both of them may rotate in the same direction (clockwise or anticlockwise) which is called conrotatory or they may rotate in opposite direction which is called disrotatory.

Let us now examine the molecular orbitals of cyclobutene i.e. σ, π, σ* and π*, and those of butadiene i.e. ψ₁, ψ₂, ψ₃ and ψ₄ with respect to their energies.

In conrotatory opening the σ orbital of cyclobutene, which is symmetric, changes to ψ₁ orbital of butadiene which is also symmetric and π orbital of cyclobutene, which is asymmetric, changes to ψ₄ orbital of butadiene which is also asymmetric. Similarly σ* and π* orbitals of cyclobutene change respectively to ψ₃ and ψ₄ orbitals of butadiene with same symmetry characteristics. Thus orbital
Symmetry is conserved and all the reactant bonding orbitals correlate with product bonding orbitals and all the reactant antibonding orbitals correlate with product antibonding orbitals symmetry wise. The reaction, therefore, is symmetry allowed. Refer Figure 13.1.

**Fig. 13.1** Contostatory Correlation and Disrotatory Correlation

On the other hand in a disrotatory opening of cyclobutene though the ground state $\sigma$ orbital changes to $\psi_3$ orbital of butadiene but the $\pi$ orbital of cyclobutene changes to $\Psi_3$ orbital and not to $\psi_3$ orbital of butadiene. Since $\psi_3$ is an excited state antibonding orbital hence the thermal transformation via disrotatory opening of cyclobutene to butadiene and vice-versa is symmetry forbidden.

**Fig. 13.2** Correlation of Orbitals in Cyclobutene and Butadiene

If cyclobutene is exposed to photochemical irradiation then one electron from $\pi$ bonding orbital is promoted to $\pi^*$ antibonding orbital. Now the three occupied
Pericyclic Reactions

orbits $\sigma$, $\pi$ and $\pi^*$ of cyclobutene correlate with $\psi_1$, $\psi_2$ and $\psi_3$ orbitals of butadiene (one of the electron from $\psi_1$ bonding orbital of butadiene is promoted to $\psi_2$ antibonding orbital on excitation). Hence disrotatory opening is symmetry allowed in photochemical interconversion of cyclobutene to butadiene and vice-versa.

(iv) Cycloaddition Reactions

In contrast to electrocyclic reactions where two double bonds of the same molecule changed to one $\sigma$ and one $\pi$ bond, the cycloaddition reactions are basically additions of two separate molecules combining through two $\pi$ bonds to form two $\sigma$ bonds

$$\text{No reaction symmetry forbidden} \quad \text{CH}_2 \quad \text{CH}_2 + \quad \text{CH}_2 \quad \text{CH}_2 \quad \text{CH}_2 \quad \text{CH}_2 \quad \text{Cycloaddition occurs photochemically}$$

Check Your Progress

1. What happens when a reaction is highly stereospecific?
2. What does FMO stand for?
3. What is the basic principle involved in pericyclic reactions?

13.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. When reactions are highly stereospecific, so much so that initiation of reaction by heat or light gives products with different stereochemical nature.
2. Frontier Molecular Orbital.
3. The basic principle involved in pericyclic reactions is that orbitals of reactants interact to form a transition state which then changes to orbitals of the products. If the transition state is of relatively low energy then the reaction will be favoured.

13.4 SUMMARY

- A large number of reactions of olefinic compounds are known which do not involve ionic or free radical intermediates and are initiated by heat or light.
Apparantly solvents and catalysts do not affect these reactions. Such reactions in which bonds are broken and made in a single concerted step through a cyclic transition state were termed as pericyclic reactions.

- An electrocyclic reaction is a type of pericyclic rearrangement where the net result is one π bond being converted into one σ bond or vice versa.
- A cycloaddition is a chemical reaction, in which “two or more unsaturated molecules (or parts of the same molecule) combine with the formation of a cyclic adduct in which there is a net reduction of the bond multiplicity.” The resulting reaction is a cyclization reaction. Many but not all cycloadditions are concerted and thus pericyclic. Nonconcerted cycloadditions are not pericyclic.
- A sigmatropic reaction in organic chemistry is a pericyclic reaction wherein the net result is one σ-bond is changed to another σ-bond in an uncatalyzed intramolecular process.
- Woodward and Hoffmann (1965) in order to explain pericyclic reactions, suggested that all concerted reactions occur with conservation of molecular orbital symmetry. This is known as conservation of molecular orbital symmetry principle.

13.5 KEY WORDS

- **Pericyclic reaction**: A pericyclic reaction is a type of organic reaction wherein the transition state of the molecule has a cyclic geometry, the reaction progresses in a concerted fashion, and the bond orbitals involved in the reaction overlap in a continuous cycle at the transition state.
- **Cycloaddition reaction**: A cycloaddition is a chemical reaction, in which two or more unsaturated molecules (or parts of the same molecule) combine with the formation of a cyclic adduct in which there is a net reduction of the bond multiplicity. The resulting reaction is a cyclization reaction.

13.6 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. What are electrocyclic reactions? Give an example.
2. What are cycloaddition reactions?
3. Discuss the application of cycloaddition reaction.
4. Give one example of cope reaction, claisen reaction and clathrotropic reaction.
Long Answer Questions

1. Discuss the mechanism of pericyclic reaction.
2. Explain the reactions of the major classes of pericyclic reaction.
3. Write an essay on the conservation of molecular orbital symmetry principle.
4. Explain the difference between electrocyclic reaction and cycloaddition reaction.

13.7 FURTHER READINGS

UNIT 14 CHELOTROPIC REACTION

Structure
14.0 Introduction
14.1 Objectives
14.2 Chelotropic Reaction
  14.2.1 Sigmatropic Rearrangement
  14.2.2 1,3-Dipolar Cycloaddition
14.3 Diels - Alder reaction
14.4 Answers to Check Your Progress Questions
14.5 Summary
14.6 Key Words
14.7 Self Assessment Questions and Exercises
14.8 Further Readings

14.0 INTRODUCTION

Cheotropic reactions also known as chelotropic reactions are a type of pericyclic reaction. A pericyclic reaction is one that involves a transition state with a cyclic array of atoms and an associated cyclic array of interacting orbitals. A reorganization of σ and π bonds occurs in this cyclic array.

A sigmatropic reaction in organic chemistry is a pericyclic reaction wherein the net result is one σ-bond is changed to another π-bond in an uncatalyzed intramolecular process. The name sigmatropic is the result of a compounding of the long-established sigma designation from single carbon–carbon bonds and the Greek word tropos, meaning turn. In this type of rearrangement reaction, a substituent moves from one part of a π-bonded system to another part in an intramolecular reaction with simultaneous rearrangement of the π system.

In organic chemistry, the Diels–Alder reaction is a chemical reaction between a conjugated diene and a substituted alkene, commonly termed the dieneophile (also spelled dienophile), to form a substituted cyclohexene derivative. It is the prototypical example of a pericyclic reaction with a concerted mechanism.

The 1,3-dipolar cycloaddition is a chemical reaction between a 1,3-dipole and a dipolarophile to form a five-membered ring. The earliest 1,3-dipolar cycloadditions were described in the late 19th century to the early 20th century, following the discovery of 1,3-dipoles. Mechanistic investigation and synthetic application were established in the 1960s, primarily through the work of Rolf Huisgen. Hence, the reaction is sometimes referred to as the Huisgen cycloaddition.

In the previous unit, you have studied about pericyclic reactions. This unit discusses different pericyclic reactions like chelotropic reaction and sigmatropic reactions. You will also study the process of Diels-Alder reaction and 1, 3-dipolar additions.
14.1 OBJECTIVES

After going through this unit, you will be able to:

- Discuss chelotropic reaction
- Carry out sigmatropic rearrangements
- Understand 1,3-dipolar additions
- Explain Diels-Alder reaction

14.2 CHELOROPIC REACTION

Chelotropic reactions also known as chelotropic reactions are a type of pericyclic reaction. A pericyclic reaction is one that involves a transition state with a cyclic array of atoms and an associated cyclic array of interacting orbitals. A reorganization of $\sigma$ and $\pi$ bonds occurs in this cyclic array.

Specifically, chelotropic reactions are a subclass of cycloadditions. The key distinguishing feature of chelotropic reactions is that on one of the reagents, both new bonds are being made to the same atom. A few examples are below. In the first case, the single atom is the carbonyl carbon that ends up in carbon monoxide. The end result is making two new bonds to one atom. The first two examples are known as chelotropic extrusions because a small stable molecule is given off in the reaction. The driving force for these reactions is often the entropic benefit of gaseous evolution (For example, CO or N$_2$).

![Chelotropic Reactions](image)

Fig. 14.1 Chelotropic Reactions

Theoretical Analysis

In the pericyclic transition state, a small molecule donates two electrons to the ring. The reaction process can be shown using two different geometries. The small molecule can approach in a linear or non-linear fashion. In the linear approach, the
electrons in the orbital of the small molecule are pointed directly at the \( \pi \)-system. In the non-linear approach, the orbital approaches at a skew angle. The \( \pi \)-system’s ability to rotate as the small molecule approaches is crucial in forming new bonds. The direction of rotation will be different depending on how many \( \pi \)-electrons are in the system. Shown below is a diagram of a two-electron fragment approaching a four-electron \( \pi \)-system using frontier molecular orbitals. The rotation will be disrotatory if the small molecule approaches linearly and conrotatory if the molecule approaches non-linearly. Disrotatory and conrotatory are sophisticated terms expressing how the bonds in the \( \pi \)-system are rotating. Disrotatory means opposite directions while conrotatory means the same direction.

Using Hückel’s Rule, one can tell if the \( \pi \)-system is aromatic or anti-aromatic. If aromatic, linear approaches use disrotatory motion while non-linear approaches use conrotatory motion. The opposite goes with an anti-aromatic system. Linear approaches will have conrotatory motion while non-linear approaches will have disrotatory motion.

14.2.1 Sigmatropic Rearrangement

Rearrangements involving migration of a \( \sigma \) (sigma) bond to a new position within the system on heating (or by photolysis) are known as **Sigmatropic rearrangements** which proceed in a concerted manner with conservation of orbital symmetry. The general reaction may be written as follows:

\[
\begin{array}{c}
\text{CH}_2\text{CH} \quad \text{CH} \quad \text{CH}_2 \\
\text{R}_1 \quad \text{R}_2 \quad \text{R}_3 \\
\end{array}
\rightarrow
\begin{array}{c}
\text{CH}_2\text{CH} \quad \text{CH} \quad \text{CH}_2 \\
\text{R}_1 \quad \text{R}_2 \quad \text{R}_3 \\
\end{array}
\]

The reactions are designated by \([i, j]\) order where \(i\) and \(j\) refer to the number of atoms to which the migrating bond joins. The above reaction is a \([1, 3]\) shift and the Cope rearrangement and Claisen rearrangement are \([3, 3]\) shift.

- **Cope rearrangement** \([1, 3]\) shift
- **Claisen rearrangement** \([3, 3]\) shift

Self-Instructional Material
14.2.2 1,3-Dipolar Cycloaddition

The 1,3-dipolar cycloaddition is a chemical reaction between a 1,3-dipole and a dipolarophile to form a five-membered ring. The earliest 1,3-dipolar cycloadditions were described in the late 19th century to the early 20th century, following the discovery of 1,3-dipoles. Mechanistic investigation and synthetic application were established in the 1960s, primarily through the work of Rolf Huisgen. Hence, the reaction is sometimes referred to as the Huisgen cycloaddition (this term is often used to specifically describe the 1,3-dipolar cycloaddition between an organic azide and an alkyne to generate 1,2,3-triazole). 1,3-dipolar cycloaddition is an important route to the regio- and stereoselective synthesis of five-membered heterocycles and their ring-opened acyclic derivatives.

Mechanistic Overview

Originally two proposed mechanisms describe the 1,3-dipolar cycloaddition: first, the concerted pericyclic cycloaddition mechanism, proposed by Rolf Huisgen; and second, the stepwise mechanism involving a diradical intermediate, proposed by Firestone. After much debate, the former proposal is now generally accepted—the 1,3-dipole reacts with the dipolarophile in a concerted, often asynchronous, and symmetry-allowed π4 + π2, fashion through a thermal six-electron Hückel aromatic transition state. Although, few examples exist of stepwise mechanism of the catalyst free 1,3-dipolar cycloaddition reactions for thiocarbonyl ylides, and nitrile oxides.

Pericyclic Mechanism

Huisgen investigated a series of cycloadditions between the 1,3-dipolar diazo compounds and various dipolarophilic alkenes. The following observations support the concerted pericyclic mechanism, and refute the stepwise diradical or the stepwise polar pathway:

- **Substituent effects**: Different substituents on the dipole do not exhibit a large effect on the cycloaddition rate, suggesting that the reaction does not involve a charge-separated intermediate.
- **Solvent effects**: Solvent polarity has little effect on the cycloaddition rate, in line with the pericyclic mechanism where polarity does not change much in going from the reactants to the transition state.
• **Stereochemistry:** 1,3-dipolar cycloadditions are always stereospecific with respect to the dipolarophile (i.e., cis-alkenes giving syn-products), supporting the concerted pericyclic mechanism in which two sigma bonds are formed simultaneously.

• **Thermodynamic parameters:** 1,3-dipolar cycloadditions have an unusually large negative entropy of activation similar to that of the Diels-Alder reaction, suggesting that the transition state is highly ordered, which is a signature of concerted pericyclic reactions.

1,3-Dipole

A 1,3-dipole is an organic molecule that can be represented as either an allyl-type or a propargyl/allenyl-type zwitterionic octet/sextet structures. Both types of 1,3-dipoles share four electrons in the π-system over three atoms. The allyl-type is bent whereas the propargyl/allenyl-type is linear in geometry. 1,3-Dipoles containing higher-row elements such as sulfur or phosphorus are also known, but are utilized less routinely.

Resonance structures can be drawn to delocalize both negative and positive charges onto any terminus of a 1,3-dipole. A more accurate method to describe the electronic distribution on a 1,3-dipole is to assign the major resonance contributor based on experimental or theoretical data, such as dipole moment measurements or computations. For example, diazomethane bears the largest negative character at the terminal nitrogen atom, while hydrazoic acid bears the largest negative character at the internal nitrogen atom.

![Major resonance structures](image)

Consequently, this ambivalence means that the ends of a 1,3-dipole can be treated as both nucleophilic and electrophilic at the same time. The extent of nucleophilicity and electrophilicity at each end can be evaluated using the frontier molecular orbitals, which can be obtained computationally. In general, the atom that carries the largest orbital coefficient in the HOMO acts as the nucleophile, whereas that in the LUMO acts as the electrophile. The most nucleophilic atom is usually, but not always, the most electron-rich atom. In 1,3-dipolar cycloadditions, identity of the dipole-dipolarophile pair determines whether the HOMO or the LUMO character of the 1,3-dipole will dominate.
Dipolarophile

The most commonly used dipolarophiles are alkenes and alkynes. Heteroatom-containing dipolarophiles such as carbonyls and imines can also undergo 1,3-dipolar cycloaddition. Other examples of dipolarophiles include fullerenes and nanotubes, which can undergo 1,3-dipolar cycloaddition with azomethine ylide in the Prato reaction.

Solvent effects

1,3-dipolar cycloadditions experience very little solvent effect because both the reactants and the transition states are generally non-polar. For example, the rate of reaction between phenyl diazomethane and ethyl acrylate or norbornene changes only slightly upon varying solvents from cyclohexane to methanol.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>relative δS</th>
<th>relative δ2</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclohexane</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>dioxane</td>
<td>1.48</td>
<td>0.80</td>
</tr>
<tr>
<td>DMSO</td>
<td>3.16</td>
<td>1.06</td>
</tr>
<tr>
<td>methanol</td>
<td>5.34</td>
<td>0.88</td>
</tr>
</tbody>
</table>

Lack of solvent effects in 1,3-dipolar cycloaddition is clearly demonstrated in the reaction between enamines and dimethyl diazomalonate. The polar reaction, N-cyclopentenyl pyrroline nucleophilic addition to the diazo compound, proceeds 1,500 times faster in polar DMSO than in non-polar decalin. On the other hand, a close analog of this reaction, N-cyclohexenyl pyrroline 1,3-dipolar cycloaddition to dimethyl diazomalonate, is sped up only 41-fold in DMSO relative to decalin.

Check Your Progress

1. What does disrotatory mean?
2. Give an example of sigmatropic rearrangement.
14.3 DIELS - ALDER REACTION

In general if the number of participating \( \pi \) electron pairs is odd the reaction is symmetry allowed but if the number of \( \pi \) electron pairs is even then the reaction is symmetry forbidden but will occur photochemically. Thus a \((4 + 2)\) cycloaddition with 3 pairs of \( \pi \) electrons (odd no.) is symmetry allowed while \((2 + 2)\) cycloaddition with 2 pairs of \( \pi \) electrons (even no.) is symmetry forbidden and occur only photochemically.

Diels-Alder and other cycloadditions are highly stereospecific. This is to be expected also as the addition of two molecules with \( \pi \) electrons may occur either on the same or opposite side. If the new bond formation occurs on the same side of the double bond it is termed as suprafacial addition while if the new bonds are formed on the opposite side of \( \pi \) bonds it is termed as antarafacial addition. The terms \( s \) and \( a \) are written as subscripts to \( \pi \) electron numbers to designate suprafacial and antarafacial additions.

By consideration of the correlation diagram for \((4s + 2\pi)\) cycloaddition between butadiene and ethylene it becomes clear that it is a symmetry allowed process because in the transformation of reactant bonding orbitals \( \psi_1, \pi \) and \( \psi_2 \) to product orbitals \( \sigma_1, \sigma_2 \) and \( \pi \) symmetry is conserved.

![Fig. 14.2 Correlation of Orbital Symmetry in the \((4s + 2\pi)\) Cycloaddition (Diels-Alder) Reaction](image)
According to FMO method to determine whether or not a cycloaddition reaction is symmetry allowed, the highest occupied molecular orbital (HOMO) of one reactant and the lowest unoccupied molecular orbital (LUMO) of another reactant or vice-versa is examined. If these orbitals can give rise to an overlap with symmetry conservation, then the reaction is symmetry allowed. Thus in Diels-Alder reaction of butadiene and ethylene the HOMO of one and LUMO of another result in positive overlap with conservation of symmetry.

![Diagram showing orbital overlap](image)

Interaction between HOMO and LUMO of butadiene and ethylene or vice versa are thus symmetry allowed but in a reaction between two molecules of ethylene it is not. However irradiation of ethylene with hn promotes one electron to antibonding orbital which now becomes the HOMO of excited state. This HOMO of excited state can give rise to a positive symmetry allowed with LUMO of other ethylene molecule and hence the reaction is thermally forbidden but photochemically allowed.

![Diagram showing orbital overlap](image)

In a Diels-Alder reaction between two moles of cyclopentadiene or between maleic anhydride and cyclopentadiene it is the endo product rather than exo product which is formed. This is because the transition state for endo product involves secondary interactions between frontier orbitals and hence is more stabilised as compared to transition state for exo product.

Check Your Progress

3. Diels-Alder reaction is an example of which type of reaction?
4. What does HOMO stand for?
14.4 ANSWERS TO CHECK YOUR PROGRESS
QUESTIONS

1. Disrotatory means opposite directions while conrotatory means the same direction.
2. Claisen rearrangement.
3. Pericyclic reaction.
4. Highest Occupied Molecular theory.

14.5 SUMMARY

- Cheletronic reactions also known as chelotropic reactions are a type of pericyclic reaction. A pericyclic reaction is one that involves a transition state with a cyclic array of atoms and an associated cyclic array of interacting orbitals. A reorganization of $\sigma$ and $\pi$ bonds occurs in this cyclic array.
- The 1,3-dipolar cycloaddition is a chemical reaction between a 1,3-dipole and a dipolarophile to form a five-membered ring. The earliest 1,3-dipolar cycloadditions were described in the late 19th century to the early 20th century, following the discovery of 1,3-dipoles.
- Rearrangements involving migration of a $\sigma$ (sigma) bond to a new position within the system on heating (or by photolysis) are known as Sigmatropic rearrangements which proceed in a concerted manner with conservation of orbital symmetry.
- Diels-Alder and other cycloadditions are highly stereospecific. This is to be expected also as the addition of two molecules with $\pi$ electrons may occur either on the same or opposite side. If the new bond formation occurs on the same side of the double bond it is termed as suprafacial addition while if the new bonds are formed on the opposite side of $\pi$ bonds it is termed as antarafacial addition.

14.6 KEY WORDS

- **Pericyclic reaction:** A pericyclic reaction is one that involves a transition state with a cyclic array of atoms and an associated cyclic array of interacting orbitals. A reorganization of $\sigma$ and $\pi$ bonds occurs in this cyclic array.
- **Sigmatropic rearrangements:** Rearrangements involving migration of a $\sigma$ (sigma) bond to a new position within the system on heating (or by photolysis) are known as Sigmatropic rearrangements which proceed in a concerted manner with conservation of orbital symmetry.
14.7 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions
1. Discuss the mechanism of Cope's rearrangement.
2. Discuss the mechanism of Claisen rearrangement.
3. Discuss the mechanism of 1,3 dipolar addition.
4. In a Diels-Alder reaction between two moles of cyclopentadiene or between maleic anhydride and cyclopentadiene it is the endo product rather than exo product which is formed. Give reasons.

Long Answer Questions
1. Discuss chelotropic reactions in detail.
2. Explain the general reaction of sigmatropic rearrangement.
3. Discuss the mechanism of Diels-Alder reaction.
4. What are the solvent effects of 1,3 dipolar addition?

14.8 FURTHER READINGS
