ALAGAPPA UNIVERSITY

[Accredited with 'A+' Grade by NAAC (CGPA:3.64) in the Third Cycle
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(A State University Established by the Government of Tamil Nadu)

KARAIKUDI – 630 003

Directorate of Distance Education

M.Sc. [Chemistry]

I - Semester

344 12

ORGANIC CHEMISTRY - I

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Unit (1.0-1.4, 1.4.2-1.9, 2, 3.0-3.3, 3.5-3.9, 4.0-4.1, 4.3, 4.4-4.9, 5.2, 8.0-8.2, 8.4-8.10, 9.0-9.2, 9.4.2, 9.5-9.9, 10.2.1, 10.2.2, 11, 12, 13, 14)

Vikas® Publishing House: Units (1.4.1, 3.4, 4.2, 4.3.1, 5.0-5.1, 5.3-5.9, 6, 7, 8.3, 9.3, 9.4, 9.4.1, 9.4.3, 10.0-10.2, 10.3-10.7)

VIKAS® PUBLISHING HOUSE PVT. LTD.
E-28, Sector-8, Noida - 201301 (UP)
Phone: 0120-4078900 • Fax: 0120-4078999
Regd. Office: 7361, Ravindra Mansion, Ram Nagar, New Delhi 110 055
• Website: www.vikaspublishing.com • Email: helpline@vikaspublishing.com

Work Order No. AU/DDE/DE1-238/Preparation and Printing of Course Materials/2018 Dated 30.08.2018 Copies - 500

SYLLABI-BOOK MAPPING TABLE

Organic Chemistry - I

Syllabi	Mapping in Book
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BLOCK -II: STEREOCHEMISTRY OF ORGANIC COMPOUNDS **Unit-5: Introduction to Stereochemistry:** Introduction to molecular symmetry and chirality - examples from common objects to molecules - axis, plane, center, alternating axis of symmetry. Stereoisomerism - definition based on symmetry and energy criteria - configuration and conformational stereoisomers.Center of chirality - molecules with C, N, S based chiral centers - absolute configuration - enantiomers - racemic modifications. **Unit-6: Nomenclature:** R and S nomenclature using Cahn-Ingold-Prelog rules - molecules with a chiral center and Cn - molecules with more than one center of chirality - definition of diastereoisomers - constitutionally symmetrical and unsymmetrical chiral molecules - erythro, threo nomenclature - E and Z nomenclature - out/in isomers. **Unit-7: Stereochemistry and Absolute Configuration:** Axial, planar and helical chirality - examples - stereochemistry and absolute configuration of allenes, biphenyls and binaphthyls, ansa and cyclophanic compounds, spiranes, exo-cyclic alkylidenecycloalkanes.	**Unit 5:** Introduction to Stereochemistry **(Pages 88-140);** **Unit 6:** Nomenclature **(Pages 141-153)**; **Unit 7:** Stereochemistry and Absolute Configuration **(Pages 154-168)**
BLOCK-III: REACTION MECHANISM AND MOLECULAR REARRANGEMENT **Unit-8: Kinetics of Reaction Mechanisms:** Classification of organic reactions - Principle of microscopic reversibility - Hammond postulate - Kinetic and thermodynamic control of chemical reactions - Kinetic and non- kinetic methods for determining organic reaction mechanisms **Unit-9: Carbocation:** Structure and stability of carbocations, Classical and non-classical carbocations, Neighbouring group participation and rearrangements including Wagner-Meerwein, Pinacol-pinacolone, semi-pinacol rearrangement **Unit -10: Molecular Rearrangements:** Mechanisms of Wagner - Meerwein, Demzonev, Wolff, Baeyer-Villiger, Stern, Beckmann and Favorskii rearrangements.	**Unit 8:** Kinetics of Reaction Mechanisms **(Pages 169-187);** **Unit 9:** Carbocation **(Pages 188-201);** **Unit 10:** Molecular Rearrangements **(Pages 202-208)**
BLOCK -IV: SUBSTITUTIONS REACTION **Unit-11: Aliphatic Nucleophilic Substitutions:** Nucleophiles and nucleofuge - SN1, SN2 and SNi mechanisms with examples - Factors influencing the Aliphatic nucleophilic substitutions- kinetics of Aliphatic nucleophilic substitutions- stereochemistry- competition between SN1 and S_N2 **Unit-12: Aliphatic Electrophilic Substitutions:** S_E1, S_E2 and SE_i reaction and mechanism. **Unit-13: Aromatic Electrophilic Substitutions:** Aromatic electrophilic substitution reaction, O/P ratio, ring activator, deactivator, arenium ion mechanism, typical reaction and Mechanisms of nitration, diazonium coupling, sulphonation, halogenation, Friedel craft alkylation and acylation - Gatermann Koch formylation - VilsmierHaak reaction. **Unit-14: Aromatic Nucleophilic Substitutions:** Addition-elimination reaction, elimination -addition reaction and mechanism- benzyne mechanism - Von-Richter reaction.	**Unit 11:** Aliphatic Nucleophilic Substitutions **(Pages 209-218);** **Unit 12:** Aliphatic Electrophilic Substitutions **(Pages 219-225);** **Unit 13:** Aromatic Electrophilic Substitutions **(Pages 226-249);** **Unit 14:** Aromatic Nucleophilic Substitutions **(Pages 250-288)**

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BLOCK IV: SUBSTITUTIONS REACTION

INTRODUCTION

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Organic compounds are all around us. 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, compounds containing 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. The range of application of organic compounds is enormous and also includes, but is not limited to, pharmaceuticals, petrochemicals, food, explosives, paints, and cosmetics. Many modern, high-tech materials are at least partially composed of organic compounds.

This book, *Organic Chemistry I*, is divided into four blocks that are further divided into fourteen units which will help to understand the basic concepts of inorganic chemistry, such as basics of organic chemistry, bicyclic, polycyclic and heterocyclic compounds, mesomeric effect, steric inhibition of resonance, steric enhancement of resonance, hyperconjugation, effect of structure on the dissociation constants of acids and bases, electron delocalization and resonance, aromatic, antiaromatic, homoaromatic and non-aromatic compounds, molecular orbital picture of aromaticity- HMO theory, aromaticity on cyclopentadienyl anion, fulvene, ferrocene, azulene, tropolones, annulens and tropylium cations. Aromaticity on larger annulenes, hetero annulenes and fullerenes, introduction to molecular symmetry and chirality, examples from common objects to molecules, axis, plane, center, alternating axis of symmetry, stereoisomerism, configuration and conformational stereoisomers, center of chirality, molecules with C, N, S based chiral centers, absolute configuration, R and S nomenclature using Cahn-Ingold-Prelog rules, molecules with a chiral center and Cn – molecules with more than one center of chirality, definition of diastereoisomers, constitutionally symmetrical and unsymmetrical chiral molecules, axial, planar and helical chirality, stereochemistry and absolute configuration of allenes, biphenyls and binaphthyls, ansa and cyclophanic compounds, spiranes, exo-cyclic alkylidenecycloalkanes, classification of organic reactions, kinetic and thermodynamic control of chemical reactions, structure and stability of carbocations, classical and non-classical carbocations, neighbouring group participation and rearrangements including Wagner-Meerwein, Pinacol-pinacolone, semi-pinacol rearrangement, mechanisms of Wagner (Meerwein, Demzonev, Wolff, Baeyer-Villiger, Stern, Beckmann and Favorskii rearrangements), nucleophiles and nucleofuge, factors influencing the aliphatic nucleophilic substitutions, kinetics of aliphatic nucleophilic substitutions–stereochemistry,Von-Richter reaction.

The book follows the self-instruction mode or the SIM format wherein each unit begins with an 'Introduction' to the topic followed by an outline of the 'Objectives'. The content is presented in a simple, organized and comprehensive form interspersed with 'Check Your Progress' questions and answers for better understanding of the topics covered. A list of 'Key Words' along with a 'Summary' and a set of 'Self Assessment Questions and Exercises' is provided at the end of the each unit for effective recapitulation.

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BLOCK - I

FUNDAMENTALS OF ORGANIC CHEMISTRY

UNIT 1 IUPAC NOMENCLATURE OF ORGANIC COMPOUNDS

Structure

1.0 INTRODUCTION

An organic compound is generally any chemical compound that contains carbon. Due to carbon's ability to catenate, millions of organic compounds are known. Study of the properties and synthesis of organic compounds is the discipline known as organic chemistry. For historical reasons, a few classes of carbon-containing compounds, along with a handful of other exceptions, are not classified as organic compounds and are considered inorganic. No consensus exists among chemists on precisely which carbon-containing compounds are excluded, making the definition of an organic compound elusive. Although organic compounds only make up a small percentage of the Earth's crust, they are of central importance because all known life is based on organic compounds. Most synthetically produced organic compounds are ultimately derived from petrochemicals consisting mainly of hydrocarbons.

In chemical nomenclature, the IUPAC nomenclature of organic chemistry is a systematic method of naming organic chemical compounds as recommended by the International Union of Pure and Applied Chemistry (IUPAC). It is published in the Nomenclature of Organic Chemistry (informally called the Blue Book). Ideally, every possible organic compound should have a name from which an unambiguous structural formula can be created. There is also an IUPAC nomenclature of inorganic chemistry.

In this unit, you will study about organic compounds and their classification as acyclic and cyclic. Further in this unit, you will understand the nomenclature of organic compounds.

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1.1 OBJECTIVES

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

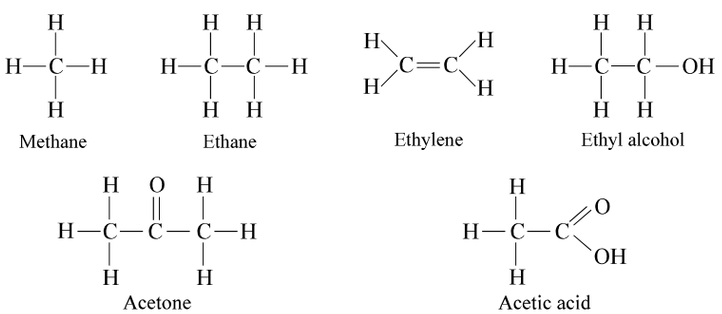
- Understand the concept pf organic compounds
- Discuss classification of organic compounds
- Know about IUPAC nomenclature of organic compounds
- Understand rules for IUPAC nomenclature

1.2 ORGANIC COMPOUNDS

Organic Chemistry is the study of the compounds of carbon. The carbon atoms have a unique property of combining with other carbon atoms repeatedly, hence very large number of carbon compounds are possible. In fact about ten million organic compounds are already known and a large number (about half a million) of new compounds are being added every year to the domain of organic chemistry. The study of such a vast subject would be unnecessarily complicated if it is not divided into classes or groups based on the similarities of structures and properties of the group members. The two main types into which all known organic compounds may be classified are **acyclic** and **cyclic**.

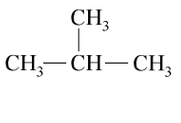
Acyclic Compounds

The acyclic compounds are those in which the carbon atoms are linked to each other in such a manner that the molecule is having an open chain structure. They are also known *open chain compounds* or *aliphatic compounds*. Thus simple compounds like methane, ethane, ethylene, ethyl alcohol, acetone, acetic acid etc., are all acyclic or aliphatic compounds because they have an open chain of carbon atoms in their molecules.

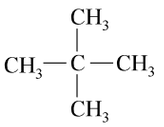


NOTES

These open chain compounds may have a straight or branched chain of carbon atoms and are accordingly referred to as *straight chain* or *branched chain* aliphatic compounds. For example all the compounds mentioned above are straight chain type and compounds like iso-butane, neo-pentane etc., are branched chain type.



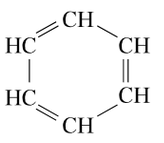
Isobutane



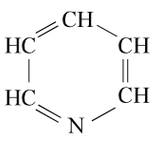
Neopentane

Cyclic Compounds

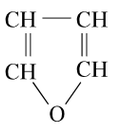
When the carbon atoms are linked to each other or to the atoms of some other elements in a manner to form a closed chain or ring type structure; the compounds are known as cyclic compounds. The compounds with only one ring of atoms in the molecule are known as *monocyclic* but those with more than one ring of atoms are termed as *polycyclic*. Again the ring may be made up of only carbon atoms or it may contain hetero (*hetero* meaning different) atoms like N, O, S, etc., besides the carbon in the rig. The former type of compounds are known as *Homocyclic* or *Carbocyclic* where as the latter are referred to as *Heterocyclic*. Benzene is an example of carbocyclic compound and pyridine, furan and thiophene etc., are heterocyclic compounds.



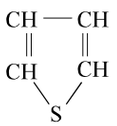
Benzene (Carbocyclic)



Pyridine

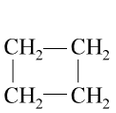


Furan
(Heterocyclic)

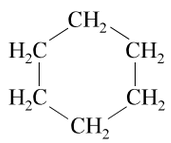


Thiophene

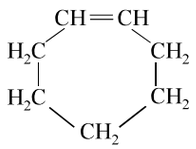
The carbocyclic or homocyclic compounds may again be divided into two types: (*i*) *Alicyclic* compounds, and (*ii*) *Aromatic* compounds. Alicyclic compounds, although possess a ring structure made up of carbon atoms they behave more or less like aliphatic compounds. Cyclobutane, cyclohexane, cycloheptene etc., are examples of alicyclic compounds.



Cyclobutane



Cyclohexane



Cycloheptene

A large number of cyclic compounds having alternate single and double bonds show unusual stability towards addition reactions and undergo substitution reactions despite the unsaturation in the molecule. Such compounds are designated as *aromatic* type. Most of these aromatic compounds have a benzene ring consisting of six carbon atoms with alternate single and double bonds. These compounds are

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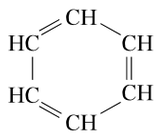
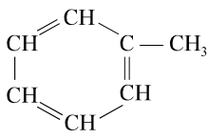
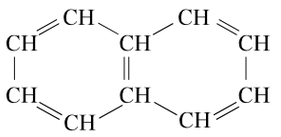
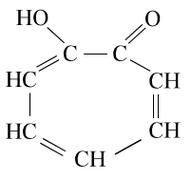
known as *benzenoid aromatics*. On the other hand some of the aromatic compounds have structural units different from benzenoid type and these are known as *non-benzenoid aromatics*.

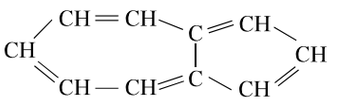
Thus benzene, toluene and naphthalene are benzenoid aromatic compounds while tropolone and azulene are non-benzenoid aromatic compounds.


Benzene


Toluene

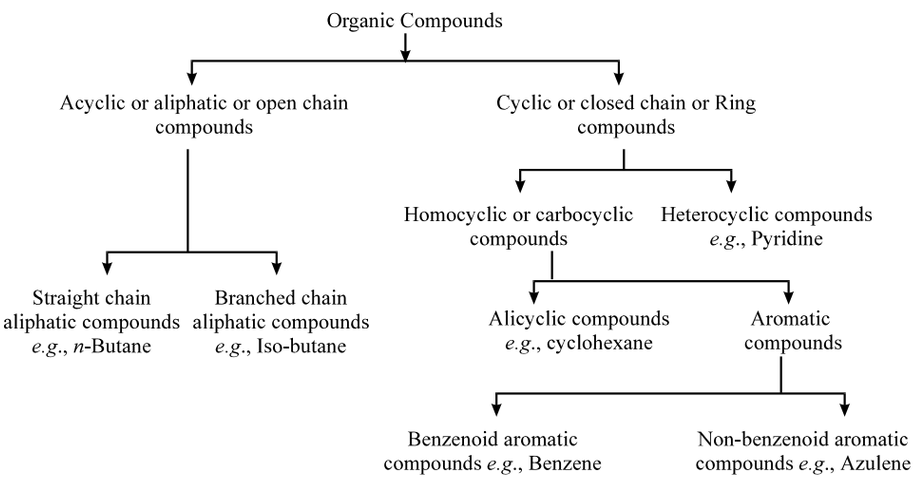

Naphthalene


Tropolone


Azulene

The behaviour of heterocyclic compounds is similar to either aliphatic or aromatic compounds depending on their structure. Thus compounds like piperidine resemble alicyclic compounds whereas compounds like pyridine resemble aromatic compounds in their chemical behaviour. The compounds of aliphatic series differ in many ways from the compounds of aromatic series.

The short schematic classification of the organic compounds is given below:



Classes of organic compounds

The above classification is based on basic skeleton of carbon atoms. To these carbon atoms are attached hydrogen atoms or groups made up of other atoms. The molecules made up of only carbon and hydrogen are known as *hydrocarbons*. All other compounds are considered to be the derivatives of hydrocarbons obtained by the replacement of one or more hydrogen atoms with other atoms or groups.

The groups are generally composed of *heteroatoms* (atoms other than C and H) like O, N, S, halogens etc., and are known as *functional groups*, since the reactivity or functions of the compounds are largely governed by these groups. *A functional group is an atom or a group of atoms which defines the structure of a particular family of organic compounds and also determines their properties*. In most of the reactions functional groups are the site of chemical reactions. Hydrocarbons having only σ bonds are referred to as saturated and are generally less reactive. If π bonds are present then the hydrocarbon is referred to as unsaturated and these owe their reactivity to multiple bonds. *Thus the double and triple bonds in hydrocarbons are also considered as their functional groups*. Every functional group has its own chemical characteristics and it is generally on the basis of the type of functional group, that an otherwise unmanageable large number of organic compounds, have been grouped into only limited number of classes.

Some of the important functional groups present in organic compounds are listed in the Table 1.1.

Check Your Progress

1. What are the main two types of organic compounds?
2. What are acyclic compounds?
3. What are cyclic compounds?

1.3 IUPAC NOMENCLATURE OF ORGANIC COMPOUNDS

The earlier system of naming a compound depending on the source from which it was obtained or on the basis of its structure or properties is known as *trivial system*. Thus the names urea (from urine) methanol (meaning spirit of wood), citric acid (from citrus plant) etc., were based on the source of their occurrence. Similarly glucose (sweet), pentane (five), hexane (six) etc., were derived from the Greek words describing their properties and structure. The names based on trivial system are called *trivial* or *common names*.

However, with the enormous increase in the number of organic compounds it became very difficult to assign trivial names to each compound. Moreover, the trivial names often did not have any logic and depended on the likes or dislikes of the discoverer and often a single compound was given different names by different workers. Under these circumstances it became essential that a system of nomenclature be so devised that the name must clearly indicate one and only one structure for that compound. With this objective, the International Chemical Congress met in Geneva in 1892 and formulated a system, based on simple and rationally

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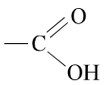
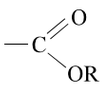
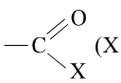
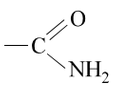
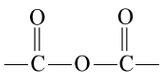
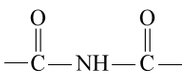
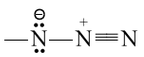
Table 1.1 *Important Functional Groups and with Classes of their Compounds*

Sl. No.	*Functional group*	*Name of the group*	*Class of compound*
1.	— F, — Cl, — Br, —I (Represented as X)	Fluoro, Chloro, Bromo, Iodo, (Halo)	Alkyl halides or Halogen compounds
2.	— OH	Hydroxy	Alcohols or Alkanols
3.	— OR	Alkoxy	Ethers
4.	— SH	Mercapto	Thio alcohols or Mercaptans or Thiols
5.	—SR		Thioethers or Sulphides
6.		Formyl	Aldehydes or Alkanals
7.		Carbonyl	Ketones or Alkanones
8.		Carboxy	Carboxylic acids or Alkanoic acids
9.		Ester	Esters
10.	 (X = Cl, Br or I)	Acyl halide	Acid halides or Acyl halides
11.		Amide	Acid amides or Amides
12.		Anhydride	Acid anhydrides
13.	$—NH_2$	Amino	Amines
14.		Imino	Imines
15.	—C≡N	Cyano	Cyanides or Nitriles
16.	—N⇉C	Isocyanide	Isocyanides or Carbylamines
17.		Nitro	Nitro compounds
18.	—N=O	Nitroso	Nitroso compounds
19.		Imido	Imides
20.	—N=C=O	Isocyanate	Isocyanates
21.	—C≡N→O	Cyanate	Cyanates
22.	—N=C=S	Isothiocyanate	Isothiocyanates
23.		Azide	Azides
24.	—N=N—	Azo	Azo compounds
25.	$— SO_2 — OH$	Sulphonic acid	Sulphonic acids
26.	$— SO_2 — NR_2$	Sulphonamide	Sulphonamides
27.	$—SO_2 — Cl$	Sulphonyl chloride	Sulphonyl chlorides
28.	$— PH_2$	Phosphine	Phosphines

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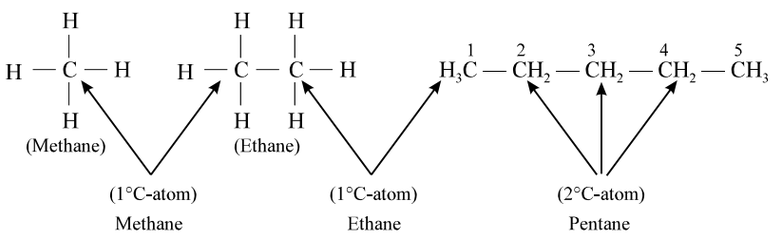
applicable principles, for naming the organic compounds. This system was known as **Geneva System** of nomenclature.

This system was revised and adopted by the International Union of Chemistry (IUC) at Liege in 1930 and became known as **IUC System of Nomenclature**. This IUC system too was found to be inadequate. The IUC later changed its name to **International Union of Pure and Applied Chemistry** and modified the system of nomenclature. The new system, now widely accepted, is in accordance with the rules published by the International Union of Pure and Applied Chemistry (IUPAC) in 1957 and revised in 1967, and is known as **IUPAC System of Nomenclature**.

This IUPAC system of nomenclature has been grafted over the existing naming practice and therefore certain common names, with which the chemists are thoroughly familiar, are still used for example, the names acetylene, ethylene, and allene ($H_2C{=}C{=}CH_2$) *are still retained*. The name assigned to a compound on the basis of IUPAC rules is known as its **systematic name** whereas the name which has been retained for a compound on account of its familiarity or long usage is known as **common name**.

Some other common terms used are:

(*i*) **Primary (1°), Secondary (2°), Tertiary (3°) and Quaternary (4°) carbon atoms**. In further discussion you will see that abbreviations 1°, 2°, 3° and 4° are used. Wherever they are used they stand for primary, secondary, tertiary and quaternary carbon atoms. This can be understood by taking example of methane, ethane and pentane as given below. The carbon atoms of pentane are numbered 1 to 5 starting from one end.



There are two types of carbon atoms in these hydrocarbons:

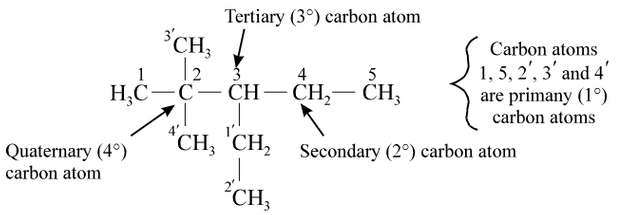
(*a*) *The carbon atoms which are attached either to no other carbon atom (methane) or to only one other carbon atom. Such carbon atoms are called primary (1°) carbon atoms.*

(*b*) The carbon atoms 2, 3 and 4 of pentane which are attached to two other carbon atoms. Such carbon atoms are called secondary (2°) carbon atoms.

Now look at the following hydrocarbon 3-ethyl-2,2-dimethyl pentane. The carbon atoms numbered 1, 5, 2′, 3′ and 4′ are attached to only one carbon atom.

These are primary (1°) carbon atoms. Carbon atoms 4 and 1′ are secondary (2°) carbon atoms as they are attached to two other carbon atoms number 3 and 2′ and numbers 3 and 5 respectively.

NOTES



(*ii*) *The carbon atom number 3 is attached to three other carbon atoms number 4, 2 and 1′*. Such carbon atoms are called *tertiary (3°) carbon atoms*.

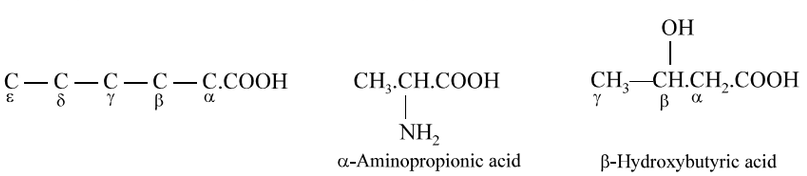
(*iii*) *Lastly the carbon atom number 4 is connected to four other carbon atoms number 1, 3, 3′ and 4′*. Such carbon atoms are called *quaternary (4°) carbon atoms*.

The hydrogen atoms attached to 1°, 2° and 3° carbon atoms are sometimes called primary, secondary and tertiary hydrogen atoms.

Further, while writing the names of the compounds it must be noted that the names of some compounds are written as one word whereas the names of other compounds are written as consisting of two separate syllables. Thus the names like methyl chloride, ethyl alcohol etc., are written in two parts because the name suggets that the compound is made up of two or more independent units. Thus ethyl group and alcoholic —OH group when combined give ethyl alcohol and therefore ethyl alcohol should be written in two separate syllables. On the other hand names like chloromethane, nitroethane etc., are written as one word because the name suggests that a group has replaced the hydrogen of the hydrocarbon. Thus, the name of groups replacing hydrogens in a compound are prefixed in the name of the compound and it is written as one word.

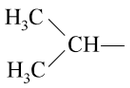
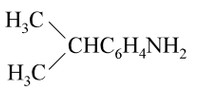
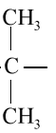
Some of the common abbreviations used for various groups are given in Table 1.2.

Sometimes the names of compounds include the use of a Greek letter α, β, γ, δ etc., as in names like α-amino acids, β-hydroxyacids. These letters are used to designate the position of groups or atoms at various carbon atoms in the chain with respect to a functional group. Thus if a functional group like —COOH, —CO—, —NO_2 etc., is present, the carbon atom to which this group is attached is known as α, the next to α carbon atom is β, and the next one is γ and then δ, ε etc.



NOTES

Table 1.2 *Commonly used Abbreviations*

Abbreviations	*Name of groups*	*Examples*
R—	Alkyl	—CH_3, —C_2H_5
X—	Halide (F, Cl, Br, I)	—F in CH_3F (CH_3X) —Cl in C_2H_5Cl (C_2H_5X) —Br in CH_2Br_2 (CH_2X_2) —I in CHI_3 (CHX_3)
Me—	Methyl (CH_3—)	Me_2SO_4 or $(CH_3)_2SO_4$ R.COOMe or R.$COOCH_3$
Et—	Ethyl (C_2H_5—)	Et_2NH or $(C_2H_5)_2NH$ EtOH or C_2H_5OH
i-Pr	*iso*-Propyl 	*i*-Pr- $C_6H_4NH_2$ or 
Pr—	*n*-Propyl (CH_3—CH_2—CH_2—CH_2—)	PrOH or $CH_3.CH_2.CH_2OH$
Bu—	*n*-Butyl (CH_3—CH_2—CH_2—CH_2—)	BuOH or $CH_3.CH_2.CH_2.CH_2OH$
t-Bu	*ter*-Butyl 	*t*-BuOH or $(CH_3)_3C.OH$
Ac—	Acetyl (CH_3CO—)	AcOH or CH_3COOH
Ph— (ϕ— or Ar—)	Phenyl (C_6H_5—)	Ph. COOH, Ar. COOH ϕ COOH or C_6H_5COOH

Rules for IUPAC Nomenclature

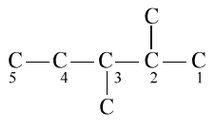
The IUPAC names of the representative members of various homologous series have been given in the previous section. However, in case of naming complex structure molecule the *International Union of Pure and Applied Chemistry* has framed a set of rules for various types of organic compounds. The guiding principle which is followed in writing the names for organic compounds is that of *substitution on a parent name*. All such names are, therefore, also known as *substitutive names*. The general rules for IUPAC nomenclature are enunciated and illustrated below:

1. *All organic compounds are considered to be the derivatives of the* **hydrocarbons** formed by the suitable replacements of the hydrogen(s) by various groups or substituents. Thus the naming of any organic compound depends on the correct selection of the parent hydrocarbon or the basic carbon skeleton.

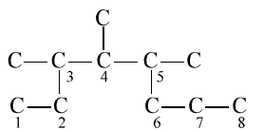
2. **Longest carbon chain**. *The first step is to select the longest possible continuous chain of carbon atoms which is called the parent chain*.

NOTES

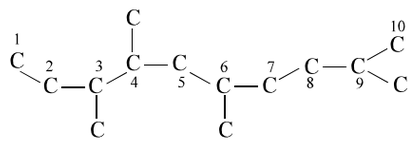
On the basis of the number of carbon atoms in the parent chain, the parent hydrocarbon is named. All other carbon chains attached to main (i.e., the longest) chain are referred to as *side chains*. Thus if the parent chain contains five carbon atoms the parent hydrocarbon is pentane. For example in structure I the longest carbon chain contains five carbon atoms which are shown in a straight line.



(I)

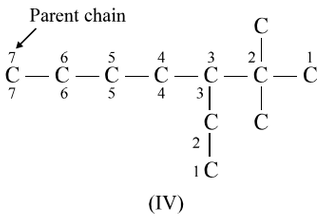


(II)

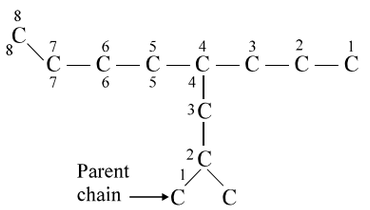


(III)

In structure II the straight line contains only five carbon atoms whereas the longest continuous chain of carbon atoms contains eight carbon atoms. A zigzag chain of carbon atoms is shown in III where the longest chain contains ten carbon atoms.



(IV)



(V)

It is possible that sometimes there may be two carbon chains having same number of carbon atoms in the molecule. In such a case the one which carries the larger number of side chains is selected as the parent chain. For example structures IV and V both contain two carbon chains of equal lengths but the one with maximum substituents has been selected as the parent chain.

While naming the carbon chain a *root word* denoting the length of the carbon chain is put before the *primary suffix* of the type of hydrocarbon. Following Table 1.3 makes the point clear.

Table 1.3 *Root words and Primary Sufix*

No. of C atoms in the chain		*Root word*	*Primary suffix*		
			-ane	*-ene*	*-yne*
1	(C_1)	Meth	Methane	—	—
2	(C_2)	Eth	Ethane	Ethene	Ethyne
3	(C_3)	Prop	Propane	Propene	Propyne
4	(C_4)	But	Butane	Butene	Butyne
5	(C_5)	Pent	Pentane	Pentene	Pentyne
6	(C_6)	Hex	Hexane	Hexene	Hexyne

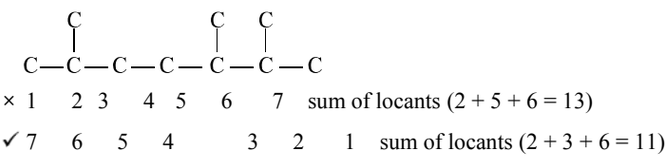
For 7, 8, 9, 10, 11 carbon atom chains the root words Hept, Oct, Non, Dec and Undec respectively are used.

3. **Lowest number for locants**

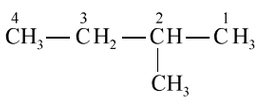
NOTES

(*i*) *The carbon atoms of the longest continuous chain, are then numbered by arabic numberals 1, 2, 3, 4, 5.....etc., from one end to the other in such a manner that the carbon atoms carrying substituent get the lowest number. The position of the side chain or substituent is indicated by the number assigned to the carbon atom to which it is attached. If there are more than one substituents then the numbering of carbon atoms is done in such a way that the sum of the numbers used to locate the substituents is minimum*. This is also known as **lowest sum rule**. The number that locates the position of a substituent is known as **Locant**.

In the example given below the numbering should be done from the right hand end as it gives the lowest sum for locants



(*ii*) *Lastly the name of the substituent is prefixed, preceded by the locant, to the name of the parent hydrocarbon. A hyphen separates the locant from the name of the substituent.* Thus the hydrocarbon given below is 2-methylbutane:



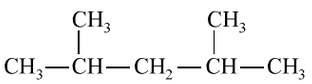
The name 2-methylbutane indicates that the parent chain has four carbon atoms (butane) and there is a methyl group at position 2.

4. **Alphabetical order of prefixes**

(*i*) *If there are more than one substituents, each substituent prefixed by its locant, is put in the alphabetical order preceding the name of the parent hydrocarbon*.

In case the same substituent is present two, three or four times then the prefix di, tri or tetra is attached to substituent's name. Its locants are written in the increasing order separated by commas amongst themselves and by a hyphen from the substituent name.

It is to be noted that the prefixes di, tri, etc., are not considered while deciding the alphabetical order of the substituent. Thus the names given to the compounds below within brackets are not correct:



2,4-Dimethylpentane
(VI)

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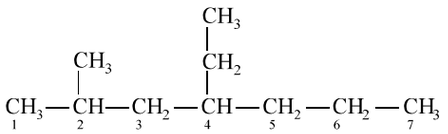
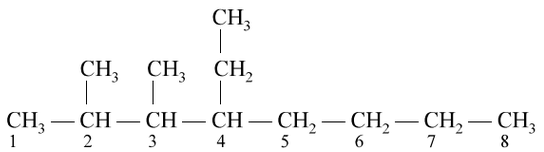


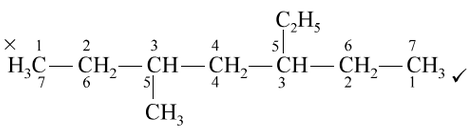
✓ 4-Ethyl-2-methylheptane
× (2-Methyl-4-ethylheptane)
(VII)



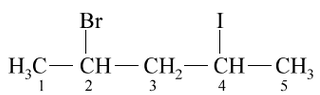
✓ 4-Ethyl-2,3-dimethyloctane
× (2,3-Dimethyl-4-ethyloctane)
(VIII)

The name 2-methyl-4-ethylheptane for hydrocarbon VII is wrong because it violates the *alphabetical rule* and the name 2,3-dimethyl-4-ethyloctane is incorrect for the compound VIII because the prefix 'di' has been included in the alphabetical order which is wrong.

(*ii*) *In case two alkyl groups are present as side chains in such a manner that the lowest sum rule is obeyed by numbering the chain from either side then the lower number is given to that which is first cited in the name for example, of the hydrocarbon given below will be 3-ethyl-5-methyl heptane.*

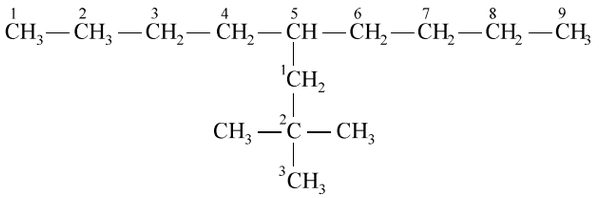


(*iii*) *If two substituents of equal priority are present in identical position with respect to the end of the carbon chain then the lower number is given to the substituent which comes first in alphabetical order*.



The compound given above will correctly be called 2-bromo-4-iodo pentane.

(*iv*) *If the substituent on the parent chain has itself branched chain then it is named as the substituted alkyl group and its carbon atoms are numbered from the carbon attached to parent chain*. Such a substituent, indicating the positions of the branched substituents on it, is written in parentheses and prefixed before the name of parent hydrocarbon. Thus in the example given below, the substituent at C atom 5 of the main chain is 2,2-dimethylpropyl group and so the name of the hydrocarbon will be 5-(2,2-dimethylpropyl) nonane.



(IX)

It is to be noted that it is the complete name of the branch that is alphabetised. Thus for example:

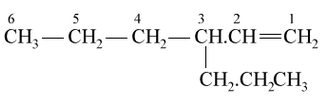
(*a*) (2,2-dimethyl) comes before propyl.

(*b*) Other prefixes which are hyphenated are not considered to be a part of the groups name when placing the group in alphabetical order *for example, sec*-butyl is placed under '*b*' not '*s*'.

5. **Numbering the multiple bonds**

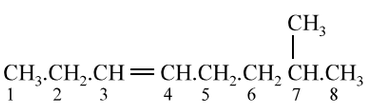
(*i*) *The double and triple bond in a molecule are regards as functional groups. If a double or triple bond is present in the molecule then the longest chain of carbon atoms is so chosen as to include the double or triple bond even if it is not the longest continuous chain of carbon atoms*. Thus in the example (X) given below the longest continuous chain is of 7 carbon atoms but, since it does not include the double bond, it is rejected and the carbon chain of 6 atoms including the double bond selected as parent chain for naming the compound.

(*ii*) *The position of the double or triple bond is indicated by prefixing the number of the C atom preceding the multiple bond. The carbon chain is numbered in a manner so as to give the least number to the multiple bond even if it violates the lowest sum rule*. Observing these rules the name given to the compound (X) is 3-propyl-1-hexene or 3-propylhexene-1 or



(X)

3-propyl hex-1-ene. Similarly the compound $CH_3.CH_2.CH_2.CH_2—C\equiv CH$ will be named as 1-hexyne.



(XI)

The compound XI will correctly be called as 7-methyl-3-octene or 7-methyloctene-3 or 7-methyloct-3-ene although the lowest sum rule gives the name as 2-methyl-5-octene (which is wrong as it gives locant 5 to double bond).

(*iii*) *If more than one double or triple bond is present in the molecule, then the longest chain of carbon atoms is so chosen that it includes maximum number of such bonds even if it is not the longest chain*.

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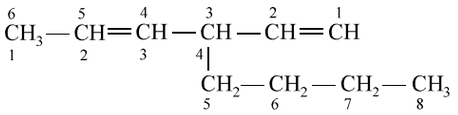
In the compound XII the longest chain consists of eight C atoms but it includes only one double bond; hence the alternative chain having six carbon atoms and including both the double bonds is accepted for naming the compound.



(XII)

Now since it has two double bonds at carbon 1 and 4 and a butyl group at carbon atom 3 it will be called as 3-butyl-1,4-hexadiene or 3-butyl hex-1,4-diene (diene—meaning 2 double bonds).

6. **Naming functional group compounds**

(*i*) *For naming monofunctional (those having one functional group) compounds, with or without multiple bonds, the longest carbon chain is so chosen as to include the functional group, and the multiple bonds if any. The parent chain selected is numbered in such a way so as to give the lowest number to the functional groups even if it violates the lowest sum rule*. The monovalent functional groups like —CHO, —COOH, —CN, —$CONH_2$ etc., occur at the end of the chain and their carbon atom is always given number 1.

(*ii*) *The names of the substituents are prefixed to the parent hydrocarbon according to IUPAC rules discussed above*.

(*iii*) *The last 'e' of the primary suffix of hydrocarbon is dropped and the secondary suffix representing the functional group is added*. The suffix 'ol' for alcohol, 'al' for aldehyde, 'one' for ketone etc., are called secondary suffixes.

(*iv*) *The number giving the position of the functional group is inserted before the name of the hydrocarbon and separated on either side by hyphens*. If the functional group is at the end of the side chain then its locant is not indicated (see examples 2 and 4 below). However, in case of a possibility of confusion the number is shifted just before the functional syllable.

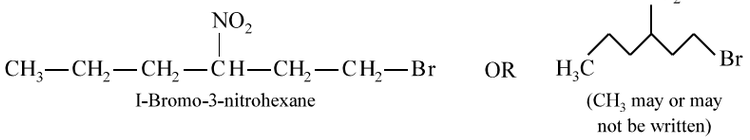
However there is no definite rule for positioning the numeral representing the functional group and three different methods are used; all being acceptable. Thus the compound $CH_3.CH_2.CH_2.CO.CH_3$ is named as 2-pentanone, pentan-2-one or pentanone-2. Similarly the compound $CH_3.CHOH.CH_2CH_3$ may be called as 2-butanol, butan-2-ol or butanol-2.

(*v*) *Halo* (—Cl, —Br and —I), *nitro* (—NO_2), *nitroso* (—NO), *alkoxyl* (—OR) *groups are not regarded as functional groups*. They have to be taken as substituents when present.

Some examples of the names of the monofunctional compounds are given below to illustrate the rules. The line structures have been also given to develop their understanding.

NOTES

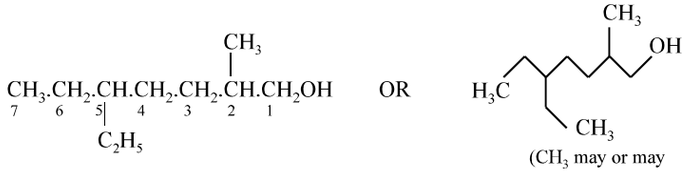
Example 1



I-Bromo-3-nitrohexane

(CH_3 may or may not be written)

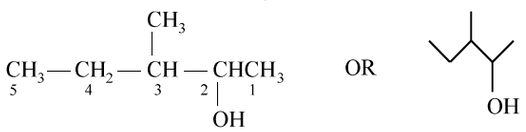
Example 2



(CH_3 may or may not be written)

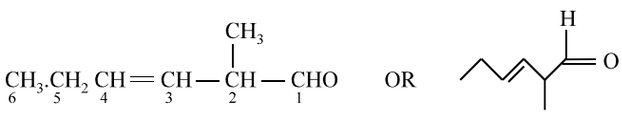
Here the longest chain is of 7 carbon atoms. Functional group is attached to carbon atom 1 and methyl and ethyl groups are at carbon atoms 2 and 5. Hence the name will be 5-ethyl-2-methyl-1-heptanol or 5-ethyl-2-methylheptan-1-ol or *5-ethyl-2-methyl heptanol*.

Example 3



If the —OH group is attached to a carbon atom, not at the end, then the numbering is to be done from the end which gives a lesser number to the carbon atom bearing —OH group. Thus the compound given above is 3-methyl-2-pentanol or 3 methyl pentan-2-ol.

Exampel 4



Here the longest carbon chain with the functional group is the 6 carbon atom chain. It has a double bond between the carbon atoms 3 and 4 hence the parent hydrocarbon is 3-hexene. The above compound is an aldehyde hence the terminal 'e' will be replaced by 'al'. Now in this case, there is locant prefixing the hydrocarbon name hence the numeral indicating the position of the functional group will be placed before the functional syllable separated by a hyphen on either side. Thus the name will be written as 2-methyl-3-hexen-1-al or 2-methyl-3-hexenal.

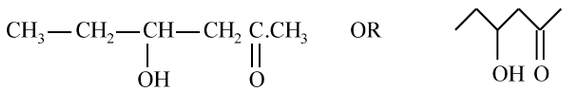
NOTES

Naming Polyfunctional compound

In compounds having more than one functional groups, excluding double or triple bonds, the 'principal' or 'senior' group forms the suffix of the name and other group(s) are treated as substituents. The order of precedence or seniority, prefix and suffix names of groups are given in Table 3.3.

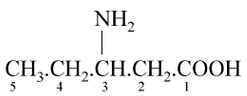
Given below are some more examples to illustrate the nomenclature of the compounds with more than one functional groups. Line structures are also given alongside.

Example 5



The longest chain is of six carbon atoms. It has a hydroxy and a ketonic group and the latter will appear as a suffix taking precedence. Hence, the name of the compound will be 4-hydroxy-2-hexanone or 4-hydroxyhexanone-2 or 4-hydroxyhexan-2-one.

Example 6



The —COOH group is the principal functional group and hence its name will appear in suffix. So the name of the compounds is 3-amino-1-pentanoic acid.

Table 1.4

Order of precedence	***Group***	***Prefix name***	***Suffix name***
1.	—C(=O)OR	Alkoxy carbonyl	alkyl alkanoate
2.	—C(=O)OH	Carboxy*	-oic acid
3.	—SO_3H	Sulpho	-sulphonic acid
4.	X–C(=O) (*e.g.*, COCl)	Haloformyl	-anoyl halide
5.	NH_2–C(=O)	Carbamoyl	-amide
6.	—C≡N	Cyano*	-nitrile
7.	H–C(=O)	Oxo	-al

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8.	$\rangle C=O$	Oxo	-one
9.	$\rangle C=S$	Thioxo	-thione
10.	—OH	Hydroxy	-ol
11.	—SH	Mercapto	-thiol
12.	$—NH_2$	Amino	-amine
13.	$\rangle C=C$	—	-ene
14.	$—C\equiv C—$	—	-yne
15.	—O—	Epoxy	—
16.	$—N=N^-$	Azo	—
17.	—NO	Nitro	—
18.	—NO	Nitroso	—
19.	—X (halogen)	Halo	—

@ From Basic Organic Nomenclature: An introduction, by Dave Woodcock 1996, 2000, Okanagan University College.

* These prefixes include carbon of the functional group in the name.

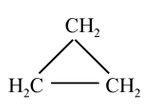
Check Your Progress

4. What does IUPAC stand for?
5. What is the systematic name of an organic compound?
6. What are tertiary carbon atoms?

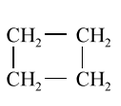
1.4 CYCLIC AROMATIC AND HETEROCYCLIC COMPOUNDS

The nomenclature of cyclic, heterocyclic and aromatic compounds will be dealt along with those compounds but some reference is being given here to enable the students to overcome any difficulty which they may face in dealing with simple problems:

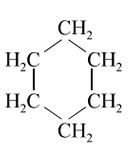
(*a*) The cyclic nature of the compound is indicated by putting the prefix '*cyclo*' before the name of the parent hydrocarbon.



Cyclopropane



Cyclobutane



Cyclohexane

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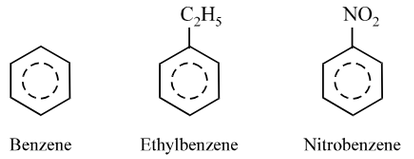
(*b*) Aromatic compounds are regarded as benzene derivatives.

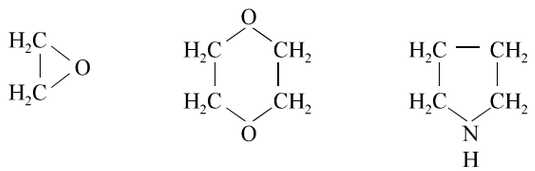


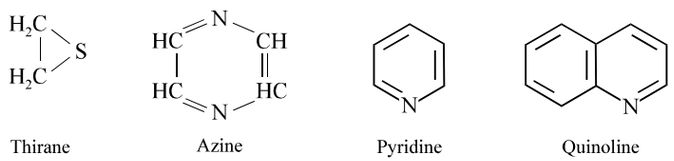
(*c*) For naming the heterocyclic compounds prefix 'oxa' is used to denote oxygen, 'aza' to signify nitrogen and 'thia' to indicate sulphur. The names of heterocyclic rings may thus be derived by adding to these the suffix name depending on the nature of ring.

Table 1.5 *Suffix used in Naming Heterocyclic Rings*

No. of atoms forming ring	*Rings containing nitrogen*		*Rings not containing nitrogen*	
	Unsaturated	*Saturated*	*Unsaturated*	*Saturated*
3	irine	iridine	irene	irane
4	ete	etidine	ete	etane
5	ole	olidine	ole	olane
6	ine	perhydro azine	in	ane

Thus:





Finally, it must be understood that for writing the structural formula of the compound starting from the IUPAC name a reverse procedure is followed.

(*i*) *Firstly, the parent hydrocarbon is located from the name and accordingly a straight chain of as many carbon atoms is written.*

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(*ii*) *Next, all the carbon atoms are numbered; the numbering may be done from any end.*

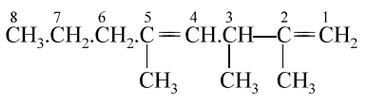
(*iii*) *Now the suffix is located which gives information about the type of functional group, its number and its position.* The group is attached to the carbon atom indicated in the name. For the suffix group having carbon (*for example,* — COOH, — CN, —C(=O)— etc.) the carbon atom of the chain is included in the group.

(*iv*) *Lastly, the groups or substituents mentioned in prefix are attached to carbon atoms indicated by locants and hydrogens filled in to satisfy rest of the valencies of the carbon atoms*.

Thus for writing the structural formula of 2,3,5-Trimethyl-1-4-octadiene we proceed as follows:

1. Write eight carbon atoms in a chain and number them.
2. Insert two double bonds at positions 1 and 4.
3. Place three methyl groups at carbon 2, 3 and 5.

Thus we have the structural formula as:



Though the IUPAC names are systematic and logical, sometimes the trivial names are preferred over them for being convenient. However, IUPAC name is always regarded correct even if the same is hardly ever used. Thus IUPAC name of naphthalene ($C_{10}H_8$), [4.4.0.] Bicyclodeca-pentene is hardly ever used being inconvenient. Another such name is benzene. These are always used and have been assimilated to a great extent in IUPAC system. Hence the actual test of name is its usage and if a name is frequently used in literature, howsoever illogical it may be, it is accepted.

Relatively complex substances like morphine, cholestrol, strychnine, camphor etc., are still better known through their common names and for some highly complex molecules no IUPAC name can be assigned.

1.4.1 Bicyclic and Polycyclic Compounds - Nomenclature

A bicyclic molecule (bi = two, cycle = ring) is a molecule that features two joined rings. Bicyclic structures occur widely, for example in many biologically important molecules like á-thujene and camphor. A bicyclic compound can be carbocyclic (all of the ring atoms are carbons), or heterocyclic (the rings atoms consist of at least two different elements), like DABCO. DABCO, a heterocyclic, bridged bicyclic compound, formally named 1, 4-diazabicyclo [2.2.2] octane. Moreover, the two rings can both be aliphatic (for example, decalin and norbornane), or can be aromatic (for example, naphthalene), or a combination of aliphatic and aromatic (for example, tetralin).

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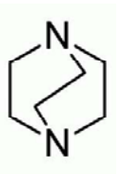
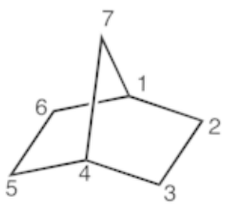


DABCO: A Heterocyclic Bridged Bicyclic Compound

There are three possible modes of ring junction for a bicyclic compound:

- In spirocyclic compounds, the two rings share only one single atom, the spiro atom, which is usually a quaternary carbon. An example of a spirocyclic compound is the photochromic switch spiropyran.
- In fused bicyclic compounds, two rings share two adjacent atoms. In other words, the rings share one covalent bond, i.e., the so-called bridgehead atoms are directly connected (for example, á-thujene and decalin).
- In bridged bicyclic compounds, the two rings share three or more atoms, separating the two bridgehead atoms by a bridge containing at least one atom. For example, norbornane, also known as bicycle [2.2.1] heptane, can be thought of as a pair of cyclopentane rings each sharing three of their five carbon atoms. The structure of camphor has the same basis as norbornane, but with some substituents added. Figure illustrates the bridged bicyclic norbornane, formally bicycle [2.2.1] heptane.



Norbornane: The Bridged Bicyclic

Nomenclature

Bicyclic molecules have a strict nomenclature. The root of the compound name depends on the total number of atoms in all rings together, possibly followed by a suffix denoting the functional group with the highest priority. Numbering of the carbon chain always begins at one bridgehead atom (where the rings meet) and follows the carbon chain along the longest path, to the next bridgehead atom. Then numbering is continued along the second longest path and so on. Fused and bridged bicyclic compounds get the prefix *bicyclo*, whereas spirocyclic compounds get the prefix *spiro*. In between the prefix and the suffix, a pair of brackets with numerals denotes the number of carbon atoms between each of the bridgehead atoms. These numbers are arranged in descending order and are separated by periods. For example, the carbon frame of norbornane contains a

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total of 7 atoms, hence the root name heptane. This molecule has two paths of 2 carbon atoms and a third path of 1 carbon atom between the two bridgehead carbons, so the brackets are filled in descending order: [2.2.1]. Addition of the prefix *bicyclo* gives the total name bicyclo[2.2.1]heptane.

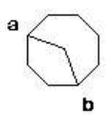
The carbon frame of camphor also counts 7 atoms, but is substituted with a carbonyl in this case, hence the suffix heptanone. We start with numbering the carbon frame at the bridgehead atom with the highest priority (methyl goes before proton), hence the bridgehead carbon in front gets number 1, the carbonyl gets number 2 and numbering continues along the carbon chain following the longest path, until the doubly substituted top carbon (number 7). Equal to norbornane, this molecule also has two paths of 2 carbon atoms and one path of 1 carbon atom between the two bridgehead carbons, so the numbers within the brackets stay [2.2.1]. Combining the brackets and suffix (now filling in the position of the carbonyl as well) gives us [2.2.1] heptan-2-one. Besides *bicyclo*, the prefix should also specify the positions of all methyl substituents so the complete, official name becomes 1,7,7-trimethylbicyclo[2.2.1]heptan-2-one.

When naming simple fused bicyclic compounds, the same method as for bridged bicyclic compounds is applied, except the third path between the two bridgehead atoms now consists of zero atoms. Therefore, fused bicyclic compounds have a "0" included in the brackets. For example, decalinis named bicycle [4.4.0] decane. The numbers are sometimes omitted when no ambiguity is created as there is no alternative possible – for example, bicyclo[1.1.0]butane is typically called simply bicyclobutane.

The heterocyclic molecule DABCO has a total of 8 atoms in its bridged structure, hence the root name octane. Note that here the two bridgehead atoms are nitrogen instead of carbon atoms. Therefore, the official name gets the additional prefix *1,4-diaza* and the total name becomes 1,4-diazabicyclo[2.2.2]octane.

Bicyclic Alkanes. II. Two Ring Carbons Common.

When the two rings of the bicyclic compound have two carbons common there are three different paths between the two common carbons following carbon, carbon bonds. Take for example the following molecule:



In this example, the carbon atoms labelled as a and b are the carbons common to the two rings, often referred to as **bridgehead carbons**, and the three different paths between a and b contain 1, 2 and 4 intervening carbon atoms.

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The generic name for compounds such as this is **Bicycle [x.y.z] alkane**

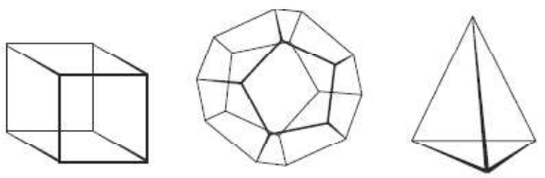
where x, y, and z are the numbers of intervening carbons on the three paths between the two bridgehead carbons cited in **decreasing** numerical order, and alk refers to the total number of carbons in the ring systems. (For a check, this number is the sum of the three numbers, x, y, and z, plus 2 for the two bridgehead carbons.)

The compound illustrated above is thus named:

Bicycle [4.2.1] nonane

Note carefully the similarities and the differences in naming these compounds and in naming the spiro compounds.

Some organic compounds contain many rings joined at common atoms; these compounds are called polycyclic compounds. Among the more intriguing polycyclic compounds are those that have the shapes of regular geometric solids. Three of the more spectacular examples are cubane, dodecahedrane, and tetrahedrane.



cubane dodecahedrane tetrahedrane

Systematic IUPAC name of Cubane: Pentacyclo [4.2.0.02,5.03,8.04,7] octane

Systematic IUPAC name of Dodecahedrane: [5]fullerane-C_{20}-Ih

Systematic IUPAC name of Tetrahedrane: Tricyclo[1.1.0.$0^{2,4}$]butane

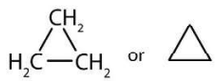
Check Your Progress

7. What is the structure of cyclopropane?
8. How are heterocyclic compounds named?

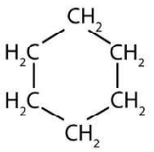
1.5 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. The two main types into which all known organic compounds may be classified are acyclic and cyclic.
2. The two main types into which all known organic compounds may be classified are acyclic and cyclic.

NOTES

3. When the carbon atoms are linked to each other or to the atoms of some other elements in a manner to form a closed chain or ring type structure; the compounds are known as cyclic compound.
4. International Union of Pure and Applied Chemistry.
5. The name assigned to a compound on the basis of IUPAC rules is known as its systematic name whereas the name which has been retained for a compound on account of its familiarity or long usage is known as common name.
6. The carbon atom number 3 is attached to three other carbon atoms number 4, 2 and 1¢. Such carbon atoms are called tertiary (3°) carbon atoms.
7.  or

cyclopropane

 or 

cyclohexane

8. For naming the heterocyclic compounds prefix 'oxa' is used to denote oxygen, 'aza' to signify nitrogen and 'thia' to indicate sulphur. The names of heterocyclic rings may thus be derived by adding to these the suffix name depending on the nature of ring.

1.6 SUMMARY

- Organic Chemistry is the study of the compounds of carbon.
- The carbon atoms have a unique property of combining with other carbon atoms repeatedly, hence very large number of carbon compounds are possible.
- The two main types into which all known organic compounds may be classified are acyclic and cyclic.
- The acyclic compounds are those in which the carbon atoms are linked to each other in such a manner that the molecule is having an open chain structure. They are also known open chain compounds or aliphatic compounds.
- When the carbon atoms are linked to each other or to the atoms of some other elements in a manner to form a closed chain or ring type structure; the compounds are known as cyclic compounds.
- The compounds with only one ring of atoms in the molecule are known as monocyclic but those with more than one ring of atoms are termed as polycyclic.

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- The carbocyclic or homocyclic compounds may again be divided into two types: (i) Alicyclic compounds, and (ii) Aromatic compounds.
- The molecules made up of only carbon and hydrogen are known as hydrocarbons.
- The name assigned to a compound on the basis of IUPAC rules is known as its systematic name whereas the name which has been retained for a compound on account of its familiarity or long usage is known as common name.
- A bicyclic compound can be carbocyclic (all of the ring atoms are carbons), or heterocyclic (the rings atoms consist of at least two different elements), like DABCO. DABCO, a heterocyclic, bridged bicyclic compound, formally named 1, 4-diazabicyclo [2.2.2] octane.
- Some organic compounds contain many rings joined at common atoms; these compounds are called polycyclic compounds. Among the more intriguing polycyclic compounds are those that have the shapes of regular geometric solids. Three of the more spectacular examples are cubane, dodecahedrane, and tetrahedrane.

1.7 KEY WORDS

- **Organic Compound:** An organic compound is generally any chemical compound that contains carbon.
- **Acyclic Compound:** A compound which is an open-chain compound, for example alkanes and acyclic aliphatic compounds.
- **Cyclic Compound:** A cyclic compound is a term for a compound in the field of chemistry in which one or more series of atoms in the compound is connected to form a ring.
- **Aromatic compound:** An organic compound that contains one or more benzene or equivalent heterocyclic rings: many such compounds have an agreeable odor.
- **Heterocyclic Compound:** A heterocyclic compound or ring structure is a cyclic compound that has atoms of at least two different elements as members of its ring.

1.8 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. What do you understand by the term class of compounds?

2. What are carbocyclic and heterocyclic compounds? Discuss.
3. What are functional groups? Explain.

Long Answer Questions

NOTES

1. Give a concise account of systematic nomenclature of organic compounds. Discuss the IUPAC system of naming organic compounds.
2. Explain aliphatic and aromatic compounds with the help of examples.
3. Write the structural formulae of the following compounds:
   (a) 3-Ethyl-2-methylhexene-1 (b) 4-Methylpentene-2
   (c) 2,2,3-Trimethylhexane (d) 1-Bromo-2-chloropentane
   (e) Pentane-2,4-dione (f) 1,3-Butadiene
4. Write structural formulae and IUPAC names of the following compounds:
   (a) Dimethyl carbinol (b) Ethylidene chloride
   (c) Crotonic acid (d) Vinyl acetylene
   (e) Methyl acetate.
5. What are bicyclic and polycyclic compounds? Give examples.

1.9 FURTHER READINGS

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NOTES

UNIT 2 ELECTRON DISPLACEMENT IN MOLECULES

Structure

2.0 INTRODUCTION

Covalent bonds are in most of the molecules we get encountered with on a daily basis, from the food we eat to the air we breathe to the fabric we wear. Covalent bonds are defined as chemical bonds between atoms where electrons are shared by each atom, rather than transferred from one atom to another, as it happens in an ionic bond. But not all atoms share electrons equally, in fact, chemistry would be a very boring topic if that were the case! Atoms can actually take more than their 'fair' share of electrons, even in a covalent bond, which leads to a variety of electronic displacements. An electronic displacement occurs when electrons move toward one side or part of a molecule. Electronic displacements are often responsible for the chemical reactivity of some molecules and the relative inertness of others. There are four different types of electronic displacements to consider: Inductive effects, Resonance, Hyperconjugation, and Electromeric effects

With the advancement of knowledge of organic chemistry it is no longer sufficient to simply isolate and study the properties of an organic compound but it has become important to correlate theoretical prediction with experimental facts and to explain with precision as to why a compound behaves in a particular manner. This information is usually acquired by a thorough understanding and systematic interpretation of the basic fundamentals governing the electronic structure of organic molecules.

In this unit, an attempt has been made to present these concepts in an empirical and simplified manner.

2.1 OBJECTIVES

NOTES

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

- Understand displacement of electrons in molecules
- Discuss covalent bonds and factors affecting a covalent bond
- Understand the concept of hyperconjugation
- Know about hydrogen bonding in molecules

2.2 ELECTRON DISPLACEMENT IN MOLECULES

An examination of the periodic table shows that besides the inert gases there are three types of elements—(*i*) those having one to three electrons in the outermost shell, (*ii*) those having five to seven electrons in the outermost shell, and (*iii*) those having four electrons in the outermost shell. Since the driving force for chemical combination is the tendency to acquire inert gas stable configuration, first type of elements will try to stabilise themselves by losing 1, 2 or 3 electrons because it is difficult to gain 7, 6 or 5 electrons than to lose 1, 2 or 3 electrons for obtaining stable arrangement. Similarly the elements of the second type will try to stabilize themselves by gaining 3, 2 or 1 electrons as losing 5, 6 or 7 electrons will be more difficult. Thus the elements of the first and the second type usually combine by either losing or gaining electrons.

The elements of third type, of which carbon is a representative, have to lose 4 electrons or gain 4 electrons in order to obtain inert gas configuration and if the element has balanced electropositive and electronegative characters then either process becomes still more difficult.

In such cases and other cases where the electronegativity difference between atoms is small, the element achieves the stable configuration by sharing of these electrons with other elements. Besides carbon, one more element is in a similar position and that is hydrogen which may attain the stable configuration by either losing or gaining one electron. It can also do so by sharing of electrons with other elements.

Shapes of *S* and *P* Orbitals

Since there is only one orientation for the *s* sub-shell there is only one *s* orbital and that too is spherical. Similarly there are three orientations for *p* sub-shell and therefore there are three *p* orbitals p_x, p_y and p_z. The superscripts *x*, *y* and *z* refer to the coordinate axis. Solution of the wave equation gives the shape of the *s* orbital as spherical and that of the *p* orbital as dumb-bell type.

There is a *s* orbital corresponding to each shell and these are designated as 1*s,* 2*s,* 3*s*...etc., where 1, 2 and 3 are the shell numbers. The only difference 1*s,* 2*s,* 3*s,*...etc., orbitals is that the radius of spherically symmetrical orbitals increases

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with principal shell numbers. Thus shapes of 1*s* and 2*s* orbitals are given in Figure. 2.1.

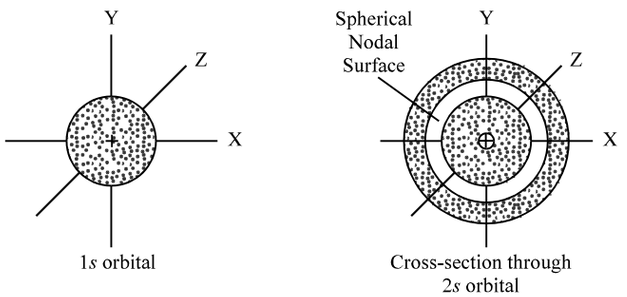

Fig. 2.1 *Shapes of 1s and 2s orbitals*

There is a region between the 1*s* and 2*s* (or between any two *s* orbitals) in which the probability of finding the electron approaches zero. Since the orbitals are spherical the nodal surface will also be spherical. In case of *p* orbitals there is a plane passing through the nucleus and at right angles to the axis of the orbital, in which the probability of finding the electron is zero. These plane are called the nodal plane. In the figures above, one lobe of the orbital has been shown as (+) and the other (–), which are only the signs of the wave functions. (These signs should not be confused with positive and negative charges as the electrons or electron clouds always have a negative charge.)

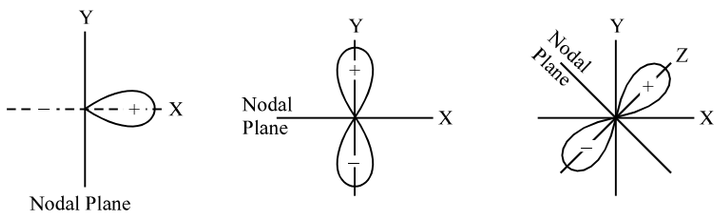

Fig. 2.2 *Shapes of the p_x, p_y, p_z orbitals*

The *K* shell, having two electrons only, does not have a *p*-orbital. The *L* shell has one *s* and three *p* orbitals designated as 2*s*, $2p_x$, $2p_y$ and $2p_z$ orbitals. *M* shell has orbitals of still higher energy designated as 3*s*, $3p_x$, $3p_y$, $3p_z$, $3d_{xz}$, $3d_{xy}$, $3d_{yz}$, $3d_{x^2y^2}$, $3d_{z^2}$; nine in all accommodating 18 electrons. Similarly *N* shell has one 4*s,* three 4*p*, five 4*d*, and seven 4*f* orbitals, 16 in all capable of accommodating 32 electrons.

Valence Bond and Molecular Orbital Methods

Solution of wave equation for molecules would give a complete description of the structure for that molecule showing precisely the shape of orbitals in which electrons are placed. However except for relatively simple molecules, it is not possible to solve the wave equation and therefore, drastic approximations are necessary to understand and depict the structure of molecules. The two important methods of approximation are known as **Valence bond** and **Molecular orbital** methods.

The valence bond (V.B.) method is the result of the work of Heitler, London and Pauling. The V.B. method considers the molecules as being made up of atoms with electrons in atomic orbitals in each atom. Thus the atoms retain their individual character to some extent even when linked to other atoms. In this method, a wave equation is written for each of various possible electronic structures (also known as Lewis structures or canonical forms) for a molecule and the total wave function for the molecule is obtained by adding the wave functions for each of these arrangements of electrons together with a coefficient '*c*' which determines its contribution to the total form

$$\psi = c_1\psi_1 + c_2\psi_2 + c_3\psi_3 + ...$$

Thus H_2 molecule may be represented as H—H or H : H; $\overset{-}{H}\ \overset{+}{H}$ or H : H, $\overset{+}{H}\ \overset{-}{H}$ or H : H and the total ψ may be obtained by summing up the wave functions for each of these canonical forms together with coefficient *c* which will be very high for H—H and low for $\overset{-}{H}\overset{+}{H}$ or $\overset{+}{H}\ \overset{-}{H}$ suggesting that H—H has greater contribution in the total structure of hydrogen molecule.

The essential feature of this approach is that to begin with electrons belonging to different atoms are treated as different and then correlated. According to quantum theory the electrons from any atom have identical characteristics. The valence bond theory takes care of it by using the concept of resonance which postulates that the actual distribution of electrons in a moecule is a 'resonance hybrid' of all the different possible arrangements commonly referred to as 'limiting structures'.

It may also be noted that the valence bond theory implies extra stabilization of molecules due to electron pairing.

In the Molecular Orbital (M.O.) method developed by Mulliken, Hund, Huckel, Jones etc., the orbitals are considered as eigenstates in atoms and bonds are considered to be formed by the overlap of atomic orbitals. Thus the electrons move in the field of more than one nucleus, i.e., molecular orbitals are assumed to be polycentric. The overlap of atomic orbitals gives rise to two new orbitals known as molecular orbitals. In one of these the electron charge is concentrated in the region between the nuclei thus holding them together. Obviously this will have lower energy than the original atomic orbital and is known as *bonding orbital*. In the other orbital the electron cloud is withdrawn from the region between the nuclei thus causing repulsion between them. This is the orbital of higher energy and is known as *antibonding orbital* (Reger Figure 2.3). This simplest combination of atomic orbitals is known as *linear combination of atomic orbitals* or *LCAO* and represented mathematically as

$$\psi = C_A\psi_A + C_B\psi_B + ...$$

where ψ_A is the wave function which the electron is considered to assume when it is near the nucleus of atom *A* and ψ_B is the wave function it assumes in the vicinity

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of atom *B* and so on. C_A is a coefficient depending upon the time an electron spends near nucleus *A* and so on.

Both these theories have their advantages and disadvanatages and most of the concepts used for explanining the structure of molecules have been obtained from one or both of these.

Concepts like resonance, hybridization of atomic orbitals, orbital box diagrams for electronic configurations are a consequence of the valence bond theory.

On the other hand, molecular orbital theory has given us concepts like bond order, orbitals (in place of bonds), bonding, antibonding and non-bonding electrons and delocalised orbitals instead of resonance.

Sigma and Pi orbitals: Qualitatively the M.O. method may be used to explain bonding in covalent compounds more effectively than V.B. method. Thus bonds are formed by the overlap of atomic orbitals and greater the area of overlap the greater will be the stability of the bond. When two atomic orbitals combine they may be do so as $\psi_A + \psi_B$, or $\psi_A - \psi_B$. If the signs of the amplitude of ψ_A and ψ_B are same the resulting amplitude of the combination will increase electron density between two nuclei and bonding would occur. If the amplitude signs of two orbitals are opposite the bonding will not occur. Figures 2.4, 2.5 and 2.6 show the bonding and antibonding orbitals formed by the overlap of *s* and *p* orbitals. *When the centres of electron density are on the axis common to the nuclei or the overlapping is coaxial the orbital is known as* σ (sigma) and corresponding antibonding orbital as σ^* (sigma star) (Reger Figure 2.7, 2.8).

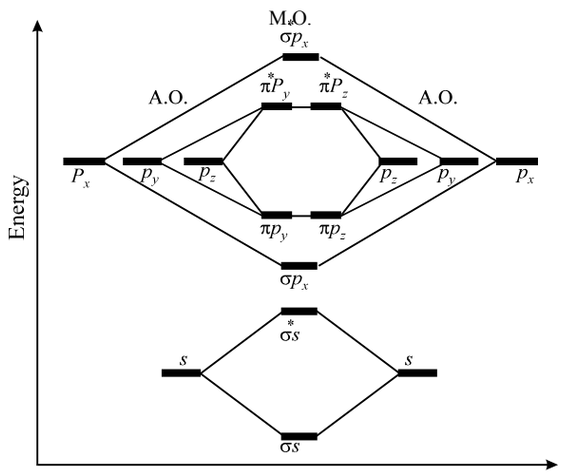

Fig. 2.3 *Combination of atomic orbitals to form bonding and antibonding orbitals*

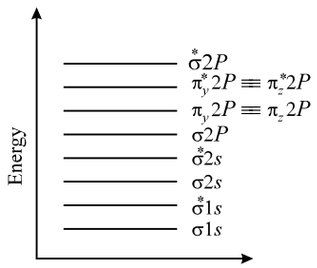

Fig. 2.4 *Schematic representation of the relative energies of various molecular orbitals*

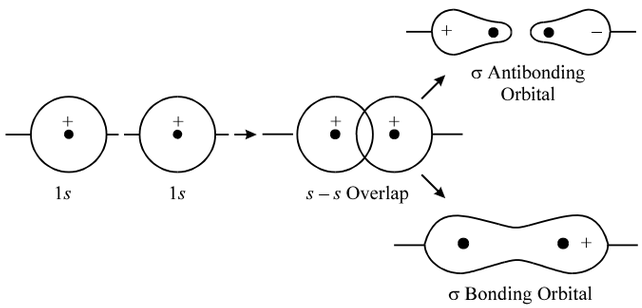

Fig. 2.5 *Overlap of two 1s orbitals as in hydrogen molecule*

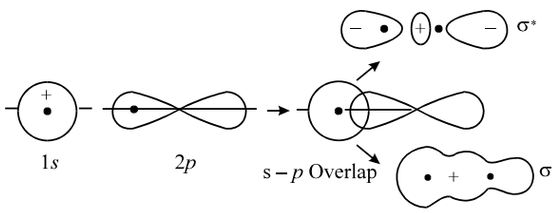

Fig. 2.6 *Coaxial overlap of 1s and 2p orbitals as in HF molecule*

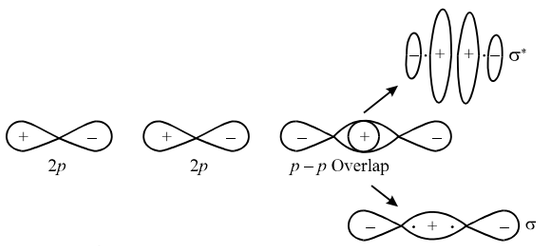

Fig. 2.7 *Coaxial overlap of 2p orbitals as in chlorine molecule*

Similarly, *d* and *f* orbitals may overlap with all kinds of orbitals resulting in the formation of molecular orbitals. Most of these σ orbitals are ellipsoidal in shape.

The σ orbitals are formed by overlapping around a common axis in the same plane. If however two orbitals overlap sideways their axis or planes become parallel to each other. The extent of overlap is small and molecular orbital formed lies above and below the nodal plane. For example sideways overlapping of two *p*-orbitals may be shown in Figure 2.8.

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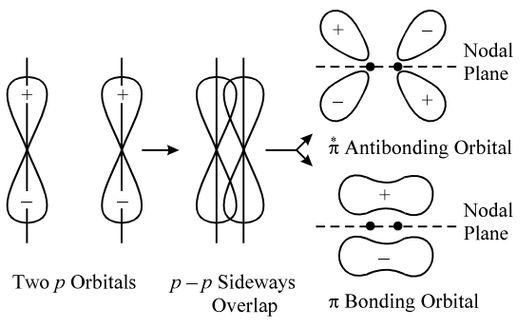


Fig. 2.8 *Sideways overlap of two p orbitals to form π bond*

The M.O. formed by sideways overlapping, having only one nodal plane along the nuclear axis, is known as π (pi) orbital. Since the space and extent of overlap of atomic orbitals is small in the π bonds as compared to σ bonds the π bonds are usually weaker than σ bonds. Also it is not possible for the atoms forming a π bond to rotate freely with respect to each other because of the shape of π orbital whereas atoms linked by a σ bond may rotate freely on their axis with respect to each other.

Hybridization of Orbitals in Carbon

The ground state electronic configuration of carbon is: $1s^2, 2s^2, 2p_x^1, 2p_y^1$. This configuration suggests that since there are only two half-filled orbitals carbon can form only two bonds and, therefore, must be divalent. However carbon atom exhibits tetracovalency in the organic compounds. To explain this it is suggested that one of the 2*s* electrons is promoted to the vacant $2p_z$ orbital of higher energy. The electronic structure of this excited carbon can then be written as:

$$1s^2, 2s^1, 2p_x^1, 2p_y^1, 2p_z^1 \quad \text{(Excited configuration).}$$

This configuration can account for the tetracovalent nature of carbon because there are four half filled orbitals and these are capable of forming four bonds. Theoretically it may be said that the energy required for promotion of one 2*s* electron to $2p_z$ orbital may be recovered in the process of formation of two additional σ bonds. Thus although the carbon atom in isolated form may have the ground state configuration of electrons, at the instance of reaction it acquires excited electronic configuration.

Such an electronic configuration will give rise to four σ bonds out of which three σ bonds will be similar to each other in every respect while the fourth σ bond will be different from these three because of the differences in constituent overlapping orbitals. This will be contrary to known facts which show that all the four valencies of carbon are equivalent to each other in every way.

To account for this it has been suggested that 2*s* and 2*p* orbitals of carbon in the excited state undergo a process of mixing up and redistribution to form new

orbitals of equivalent energy. This concept is known as **Hybridization** and the resultant new orbitals are called **Hybridized orbitals**. In fact orbitals of nearly the same energy tend to combine by mixing (hybridizing) and then the redistribution results in formation of equal number of new orbitals in many other atoms besides carbon.

Thus in an excited carbon one 2*s* and three 2*p* orbitals are available for hybridization and depending on actual number of orbitals taking part in it the hybridization can be of three types.

(*i*) ***sp*^{3} Hybridization.** If one *s* and three *p* orbitals take part in hybridization then it is called sp^3 hybridization. It results in the formation of four new equivalent hybrid orbitals also known as sp^3 orbitals. These hybrid orbitals are twin lobed (Reger Figure 2.9) but one of the lobe is much larger than the other. The hybrid orbital is said to have three-fourth *p* character and one-fourth *s* character and such a shape affords greater area for overlapping. Consequently the bond formed by hybrid orbitals are stronger. Since all these four orbitals are equivalent in every way, such a symmetrical distribution in space suggests that these hybrid orbitals must be directed towards the corners of a regular tetrahedron or in other words they have an angle of 109.5° between them. The process of hybridization lowers the energy of the system and more energy is released later on due to greater area of overlap provided by these hybrid orbitals. sp^3 hybridization in saturated compound of carbon explains the tetrahedral and tetracovalent nature of carbon atoms most satisfactorily. It is for this reason that it is also called **Tetrahedral hybridization.**

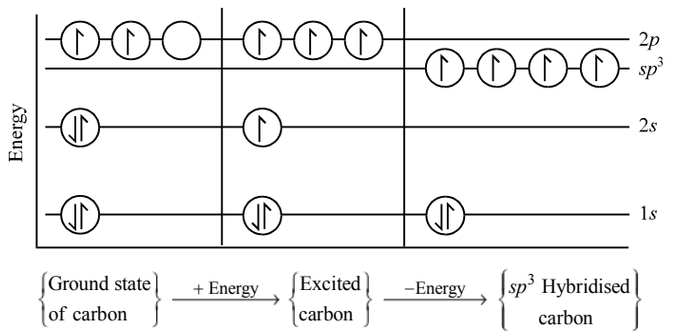


Fig. 2.9 *Electronic description of sp^3 hybridization*

Figures 2.10 and 2.11 show the formation of these hybrid orbitals and the way they combine to form molecules.

Overlap of these hybrid orbitals with *s*, *p* or other hybrid orbitals along the nuclear axis results in formation of σ bonds. Representation of the orbital diagram of methane, ethane and methyl chloride will cover all these types of σ bonds.

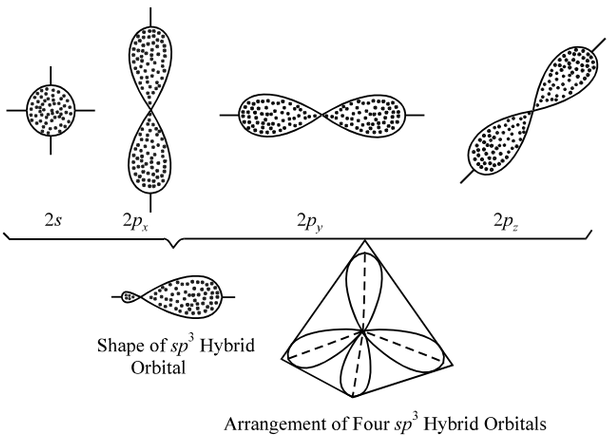
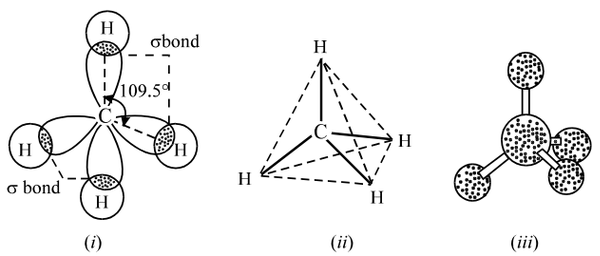
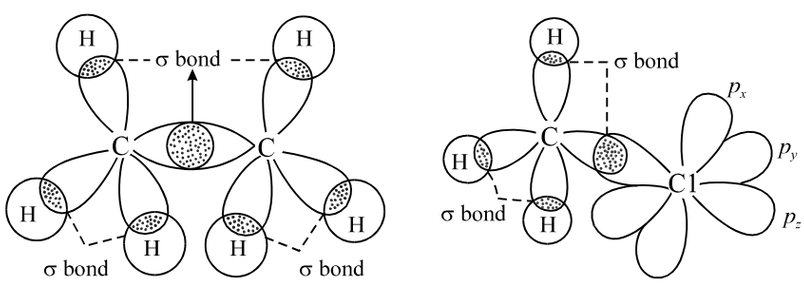


Fig. 2.10 *Hybridization and shape of sp^3 orbitals*



(*a*) Methane (4σ bonds; hybrid-*s* overlap)



(*b*) Ethane (7σ bonds; hybrid-*s* and hybrid-hybrid overlap)

(*c*) Methyl chloride (4σ bonds; hybrid-*s* and hybrid-*p* overlap)

Fig. 2.11 *Representation of the molecular orbital diagrams of some molecules having sp^3 hybridized carbon*

(*ii*) ***sp*^{2} Hybridization.** If, however, out of the four orbitals available for hybridization; one 2*s* and two 2*p* take part in hybridization then it is known as sp^2 hybridization. This results information of three new equivalent hybrid orbitals having two-thirds *p* character and one-third *s* character each. The shape of sp^2 hybrid orbitals is nearly similar to that of sp^3 hybrid orbitals. Since these three equivalent orbitals must have a symmetrical distribution these are directed towards the corner of a trigon and are planar having an angle of 120° between them. Hence this type

of hybridization is also called **Trigonal hybridization**. At each of the sp^2 hybridized carbon there is still an unhybridized half-filled *p*-orbital. The sp^2 hybrid orbitals form σ bonds by head on, inplane overlap whereas the unhybridized *p*-orbital at each sp^2 hybridized carbon can only combine by side-ways overlap and, therefore, forms a bond different from σ which is known as π bonds. Compounds having double bonds in the molecule usually have sp^2 hybridized carbon atoms, for example, ethylene.

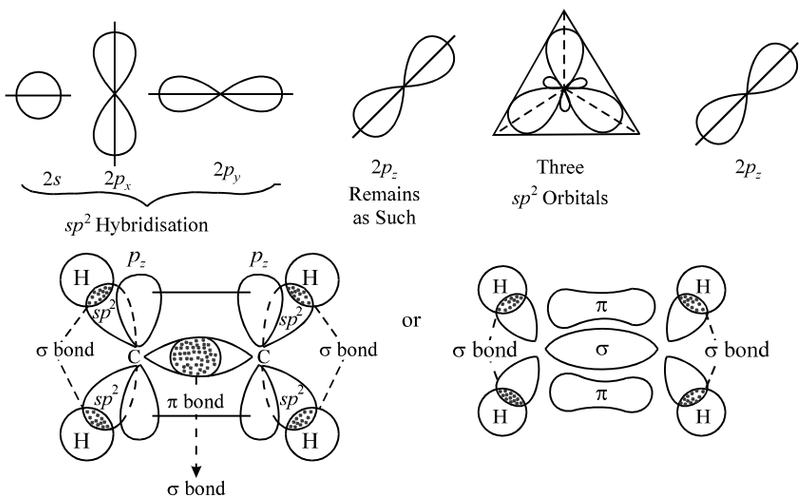


Fig. 2.12 *Molecular orbital representation of sp^2 hybridization and ethylene molecule; $CH_2 = CH_2$ (Hybrid-s and hybrid-hybrid overlap gives σ bond; p-p overlap sideways gives π bond)*

(*iii*) ***sp* Hybridization.** If only one 2*s* and one 2*p* orbital takes part in hybridization it results in the formation of only two new equivalent hybrid orbitals and the process is known as *sp* or *sp* hybridization. The hybrid orbitals have 50% *s* and 50% *p* character but the shape is nearly similar to that of sp^2 hybrid orbital. In order to be symmetrical and equivalent to one another these hybrid orbitals must be linear, in the same plane and must have an angle of 180° between them. The *sp* hybrid orbitals form σ bonds by coaxial overlapping with *s*, *p* or other hybrid orbitals.

At each of the *sp* hybridized carbon there are still two unhybridized 2*p* orbitals which may only overlap sideways giving two π bonds. This type of hybridization is usually found in compounds having triple bond like acetylene.

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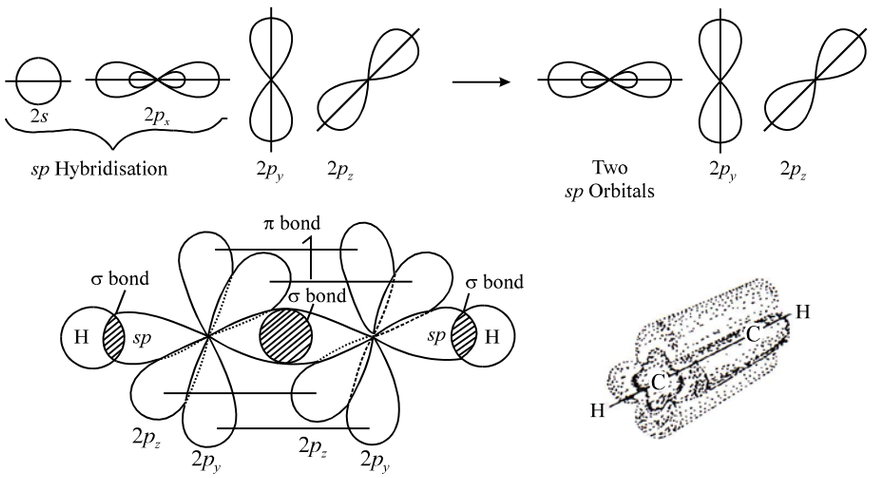

Fig. 2.13 *Molecular orbital representation of sp hybridization and acetylene molecule; CH ≡ CH (Hybrid-s; and hybrid-hybrid overlap gives σ bonds and p-p sideways overlap gives π bonds).*

Bond Distances or Bond Lengths

The average distance between two atomic nuclei in a covalent molecule is called the **bond distance** or **bond length**. This distance is such that the repulsion between atomic nuclei is balanced by the stability acquired through the overlapping of orbitals. The bond lengths are characteristic properties of a molecule and give information about its structure, properties etc. Bond lengths and bond angles are determined by *x*-ray diffraction, electron diffraction or spectroscopic methods. Similar bonds in different molecules have fairly constant lengths. The bond lengths are measured in Angstrom (Å) unit which is equal to 10^{-8} cm or 10^{-10} m or picometre (pm) and 1 pm ≡ 10^{-10} cm or 10^{-12} m.

Bond lengths generally depend on

(i) *Covalent radii of constituent atoms*: Greater the covalent radii, greater is the bond length, for example, bond lengths of

$$H—F < H—Cl < H—Br < H—I$$

(ii) *Type of the bond*: A double bond is shorter than a single bond and a triple bond is shorter than a double bond. Thus,

$$C \equiv C\ (1.2Å) < C = C\ (1.33Å) < C—C\ (1.54Å)$$

(iii) *Type of hybridization:* Bond length increases with a decrease in '*s*' character of the hybrid orbital. Thus, a C— H bond in different hybrid state of carbon has as lengths in the order

$$sp^3–s\ (1.11Å) > sp^2–s\ (1.10Å) > sp–s\ (1.08Å)$$

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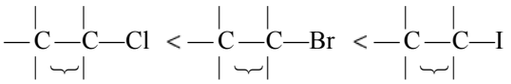
(iv) *Inductive effect*: Greater the magnitude of inductive effect, the shorter will be adjacent bond. Thus C—C bonds in different alkyl halides have bond lengths in the order



due to –I effect of halogens which is in order Cl > Br > I.

Bond lengths of some common covalent bonds are given in Table 2.1.

Table 2.1

	Bond	*Length (Å)*	*Typical compound*
C—C	$sp^3 - sp^3$	1.54	Ethane, Propane etc.
	$sp^2 - sp^2$	1.48	Butadiene
	$sp - sp$	1.38	Butadiyne
C═C	$sp^2 - sp^2$	1.34	Ethylene
	$sp - sp$	1.28	Butatriene
C≡C	$sp - sp$	1.20	Acetylene
C—H	$sp^3 - s$	1.11	Methane
	$sp^2 - s$	1.10	Benzene
	$sp - s$	1.08	Acetylene
C═O	$sp^2 - p$	1.20	Formaldehyde
	$sp - p$	1.16	CO_2
C—O	$sp^3 - p$	1.41	Ethanol
	$sp^2 - p$	1.34	Formic acid
C—N	$sp^3 - N^*$	1.41	Methylamine
	$sp^2 - N^*$	1.36	Formamide
C—Cl	$sp^3 - p$	1.78	Methyl chloride
C—Br	$sp^3 - p$	1.94	Methyl bromide
C—I	$sp^3 - p$	2.14	Methyl iodide
O—H	$p - s$	0.96	Methanol
N—H	$N^* - s$	1.01	Methyl amine

* N stands for the orbitals of nitrogen which may be hybrid.

Bond Angles

The three *p* orbitals of an atom are at the angel of 90° to each other. So bonds formed by these should have an angle of 90°. Similarly sp^3, sp^2 and *sp* orbitals in hybridized carbon atoms have an angle of 109.5°, 120° and 180° respectively.

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For example in methane, where the four groups attached to sp^3 orbitals are identical, the angle is 109.5°. But if one of these groups is different then usually the angle is distorted. Thus in bromopropane C — C — Br bond angle is 114.2°.

H—O—H bond angle in water and H—S—H bond angle in H_2S should be similar or 90° but the measured angle is 104.5° and 92.1° respectively. In hybrid orbitals due to the magnitude of bond-bond pair, usually in strained molecules the bond angles may be greatly distorted. Understanding of bond angles is essential for the study of the shape and geometry of the molecules. Bond angles in some molecules have been shown in Figure. 2.14.

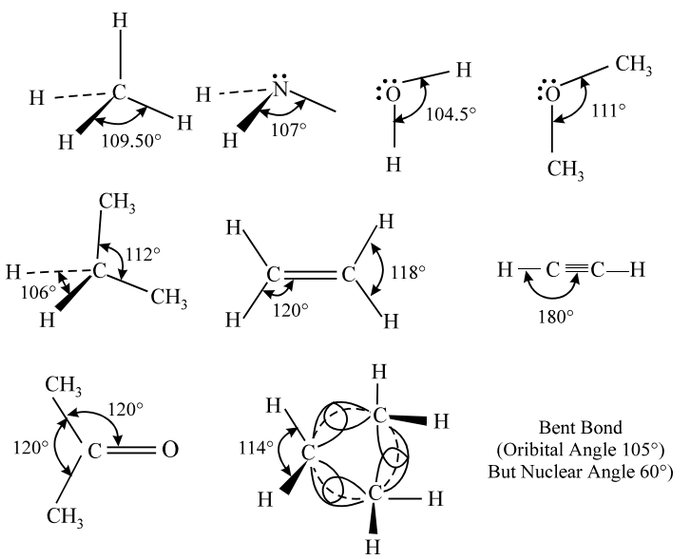

Fig. 2.14 *Bond angles in some molecules represented diagrammatically*

Bond Energies or Bond Strengths

When bonds are formed energy is reduced, consequently the energy required to break a bond into its constituents is referred to as **Bond energy** and is a measure of **Bond strength**. The greater the energy required to break a bond, the greater will be its strength. Thus bond energies provide a useful picture of the strengths of various bonds. They are expressed in kcal/mole.

There are two terms which are frequently used in connection with bond energies namely **bond dissociation energy** and **bond energy** or **empirical bond energy**. The former refers to the energy necessary to break a bond into its constituents. The H_2O molecule has two H— O bond. For breaking first H— O bond as in $H_2O \rightarrow H + OH$ the energy required is 118 kcal/mole while for another H— O bond, as in $OH \rightarrow O + H$, the energy required is 100 kcal/mole. These two values are referred to as the bond dissociation energies for first and second H—O bonds in water, while the average of the two values, i.e., 109, kcal/mole is taken as the bond energy or empirical bond energy of the O—H bond.

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In general

(i) The bond energy for sigma bond is more than that of a *pi* bond.

(ii) Amongst the bonds formed by hybrid orbitals the magnitude of bond energy increases with increase in *s*-character of the hybrid orbital. Thus the bond enrgy of sigma bond formed by *sp–sp* orbitals is gretaer than that of a bond fomed by sp^2–sp^2 bond. The bond energies of bonds formed by the overlap of different hybrid orbitals are in the order

$$sp–sp > sp–sp^2 > sp–sp^3$$

and

$$s–sp > s–sp^2 > s–sp^3$$

(iii) The bond enrgy of a triple bond is greater than that of a double bond which in turn is greater than that of the single bond. Thus

$$N \equiv N > N = N > N—N \quad \text{and} \quad C \equiv C > C = C > C—C.$$

(iv) Generally bond energy decreases as the size of atom increase. This bond energies of hydrogen halides are in the order

$$HF > HCl > HBr > HI \quad \text{or} \quad C—C > s_i—s_i > Ge—Ge > Sn—Sn$$

but P—P > N—N, S—S > O—O and Cl—Cl > F—F due to p_π–d_π back bonding.

Bond strengths are usually calculated from the values of heat of formation or heat of combustion using Hess's law of constant heat summation. Some of the important bond energies are given in Table 2.2.

It can be seen from the Table 2.2 that carbon-carbon multiple bonds are associated with higher bond energies and thus are stronger than carbon-carbon single bond.

Table 2.2

Bond	*Compound*	*Bond energy*	
		kJ mol^{-1}	(*kcal/mole at 25°C*)
C—H	Methane	416	99
C—C	Ethane	348	83
C═C	Ethylene	611	146
C≡C	Acetylene	837	199
C—Cl	Carbon tetrachloride	330	79
C—Br	Carbon tetrabromide	276	66
C—O	Methyl alcohol	358	85
O—H	Alcohols	463	110.6
C═O	Acetone	745	179
C—N	Methyl amine	305	70
N—H	Ammonia	391	93

Electronegativity

The measure of the tendency of chemically bonded atom to attract electrons is known as electronegativity. Usually the electron cloud between bonded atoms

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is symmetrical when the two atoms are similar but if one of the atoms has a greater tendency to attract the electron cloud then it shifts slightly towards that atom. The atom having greater nuclear charge and smaller atomic radii are highly electronegative. The order of electronegativities of some common elements which concern us in the study of organic chemistry is thus:

$$H < C < S < I < Br < Cl < N < O < F.$$

When the atoms forming a covalent bond are having different electronegativities, the sharing of electrons will be unequal and will result in development of polarity in the molecule. Such a covalent bond will have partial ionic character. Usually most of the bonds are intermediate between ionic and covalent. Due to their symmetrical structure compounds like methane, ethane, etc., are almost non-polar or pure covalent compounds but compounds like HF, H_2O, NH_3 etc., where the constituent atoms have large differences in their electronegativities are highly polar. Similarly compounds like methyl chloride, ethyl alcohol, dimethyl ether etc., are all having partial ionic or polar character.

In a bond between two atoms having larger difference in electronegativities the electron cloud is distorted to such an extent that one of the atom acquires a partial negative charge (δ^-) and other a partial positive charge (δ^+). This polarity or charge separation in molecules results in a *dipole* where two equal and opposite charges are separated, by a distance. The **dipole moment** of such a compound may be expressed as

$$\mu = e \times d$$

where *e* is charge in e.s.u. and *d* is distance in Å separating the two charges. Dipole moment (μ) is expressed in debyes. The unit 10^{-18} e.s.u. cm being called a debye (D).

However, simply the presence of a polar bond in a molecule is not enough to make the molecule polar. Thus there may be even number of such polar bonds or dipoles in opposite directions in space making the compound as a whole non-polar.

For example *p*-dichlorobenzene having two C— Cl dipoles has the zero dipole moment, and carbon tetrachloride having four C— Cl dipoles also has a zero dipole moment. Dipole moment of a few compounds are given here for comparison:

Compound	*Dipole moment in D*
CH_4	0
CH_3Cl	1.85
C_6H_5Cl	1.75
$C_6H_5CH_3$	0.43
C_6H_5OH	1.54
$C_6H_5NO_2$	3.93

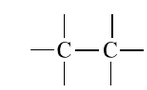
Check Your Progress

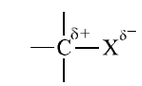
1. What are nodal planes?
2. What is Valence Bond method?
3. What is Molecular Bond method?
4. What is sigma orbital?
5. Define bond length.

2.3 FACTORS AFFECTING A COVALENT BOND

(a) Inductive Effect

In a covalent bond between two atoms having different electronegativities, the electrons pair shifts towards the more electronegative atom resulting in the origin of small fractional charges on the constituent atoms. When a carbon is joined to another carbon (C — C) by a covalent bond such as in alkanes, the sharing of electron-pair is symmetrical between them. However, if one of the hydrogen of alkane is replaced by a more electronegative atom or group like halogen (X) the electron pair of the covalent bond between them (C — X) shifts slightly towards halogen, thus distorting the molecular orbital. As a result, the halogen acquires a small negative charge (δ^-) and the carbon acquires a small positive charge (δ^+). Thus


(Symmetrical sharing of electron pair)


(Origin of fractional charges due to greater electronegativity of X)

This development of fractional charge in one bond may induce a similar polarity in an adjacent bond, which in turn may propagate it further. *Thus, induction of polarity or dipole, in an otherwise non-polar bond, and consequent electron shift along a chain of atoms is known as inductive effect.* Imagine a molecule having large number of carbon atoms linked to each other in a chain. The bonds between these carbon atoms are nonpolar. If an atom having higher electronegativity than carbon, say for example chlorine, is attached to the end of this chain of carbon atoms then because of difference in electronegativity C— Cl bond will be a highly polarised, with chlorine acquiring a small negative charge and the carbon acquiring a small positive charge. Now this positively charged carbon induces a similar polarity in adjacent C— C bond or this carbon behaves as more electronegative atom in an otherwise nonpolar bond. As a result there is a slight shift in electron density of this C— C bond and the second carbon atom also acquires a small positive charge but the magnitude of this positive charge on the second carbon will be smaller than the positive charge on first carbon atom. Similarly, the second carbon atom can induce polarity in the next adjoining C— C bond resulting in still smaller positive

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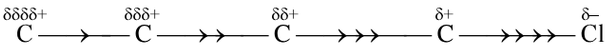
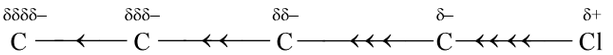
charge on third carbon atom due to lesser shifting of electrons and thus the inductive effect propagates through the carbon chain. Usually the inductive effect is negligible beyond fourth carbon atom.

The inductive effect is shown by arrows (→) pointing in the direction of electron displacement.



The progressive decrease in the inductive effect and as a result reduction in the magnitude of charges with increases in distance has been shown by decrease in the number of arrows.

Alternatively if the group attached to carbon chain in more electropositive than carbon, then the direction of inductive effect is reversed.



The inductive effect is a permanent effect in the ground state of the molecule and usually operates through single bonds. However inductive effect may also be transmitted through space or solvent molecules and is then known as **field effect**.

*According to **Ingold** atoms or groups having greater electron affinity or electron attracting power than hydrogen are said to have –I effect whereas atoms or groups having lesser electron affinity than hydrogen are said to have +I effect.* Some of the atoms and groups arranged in increasing order of inductive effect are given below:

Groups Having –I Effect

H—, C_6H_5—, —OH, —OCH_3, —I, —Br, —Cl, —F, —COOH, —CN, —NO_2.

The –I effect of the groups having hetero atoms like O, halogen, N etc. is due to the greater electronegativity of these atoms as compared to carbon. These groups thus have –I effect due to their electron attracting nature.

Groups Having +I Effect

—H, —D, —CH_3, —CH_2R, —CHR_2, —CR_3, —$CO\bar{O}$

The + I effect of most of these groups is due to electron releasing nature of alkyl groups. Deuterium (D) causes greater +I effect than hydrogen, perhaps, because of larger atomic radii which make it more electropositive than hydrogen.

A large number of phenomenon have now been explained on the basis of inductive effect. Some of these like decrease in bond lengths, origin of dipole moment, strength of acids and bases, are considered as applications of inductive effect.

Applications of Inductive Effect

(*i*) *Effect of Bond Lengths*: Usually the bond length decreases with increase in inductive effect, perhaps, because the covalent bond assumes increased ionic character. The bond length of C — F, C — Cl, C — Br and C — I bonds are in the order given below due to increase

$$C—F < C—Cl < C—Br < C—I$$

in the radius of halogen from F to I but the C — C bond lengths in following skeletal structures should be same.

C — C — F C — C — Cl C — C — Br C—C—I.

However, the inductive effect of halogen is in the order F > Cl > Br > I which results in the following order of bond lengths for C—C bonds

$$\underbrace{C—C}—F < \underbrace{C—C}—Cl < \underbrace{C—C} < Br < \underbrace{C—C}—I$$

(*ii*) *Dipole Moment*: A covalent bond acquires a dipolar character because of the inductive effect resulting in the dipole moment which is an important physical property used in structure elucidation. As the inductive effect increases dipole moment also increases.

$$\underset{1.64\ D}{CH_3 \rightarrow\!\!-\ I} \quad \underset{1.79\ D}{CH_3 \rightarrow\!\!-\ Br} \quad \underset{1.83\ D}{CH_3 \rightarrow\!\!-\ Cl}$$

(Increase in –I effect and also in dipole moment.)

Similarly the dipole moment of $CH_3—CH=CH_2$ is due to +I effect of the alkyl group.

(*iii*) *Strength of Acids*: The difference in the strength of various aliphatic acids may be explained on the basis of inductive effect. For convenience here acidity may be defined as ability to donate hydrogen ion. Thus acid strength decreases from formic acid to butyric acid. This is because the +I effect of alkyl groups increases in the order $H < CH_3 < C_2H_5 < C_3H_7$.

		pK_a value	
Increase in + I effect due to alkyl groups ↓	Formic Acid	3.77	Decrease in Acid strength ↓
	Acetic Acid	4.76	
	Propionic Acid	4.88	
	Butyric Acid	4.90	

With increase in + I effect, removal of hydrogen as proton becomes more difficult thus decreasing the acid strength. If the halogens are substituted in alkyl group, then because of – I effect due to halogens the strengths of halogen substituted acids will increase with increase in the – I effect of halogen or number of halogens attached to the alkyl group. The strength of the acetic acid has been compared with the halogen substituted acids in the data given below:

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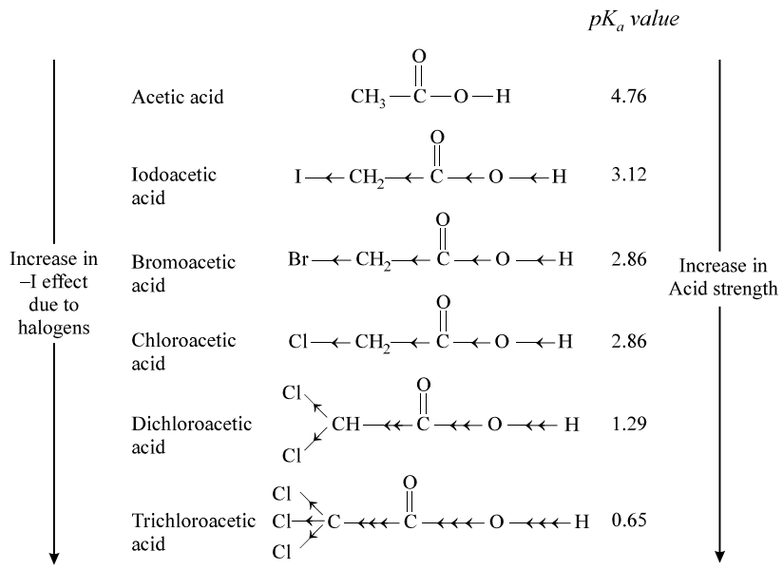
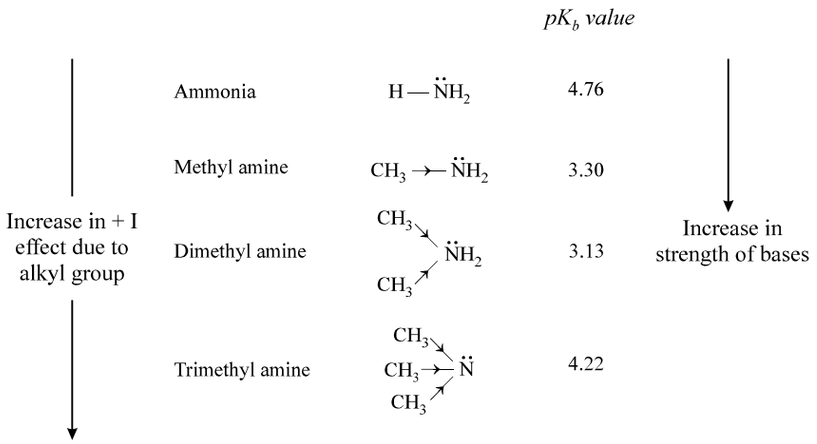


(*iv*) *Strength of Bases*: The difference in the base strength of various amines may be explained conveniently on the basis of inductive effect. Here base strength may be defined as a measure of the capacity to furnish an electron pair for sharing. Thus amines are stronger bases than ammonia because +I effect of alkyl groups increases the availability of electron pair at nitrogen atom. However, inductive effect alone does not determine the basic nature, pK_b of trimethyl amine is 4.22. The decreases in its basic character is due to the steric effect of three methyl groups. Comparative strength of a few bases is given here as an illustration of the point.



(b) Inductomeric Effect

The extent of inductive effect can be influenced temporarily prior to a reaction by the approach of a charged ion. Thus –I effect will be enhanced by the approach of a negatively charged ion and +I effect will be increased at the approach of a positively charged ion. *It is a temporary effect and brought into play only in*

the presence of charged attacking reagent. However this does not have an important role in organic reactions except in assisting the displacement of electrons in inductive effect.

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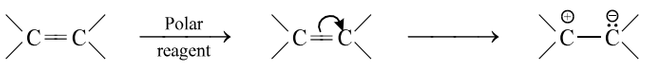
(c) Electromeric Effect

It has been discussed earlier that a multiple bond consists of σ and π bonds. Due to the nature of π bonding the electrons involved in such a combination are loosely held and easily polarisable. Therefore, when a compound having double or triple bond is approached by a charged reagent, the electrons of the bond are completely polarised or displaced towards one of the constituent atoms due to electrostatic attraction or repulsion. Thus:



The atom that now acquires the electrons pair, becomes negatively charged while the other atom gets a positive charge.

The effect, involving the complete transfer of a shared pair of electrons to one of the atoms joined by a double or triple bond at the requirement of attacking reagent, is known as Electromeric effect (E effect). It is a temporary effect and brought into play instantaneously at the demand of the attacking reagent. However, as soon as the attacking reagent is removed original electronic condition is restored.

Usually the electromeric effect precedes a polar or ionic addition reaction. In cases, where the constituent atoms linked by the multiple bond are similar, the direction of electromeric shift is not important. As displacement of electrons to either of the constituent atom will lead to similar structures. However, if one of the doubly bonded atom is linked to an electron withdrawing or electron releasing group, then the direction of electromeric shift is determined by the direction of the inductive influence of such a group. For example, in propylene, the electromeric effect can be represented in two possible manners without considering the effect of methyl group.

$$CH_3-CH=CH_2 \longrightarrow CH_3-\overset{+}{C}H-\overset{\cdot\cdot}{\underset{\cdot\cdot}{C}}H_2 \quad \text{... (2.1)}$$

$$CH_3-CH=CH_2 \longrightarrow CH_3-\overset{\cdot\cdot}{\underset{\cdot\cdot}{C}}H-\overset{+}{C}H_2 \quad \text{...(2.2)}$$

However, due to electron repelling nature of methyl group the electromeric shift will occur as in (2.1) and not as depicted in (2.2) because the latter type of shift opposes the electron releasing influence of methyl group. An opposite situation is encountered when an electron withdrawing group is present in place of electron releasing group.

In case one of the atoms involved in multiple bond is more electronegative, the electromeric shift of electrons is towards the more electronegative atom. This effect

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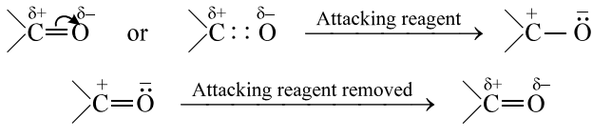
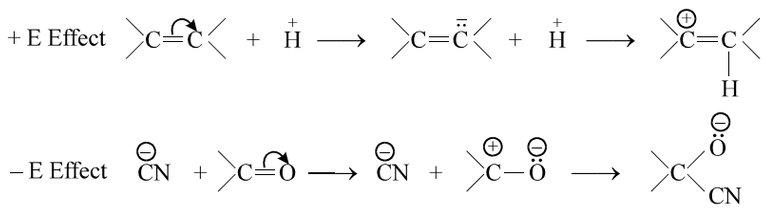
may be best illustrated by taking the example of carbonyl group. Initially there is a small negative charge on oxygen and a small positive charge on carbon atom because of greater electronegativity of the oxygen. When a charged reagent approaches the carbonyl group one of the two shared pairs of electrons (in fact π electrons) is completely transferred to oxygen. As a result of this, oxygen acquires a negative charge and carbon acquires a positive charge.



Such a carbon atom (with a positive charge) may now react with a reagent rich in electrons and then oxygen may combine with an ion deficient in electrons resulting in addition to carbonyl group.

The electromeric effect is indicated by 'E' and represented by a curved arrow showing the direction of shifting of electron pair. When the transfer of electron pair takes place towards the attacking reagent (electrophile), the effect is called +E effect and when the transfer occurs away from the attacking reagent (nucleophile) the effect is called –E effect.



In cases where inductive and electromeric effects operate simultaneously usually the electromeric effect predominates.

Applications of Electromeric Effect

Electromeric effect is very useful in explaining addition reactions of the compounds having double or triple bonds.

(*i*) *Addition to Alkenes or* > C = C <

Simple examples are addition of bromine and hydrobromic acid to ethylene.

Ethylene molecule does not have an ionic character but at the requirement of the attacking reagent the normal distribution of electrons is disturbed. In the addition of bromine the symmetrical bromine molecule gets polarised on approaching the π electrons of ethylene molecule. This polarised bromine molecule $(\overset{\delta+}{Br}—\overset{\delta-}{Br})$ then causes the electromeric displacement of π electrons to one of the carbon atom constituting the double bond. Thus one carbon atom acquires a positive and the other one a negative charge.

The electrons then attack the electrophilic (positively charged) end of the bromine molecule $(Br^{\delta+})$ which combines with this carbon releasing the bromide ion and forming a carbonium ion.

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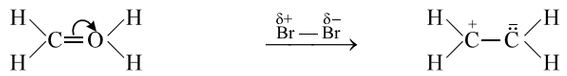
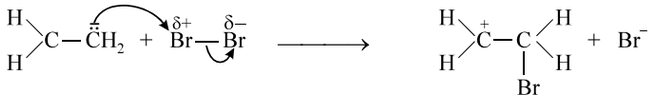
Lastly the bromide ion combines with carbonium ion to complete the addition reaction.

(*i*)

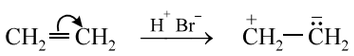


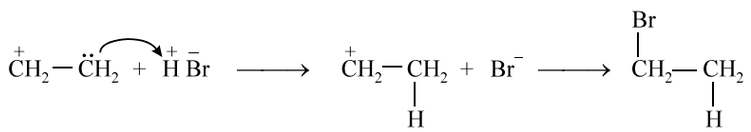
(*ii*)



(*iii*)

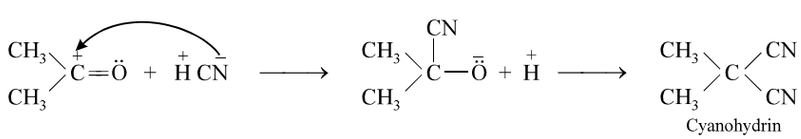
In the addition of hydrobromic acid to ethylene, at first the ionised hydrobromic acid molecule (H^+Br^-) induces electromeric effect in ethylene molecule which then takes up H^+ to form the carbonium ion. The carbonium ion in the final step combines with bromide ion to complete the addition reaction.





(*ii*) *Addition to Carbonyl Group* (> *C*═*O*)

The carbonyl group undergoes addition at carbon to oxygen double bond. Let us consider the addition of HCN to carbonyl group of acetone. The carbonyl group is initially polarised with a slight negative charge on oxygen and a slight positive charge on carbon $\rangle\overset{\delta^+}{C}=\overset{\delta^-}{O}$. The approaching ionised $\overset{+}{H}\,\overset{-}{\ddot{C}}N$ molecule then causes the transfer of π electrons towards the oxygen on account of its greater electronegativity (electromeric effect). Since the system having a positively charged carbon is less stable than the system having a negatively charged oxygen, the addition of the nucleophile to carbon precedes the addition of the electrophile on oxygen. (In alkenes the addition of electrophile precedes the addition of nucleophile.) Therefore, in this addition CN^- will add at the carbon atom followed by H^+ adding at oxygen.



Cyanohydrin

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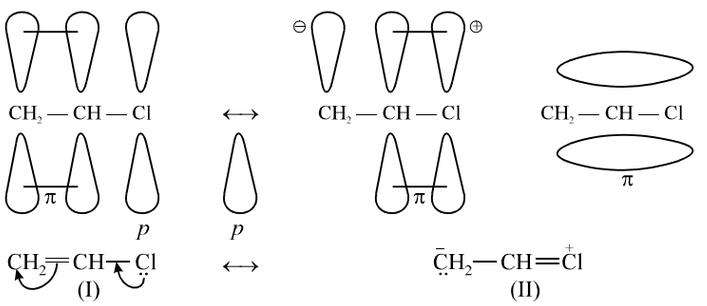
Conjugation, Mesomerism and Resonance

If the single and double bonds are present alternately in a molecule, it is said to contain double bonds in *conjugation* and the molecule is called a conjugated molecule. For example in 1,3-butadiene the double bonds are in conjugation.

$$CH_2 = CH - CH = CH_2 \quad \text{(1,3-Butadiene)}$$

Alternatively the double (or triple) bonds may be in conjugation with a lone pair of electrons (or non-bonding electrons) on an adjacent atom. Thus in vinyl chloride the double bond is in conjugation with the lone pair of electrons at chlorine.



It has been observed that in butadiene or vinyl chloride and other similar conjugated compounds the double bond does not behave as an isolated double bond. In case of butadiene the addition of a molecule of bromine results in a mixture of 1,2 and 1,4-addition products, whereas its structure explains only 1,2-addition.

$$CH_2 - CH - Cl \xrightarrow{Br_2} CH_2 = CH - CHBr - CH_2Br$$

1,2-Dibromo derivative (Theoretical product)

$$CH_2 = CH - CHBr - CH_2Br + CH_2Br - CH = CH - CH_2Br$$

1,2-Dibromo derivative — 1,4-Dibromo derivative (Actually obtained)

On the other hand, the chlorine in vinyl chloride is very firmly bound and cannot be replaced by usual substitution reactions as in the case with C_2H_5Cl. *Thus we see that conjugation effect in molecules results in large deviations from their usual behaviour.*

To explain such differences in the actual and expected behavior of conjugated molecules and the fact that many such compounds can be represented by two or more electronic structures, which are capable of explaining some or several properties of these compounds, Robinson and Ingold (1933) gave the concept of **mesomerism** or **mesomeric effect**.

Mesomerism. The early successes of classical structural theory led to the generally followed practice of representing the molecules by structural formulae. It has been observed that when a compound is conjugated such classical structural formulae are inconsistent with all the properties of that compound. For example a carboxylic

group is represented as — C(=O)(—O) and therefore, should exhibit the reactions of > C═O and — OH groups, which is evident from the structural formula but it is not so. Similarly the structure of benzene given by Kekule does not explain the important features of the molecule. To account for the properties of benzene it was suggested by Robinson and Ingold that when a molecule (like benzene) can be represented by two or more electronic structures satisfying all the valency rules and all of which are capable of explaining some but not all the properties of the compound the molecule is having neither of these structures but the real structure of the molecule lies in between these structures. The real structure cannot be represented on paper because of the limitations of the classical structural theory. This concept is known as **concept of mesomerism**.

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Thus benzene can be represented as having two structures shown here.

To show that the structure of the real molecule lies in between these structures a double headed arrow (↔) is placed between the possible structures. Since the real structure of the molecule lies in between these two structures the energy corresponding to real structure is lower than the energies of either of these. Such structures can be written by simply shifting the electrons from one position to another, hence it can be said that the electrons of the molecule have acquired a greater degree of freedom or electrons are now *delocalised.* The difference in the energy of the real molecule of benzene and that of the structures shown above is known as **delocalization energy** or **stabilization energy due to conjugation** or **energy of mesomerism**. This lowering of energy makes the actual molecule more stable than represented by either of these structures. This delocalization energy may be obtained from the difference in the values for heat of combustion or heat of hydrogenation of the actual molecule and those calculated for the above structures.

Resonance. Simultaneous to the development of the concept of mesomerism, Heisenberg (1926) gave the theory of *resonance* based on quantum mechanics. This was applied qualitatively to organic compounds by Pauling as the concept of resonance. The concept of resonance practically says more or less the same thing as mesomerism but it is a consequence of valence bond method of representing molecular parameters. The problem in case of benzene and other conjugated systems is that no single classical structure adequately represents the molecule and several structures must be written for it. None of these structures completely describe the molecule but each contributes, to the total picture or behaviour of the molecule and the actual molecule is considered as a hybrid of all these structures. This crudely parallels the mathematical expression written for the molecule in V.B. method. Thus the above two Kekule structures for benzene having localized bonds do not represent benzene but a resonance hybrid of the two (or more) will represent the molecule more accurately. All the bonds which are double in one structure are single in the other structure. Thus the actual bonds in benzene are intermediate between double and single bonds.

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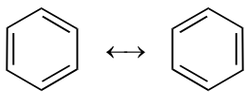
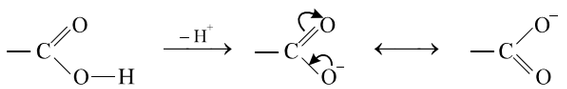


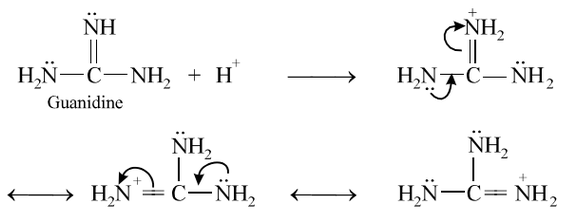
Fig. 2.15 *Bonds in Benzene*

Such a qualitative, empirically based concept, bearing resemblance to V.B. approach and developed by Pauling, is called *Theory of Resonance.* It states that a molecule for which several classical structural formulae may be written, cannot be satisfactorily represented by any one of these formulae known as **limiting structures** or **canonical structures** but only by the superposition of the whole set. The limiting structures are considered to be in resonance and the real molecule as a resonance hybrid of these. The resonance in a molecule is depicted by writing a double headed arrow between limiting structures. The limiting structures do not correspond to real ground state. These contributing limiting structures can only be selected on the basis of chemical consideration. At this point the resonance and V.B. concepts may be distinguished because the mathematics provides no basis for selecting one or the other resonance structure as is done in resonance representation. In V.B. scheme the wave function of the molecule can be obtained not only as a linear combination of wave functions with appropriate coefficients. *In this respect the concept of resonance coincides with the concept of mesomerism.*

Usually the significance of various physical phenomenon is explained by assuming various limiting structures as responsible for specific properties of a compound. Thus the acidic properties of —COOH group are explained by assuming that the carboxylate anion obtained by dissociation of a proton is stabilized by resonance.



Similarly the basicity of guanidine is explained in terms of resonance stability acquired by resulting cation due to resonance.



However, one should be careful that from illustration given above it is extremely easy to misunderstand that such structures are real or there is some such phenomenon as electron resonance.

The concept of resonance is used to describe long range delocalization of electrons leading to an extra stability. In a conjugated molecule the conjugated electrons can get delocalized. Hence such electrons must either be non-bonding electrons or loosely bonded π (pi) electrons hereafter called molecule electrons.

In order to get localized there should be some vacant orbital (or an orbital which can accept a pair of electrons after some adjustment in another part of the molecule) where the mobile electrons may be shown to be moving.

The essential condition of conjugation is that there must be a gap of one bond between mobile electrons and the vacant orbital. Thus, resonance is not possible in following molecule as there is a gap of two bonds between mobile electrons

$$CH_2=CH-CH_2-CH=CH_2 \quad \text{(Resonance not possible)}$$

Gap of two bonds

but is possible in $CH_2=CH-\overset{\oplus}{C}H_2$ as there is a gap of only one bond between mobile electrons and vacant orbital at positively charged carbon.

Conditions and Rules for Resonance. Wheland has suggested following conditions for resonance:

(1) The positions of all the atomic nuclei in limiting structures must be same or very nearly same.

(2) The limiting structures must have the same number of paired and unpaired electrons.

(3) The limiting structures must not exhibit large differences in the average positions of the electrons.

(4) The energies of the various limiting structures must be same or nearly the same.

(5) All the limiting structures must be written in accordance with usual structural scheme.

(6) All the limiting structures do not contribute equally to the real molecule but each structure contributes in proportion to its stability. Equivalent limiting structures contribute equally. Usually all the atoms taking part in the resonance lie in a plane and the stability of a structure depends on following factors:

(*a*) Structures with more covalent bonds are more stable than those with lesser covalent bonds. Limiting structures having same number of sigma and pi bonds are known as isovalent structures. If the number is different then the structures are called *heterovalent*. In general, isovalent structures are more important than heterovalent structures, for example,

Isovalent structures

$$CH_2=CH-\ddot{\underset{\cdot\cdot}{Cl}}: \leftrightarrow \overset{\ominus}{C}H_2-CH=\overset{\oplus}{Cl}:$$

(I) (II) Significant contribution

Heterovalent structures

$$CH_2=CH-CH=CH_2 \longleftrightarrow \overset{\oplus}{C}H_2-CH=CH-\ddot{C}H_2^{\ominus}$$

(III) (IV) Insignificant contribution

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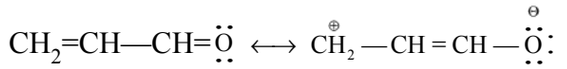
(*b*) Stability decreases if there are isolated charges or there is increase in charge separation. Structures with similar charges on adjacent atoms are not significant.

(*c*) Structures with a negative charge on more electronegative atom are more stable than those in which the negative charge is on less electronegative atom. Amongst heterovalent structures those having negative charge on more electronegative atom (like oxygen or chlorine) are important contributing structures, e.g.



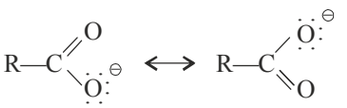
(V) (VI) Significant contribution

(*d*) Structures with strained bond angles or bond lengths are less stable.

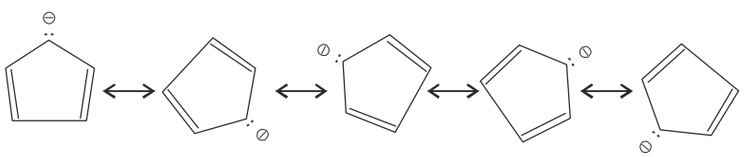
For writing resonance contributing structures only electrons may be shifted from one place to another within the molecule but not the atoms.

Resonance Energy. The extra stabilization of a molecule because of resonance or delocalization is expressed in terms of resonance or delocalization energy. The magnitude of resonance energy is large when

(a) Limiting structures are identical, for example, in carboxylate anion.



(b) Number of limiting structures of comparable energy is large



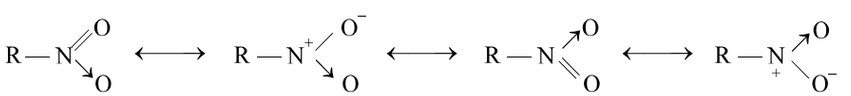
Cyclopentadienyl anion (All limiting structures are of identical energy)

(c) Number of conjugated pi-electrons in a planar cyclic compound is $(4n + 2)$ where 'n' may have values of 0, 1, 2... etc. For $n = 1$ the most important case is benzene which has extra resonance stabilization due to aromaticity.

The resonance energy is generally equal to the difference in enthalpy of combustion of actual compound and that calculated for the most important limiting structure.

Applications. As has been seen the concept of resonance is most useful in explaining the unusual behaviour like stability of the conjugated systems. The resonance representation of some such molecules is given below:

(*i*) *Nitroalkane*



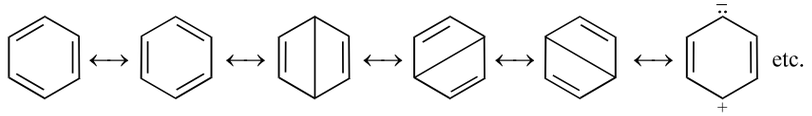
(*ii*) *Butadiene*

$$CH_2{=}CH{-}CH{=}CH_2 \longleftrightarrow \overset{+}{C}H_2{-}CH{=}CH{-}\overset{-}{C}H_2 \longleftrightarrow \overset{-}{C}H_2{-}CH{=}CH{-}\overset{+}{C}H_2$$

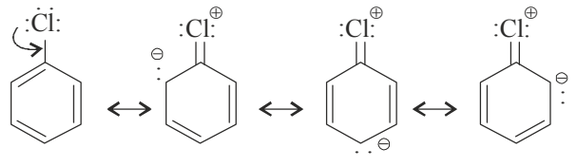
(*iii*) *Diazomethane* $CH_2{=}\overset{+}{N}{=}\overset{+}{N} \longleftrightarrow \overset{-}{C}H_2{-}\overset{+}{N}{\equiv}N$

(*iv*) *Allyl cation* $CH_2{=}CH{-}\overset{+}{C}H_2 \longleftrightarrow \overset{+}{C}H_2{-}CH{=}CH_2$

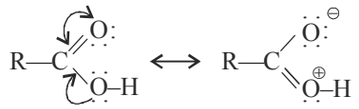
(*v*) *Benzene*



(*vi*) *Chlorobenzene*



(*vii*) *Carboxylic acids*



There are two important features which may be observed in the above representation of resonance structures:

1. The electrons are not necessarily present where they are expected to be but are delocalized giving the molecule an extra stability.
2. A more significant case is that of chlorobenzene and vinyl chloride. Normally chlorine withdraws electrons towards itself by *–I* effect but in its limiting structures chlorine has get a positive charge and seems to be donating electrons towards carbon skeleton.

   Does this mean that chlorine has lost its *–I* effect? No, as the *–I* effect is a permanent effect but in addition it now has an electron donating resonance effect (called *+R* or *+M* effect) due to conjugation.

   In carboxylic acids oxygen of the — OH group has given its electron pair towards carbon (*+R* or *+M* effect) due to conjugation despite the *–I* effect of the oxygen.

   Since in both the above cases inductive and resonance effects are operating in opposite direction one of them will prevail in deciding the overall electron density distribution in the molecule. In case of chlorobenzene, chlorine has a *–I* effect and also a *+R* effect such that *–I* > *+R*. Thus chlorine withdraws electron density from benzene ring by *–I* effect but comparatively increases the electron density at *o*- and *p*- positions of benzene ring by *+R* effect.

Although both mesomerism and resonance are used to explain the molecular properties in terms of electronic structural formulae yet the *concept of mesomerism has evolved from purely chemical considerations, whereas the resonance*

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concept has been developed by analogy to quantum and wave mechanics, and applied to organic structural representations. However both these terms are used somewhat interchangeably by organic chemists.

The concept of mesomerism and resonance may be distinguished from each other by taking the example of ethylene molecule. Its structural formula $CH_2 = CH_2$ is capable of explaining its properties satisfactorily. Therefore the concept of mesomerism cannot be applied to ethylene. On the other hand in the concept of resonance certain rules are provided for writing the contributing structures whether or not there is a discrepancy in its properties and the structure written for it. Thus ethylene may be considered as resonance hybrid of following contributing structures:

$$CH_2 = CH_2 \leftrightarrow \overset{\oplus}{C}H_2 - \overset{\ominus}{\ddot{C}}H_2 \leftrightarrow \overset{\ominus}{\ddot{C}}H_2 - \overset{\oplus}{C}H_2$$

Some important applications of resonance effect are given below:

1. *Effect on bond lengths*. In resonance description of molecules very often a bond between two particular atoms in represented as a single bond in one limiting structure and as a double bond in another limiting structure.

   Since the molecule is a hybrid of these structures such a bond acquires partial single and partical multiple bond character. Hence the bond length is somewhere between that of the single and multiple bond. For example all C— C bonds in benzene are equal to 1.39Å whereas the usual bond length for single and double bonds are 1.54Å and 1.33Å respectively. In carboxylate anion both C— O bonds are equal to 1.27Å and this value lies in-between the lengths for C— O single and double bonds. In 1, 3-butadiene C_1 to C_2 and C_3 to C_4 bond length is 1.35Å (greater than 1.3 Å expected for a double bond) and C_2— C_3 bond length is 1.47Å (less than expected value of 1.54Å for a single bond.) In nitro compounds the two N— O have identical bond lengths due to two identical contributing structures.

   Thus the shortening of single bond distances and lengthening of multiple bond distances in most of the conjugated molecules are explained on the basis of resonance concept.

2. *Effect on stability*. Resonance hybrid is always more stable than any of the limiting structures. Thus benzene molecule is about 36 kcal mol^{-1} more stable as compared to contributing Kekule structures. The difference of energy of actual molecule from limiting structures is called resonance energy.

3. *Effect on strengths of acids and bases*. Compounds with — OH group in alcohols are neutral and act as nucleophiles but when — OH group is attached to a conjugated system as in phenol it acquires acidic character due to resonance involving limiting structures having +ve charge on oxygen which results in easy loss of $H^{\oplus}$

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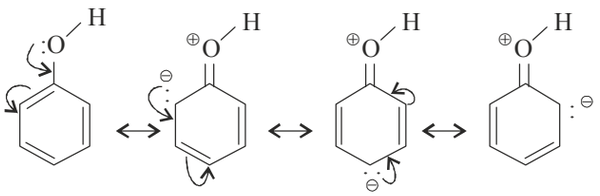
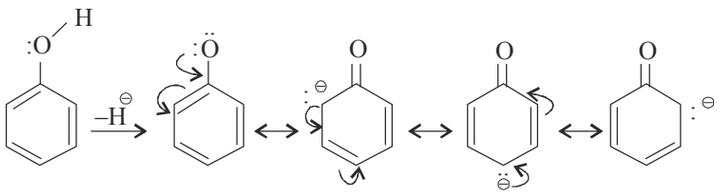


Resonance contributing structures of phenol

Also the phenoxide ion formed as a result of loss of proton is more stabilized by resonance as compared to phenol, because

(a) only one kind of charge is there on all the limiting structures unlike phenol which has dipolar limiting structures



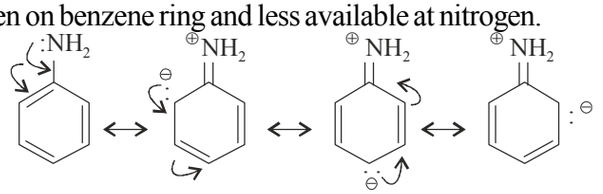
Resonance contributing structures of phenoxide ion

(b) phenoxide ion has negative charge on oxygen and ring carbon atoms while phenol has positive charge on oxygen –an electronegative atom.

The basic character of amines is due to the lone pair of electrons at nitrogen. Usually the base strength of amines increases with increase in number of alkyl groups attached to nitrogen due to their +*I* effect (except in case of tertiary amines which are weaker bases due to steric factor).

$NH_3 < R—NH_2 < R_2NH > R_3N$ (Abnormal due to steric factor)

If —NH_2 is attached to a conjugated system like benzene, the lone pair at nitrogen gets delocalized over the benzene ring due to +*R* effect of —NH_2 group, making aromatic amines much less basic than aliphatic amines. Resonance structure of aniline shows delocalization of electron pair of nitrogen on benzene ring and less available at nitrogen.

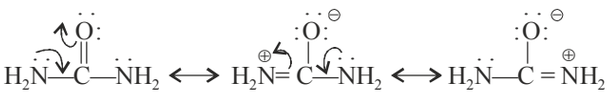


Resonance contributing structures of aniline

As the number of aryl group increases, the basic character of aromatic amines decreases. Thus

$$C_2H_5NH_2 > C_6H_5NH_2 > (C_6H_5)_2\,NH > (C_6H_5)_3\,N$$

Urea is a monoacid base though it has two nitrogens with lone pairs. The resonance structure of urea shows that both the nitrogens of urea are somewhat deficient in electrons and oxygen is rich in electrons. Since there is only one oxygen it behaves as a monoacid base



Resonance contributing structures of urea

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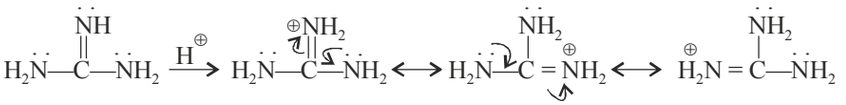
Guanidine is a strong base due to greater resonance stabilization of its conjugate acid.

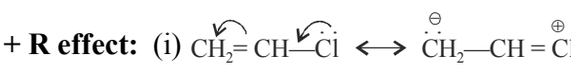


Guanidine Conjugate acid of Guanidine (more stable)

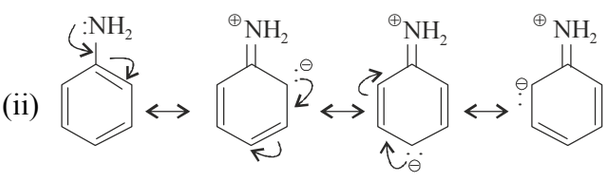
4. *Effect of resonance on electron displacement*. While writing the resonance limiting structures, it is customary to show shift of electrons from one position to another but since the limiting structures have no real existence the movement of electrons is not taking place. Electrons in a molecule occupy a definite position which is not completely defined by any limiting structure.

   Some groups when linked to a conjugated system release electrons because of resonance (regardless of their inductive effects) and are said to have +*R* or +*M* effect. Examples of such groups are –X (halogen), — OH, and — NH_2. All these groups have –*I* but –*R* effect. The essential feature of such groups is that they have a lone pair at the atom directly linked to conjugated system which participates in resonance, for example:

   + R effect: (i)



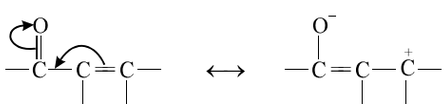
(ii)



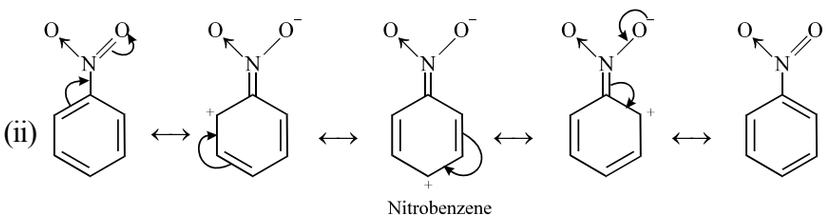
In both these examples of +*R* effect, the usual inductive effect (–*I*) is opposing the resonance effect (+*R*). In contrast those groups which when linked to a conjugated system withdraw electrons due to resonance are said to have –*R* or –*M* effect, for example, — NO_2, — CN, > CO, — SO_3H etc. The important feature of these groups is that the atom directly linked to the conjugated system does not have a lone pair and is attached to a more electronegative atom by a multiple bond.

–R effect:

(*i*)



α,β-Unsaturated carbonyl compounds



Steric Inhibition of Resonance

The word steric is derived from 'stereos' meaning space. Steric effect essentially arises because of the fact that each atom of molecule occupies some space. If two atoms are brought closer, then their van der Waal's radii, their electron clouds repel each other and this process in energetically unfavourable. Steric effect plays an important role in organic chemistry. Consider the example shown in Figure 2.16.

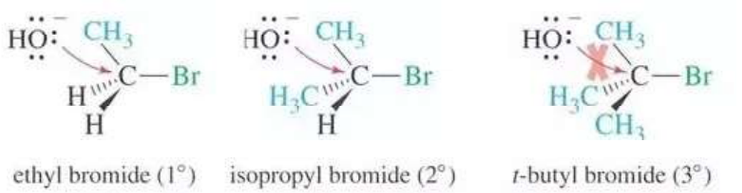


Fig. 2.16 *S_N2 Reaction*

The Figure 2.16 shows the S_N2 reaction in which there are three substrates. Hydroxide ion is attacking carbon which is attached to bromine. Bromine leaves as hydroxide attacks on the central carbon atom.

In the first substrate central carbon is attached to two hydrogens and one methyl group and in the second substrate two methyl groups and one hydrogen. In the third substrate three methyl groups. Methyl group occupies significant space, so when hydroxide ion approaches the central carbon atom, methyl group starts repelling the hydroxide ion. Presence of two methyl groups makes the compound more stable. In the case of three methyl groups, reaction hardly occurs. So one can say that Methyl group has steric effect on the hydroxide ion. This steric effect sometimes leads to low reaction rates.

Steric Enhancement of Resonance

The rate constants and the activation energies for the alkaline hydrolysis of some substituted ethyl benzoates provide evidence for the phenomenon of steric enhancement of resonance. For example, for 3-substituted-4-alkoxybenzoic esters the rate constants can be evaluated on the basis of the principle of additivity of substituent effects, which can be significantly higher as compared to the observed values. It indicates that the 3-substituent does not sterically inhibit the resonance

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interaction of the alkoxy and ester groups but it actually enhances it. The observed rate constants of 4-alkoxy-3-methyl-N, N-dimethylanilines are considerably higher than the predicted values on the basis of additivity of group effects. As a result there is enhanced resonance interaction of the alkoxy group with the dimethylamino group increasing the nucleophilicity of the dimethylamino group. A similar steric enhancement of resonance is also possible for 3-methyl-4-methylthio-N, N-dimethylaniline.

Check Your Progress

6. What is inductive effect?
7. What is electromeric effect?
8. State the theory of resonance.

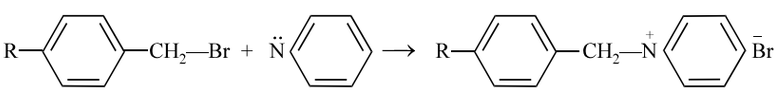
2.4 HYPERCONJUGATION

When an H — C bond is attached to an unsaturated carbon atoms, the σ (sigma) elecrons of this H — C bond enter into conjugation with unsaturated system. Such conjugation between electrons of single and multiple bonds is known as *hyperconjugation.* However since σ electrons are less polarizable than π or *n* (nonbonding) electrons, the contribution of the ionic forms involving σ bonds will be less significant than that of ionic forms involving π and *n*-electrons.

The concept of hyperconjugation was developed on the discovery of anomalous electron releasing pattern of alkyl groups. The inductive (+*I*) effect of alkyl groups is normally in the order

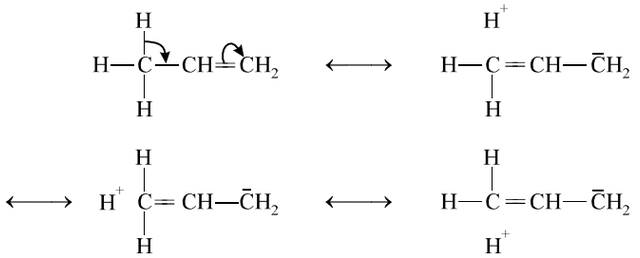
$$-CH_3 < -CH_2-CH_3 < -CH(CH_3)_2 < -C(CH_3)_3$$

However, Baker and Nathan observed that when alkyl groups are attached to an unsaturated system, the order of inductive effect is disturbed and in some cases actually reversed. For example in the following reaction:



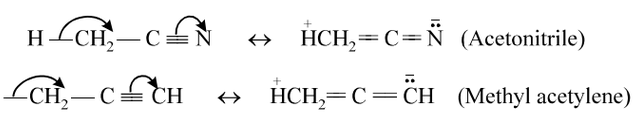
the rate of reaction should increase in the order of the increase in inductive effect of group — R but surprisingly the rate of reaction actually decreases in that order. Thus alkyl groups are capable of releasing electrons by a mechanism different from the inductive effect and the methyl group is the most successful exponent of this electron release phenomenon.

The dipole moment of propylene (0.4 D) and its greater stability than ethylene can be explained by considering the resonance contributions of structures such as:



in which no covalent bond is shown between a carbon and hydrogen atom. The hyperconjugation is therefore, also known as *no-bond resonance*. The hydrogen is taken as the positive end because of its smaller electronegativity. At this point it must be emphasized that the hydrogen does not actually become free or leave the molecule because if it moved from its original position one of the necessary condition, for resonance to occur, will be violated. Since the hyperconjugation depends on the presence of hydrogen at α-carbon, this appears to be the reason for the reversal of electron releasing ability of alkyl groups in the order $CH_3 —> C_2H_5 —> (CH_3)_2CH > (CH_3)_3C$ due to hyperconjugation. The number of α-hydrogens is maximum in methyl group and nil in *t*-butyl group.

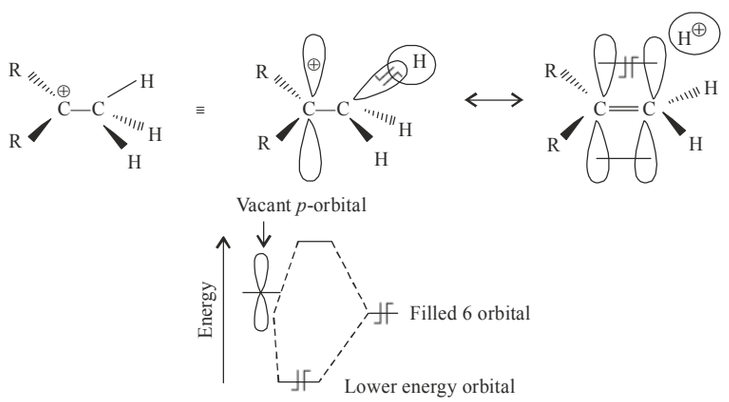
Other application of hyperconjugation is the explanation of shortening of C—C single bond adjacent to a triple bond, for example, in acetonitrile and methyl acetylene:



Similarly the heat of combustion or heat of hydrogenation of 1-butene (with two α-hydrogen atoms) is higher than of isobutylene (with six α-hydrogen atoms).

Orbital Picture of Hyperconjugation

It appears that the vacant p-orbital on adjascent carbon interacts with sigma electrons of C—H bond as shown here. The stabilization arises because the orbital interaction leads to electrons being in lower energy orbitals. Alternatively methyl group may act as a compound atom.



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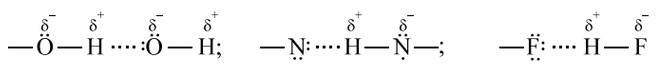
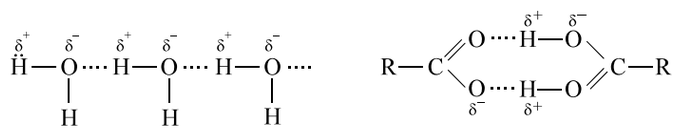
2.5 HYDROGEN BONDING

It has been observed that when a hydrogen atom in a compound is bonded to a highly electronegative atoms such as N, O or F, then marked differences are observed in its usual properties like boiling point, solubility etc. Sometimes the chemical properties of these compounds also differ as compared to similar compounds not having hydrogen attached to N, O and F. For example the boiling point of organic compounds usually increases with increase in molecular weight but, though ethyl alcohol C_2H_5OH (boiling point 78.2°) and dimethyl ether CH_3—O— CH_3 (boiling point–24.9°) have the same molecular weight, yet there is large difference in their boiling points.

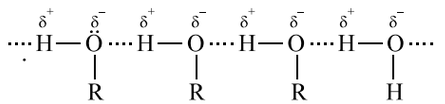
It is argued that when hydrogen is attached to such electronegative atoms the bonding electrons are drawn strongly towards the electronegative atom creating a dipole in the molecule. The hydrogen atom therefore, acquires a small positive charge and becomes extraordinarily capable of attracting a negatively charged atom of a molecule. This attraction results in association of such molecules through the H-atom known as **Hydrogen bond**. This is represented by a dotted line. It has much less strength than covalent bond and is essentially the result of electrostatic interactions, delocalisation effects and dispersion effects. The H-bonding may be represented as:



The H-bonding in water, alcohols and acids may be represented as:



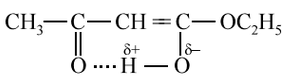
Water Acids



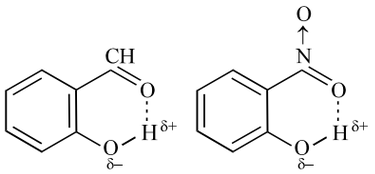
Alcohols

The type of H-bonding resulting in association of two or more molecules of the same or different compound is known as **Intermolecular hydrogen bonding**. Intermolecular association through hydrogen bond results in unusually high boiling points of the liquids. Thus the high boiling points of water, alcohols, amines and acids as compared to monomeric molecules of comparable molecular weight may be explained on the basis of H-bonding.

Intramolecular Hydrogen Bonding. In some compounds the H-bonding may occur within the molecule itself. Ethyl acetoacetate; salicylaldehyde and *o*-nitrophenol are example of this type.



Ethyl acetoacetate

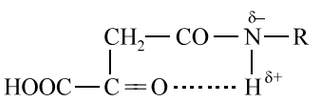


This type of H-bonding prevents the association of such molecules. It is used to explain the stability of enolic forms of ethyl acetoacetate and the low boiling points of *o*-nitrophenol and salicylaldehyde as compared to the corresponding *p*-isomers which can undergo intermolecular hydrogen bonding resulting in association. Usually the intramolecular H-bonding occurs in cases where a six-membered ring can be formed easily through H-bonding.

Hydrogen bonding is important in solid and liquid phases. However the existence of H-bonds has been shown in solution and gaseous phase also. The energies of H-bond are usually in the range of 5 to 8 kcal/mole. For detection of H-bonding solubility behaviour, dipole moment and spectroscopy (I.R.; Raman spectra) are generally used.

Application of H-Bonds

1. Intermolecular H-bonding raises the boiling point and melting point and has been used to explain unusually high boiling point. and melting point of a large number of compounds including water, alcohols, amines and acids etc.
2. The solubility of certain organic compounds in hydroxylic solvents is explained because of the formation of H-bonds between solute and solvent.
3. H-bonding explains the lack of ideal behaviour in gases, solutions and ionisation constants of acids.
4. It has a strong influence on the configuration of a molecule in space and can prevent the interconversion of isomers.
5. It explains the absorption of dyes etc., by textile fibres like cellulose (contains —OH groups) and proteins (contains > NH groups).
6. Lack of chemical reactivity of > C==O group in certain compounds like α-keto succinamic acid is because of H-bonding.



α-Ketosuccinamic acid

7. H-bond serves as a useful bonding forces in biological systems. The structures of proteins and nucleic acids show that H-bonds play an important role in retaining the helix configuration.

NOTES

Check Your Progress

9. What is hyperconjugation?
10. What is intermolecular hydrogen bonding?

2.6 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. In case of *p* orbitals there is a plane passing through the nucleus and at right angles to the axis of the orbital, in which the probability of finding the electron is zero. These plane are called the nodal plane.
2. The V.B. method considers the molecules as being made up of atoms with electrons in atomic orbitals in each atom. Thus the atoms retain their individual character to some extent even when linked to other atoms.
3. In the Molecular Orbital (M.O), the orbitals are considered as eigenstates in atoms and bonds are considered to be formed by the overlap of atomic orbitals. Thus the electrons move in the field of more than one nucleus, i.e., molecular orbitals are assumed to be polycentric.
4. When the centres of electron density are on the axis common to the nuclei or the overlapping is coaxial the orbital is known as σ (sigma).
5. The average distance between two atomic nuclei in a covalent molecule is called the bond distance or bond length.
6. Induction of polarity or dipole, in an otherwise non-polar bond, and consequent electron shift along a chain of atoms is known as inductive effect.
7. The effect involving the complete transfer of a shared pair of electrons to one of the atoms joined by a double or triple bond at the requirement of attacking reagent, is known as Electromeric effect.
8. It states that a molecule for which several classical structural formulae may be written, cannot be satisfactorily represented by any one of these formulae known as limiting structures or canonical structures but only by the superposition of the whole set.
9. When an H—C bond is attached to an unsaturated carbon atoms, the σ (sigma) electrons of this H—C bond enter into conjugation with unsaturated system. Such conjugation between electrons of single and multiple bonds is known as hyperconjugation.
10. The type of H-bonding resulting in association of two or more molecules of the same or different compound is known as Intermolecular hydrogen bonding.

2.7 SUMMARY

NOTES

- The two important methods of approximation to understand and depict the structure of molecules are Valence bond and Molecular orbital methods.
- Concepts like resonance, hybridization of atomic orbitals, orbital box diagrams for electronic configurations are a consequence of the valence bond theory.
- When the centres of electron density are on the axis common to the nuclei or the overlapping is coaxial the orbital is known as σ (sigma).
- The M.O. formed by sideways overlapping, having only one nodal plane along the nuclear axis, is known as π (pi) orbital.
- 2*s* and 2*p* orbitals of carbon in the excited state undergo a process of mixing up and redistribution to form new orbitals of equivalent energy. This concept is known as Hybridization and the resultant new orbitals are called Hybridized orbitals.
- The average distance between two atomic nuclei in a covalent molecule is called the bond distance or bond length. This distance is such that the repulsion between atomic nuclei is balanced by the stability acquired through the overlapping of orbitals.
- When bonds are formed energy is reduced, consequently the energy required to break a bond into its constituents is referred to as Bond energy and is a measure of Bond strength. The greater the energy required to break a bond, the greater will be its strength.
- The bond energy for sigma bond is more than that of a pi bond.
- The measure of the tendency of chemically bonded atom to attract electrons is known as electronegativity.
- Induction of polarity or dipole, in an otherwise non-polar bond, and consequent electron shift along a chain of atoms is known as inductive effect.
- Inductomeric effect is a temporary effect and brought into play only in the presence of charged attacking reagent. However this does not have an important role in organic reactions except in assisting the displacement of electrons in inductive effect.
- The effect involving the complete transfer of a shared pair of electrons to one of the atoms joined by a double or triple bond at the requirement of attacking reagent, is known as electromeric effect.
- If the single and double bonds are present alternately in a molecule, it is said to contain double bonds in conjugation and the molecule is called a conjugated molecule.

NOTES

- Robinson and Ingold (1933) gave the concept of mesomerism or mesomeric effect.
- The extra stabilization of a molecule because of resonance or delocalization is expressed in terms of resonance or delocalization energy.
- Since σ electrons are less polarizable than π or *n* (nonbonding) electrons, the contribution of the ionic forms involving σ bonds will be less significant than that of ionic forms involving π and *n*-electrons.
- When a hydrogen atom in a compound is bonded to a highly electronegative atoms such as N, O or F, then marked differences are observed in its usual properties like boiling point, solubility etc. Sometimes the chemical properties of these compounds also differ as compared to similar compounds not having hydrogen attached to N, O and F.

2.8 KEY WORDS

- **Electron:** A stable subatomic particle with a charge of negative electricity, found in all atoms and acting as the primary carrier of electricity in solids.
- **Covalent bond:** A covalent bond, also called a molecular bond, is a chemical bond that involves the sharing of electron pairs between atoms. These electron pairs are known as shared pairs or bonding pairs, and the stable balance of attractive and repulsive forces between atoms, when they share electrons, is known as covalent bonding.
- **Resonance:** Resonance or mesomerism is a way of describing delocalized electrons within certain molecules or polyatomic ions where the bonding cannot be expressed by one single Lewis structure.
- **Hydrogen bond:** A weak bond between two molecules resulting from an electrostatic attraction between a proton in one molecule and an electronegative atom in the other.
- **Hybridization:** Orbital hybridization is the concept of mixing atomic orbitals into new hybrid orbitals suitable for the pairing of electrons to form chemical bonds in valence bond theory.

2.9 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. In what respect atomic orbitals differ from molecular orbitals? Explain the following terms:
   (a) Sigma bond (b) Pi bond (c) *sp* hybridization.

2. Arrange the following acids in the increasing order of acid strength and justify:

   $ClCH_2COOH$, CH_3COOH, C_6H_5COOH.

3. Write a short note on electromeric effects.
4. What are the applications of electromeric effect?
5. What are the applications of inductive effect?

Long Answer Questions

1. Explain the significance of term hybridization. How does it explain the tetracovalent nature of carbon and that methane has a bond angle of 109.5° rather than 90°?
2. Write short notes on *sp*, sp^2 and sp^3 hybridization.
3. Draw explanatory diagrams of the orbital pictures of methane, ethylene, acetylene and ethane.
4. Explain the following terms in connection with the structure of organic compounds:
   (a) Electronegativity (b) Conjugation
   (c) Mesomerism (d) Resonance
   (e) Hyperconjugation
5. What are hydrogen bonds? What type of compounds form hydrogen bonds? How does its strength compare with other types of bonds?

2.10 FURTHER READINGS

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UNIT 3 AROMATICITY

NOTES

Structure

3.0 INTRODUCTION

The literal meaning of 'aromaticity' is 'fragrance,' but the word has a special meaning in chemistry. Aromaticity has to do with the unusual stability of the compound benzene and its derivatives, as well as certain other unsaturated ring compounds. The structures of these compounds are often shown to contain double bonds, but they do not actually behave like double bonds. For example, reagents such as bromine react with benzene by substitution rather than addition. Benzene and its derivatives had long been referred to as aromatic because of their distinctive odors.

In the simple aromatic ring of benzene the delocalization of six π electrons over the C_6 ring is often graphically indicated by a circle. The fact that the six C-C bonds are equidistant is one indication that the π electrons are delocalized; if the structure were to have isolated double bonds alternating with discrete single bonds, the bond would likewise have alternating longer and shorter lengths. In valence bond theory, delocalization in benzene is represented by resonance structures.

In this unit, you will study about aromatic compounds and their characteristics. You will also get yourself acquainted with theories of aromaticity. In the end, you will learn about antiaromatic, homoaromatic and non-aromatic compounds.

3.1 OBJECTIVES

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

- Understand the concept of aromaticity
- Know about aromatic, antiaromatic, homoaromatic and non-aromatic compounds
- Discuss molecular orbital theory of aromaticity

3.2 AROMATICITY

NOTES

Originally the term *aromatic* was coined for odiferous compounds and referred to a classification of organic compounds based on the physiological property of odour. Many of these organic compounds resemble benzene in their chemical behaviour particularly in undergoing substitution reaction despite unsaturation in the molecule and are said to exhibit aromatic character or aromaticity. It was also realized that the molecules of most of these organic compounds possess a benzene ring or a condensed system of benzene rings. Thus the term aromatic was synonymous to *benzenoid* (meaning the presence of benzene ring) and it was considered that the concept of aromatic character or aromaticity would be clear as soon as the problem of the structure of benzene was finally solved. However in recent years it has been pointed out that compounds other than benzene or its derivatives resemble them in chemical behaviour. Compounds such as azulenes, tropolones etc. are called '*non-benzenoid*' aromatics. The important characteristics observed for aromatic compounds are:

(1) They are usually cyclic compounds. Their molecules have been shown to be planar by X-ray and electron diffraction methods.

(2) Inspite of high degree of unsaturation these compounds are resistant to usual addition reactions of unsaturated compounds.

(3) Despite unsaturation these compounds undergo substitution reactions. Important of these substitution reactions are *electrophilic substitution reactions* like those of benzene, for example, halogenation, nitration, sulphonation, Friedel Craft alkylation and acylation reactions.

(4) They show unusual stability as shown by their low heat of hydrogenation and heat of combustion.

These distinctive properties of aromatic compounds must be somehow related to their structural features, some of which at least should be common to all compounds exhibiting aromaticity.

Theories of Aromaticity

The earliest attempts to explain aromaticity date back to 1865 when Kekule assigned a dynamic formula to benzene involving interconversion of the two Kekule forms. In 1890 E. Bamberger suggested that aromatic character was associated with compounds having six residual affinities. He argued that a hexacentric system alone was capable of this stability. He could explain the aromaticity of compounds like pyridine, pyrrole and furan by assuming that in case of pyrrole and furan, lone pair of nitrogen was considered to be contributing to the six residual affinities.

1. **Aromatic Sextet Theory**. In 1925 *Robinson* proposed sextet theory to explain aromaticity. According to this theory if there were six electrons more than required to link together the atoms of a planar system (carbocyclic or heterocyclic), then

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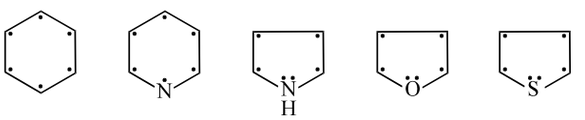
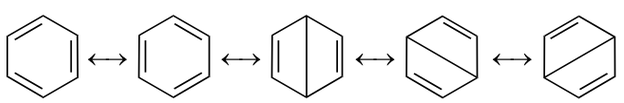
this closed group resists disruption. This closed group of six electron was called the '*sextet*' and this was responsible for *aromatic character* or *aromaticity*. Such a group is possible in benzene and heterocyclic compounds and therefore they exhibit aromatic character.



Benzene Pyridine Pyrrole Furan Thiophene

2. **Valence Bond Theory**. Benzene molecule has been found to be flat hexagon where C — C bond length is 1.397 Å and C — C — H valency angle is 120°. The value of bond length lies between the value for single bond (1.54 Å) and that of a double bond (1.33 Å). Hence the bonds in benzene have double bond character. The regular hexagon structure accounts for all the bonding electron except six. All this data satisfies the condition for a molecule to have resonating structure. V.B. theory calculation showed that there could be five canonical structures for benzene. Out of these five hypothetical structures, the Kekule structures (I and II) contribute 80% and the Dewar structures (III to V) 20% to the resonance hybrid structure of benzene. The heat of hydrogenation of the hypothetical cyclohexatriene would be –359 kJ mol^{-1} but the observed value for benzene is – 200.5 kJ mol^{-1}. Hence benzene is more stable than the triene by 150.5 kJ mol^{-1}. This value is the resonance stabilisation energy of benzene which gives its stability and the aromaticity. There are other compounds which have resonance energy and stability somewhat similar to benzene. The resonance energy of such compounds is given in the brackets.

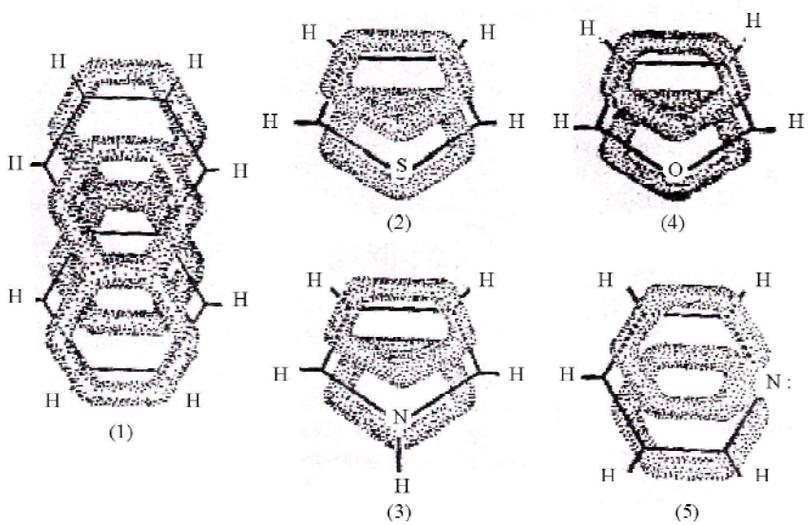


I II III IV V

Naphthalene	(255.2 kJ mol^{-1})	Pyrrole	(88.2 kJ mol^{-1})
Anthracene	(351.5 kJ mol^{-1})	Furan	(67.2 kJ mol^{-1})
Azulene	(193.2 kJ mol^{-1})	Thiophene	(123.5 kJ mol^{-1})
Tropolone	(109.2 kJ mol^{-1})	Pyridine	(125.5 kJ mol^{-1})

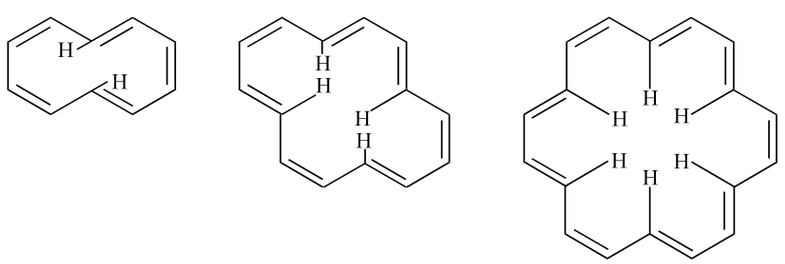
3. **Molecular Orbital Theory**. The molecular orbital structure of benzene shows benzene to be a hexagon sandwiched between two delocalised 6 π electron orbitals. Delocalisation of the three localised molecular orbitals lowers the energy of the molecule by an amount which is called the energy of delocalisation. This delocalisation energy is the same as resonance energy of the valence bond theory.

Hence it was concluded that a cyclic system having a delocalised 6 π electron molecular orbital will show stability and aromatic character similar to naphthelene and heterocyclic compounds like pyridine, thiophene, furan and pyrrole.



Huckel's Rule for Aromaticity. E. Huckel (1937) carried out M.O. calculation for monocyclic systems where each carbon atom contributed one π electron and came to the conclusion that stability and aromatic character is based on the presence of $(4n + 2)\pi$ electron in such systems, where 'n' is a positive integer. For value of $n = 1$ the Huckel's number is 6. The rule holds good in case of compounds like naphthalene (10π electron), pyridine (6π electron), furan, thiophene and pyrrole.

Sondheimer *et al*. (1962) prepared *annulenes* (conjugated monocyclic polyenes) with molecular formula C_nH_n, having 10, 12, 14, 16, 18, 20, 24 and 30 π electrons. Of these only those having 10, 14, 18 and 30 π electron come under the $(4n + 2)\pi$ electron Huckel rule. Their aromatic character was studied by NMR which revealed that they had no aromatic character. Of these [10] and [14] annulenes were not planar.



[10] Annulene [14] Annulene [18] Annulene

[No aromatic character]

Huckel's $(4n + 2)\pi$ rule when applied to polycentric system was not successful in all cases. It was suggested that $(4n + 2)\pi$ rule should be applied to peripheral conjugated π electrons. *Naphthalene* has 10 and *anthracene* 14 π electrons which are all peripheral but *pyrene* has 16π electrons of which only 14 are peripheral. All the three compounds show aromatic character.

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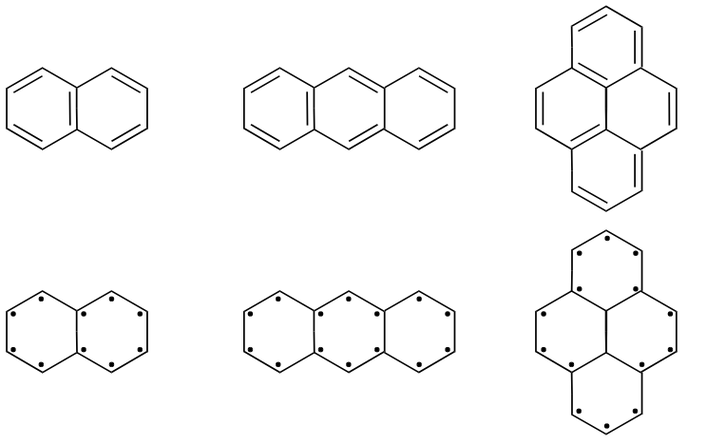


Naphthalene (10 π electrons) | Anthracene (14 π electrons) | Pyrene (14 π electrons-peripheral)

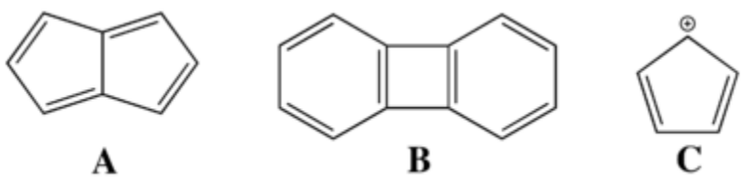
3.2.2 Elctron Delocalization and Resonance

Already discussed in Unit 2 (Refer 2.3 of Unit 2)

3.3 ANTIAROMATIC, HOMOAROMATIC AND NON-AROMATIC COMPOUNDS

Antiaromatic compounds

Antiaromaticity is a characteristic of a cyclic molecule with a π electron system that has higher energy due to the presence of 4n electrons in it. Unlike aromatic compounds, which follow Hückel's rule ([4*n*+2] π electrons) and are highly stable, antiaromatic compounds are highly unstable and highly reactive. To avoid the instability of antiaromaticity, molecules may change shape, becoming non-planar and therefore breaking some of the π interactions. In contrast to the diamagnetic ring current present in aromatic compounds, antiaromatic compounds have a paramagnetic ring current, which can be observed by NMR spectroscopy.



A **B** **C**

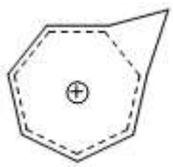
A: Pentalene *B: Biphenylene* *C: Cyclopentadienyl Cation*

Examples of antiaromatic compounds are pentalene (A), biphenylene (B), cyclopentadienyl cation (C). The prototypical example of antiaromaticity, cyclobutadiene, is the subject of debate, with some scientists arguing that antiaromaticity is not a major factor contributing to its destabilization.

Homoaromatic compounds

NOTES

Homoaromaticity, in organic chemistry, refers to a special case of aromaticity in which conjugation is interrupted by a single sp^3 hybridized carbon atom. Although this sp^3 center disrupts the continuous overlap of p-orbitals, traditionally thought to be a requirement for aromaticity, considerable thermodynamic stability and many of the spectroscopic, magnetic, and chemical properties associated with aromatic compounds are still observed for such compounds. This formal discontinuity is apparently bridged by p-orbital overlap, maintaining a contiguous cycle of π electrons that is responsible for this preserved chemical stability.



The homoaromatic homotropylium cation ($C_8H_9^+$)

The concept of homoaromaticity was pioneered by Saul Winstein in 1959, prompted by his studies of the 'tris-homocyclopropenyl' cation. Since the publication of Winstein's paper, much research has been devoted to understanding and classifying these molecules, which represent an additional class of aromatic molecules included under the continuously broadening definition of aromaticity. To date, homoaromatic compounds are known to exist as cationic and anionicspecies, and some studies support the existence of neutral homoaromatic molecules, though these are less common. The 'homotropylium' cation ($C_8H_9^+$) is perhaps the best studied example of a homoaromatic compound.

The term 'homoaromaticity' derives from the structural similarity between homoaromatic compounds and the analogous homo-conjugated alkenes previously observed in the literature. The IUPAC Gold Book requires that Bis-, Tris-, etc. prefixes be used to describe homoaromatic compounds in which two, three, etc. sp^3 centers separately interrupt conjugation of the aromatic system.

IUPAC naming system illustrated by the Homotropylium cation derivatives

Non-Aromatic Compounds

Hydrocarbons are mixes made out of carbon and hydrogen alone and they are classified into two main groups, aromatic and non-aromatic compounds.

NOTES

The aromatic hydrocarbons contain ring or cyclic system with delocalised electron cloud while the non-aromatic hydrocarbons do not contain such ring/ cyclic system. A nonaromatic is found to be either non-cyclic or not in a planar form. These incorporate basically the alkanes, which are immersed hydrocarbons, alkenes which are saturated hydrocarbons, alkenes which contain one or more double bonds and finally the alkenes which contain one or more triple bonds.

The non-aromatic compounds without ring structure are named aliphatic though those with a ring structure like cyclohexane are named alicyclic. The aromatic hydrocarbons regularly comprise of fused rings as in case of benzo pyrene.

Properties of Nonaromatic Compounds

Stability: The nonaromatic compounds are more stable than an antiaromatic compound but is considered to be less stable than aromatic compounds.

Reactivity Index: In case of reactivity - the nonaromatic compounds are more reactive than aromatic compounds. The reason behind the less reactivity of aromatic compound the presence of delocalised electron cloud below and above the plane in aromatic compound but it is not present in nonaromatic.

Examples

A nonaromatic is found to be either non-cyclic or not in a planar form. Lots of nonaromatic compound exists like 1-octyne, 1-nonyne, 1, 4-cyclohexadiene, 1, 3, 5-cyclo heptatriene etc.

Check Your Progress

1. What is the meaning of benzoid?
2. Who proposed the sextet theory of aromaticity?
3. Name two antiaromatic compounds.
4. Name two non-aromatic compounds.

3.4 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. It means presence of benzene ring.
2. In 1925 Robinson proposed sextet theory to explain aromaticity.
3. Pentalene and Biphenylene.
4. 1-octyne and 1-nonyne.

3.5 SUMMARY

NOTES

- Many of the organic compounds resemble benzene in their chemical behaviour particularly in undergoing substitution reaction despite unsaturation in the molecule and are said to exhibit aromatic character or aromaticity.
- Aromatic compounds are usually cyclic compounds. Their molecules have been shown to be planar by X-ray and electron diffraction methods.
- Despite unsaturation these compounds undergo substitution reactions. Important of these substitution reactions are electrophilic substitution reactions like those of benzene, for example, halogenation, nitration, sulphonation, Friedel Craft alkylation and acylation reactions.
- In 1925 Robinson proposed sextet theory to explain aromaticity. According to this theory if there were six electrons more than required to link together the atoms of a planar system (carbocyclic or heterocyclic), then this closed group resists disruption. This closed group of six electron was called the 'sextet' and this was responsible for aromatic character or aromaticity. Such a group is possible in benzene and heterocyclic compounds and therefore they exhibit aromatic character.
- The molecular orbital structure of benzene shows benzene to be a hexagon sandwiched between two delocalised 6 electron orbitals. Delocalisation of the three localised molecular orbitals lowers the energy of the molecule by an amount which is called the energy of delocalisation. This delocalisation energy is the same as resonance energy of the valence bond theory.
- Antiaromaticity is a characteristic of a cyclic molecule with a π electron system that has higher energy due to the presence of $4n$ electrons in it.
- Homoaromaticity, in organic chemistry, refers to a special case of aromaticity in which conjugation is interrupted by a single sp^3 hybridized carbon atom.
- A nonaromatic is found to be either non-cyclic or not in a planar form.

3.6 KEY WORDS

- **Aromaticity:** The term aromaticity is used to describe a cyclic, planar molecule with a ring of resonance bonds that exhibits more stability than other geometric or connective arrangements with the same set of atoms.
- **Resonance:** The property of having a molecular structure which cannot adequately be represented by a single structural formula but is a composite of two or more structures of higher energy.
- **Benzene:** The benzene molecule is composed of six carbon atoms joined in a ring with one hydrogen atom attached to each. As it contains only carbon and hydrogen atoms, benzene is classed as a hydrocarbon.

3.7 SELF ASSESSMENT QUESTIONS AND EXERCISES

NOTES

Short Answer Questions

1. Write a brief note on nonbenzenoid aromatic compounds.
2. Explain aromatic sextet theory.
3. What do you understand by valence bon theory?
4. Write a short note on antiaromatic compounds.
5. Write a short note on homoaromatic compounds.

Long Answer Questions

1. What do you understand by term Aromaticity?
2. Discuss the important characteristics of aromatic compounds.
3. Explain molecular orbital theory.
4. What is Huckel's rule of aromaticity? Explain.
5. What are nonaromatic compounds? Discuss its properties.

3.8 FURTHER READINGS

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UNIT 4 ALTERNANT AND NON-ALTERNANT HYDROCARBONS

Structure

4.0 INTRODUCTION

In organic chemistry, a hydrocarbon is an organic compound consisting entirely of hydrogen and carbon. Hydrocarbons are examples of group 14 hydrides. Hydrocarbons from which one hydrogen atom has been removed are functional groups called hydrocarbyls. Because carbon has 4 electrons in its outermost shell (and because each covalent bond requires a donation of 1 electron, per atom, to the bond) carbon has exactly four bonds to make, and is only stable if all 4 of these bonds are used. Aromatic hydrocarbons (arenes), alkanes, cycloalkanes and alkyne-based compounds are different types of hydrocarbons.

Alternant hydrocarbon is a member of a class of conjugated molecules whose carbon atoms can be divided into two sets so that members of one set are formally bonded only to members of the other set. Non-alternant hydrocarbons always feature at least one ring constructed with an odd number of carbon atoms, whereas alternant hydrocarbons have no such rings.

Non-benzenoid aromatic compound are chemical compounds with conjugated pi-electron system with ring of 5 to 7 carbon atoms. They exhibit aromaticity due to alternate pi-bonds in the molecule. They do not have benzene ring therefore called as non-benzenoid compounds. The chemical reactions of these compounds are like benzenoid compounds only.

In this Unit, you will get acquainted with alternant and non-alternant hydrocarbons. Further in this Unit, you will understand the concept of aromaticity on various non-benzenoid compounds.

NOTES

4.1 OBJECTIVES

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

- Describe alternant and non-alternant hydrocarbons
- Discuss aromaticity on cyclopentadienyl anion, fulvene, ferrocene, azulene, tropolones, annulens and tropylium
- Discuss aromaticity on aromaticity on higher annulens, hetero annulens and fullerenes(C_{60})

4.2 ALTERNANT AND NON-ALTERNANT HYDROCARBONS

An alternant hydrocarbon is any conjugated hydrocarbon system which does not possess an odd-membered ring. For such systems it is possible to undertake a starring process, in which the carbon atoms are typically divided into two sets such that all the carbons in one set are marked with a star so that no two starred or unstarred atoms are bonded to each other. Here the starred set contains the highest number of atoms. When this condition is fulfilled, then the secular determinant in the Hückel approximation has a simpler form, since cross-diagonal elements between atoms in the same set are essentially 0.

Alternant hydrocarbons show the following three very interesting properties:

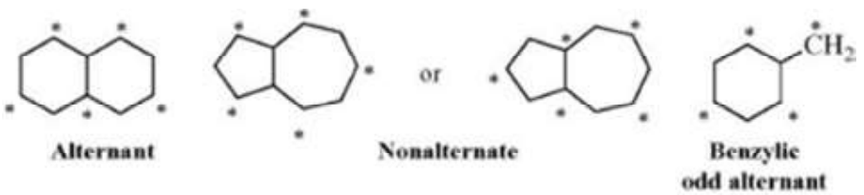
- The molecular orbital energies for the π system are paired, that is for an orbital of energy $E = \alpha + x\beta$ there is one of energy $E = \alpha - x\mathbf{b}$.
- The coefficients of two paired molecular orbitals are similar at the same position, except for a sign change in the unstarred set.
- The population or electron density at all sites is equal to unity in the ground state, so the distribution of ð electrons is uniform across the whole molecule.

Moreover, if the alternant hydrocarbon contains an odd number of atoms then there must be an unpaired orbital with zero bonding energy (a non-bonding orbital). For this orbital, the coefficients on all the orbitals belonging to the smaller (unstarred) set are 0, and the sum of the coefficients of the (starred) orbitals around them must also be 0. The most-widely accepted method to molecular orbital calculations on planar hydrocarbons is possible due to Hückel. Following is the most significant distinctions made at the Hückel level between alternant (1) and non-alternant hydrocarbons (2).

1 2

Non-alternant hydrocarbons always feature at least one ring constructed with an odd number of carbon atoms, whereas alternant hydrocarbons have no such rings.

Fundamentally, the aromatic hydrocarbons can be divided into alternant and non-alternant hydrocarbons. In alternant hydrocarbons, the conjugated carbon atoms can be divided into two sets in such a manner that no two atoms of the same set are directly linked. For convenience, one set may be starred. Naphthalene is an alternant and azulene a non-alternant hydrocarbon as shown below:



In alternant hydrocarbons, the bonding and antibonding orbitals occur in pairs; that is, for every bonding orbital with an energy $-E$ there is an antibonding one with energy $+E$ (Refer Figure 4.1). Even-alternant hydrocarbons are those with an even number of conjugated atoms, that is, an equal number of starred and unstarred atoms. For these hydrocarbons all the bonding orbitals are filled and the (electrons are uniformly spread over the unsaturated atoms. Figure illustrates 'Energy Levels' in odd-alternant hydrocarbon (odd a h) and even-alternant hydrocarbon (even a h) in which the arrows represent electrons. The orbitals are shown as having different energies, but some may be degenerate.

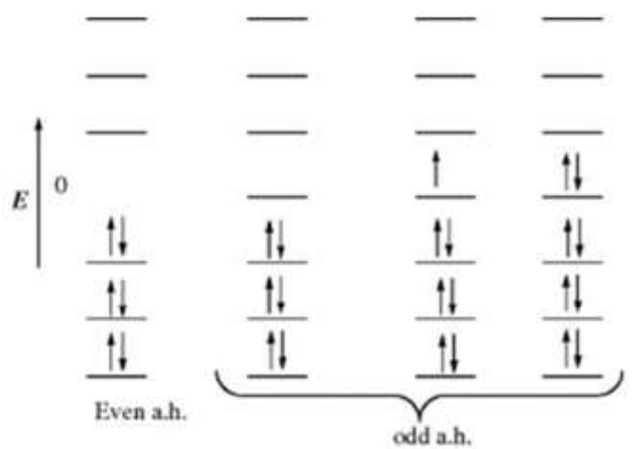


Fig. 4.1 *Energy Levels in Odd- and Even-Alternant Hydrocarbons*

NOTES

As with the allylic system, odd-alternant hydrocarbons (which must be carbocations, carbanions, or radicals) in addition to equal and opposite bonding and antibonding orbitals also have a nonbonding orbital of zero energy. When an odd number of orbitals overlap, an odd number is created. Since orbitals of alternant hydrocarbons occur in $+E$ and $+E$ pairs, one orbital can have no partner and must therefore have zero-bonding energy. For example, in the benzylic system the cation has an unoccupied nonbonding orbital, the free radical has one electron there and the carbanion has two (Refer Figure 4.2). As with the allylic system, all three species have the same bonding energy. The charge distribution (or unpaired-electron distribution) over the entire molecule is also the same for the three species and can be calculated by a relatively simple process. Figure 4.2 illustrates the 'Energy Levels for the Benzyl Cation, Free Radical and Carbanion'. Since á is the energy of a *p* orbital, the nonbonding orbital has no bonding energy.

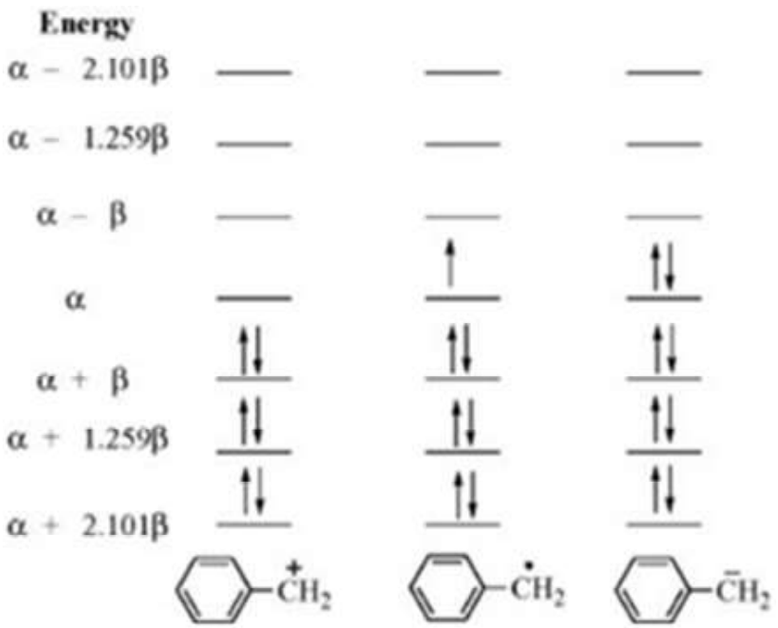


Fig. 4.2 *Energy Levels for the Benzyl Cation*

For non-alternant hydrocarbons, the energies of the bonding and antibonding orbitals are not equal and opposite and charge distributions are not the same in cations, anions, and radicals.

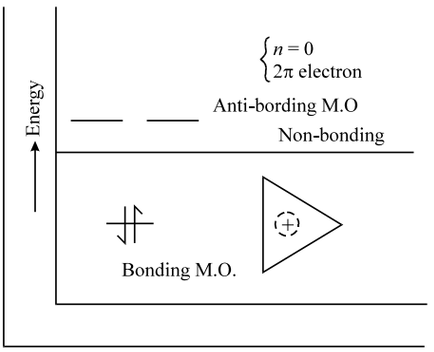
Check Your Progress

1. What is an alternant hydrocarbon?
2. Give an example of alternant hydrocarbon.
3. Give an example of non-alternant hydrocarbon.

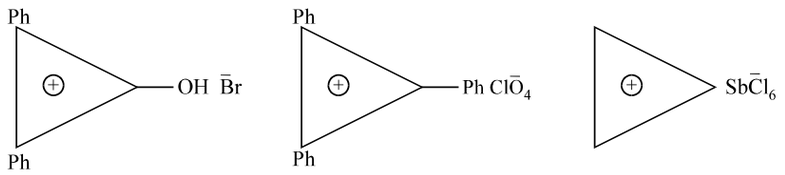
4.3 AROMATICITY ON CYCLOPENTADIENYL ANION, FERROCENE, AZULENE

NOTES

Aromaticity of Non-Benzenoids. The compounds which do not contain any benzene ring are called non-benzenoids. Various non-benzenoid systems or compounds are known which contain 2, 6 or 10 pi electrons and show aromatic character.

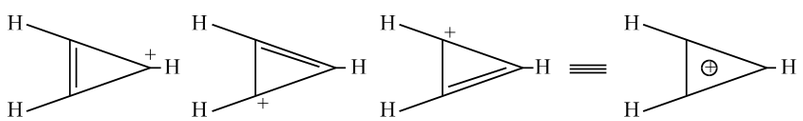


(*i*) 2π *Electron System*: A number of cyclo-propenium salts have been prepared which contain 2π electron cyclopropenyl cation. The cation correspond to the value $n = 0$ in the Huckel's formula of $(4n + 2)\pi$ electron.



Hydroxy diphenyl-cyclopropenyl bromide | Triphenylcyclopropenyl perchlorate | Cyclopropenyl hexachloroantimonate

This cation is formed by the transfer of an electron from antibonding M.O. to the anion. The cation can be represented as a resonance hybrid (V.B. theory) which explains the stabilisation and aromaticity. From M.O. theory, the empty $2p_z$ orbital from which the electron has been lost overlaps the two single electron orbitals to form a closed orbital containing two electrons.



Resonating structures of cyclopropenyl cation | Resonance hybrid

(*ii*) 6π *Electron Systems*: We have discussed the aromatic character of benzene and other heterocyclic compounds possessing 6π electron. Benzene has three bonding and three antibonding orbitals. Six π electron fill the three bonding orbitals completely to form a closed system of π electron.

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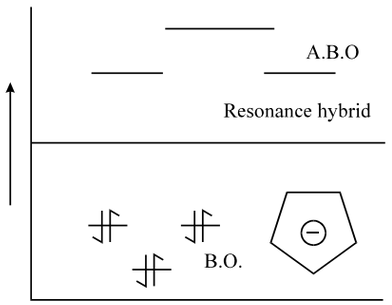
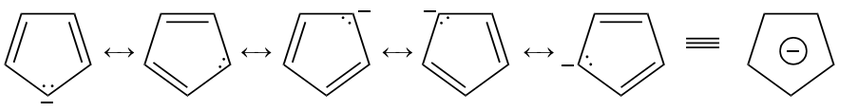


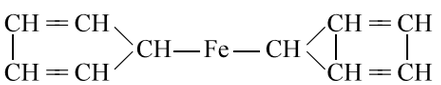
Cyclopentadienyl anion

The 5π electrons system with a planar or nearly planar structure can get an electron to become a 6π electron system. Cyclopentadienyl anion formed (from potassium cyclopenta dienide) in this manner is stabilised by resonance.

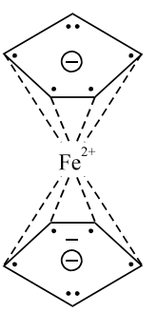


Resonating structures of cyclopentadienyl anion Resonance hybrid

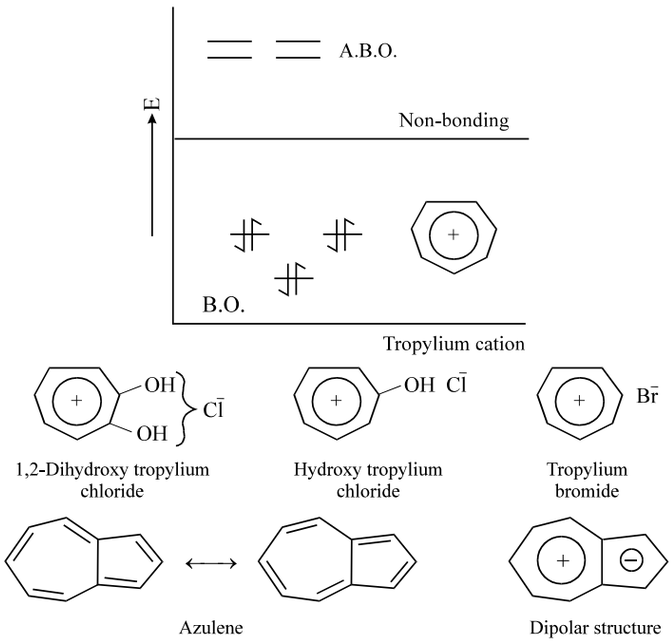
Dicyclopentadienyl iron (**ferrocene**) is another compound which has aromatic properties.



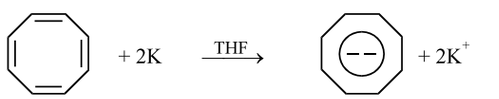
In tropylium salts one π electron is lost from anti bonding orbital to give the tropylium cation (cycloheptatrienyl) which thus is left with only 6π electrons. This ion is a resonance hybrid of seven canonical structure. Several tropylium derivatives are known which all show aromatic properties.



Azulene is a non-benzenoid containing a seven-membered ring fused into a five-membered ring. It has 10 π electrons in all, two being common to both rings. Now if one π electron is transferred from the seven π electron ring to five π electron ring then the molecule will have a dipole structure, each ring containing six π electrons. Azylene also behaves chemically as an aromatic compounds.



(*iii*) 10 π **Electron System.** Cyclo-octatetraene has 8π electrons and is a very reactive compound like olefins. However, if it is made to react with potassium in tetrahydrofuran (THF) dipotassium cyclo-octatetraenide is formed which has the cyclo-octatetetraenyl dianion. In the formation of the dianion two π electrons are gained, one to each non-bonding M.O. and a close shell having 10 π electrons is formed. NMR studies have confirmed its aromatic character.



Cyclo-octateraenyl dianion

It is now realised that energetic stabilisation of a molecule does not necessarily have any relationship with low chemical reactivity because the chemical reactivity depends on the free energy difference between that of the reactants and the transition state. Thus a molecule might be stable or aromatic and yet highly reactive. Therefore J.A. Elvidge in 1965 pointed out that Huckel's rule refers only to the energy (or stability) in the ground state of the molecule and the term aromaticity should be applied to the ground state properties of the molecule. *Perhaps the best way to ascertain the aromaticity of a compound is the study of its NMR spectra. The protons of aromatic compounds show the same chemical shift in NMR as the protons of benzene. Thus an aromatic compound will sustain an induced current in NMR.*

On the basis of the foregoing discussion the criteria for aromaticity is as follows:

(*i*) The compounds must have high degree of unsaturation yet unusual stability due to large delocalisation or resonance energy.

NOTES

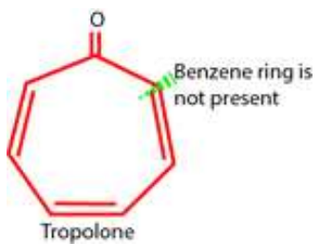
(*ii*) It must have the property of undergoing electrophilic substitution reaction instead of addition reaction.

(*iii*) The molecule must have cyclic clouds of delocalised $(4n + 2)\pi$ electrons.

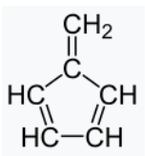
(*iv*) The compounds must have the ability to sustain an induced current in NMR.

4.3.1 Aromaticity on Fulvene, Tropolones, Annulens, Higher Annulens, Hetero Annulens and Fullerenes (C_{60}).

Tropolone is an example of non-benzenoid compound which is aromatic in nature but does not have any benzene ring. The aromaticity is due to conjugated pi-electron system in the molecule.

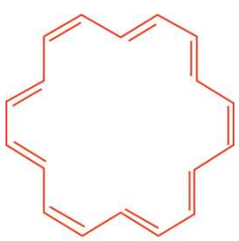


Fulvene is one of several hydrocarbons with the same formula as benzene, C_6H_6. The fulvenes are the class of molecules based on this simple hydrocarbon frame, the parent chemical, fulvene itself, is rarely encountered.



Annulenes

Benzene has 6 electrons; an aromatic compound, but cyclobutadiene with 4 pi-electrons and cyclooctatraene with 8 pi-electrons are non-aromatic compounds. Conjugated polyenes which are also called as annulenes follow Huckel's rule and aromatic compounds. For example, 10-annulene and 18-Annulene follow Huckel rule so aromatic in nature.



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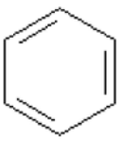
Annulenes are monocyclic compounds containing substituting ring double bonds, for example benzene, but of various sizes. As indicated by methodical terminology, benzene is a [6]annulene, while cyclobutadiene is [4]annulene, though cyclooctatetraene is a [8]annulene.

The general formula annulenes compound is C_nH_n (when n is an even number) or C_nH_{n+1} (when n is an odd number).

The initial three annulenes are cyclobutadiene, benzene, and cyclooctatetraene ([8]annulene). Some annulenes, in particular cyclodecapentaene or [10]annulene, cyclododecahexaene or [12]annulene and cyclotetradecaheptaene ([14]annulene)

[4] An-nu-lene.



[6] An-nu-lene.

[8] An-nu-lene.

Electron System in Annulenes

Two Electron System: Huckel rule predicts cyclopropenyl cation to be aromatic. It has two electrons (n=0) engaged in cyclic delocalization. Example: trichloro, diphenyl

Four Electron System: 4n systems in a closed loop which is antiaromatic, less stable than the relating open chain counterpart.

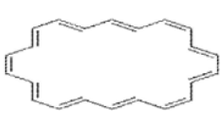
Six Electron System: 6n systems in a closed loop which is antiaromatic, less stable than the relating open chain counterpart like benzene.

Aromaticity on Larger Annulene

None of the larger annulenes are as steady as benzene, as their reactivity more closely resembles a conjugated polyene than an aromatic hydrocarbon like [18]annulene. [18]-annulene is relatively planar, with CC bonds between 137-143 pm. It responds more like a polyene than benzene and it undergoes addition reaction with H_2 and Br_2.

While the total aromatic stabilization energies (ASE) of the [n]annulenes, from C_6H_6 to $C_{66}H_{66}$, meet to ca. 22 kcal/mol, the ASEs per σ-electron diminish especially. When the Bond length increases it reduces stabilization of the annulene compounds and it also changes the magnetic properties of a compound also.

Example: Cyclodocosahendecaene ([22]-annulene)



Cyclodocosahendecaene ([22]-annulene)

NOTES

Hetero Annulenes

On the basis of molecular structure and their energy classification, a range of monocyclic and bridged annulenes and hetero-annulenes chemical compound will come in to frame. In aromatic heterocyclic compounds or molecules, it is not only the structure of carbon atoms' orbitals that participate in the formation of the aromatic π system. Orbitals of the heteroatom(s) also participate in the π system here too. Pyridine, for example, is such an aromatic heterocyclic compound. Each of the six ring atoms is sp^2-hybridized, while the molecule possesses six π electrons. The lone electron pair of pyridine's nitrogen atom occupies an sp^2 orbital. These electrons are thusly not π electrons. The staying two sp^2 orbitals of the nitrogen cover with sp^2 orbitals of the contiguous carbons, shaping two σ bonds. The π framework is the aftereffect of the covering of the nitrogen's and carbons' p orbitals, which are perpendicular to the ring plane. So the annulenes compound having hetero formation are called hetero annulene compound.

Fullerenes (C_{60})

Fullerenes are a family of carbon compounds having at least 60 carbon atoms forming carbon spheres, where carbon atoms are arranged in semi-regular polyhedra distributed over the sphere. The fullerene family was discovered in 1985 by Smalley, Curl and Kroto and are extremely plenteous at the Earth's surface and in the universe. They are the third allotropic type of carbon after diamond and graphite. Fullerenes have the property of shaping shut pens (with the C_{60} molecule) with a structure like that of a football.

The C60 molecule has 60 carbon atoms arranged at the summits of 0.7 nm distance across customary polyhedron with hexagonal and pentagonal countenances.

Types of fullerene

Buckyball clusters: Smallest member is C_{20} (unsaturated version of dodecahedrane) and the most common is C_{60}.

Nanotubes: These are very small hollow tubes having single or multiple walls.

Megatubes: Having bigger diameter than nanotubes and prepared with walls of different thickness.

Polymers: Long Chain of one dimension, two-dimensional and three-dimensional polymers are formed under high-pressure high-temperature conditions.

Nano "Onions": Multiple carbon layers having spherical structures surrounding a buckyball core.

NOTES

Check Your Progress

4. What are non-benzenoid compounds?
5. Why does the energetic stabilization of a molecule not have any relationship with low chemical reactivity?
6. What is fulvene?

4.4 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. An alternant hydrocarbon is any conjugated hydrocarbon system which does not possess an odd-membered ring.
2. Naphthalene is an alternant hydrocarbon.
3. Azulene is a non-alternant hydrocarbon.
4. The compounds which do not contain any benzene ring are called non-benzenoids.
5. The energetic stabilization of a molecule does not necessarily have any relationship with low chemical reactivity because the chemical reactivity depends on the free energy difference between that of the reactants and the transition state.
6. Fulvene is one of several hydrocarbons with the same formula as benzene, C_6H_6.

4.5 SUMMARY

- Fundamentally, the aromatic hydrocarbons can be divided into alternant and non-alternant hydrocarbons.
- An alternant hydrocarbon is any conjugated hydrocarbon system which does not possess an odd-membered ring.
- Non-alternant hydrocarbons always feature at least one ring constructed with an odd number of carbon atoms, whereas alternant hydrocarbons have no such rings.
- The compounds which do not contain any benzene ring are called non-benzenoids.
- Various non-benzenoid systems or compounds are known which contain 2, 6 or 10 pi electrons and show aromatic character.
- Benzene has three bonding and three antibonding orbitals.
- Dicyclopentadienyl iron (ferrocene) is another compound which has aromatic properties.

NOTES

- *Azulene* is a non-benzenoid containing a seven-membered ring fused into a five-membered ring. It has 10 electrons in all, two being common to both rings.
- Cyclo-octatetraene has 8π electrons and is a very reactive compound like olefins.
- Tropolone is an example of non-benzenoid compound which is aromatic in nature but does not have any benzene ring.
- The general formula annulenes compound is C_nH_n (when n is an even number) or C_nH_{n+1} (when n is an odd number).
- Fullerenes are a family of carbon compounds having at least 60 carbon atoms forming carbon spheres, where carbon atoms are arranged in semi-regular polyhedra distributed over the sphere.

4.6 KEY WORDS

- **Aromaticity:** The term aromaticity is used to describe a cyclic, planar molecule with a ring of resonance bonds that exhibits more stability than other geometric or connective arrangements with the same set of atoms.
- **Benzenoid:** Having the six-membered ring structure or aromatic properties of benzene.
- **Non-benzenoid:** Non benzenoid aromatic compound are chemical compounds with conjugated pi-electron system with ring of 5 to 7 carbon atoms. They exhibit aromaticity due to alternate pi-bonds in the molecule.
- **Alternant hydrocarbons:** A member of a class of conjugated molecules whose carbon atoms can be divided into two sets so that members of one set are formally bonded only to members of the other set.

4.7 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. Write a short note on ferrocene.
2. What is azulene? Also draw its structure.
3. Discuss aromaticity on fulvene and tropolones.
4. Discuss Aromaticity on larger annulene.
5. Write a short note on hetero annulenes.

NOTES

Long Answer Questions

1. Explain alternant and non-alternant hydrocarbons.
2. Discuss 2π electron system
3. Discuss 6π electron system.
4. Discuss 10π electron system.
5. What is fullerenes? Describe its types.

4.8 FURTHER READINGS

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NOTES

BLOCK - II

STEREOCHEMISTRY OF ORGANIC COMPOUNDS

UNIT 5 INTRODUCTION TO STEREOCHEMISTRY

Structure

5.0 INTRODUCTION

Stereochemistry is defined as a subdiscipline of chemistry which involves the study of the relative spatial arrangement of atoms that together forms the structure of molecules and their manipulation. The study of Chiral molecules which is one of the elements of symmetry is an important branch of stereochemistry. In other words, stereochemistry belongs to that department of chemistry which take care of the three-dimensional structures of molecules and how they are an impact on the chemical and the physical properties of the substance. There are two types of stereoisomers.They are known as enantiomers and diastereomers. The mirror images which are also non-superimposable isomers are known as the Enantiomers and the isomerism which are exhibited by the same are known as Enantiomerism. There is another type of Isomerism which does not behave as the mirror image of each other.

Chirality is a geometric property of some molecules and ions. A chiral molecule/ion is non-superposable on its mirror image. The presence of an asymmetric carbon center is one of several structural features that induce chirality in organic and inorganic molecules. The term chirality is derived from the Ancient Greek word for hand.

In this unit, you will study abut stereochemistry, molecules with C.N.S based Chiral centers, stereoisomerism in detail.

5.1 OBJECTIVES

NOTES

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

- Understand about stereochemistry
- Discuss about the molecules with C.N.S based Chiral centers
- Explain stereoisomerism and its definition based on energy criteria

5.2 INRODUCTION TO STEREOCHEMISTRY

The compounds having same molecular formula but differing at least in some physical characteristics or chemical properties are known as *isomers* and the phenomenon is known as *isomerism*. The term isomer was coined by Berzelius and was derived from Greek words meaning 'equal or like parts' (*isos* = equal; *meros* = parts). Obviously this difference in properties must be due to some difference in the arrangement of atoms within the molecules of the isomers. Depending on the type of this difference in arrangement of atoms, there can be two types of isomerism: **Structural Isomerism** and **Stereoisomerism**.

- **Structural Isomerism:** *This type of isomerism arises from the difference in the arrangement of atoms within the molecule resulting in two or more different structural formulae*, and the isomers are known as structural isomers. Thus, the structural isomers have same molecular formula but different structures.
- **Stereoisomerism:** *When the isomers have the same structural formulae but they differ in relative arrangement of atoms or groups in space, the phenomenon is termed as stereoisomerism* and the isomers are known as *stereoisomers.* The spatial arrangement (or arrangement in space) of atoms or groups is also referred to as *configuration* of the molecule.

Structural Isomerism

Structural isomerism depends on the mode of linking of atoms which gives rise to the following four types signifying the main difference in their structural features:

- Skeletal or chain isomerism
- Position isomerism
- Functional isomerism
- Metamerism.

Skeletal or Chain Isomerism

Isomers differing in the structure of carbon chains are known as skeletal or chain isomers and the phenomenon as skeletal or chain isomerism. The simplest compound exhibiting this type of isomerism is of molecular formula C_4H_{10} (butane).

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There are two compounds corresponding to this formula which differ only in the nature of carbon skeleton.

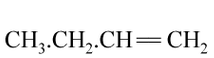
n-Butane (B.P. = –0.5°C) *Straight Chain Carbon Skeleton*

Isobutane (B.P. = – 10.2°C) *Branched Chain Carbon Skeleton*

Similarly, pentane (C_5H_{12}) exists in three isomeric forms because the five carbon atoms can be linked in three different forms of chains. The number of chain isomers goes on increasing with increase in the number of carbon atoms (*cf.* Alkanes) in the chain.

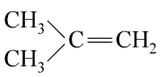
It is also possible that one of the isomer may have an open chain skeleton while the other may have a closed chain or ring (cyclic) skeleton. Thus C_4H_8 may have the following skeletal isomers all of which are known:

Straight Chain



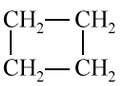
1-Butene (*n*-Butylene)

Branched Chain



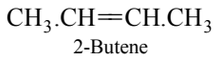
2-Methyl-2-propene (Isobutylene)

Closed Chain or Ring

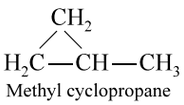


Cyclobutane

and



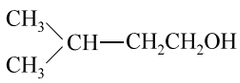
2-Butene



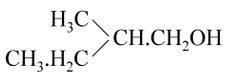
Methyl cyclopropane

This type of isomerism is also shown by other classes of compounds besides the hydrocarbons, e.g., *n*-amyl alcohol, isoamyl alcohol and *ter*-amyl alcohol, all have the same molecular formula ($C_5H_{12}O$) and are skeletal or chain isomers. Thus:

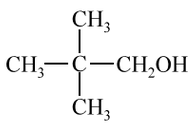
1-Pentanol (*n*-Amyl alcohol)



3-Methyl-1-butanol (Isoamyl alcohol)



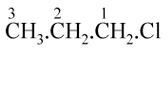
2-Methyl-2-butanol



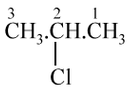
2,3-Dimethyl-1-propanol (*ter*-Amyl alcohol)

Position Isomerism

In compounds containing similar carbon chain, the difference in position occupied by a particular atom or group in the carbon chain, gives rise to position isomerism. These isomers which differ only in the position of a group or atom in the carbon chain are known as *position isomers*. Thus the molecular formula C_3H_7Cl represents following position isomers.



1-Chloropropane
(*n*-Propyl chloride)



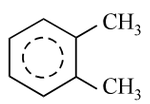
2-Chloropropane
(Isopropyl chloride)

NOTES

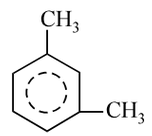
The unsaturated hydrocarbons also exhibit this type of isomerism because of difference in the position of the double or triple bond. Thus:

Mol. Formula		
C_4H_8	$CH_3.CH_2.CH=CH_2$ 1-Butene	$CH_3.CH=CH.CH_3$ 2-Butene
C_4H_6	$CH_3.CH_2.C\equiv CH$ 1-Butyne (Ethyl acetylene)	$CH_3.C\equiv C.CH_3$ 2-Butyne (Dimethyl acetylene)

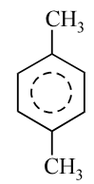
The disubstituted benzene exists in three isomeric forms—*ortho*, *meta* and *para*, which are position isomers differing only in the position of the two substituents. The three xylenes (mol. formula C_8H_{10}) exhibit this type of isomerism and are given below:



ortho-Xylene
(1,2-Dimethylbenzene)



meta-Xylene
(1,3-Dimethylbenzene)



para-Xylene
(1,4-Dimethylbenzene)

Functional Isomerism

Isomerism exhibited by compounds differing in functional groups is known as functional isomerism. As the functional group largely determines the properties of a compound, such compounds differ in their physical and chemical properties. Compounds exhibiting this type of isomerism are called *functional isomers.*

(*i*) Dimethyl ether and ethyl alcohol both have the same molecular formula (C_2H_6O) but belong to two different classes of compounds.

$CH_3.O.CH_3$	C_2H_5OH
Methoxymethane (Dimethyl ether)	Ethanol (Ethyl alcohol)

(*ii*) Propionaldehyde and acetone both have the same molecular formula (C_3H_6O) but propionaldehyde has an aldehydic group (—CHO) whereas acetone has a ketonic group (>C = O).

$CH_3.CH_2.CHO$	$CH_3.CO.CH_3$
Propionaldehyde	Acetone (Propanone)

(*iii*) Propionic acid and methyl acetate are functional isomers (mol. formula $C_3H_6O_2$) having acid and ester functional groups respectively.

$CH_3.CH_2.COOH$	CH_3COOCH_3
Propionic acid	Methyl acetate

Metamerism

Compounds of the same homologous series show this type of isomerism because of unequal distribution of carbon atoms (or difference in size of alkyl groups) on either side of the functional group in the molecules. Only those compounds which have a polyvalent functional group can exhibit metamerims. Thus diethyl ether and methyl propyl ether, both having the same molecular formula and the same functional group (*i.e.* ether linkage) are metamers because of difference in alkyl groups on either side of ether linkage.

$C_2H_5O.C_2H_5$	$CH_3.O.C_3H_7$
Diethyl ether	Methyl propyl ether

Ketones as well as amines also *exhibit metamerism.*

Mol. formula		
$C_5H_{10}O$ (Ketone)	$C_2H_5.CO.C_2H_5$ Diethyl ketone	$CH_3.CO.C_3H_7$ Methyl propyl ketone
$C_6H_{15}N$ (Amine)	$C_3H_7.NH.C_3H_7$ Dipropyl amine	$C_2H_5.NH.C_4H_9$ Butyl ethyl amine

5.2.1 Stereoisomerism

Compounds having the same atoms or groups with a different spatial arrangement are called stereoisomers. This type of isomerism is called stereoisomerism and is of two kinds:

- Geometrical Isomerism
- Optical Isomerism.

Geometrical Isomerism

As early as in 1874, **Le Bel** and **van't Hoff** had suggested that the valencies of carbon atoms are distributed symmetrically in spaces and are directed towards the corners of the regular tetrahedron with carbon at its centre. The angle between these valencies is 109°28′. Accordingly any saturated compound having two carbon atoms may be picturised as having the two carbon tetrahedra joined corner to corner. In such a case the tetrahedra are capable of rotating freely on their axes (bond) with respect to each other. *This is known as the concept of free rotation around carbon to carbon single bond.*

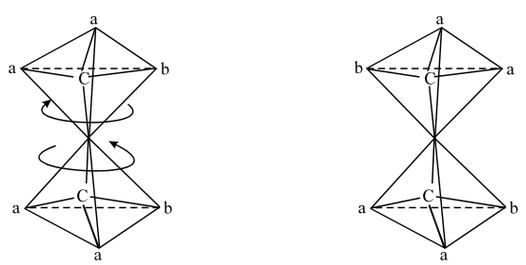


Fig. 5.1 *Showing Two Tetrahedral Carbon Atoms Linked to Each other through a Single Bond. Because of Freedom of Rotation Around C— C Bond Axis*

Both of the above Structures are Indentical Molecules.

NOTES

Actually, there is only one compound corresponding to above different structures and the molecule can assume either of these structures by simple rotation on its axis. Structures which may be wirtten by simple rotation of one carbon with respect to the other, resulting in different configuration or spatial arrangement of atoms or group within the molecule and which may not be isolated are known *as conformers.*

On the other hand if the two carbon atoms are joined through a double bond then the freedom of rotation ceases to exist. In other words the two carbon atoms are fixed with respect to each other and rotation can only be brought about by rotating the molecule as a whole. *This is known as the concept of restricted rotation around carbon to carbon double bonds.* As a result of this restricted rotation two different arrangements, of the substituent groups attached to these two carbon atoms, become possible.

Such isomers, which posses the same structural formula but differ in spatial arrangement of the groups around the double bond or some other similar feature (e.g. a ring) are known as geometrical isomers and the phenomenon is known as geometrical isomerism. The isomer which has similar groups on the same side of the double bond is called '*cis*', (Latin, *cis* = same side) and the other which has similar groups on the opposite side of the double bond is known as '*trans*' (Latin, *trans* = across) isomer. *This type of isomerism is, therefore, also known as cis-trans isomerism.*

In modern concept a *single bond is considered to be an axially symmetrical* σ *bond permitting free rotation about its axis. The double bond is considered to be consisting of a* σ *and a* π *bond*. The presence of a π bond is capable of explaining the rigidity or restricted rotation associated with a multiple bond (Reger Figure. 5.2). *If the carbon atoms are rotated with respect to each other* π *molecular orbital is distorted. The two '*p*' atomic orbitals remain no longer parallel and no orbital overlap can occur. It is this energy barrier which prevents the rotation and substituents are held in a rigid planar geometrical conformation.*

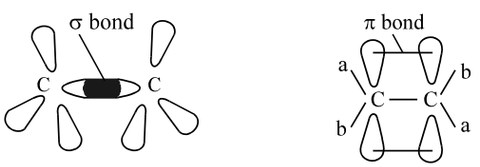
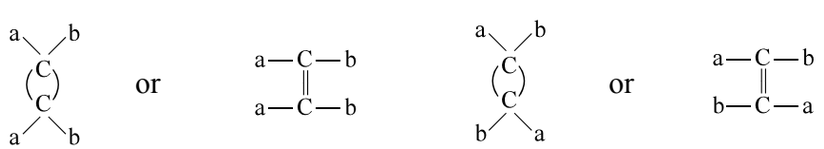


Fig. 5.2 *Modern Concept of Single and Double Bond*

A simple and convenient method of representing the geometrical isomers is to use a planar model rather than the tetrahedral model. Thus the above models may be represented as:

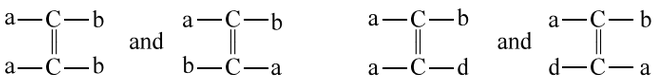


It is essential to point out here that if the two groups attached to any carbon atom are identical then both the structures would be one and the same and no isomers will be possible. For example:

Identical structures (One different substituent)

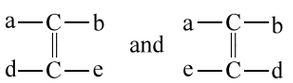
Identical structures (Two different substituent on same carbon atoms)

In all other cases where the carbon atoms joined by a double bond have different substituents, geometrical isomerism is possible.



Non-identical structures (Two different substituent on different carbon atoms)

Non-identical structures (Three different substituents)



Non-identical structures (Four different substituents)

Thus compounds like 1,2 disubstituted alkenes, unsaturated dibasic acids, oximes (having carbon to nitrogen double bond) are capable of exhibiting geometrical isomerism. However, it should be pointed out that in cases where all the four substituents are different (abC = Cde) it is not possible to decide the *cis* and *trans*-configurations.

Examples

(*i*) *1,2-Dichloroethane*

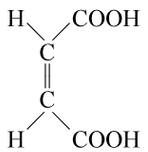
cis- *trans-*

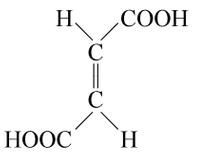
(*ii*) *2-Butene*

cis- *trans-*

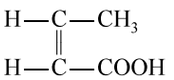
NOTES

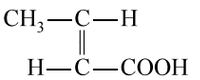
(*iii*) *Maleic and Fumaric Acids*


Maleic acid (*cis*-)

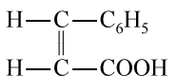

Fumaric acid (*trans*-)

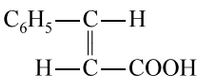
(*iv*) *Crotonic and Isocrotonic Acids*


Isocrotonic acid (*cis*-)

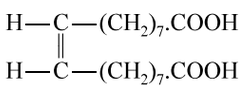

Crotonic acid (*trans*-)

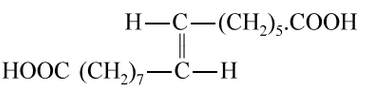
(*v*) *Cinnamic and Allocinnamic Acids*


Allocinnamic acid (*cis*-)


Cinnamic acid (*trans*-)

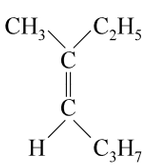
(*vi*) *Oleic and Elaidic Acids*

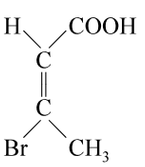

Oleic acid (*cis*-)


Elaidic acid (*trans*-)

E-Z System for Designating Isomeric Alkenes

As pointed out above, the use of terms *cis* and *trans* to designate isomeric alkenes becomes meaningless if the alkene is tri- or tetra-substituted. Thus in compounds shown below it is not possible to decide whether they are *cis* or *trans* because no two groups are same.


(A)


(B)

Therefore a convention for designating isomeric alkenes, known as E-Z system has been suggested which is based on the sequence or priorities of groups[1] in R-S system of Cahn, Ingold and Prelog. In this system we arrange the two groups attached to each carbon atom involved in the double bond in order of priority. Then the group of higher priority on one carbon is compared with the group of higher priority on other carbon atom. If both the groups of higher priority are on the same side of the double bond then the alkene isomer is designated as Z (from German; *Zusammen* meaning *together*) isomer, but if the groups of the higher priority are on the opposite sides of the double bond, the alkene is designated as E (German; Entgegen meaning opposite) isomer.

NOTES

Thus, in compound (A) shown above the order of priority of groups will be

$$C_2H_5 > CH_3 \quad \text{and} \quad C_3H_7 > H$$

As both the groups of higher priority are on the same side of the double bond, the compound is having Z configuration.

In compound (B) the order of priority is

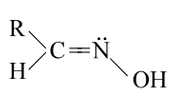
$$COOH > H \quad \text{and} \quad Br > CH_3$$

Since the groups of higher priority are on the opposite side of the double bond, the compound B is having E configuration.

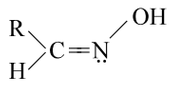
In examples given below it would be found that most *cis* isomers are designated as Z while *trans* isomers are mostly designated E. However there are many exceptions also.

(*i*) **Geometrical Isomerism of Oximes and Related Compounds:** The compounds having a carbon to nitrogen double bond (as in oximes) and nitrogen to nitrogen double bond (as in azo compounds) also exhibit geometrical isomerism because nitrogen too has the same hybridization state—as carbon *i.e.*, sp^2 in doubly bonded nitrogen.

Therefore, if a carbon is replaced by nitrogen in the formation of a double bond the geometrical isomerism will be exhibited. Thus compounds of the type of oximes (>C═N.OH) and azo (R.N═N.R) in which carbon to nitrogen or nitrogen to nitrogen double bond is present show this type of isomerism because the unshared pair of electrons at nitrogen occupies a fixed position and other group attached to nitrogen lies on the other side. The terms '*syn*' and '*anti*' are used in place of '*cis*' and '*trans*' respectively to designate isomeric oximes and azo compounds. In case of aldoximes (RCH═N.OH) the '*syn*' isomer is the one where hydrogen and hydroxyl groups lie on the same side of the double bond whereas in the '*anti*' isomer the two groups are on the opposite side. Thus:

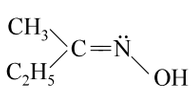


syn-Aldoxime

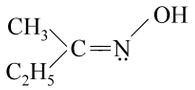


anti-Aldoxime

In the case of ketoximes ($R.\overset{R'}{\overset{|}{C}}=N.OH$) where two different alkyl groups[1] R and R′ exist, the designation is arbitrary. Thus in case of methyl ethyl ketoxime:

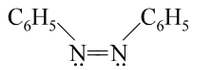


syn-Ethyl methyl ketoxime
or *anti*-Methyl ethyl ketoxime
or Z configuration

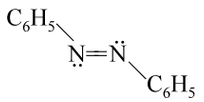


anti-Ethyl methyl ketoxime
or *syn*-Methyl ethyl ketoxime
or E configuration

The azo compounds like azobenzene exhibit geometrical isomerism as shown below:



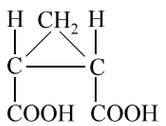
cis- or *syn*-Azobenzene



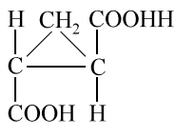
trans- or *anti*-Azobenzene

NOTES

(*ii*) **Geometrical Isomerism of Cyclic Compounds:** Just as a double bond imposes restrictions on the free rotation similarly a ring structure will also prevent free rotation of carbon atoms about their axis. The geometrical isomerism will, therefore, also arise in the cyclic or ring compounds. For example, cyclopropane-dicarboxylic acid exists in two isomeric forms — '*cis*' and '*trans*'. (Besides this it also exhibits optical isomerism.)



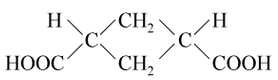
cis-



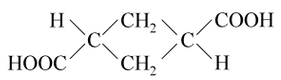
trans-

Cyclopropane-dicarboxylic acid

Similarly cyclobutane and other higher ring systems also exhibit this type of isomerism.

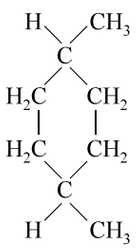


cis-

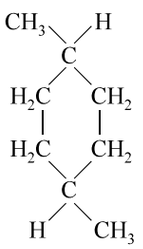


trans-

Cyclobutane-dicarboxylic acid



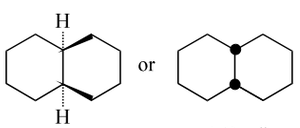
cis-



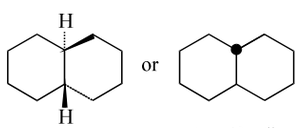
trans-

1,4-Dimethyl cyclohexane

In fused ring systems the rings which are fused through adjacent carbon atoms may be fused in *cis*- or *trans*-positions giving two isomers. For example, decalin exhibits geometrical isomerism:



cis-Decalin



trans-Decalin

(The thick line shows that the bond lies above the plane of the paper whereas dotted line shows the bond below the plane of paper).

(*iii*) **Geometrical Isomerism in Inorganic Compounds:** The coordination compounds usually exhibit geometrical isomerism. In such compounds if the geometry is square planar or octahedral the cis-trans isomerism is observed. For example:

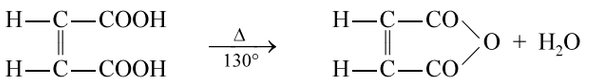
cis- *trans-*

Dichloro-diamino platinum (square planar geometry)

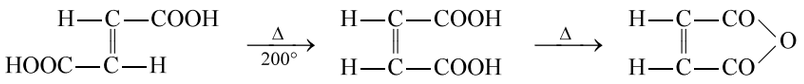
NOTES

(*iv*) **Properties of Geometrical Isomers:** The geometrical isomers are generally two different compounds having appreciable difference in their physical and chemical properties—though the differences in the latter are few. Thus *cis*-isomer, in general have lower melting point and higher values for density, refractive index, dipole moment, etc., as compared to *trans*-isomers.

If the two groups in *cis*-isomer are carboxylic groups then it may form anhydride readily losing a water molecule whereas *trans*-isomer may not form the anhydride unless it is isomerized to *cis*-form. For example, maleic acid readily forms an anhydride whereas fumaric acid first isomerizes to maleic acid at a higher temperature and then forms maleic anhydride.



Maleic acid (*cis*-) Maleic anhydride (*cis*-)



Fumaric acid (*trans*-) Maleic acid (*cis*-)

(*v*) **Determination of Configuration of Geometrical Isomers:** If a given pair of compounds shows geometrical isomerism then it is useful to find out that which one has a *cis* and which one a *trans*-configuration. This assignment of the structure to a pair of isomers is known as determination of configuration. As such, there is not standard method for finding out the configuration of geometrical isomer but by comparisons with known structures certain empirical relationships have been worked out. Determination of some of the physical and chemical properties of a pair of isomers usually gives an idea about the configuration. The following methods are in common use:

(*a*) **Study of the Physical Properties:** The physical properties of *cis-trans* isomers are usually different and show a regular behaviour. Some of these are listed in Table 5.1 below:

Table 5.1 *Physical Properties o as Trans Isomers*

Sl. No.	*Property*	*cis-Isomer*	*Trans-Isomer*[1]
1.	Melting Point	Lower	Higher
2.	Boiling Point	Higher	Lower
3.	Solubility	Higher	Lower
4.	Density	Higher	Lower
5.	Dipole Moment	Higher	Lower
6.	Refractive Index	Higher	Lower
7.	Heat of Combustion	Higher	Lower
8.	Stability	Lower	Higher

NOTES

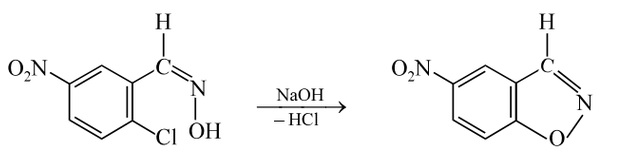
By comparison of some of these properties of the isomers, their configuration may be decided.

Besides these the spectroscopic methods, particularly ultraviolet, infrared and nuclear magnetic resonance are also used to determine the configuration. Thus in UV the *cis*-isomer always absorbs at a lower wavelength and has a lower molar extinction coefficient. In IR the stretching frequency is not shown by *trans*-isomer in general whereas *cis*-isomer shows a strong absorption in the region.

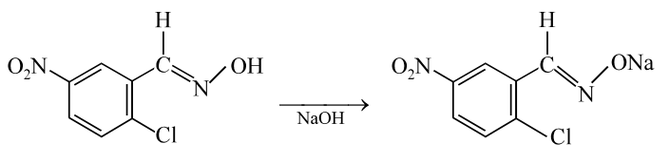
X-ray and electron-diffraction may also be used to determine the configuration of geometrical isomers.[1]

(*b*) *Study of the chemical properties*. Although because of the similarity of the functional groups there is little difference in the chemical reactivities of the geometrical isomer—but still this minor or small chemical difference may be used for the determination of the configuration. Either the method of formation of cyclic derivatives or the method of chemical correlation is used. The former may be illustrated by taking the example of maleic and fumaric acids. The two acids are having the carboxylic groups either in *cis*- or *trans*-positions—the one which is having the two carboxylic groups in *cis*-position will readily lose a water molecule and form the anhydride whereas the isomer which has the two groups trans with respect to each other will not eliminate the water molecule to form the anhydride easily. Thus it has been found that maleic acid loses water to form maleic anhydride readily whereas the fumaric acid does not cyclize easily. Thus maleic acid must have *cis*-configuration.

Similarly out of the two isomers of 2-chloro-5-nitrobenzaldoxime one is readily cyclized on treatment with NaOH whereas the other does not. Obviously the former is *anti*- and the latter *syn*-oxime.



anti-Oxime Indoxazole



syn-Oxime Sodium salt

In the correlation method the compound of unknown configuration is converted to or derived from a compound of known configuration and if it is assumed that no rearrangement occurs, then the configuration of unknown compound must be the same, as that of the known compound. Thus trichlorocrotonic acid on hydrolysis gives fumaric acid, which is known to have trans-configuration, and on selective reduction gives crotonic acid. Thus both crotonic acid and trichlorocrotonic acid must have *trans*-configuration.

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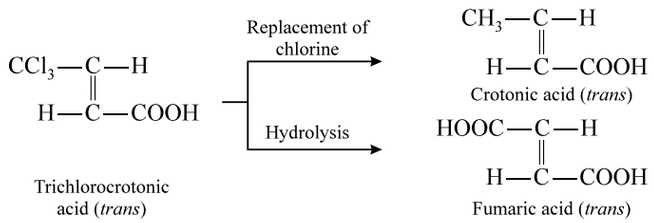
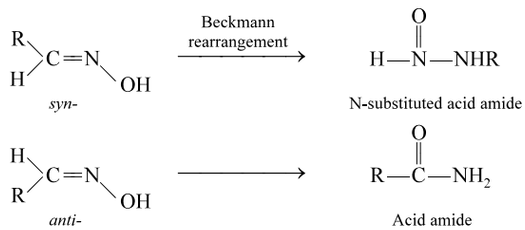
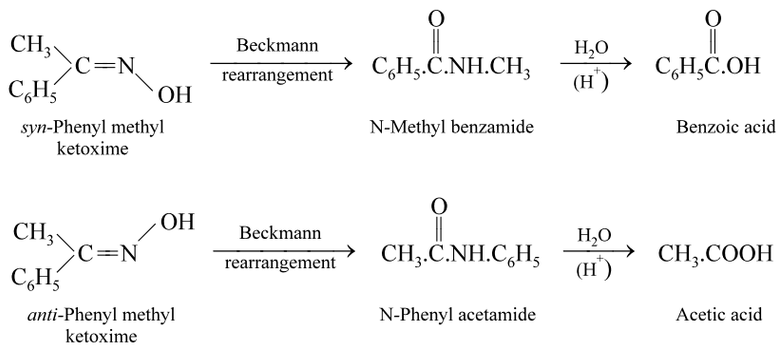


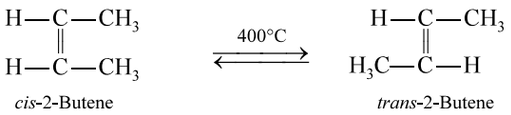
(*c*) **The Configuration of Oximes:** The configuration of oximes is best determined by a rearrangement reaction known as **Beckmann rearrangement** (1886). When an oxime is treated with reagents like acetic anhydride, PCl_5, etc., it is converted to an acid amide or substituted acid amide by a molecular rearrangement. It has been observed that in such rearrangements the alkyl groups, *anti*- to OH groups, migrates to nitrogen preferentially. Thus a pair of isomeric oximes will give different substituted amides.



Thus *syn*-aldoximes give N-substituted acid amides whereas *anti*-aldoximes give acid amides. In case of ketoximes two different substituted amides are obtained which may be distinguished by simple hydrolysis resulting in the formation of entirely different acids.



(*d*) **Interconversion of Geometrical Isomers:** Under suitable conditions geometrical isomers may be converted into each other. This is conveniently done by application of catalysts, heat or U.V. light. In general the ease of interconversion is in the order N = N > C = N > C = C for different types of geometrical isomers. The isomerisation is brought about by rotation around the bond axis which is only possible when the double bond becomes loose or breaks partially to allow such a free rotation. For example, maleic acid may be converted to fumaric acid on heating above its melting point. Similarly butenes can be isomerised by heating.



cis-2-Butene *trans*-2-Butene

NOTES

Optical Isomerism

It has been observed that geometrical isomers show a marked difference in their physical properties accompanied with some differences in their chemical properties as well. The optical isomers, on the other hand, have same chemical and physical properties except that they show a pronounced difference in their behaviour towards *plane polarised light. The property by virtue of which the substances rotate the plane of the plane polarised light is referred to as optical activity.*

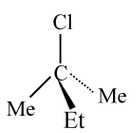
(*i*) **Symmetric, Asymmetric and Dissymmetric Molecules**. An object or molecule is considered symmetric if it possesses a **plane of symmetry, a centre of symmetry** or **an alternating axis of symmetry**. A molecule has a **plane of symmetry** if on passing a plane through it one half of the molecule is the mirror image of the other half or if a line from any atom or group on one side of the plane, drawn perpendicular to the plane and extended to an equal distance on the other side meets a similar atom or group at its end.

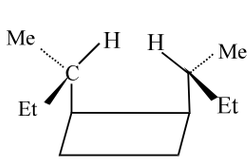
The **Centre of Symmetry** is a point in the molecule passing through which, if a line is drawn, from any atom or group and then extended to equal distance in the opposite direction, meets an identical atom, or group at its end.

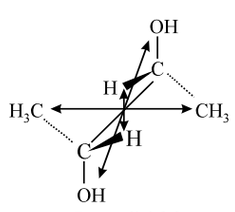
The **Axis of Symmetry** is an axis through which rotation of the molecule, by certain angle, will result in an arrangement indistinguishable or identical with initial molecule.

The **Alternating Axis of Symmetry** is an axis through which if the molecule is rotated by a certain angle and then reflectd across a plane at right angles to the axis, another identical structure is obtained. One-fold alternating axis corresponds to plane of symmetry and the two-fold alternating axis to centre of symmetry.

Symmetrical objects like books, animals, eggs etc., have a plane of symmetry. sp^1, sp^2 hybridized carbon atoms and sp^3 carbons (having at least two identical substituents) too have a plane of symmetry. The sign of swastika 卐 does not have a plane of symmetry but has a centre of symmetry. Some of the molecules having a plane of symmetry, centre of symmetry or alternating axis of symmetry are shown below:







Butanediol-2,3

Fig. 5.3 *Molecules with a Plane of Symmetry.*

Fig. 5.4 *Molecule having Centre of Symmetry (Double Headed Arrows Passing through the Centre Meet Identical Groups on Either Side at Equal Distance).*

NOTES

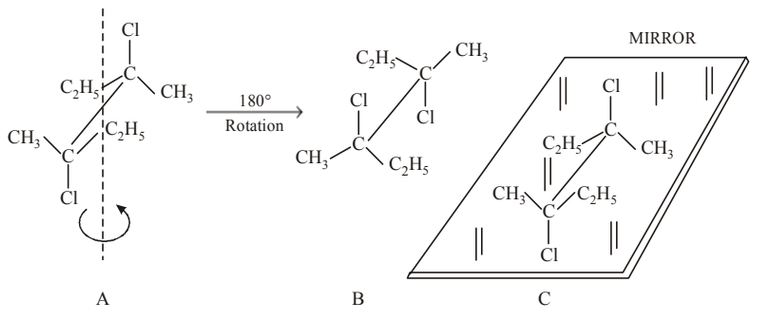


Fig. 5.5 *Molecule having a Two-fold Alternating Axis of Symmetry*

(A) Line passing through the Centre of 3,4-dichloro-3,4-dimethyl hexane,

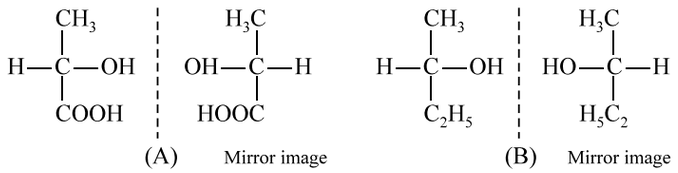
(B) Same as initial compound.

(C) Reflection obtained in a plane perpendicular to the line passing through the centre.

A molecule with no element of symmetry of any kind is **asymmetric**. Objects like hand, tree etc., are asymmetric. *A tetrahedral or sp^3 hybridized carbon attached to four different groups is asymmetric and is known as* **asymmetric carbon atom**. A molecule with no plane of symmetry is known as **dissymmetric**. Dissymmetric molecules may have an axis of symmetry but the main criterion for dissymetry is that a given molecule should not be superimposable on its mirror image. Thus all asymmetric molecules are dissymmetric but all dissymetric molecules are not necessarily asymmetric. **Non-dissymmetric** molecules are superimposable upon their mirror images.

The most commonly cited example of right and left hands is perhaps the best illustration of two objects similar in every respect expect that they are related to each other as object to its mirror image and cannot be exactly superimposed on each other. Thus an object or *a molecule which cannot be superimposed on its mirror image must be assymmetric.* Such a pair of molecules related to each other as an object to its mirror **image** are known as **enantiomorphs** or **enantiomers**.

The terms **chiral** and **achiral** are also used to designate dissymmetric and non-dissymmetric molecules respectively. A *chiral* (Greek, *cheir* meaning *hand*) molecule is not superimposable on its mirror images while *achiral* molecule is superimposable on its mirror image. The *chirality* of the molecules in most cases is due to the presence of a single *chiral* (asymmetric) atom. A chiral atom is any atom devoid of plane of symmetry and is also known as *chiral centre. Enantiomorphs exist only in case of chiral molecules.* Therefore the ultimate test for chirality is that the molecule should be non-superimposable on its mirror image. Thus a molecule will not be chiral if it possesses a plane of symmetry. Molecules shown below are chiral because they cannot be superimposed on their miror images.



(*ii*) **Optical Activity:** Most of the physical and chemical properties of the optical isomers are identical. Since the phenomenon of optical isomerism is caused by the asymmetry of the molecules, the detection of the difference in the properties can be measured only when an asymmetric measuring tool is used. The most common of such a tool is plane-polarized light.

Plane Polarized Light: Light is propagated by a wave motion. The vibrations of the waves are perpendicular to the direction of propagation and are symmetrical about the line of propagation. Thus if an imaginary cross-section of a beam of light is examined it will be observed that these vibrations occur in all directions at right angles to the line of progagation. Ordinary light is thus having symmetry. However if such a beam of light is passed through a Nicol prism, the resulting beam has all waves vibrating in the same plane. *Light, whose vibrations occur in a single plane only, is known as* **plane polarised light** *and the phenomenon is known as* **polarization**.

When plane polarized light is passed through certain substances or their solutions its plane of polarization is rotated either towards right (clockwise) or towards left (anticlockwise) by a certain angle. *The substances which rotate the plane of polarization of the plane polarized light are known as* **optically active** *and the phenomenon is referred to as* **optical activity**. Those substances which rotate the plane of polarized light to right or clockwise are called **dextro-rotatory** indicated by the sign '*d*' or (+) and those which rotate it to the left or anticlockwise are called **laevo-rotatory** indicated by sign '*l*' or (–).

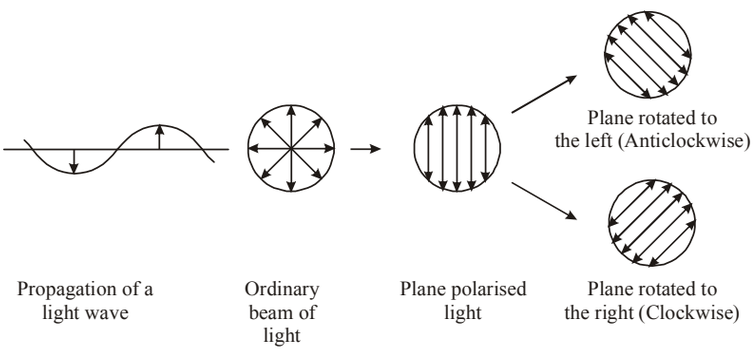


Fig. 5.6 *Imaginary Cross-sections of Light Beams*

NOTES

The extent or angle of rotation depends on the following factors:

- Nature of the substance.
- Wavelength of the light used.
- Concentration of the solution (if substance is taken in solution).
- Thickness of the layer or length of path through which polarised light passes.
- Nature of solvent (for solutions only).
- Temperature of measurement.

The apparatus used to measure the optical activity is known as polarimeter and has been schematically represented in Figure. 5.7.

The measurement of optical activity is reported in terms of specific rotation which is a constant; characteristic for a particular substance,

$$\text{Specific rotation } [\alpha]_{\lambda}^{t^{\circ}C} = \frac{\alpha_{obs.}}{l \times c}$$

where α_{obs} is the rotation observed, l is the length of solution in decimetres, c the concentration is grammage of substance in 1 ml of solution.

Specific rotation is equal to observed rotation in degrees when the polarised light passes through one decimetre (or 10 cm) of the solution of the substance having the concentration of one gram per millilitre. It is calculated by the expression given above. Usually for measurement purposes the light used is the sodium D line corresponding to 589 mμ wavelength. It is also necessary to mention the solvent, if any, used for measurement. Thus the specific rotation of sucrose may be represented as:

$$[\alpha]_{D}^{20^{\circ}} = +66.5^{\circ} \text{ (Water; Concn. 0.02 g/ml)}$$

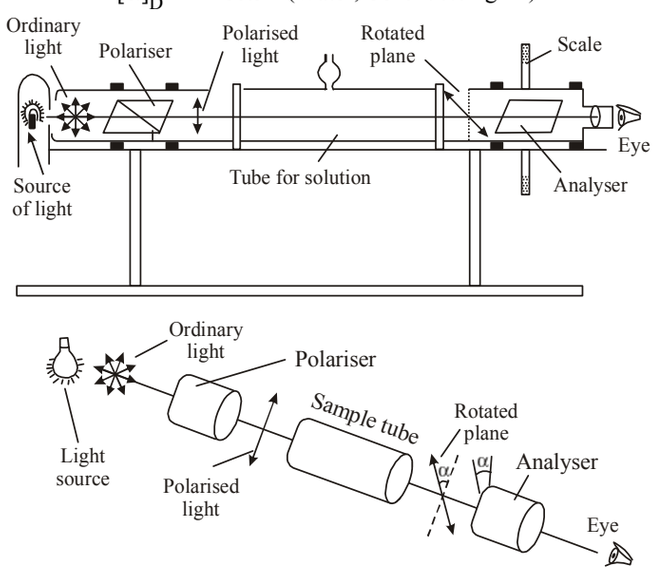


Fig. 5.7 *Schematic Representation of a Polarimeter.*

Here 'D' stands for the sodium D line wavelength, 20° is the temperature of measurement in °C, the sign (+) stands clockwise or dextro-rotation and the solvent is water. The electrical effects between solute and solvent molcules may cause considerable variations in the value of specific rotation, hence the solvent and the concentration of measurement is also mentioned in parentheses. Similarly the specific rotation of the two forms of phenyl lactic acid may be written as:

$$[\alpha]_D^{20^\circ} = +52.0^\circ \text{ (Water; Concn. 0.02 g/ml)} \text{ (Dextro-rotatory)}$$

$$[\alpha]_D^{20^\circ} = -52.0^\circ \text{ (Water; Concn. 0.02 g/ml)} \text{ (Laevo-rotatory)}$$

Just as (+) sign stands for dextro or clockwise rotation, the (–) sign indicated anticlockwise or laevo-rotation.

(*iii*) **Cause of Optical Activity**. Pasteur had suggested that optical isomerism arises from molecular dissymmetry. In 1874, the French chemist Le Bel and Dutch chemist van't Hoff almost simultaneously and independently, tried to explain the cause of optical activity.

Le Bel and van't Hoff suggested that the optical activity of substances in solutions or in liquid state depends upon the asymmetry of the molecule. According to them a carbon atom is supposed to be situated at the centre of a imaginary regular tetrahedron and its four valencies are directed towards its four corner. Now if four different atoms or groups are attached to a carbon atom the molecule becomes asymmetric. Hence if a substance has at least one asymmetric carbon atom it will be optically active. However, the presence of asymmetric carbon atoms may not make a compound necessarily optically active; what is essential is the asymmetry of the molecule as a whole.

Let there be a carbon atom having four different atoms or groups *a*, *b* and *x* and *y* attached to its valencies at the four corners of the regular tetrahedron. Obviously two arrangements are possible which will be related to one another as an object to its mirror image. They will not be superimposable upon each other.

The arrangement of groups is different in Figure. 5.8 (I) and (II). For example if one has to go from '*a*' to '*y*' through '*b*' and '*x*', one will have to go in clockwise direction in structure I and in anticlockwise direction in structure II. Again if one tries to superimpose structure I over

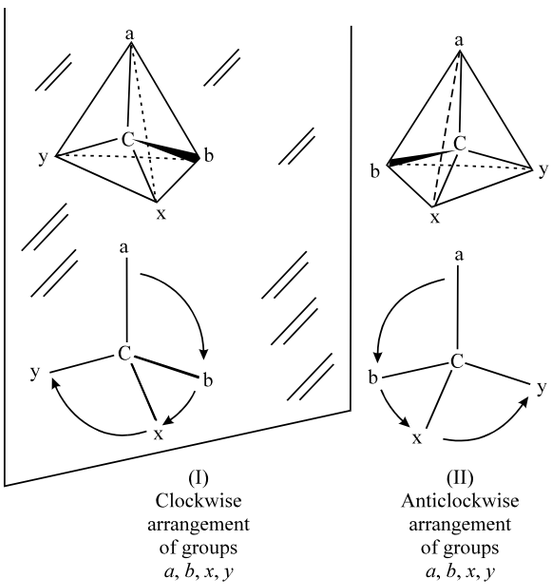
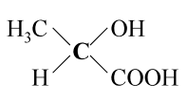


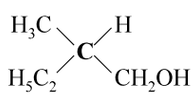
Fig. 5.8 *Two Arrangements of Groups at Asymmetric Carbon show Relation as Object and its Mirror Image*

structure II group '*a*', '*x*' and '*b*' will overlap each other but group '*y*' from each one of the structures will go on opposite sides. Clearly the two models represent two isomeric spatial arrangements or two compounds having different configuration. The compounds represented by structures I and II are enantiomers.

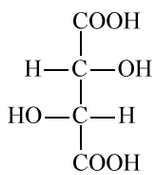
Now it has been proved beyond doubt that optical activity is due to aymmetric character of the molecule, whether the asymmetry is due to the presence of any asymmetric carbon atom or due to some other reason. The formulae of a few compounds are given below and each has at least one asymmetric carbon atom, and hence optically active. (Asymmetric carbon atoms are in thick type.)



Lactic acid

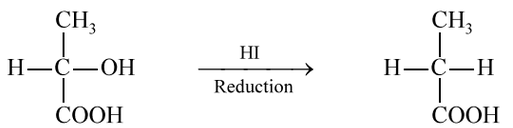


Amyl alcohol



Tartaric acid

If the asymmetric character of any of the above molecules is changed the compound becomes inactive *e.g.*, if lactic acid is reduced it gives propionic acid, which is optically inactive.



(No asymmetry)

NOTES

The number of optical isomers are given by 2^n where n is the number of asymmetric carbon atoms. Thus if there is one such carbon atom the number of isomers must be ($2^1 = 2$) two only, similarly for two asymmetric carbons the number of isomers will be ($2^2 = 4$) four and for three ($2^3 = 8$) it will be eight and so on. If the nature of asymmetic carbon atoms is same (*i.e.*, the groups attached to them are same) then the number of optically active isomers is considerably less than predicted by this formula. For example, if a compound is having two dissimilar asymmetric carbons A and B then the isomers possible are

(1) + A + B (2) – A – B
(3) + A – B (4) – A + B

} + and – sign indicate dextro or laevo rotation of asymmetric carbon atoms.

Here + A and + B are the mirror images of – A and – B respectively. So + A + B and – A – B is a pair of enantiomorphs. Similarly + A – B and – A + B constitute another pair of enantiomorphs. But + A + B and + A – B or – A + B are not related as object and mirror images of each other—though they are isomeric and similarly – A – B and + A – B or – A + B are also not enantiomorphs. The isomers which are not related to each other as object and also not enantiomorphs. The isomers which are not related to each other as object and mirror images are known as **diastereoisomers**. These may differ in physical and chemical properties.

A compound having two similar asymmetric carbons A and A may have following isomers:

(1) + A + A (2) –A –A (3) + A –A or – A + A

Let the first one be dextro-rotatory, then the second will be laevo-rotatory. The third will have a plane of symmetry and therefore will be optically inactive despite the presence of two asymmetric carbon atoms. The optical inactivity in the molecule + A – A has arisen due to equal and opposite activity of each half of the molecule. Thus the optical inactivity has come due to the compensation of the activity of one half by the other half and this is known as the *internal compensation*. Such molecules which are optically inactive due to internal compensation are called *meso*-form (or *m*-form).

The optical inactivity could also arise due to the presence of equal amounts of the dextro and laevo forms when the compound is prepared or obtained by mixing the *d*- and *l*-forms in equal molecular proportions. This inactivity is due to equal and opposite optical activity of each isomer and therefore is regarded as arising from *external compensation.* Such a mixture is called the *dl* or (±)-form.

These two inactive forms, m- and dl-, differ in the fact that whereas the dl-form could be resolved into the ***dextro*** *and* ***laevo*** *forms, it is not possible to do so with meso-form*.

While writing the configuration of the optical isomers a three dimensional (tetrahedral) structure is represented in the planar form on the paper. The two important methods for such planar representations are:

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- Perspective formula
- Fischer projection formula

In the perspective formula two groups attached to carbon atom are shown to be coplanar with it while a dotted line represents the bond and atom (or group) below the plane of the paper and a heavy thick line represents and the bond and atom (or group) above the plane.

In the representation of stereoisomers by Fischer projection formula the three dimensional molecule is considered such that the groups written to left and right of asymmetric carbon atom are projected from above the plane of paper. Similarly the groups written above and below asymmetric carbon atom are projected from beneath the plane. Figure 5.9 shows the representation of a pair of enantiomers by perspective and projection formulae. The two sets of formulae A, B and C, D correspond to each other and are represented in perspective and projection form.

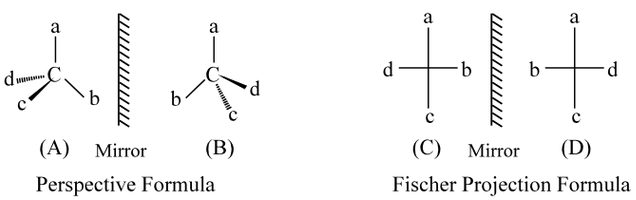


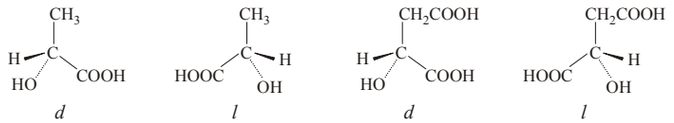
Fig. 5.9 *Representation of Asymmetric Molecules*

While using Fischer projection formulae the following rules must be kept in mind:

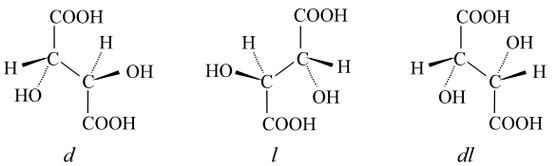
- Fischer projection formulae should not be taken out of the plane but can be rotated by 180° in the same plane. Rotation of formula by any other angle leads to change in configuration.
- The groups attached to asymmetric carbon atom may be interchanged clockwise or anticlockwise. The interchange of two groups changes the configuration forming enantiomer of original. Thus any odd number of interchange of groups (exchanging position of two groups is one interchange) changes the configuration while even number of interchanges do not change the original configuraton.

  Perspective formulae are used for compounds having one or two asymmetic (chiral) carbon atoms but when many such atoms are present then Fischer projection formulae are more convenient.

(*iv*) **Compounds with Asymmetric Carbon Atoms:** Compounds like lactic acid, malic acid, tartaric acid, amyl alcohol etc., possess asymmetric carbon atoms and exhibit optical isomerism because of the asymmetric carbon they possess. They may be represented as follows:



Lactic acids Malic acids



Tartaric acid

(*v*) **Compounds with Asymmetric Atoms other than Carbon:** Atoms which resemble carbon in the arrangement of valencies may behave in a similar manner when four different groups are attached to them. Thus quaternary ammonium salts, compounds of phosphorus, arsenic, antimony etc., have been shown to be optically active because of the N, P, As and Sb atoms, respectively. Methyl ethyl propyl phenyl quaternary ammonium chloride is an optically active compound containing tetravalent nitrogen.

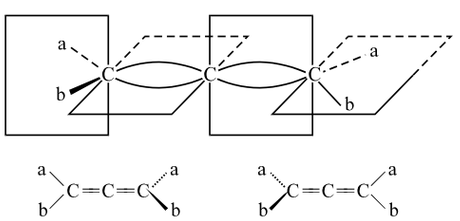
Methyl Ethyl Propyl Phenyl Quaternary Ammonium Chloride

(*vi*) **Compounds having no Asymmetric Carbon Atoms:** Many compounds have no asymmetric carbon atoms, nevertheless they are optically active because the molecule as a whole is asymmetric or chiral. The condition arises because of restricted rotation in the molecule giving rise to perpendicular dissymmetric plane. For example compounds of the type of allenes, spiranes and biphenyls exhibit optical isomerism though there may not be any asymmetric carbon atom in the molecule.

(*a*) **Allenes:** May be respresented by a general formula,

$$ab.C = C = C.ab$$

where *a* and *b* are different groups. Isomeric allenes where *a* is C_6H_5 and *b* is $C_{10}H_7$ have been separated.



Isomeric allenes

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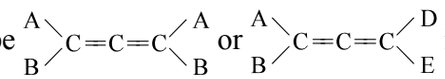
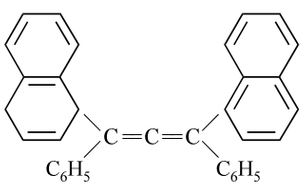
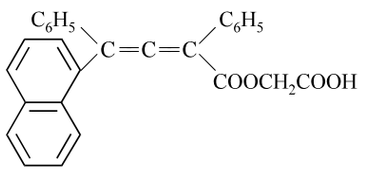
The central carbon atom of allenes is '*sp*' hybridised and has two unhybridised *p*-orbitals perpendicular to each other. Remaining two terminal carbon atoms are 'sp^2' (trigonal) hybridised, each having one unhybridised *p*-orbital. The two '*sp*' hybrid orbitals of central atom form sigma (σ) bond with sp^2 hybrid orbitals of each of the two terminal carbon atoms.The remaining two *p*-orbitals (which are perpendicular to each other) of the central atom ovelap laterally with the available *p*-orbitals of the terminal carbon atoms forming two pi (π) m.o.'s which are perpendicular to each other, one lying in the plane of the paper and the other perpendicular to the plane of the paper as shown in the structure above.

Geometry of allenes of the type  is such that Groups (A, B) at one terminal carbon become perpendicular to the groups (A, B or D, E) at the other terminal carbon atom. Therefore the mirror image of such a molecule is not superimposable on it. The molecule becomes chiral and hence it will exists in two enantiomeric forms.

Mills and coworkers (1935) resolved dinaphthyldiphenylallene (I) by catalytic asymmetric dehydration of 1,3-di-1-naphthyl-1,3-diphenylprop-2-enol. Kohler *et al*. (1935) resolved the ester of 3-(1-naphthyl)-1,3-diphenyl-allene-1-carboxylic acid (II) using brucine.

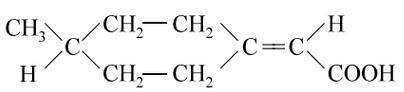


(I)



(II)

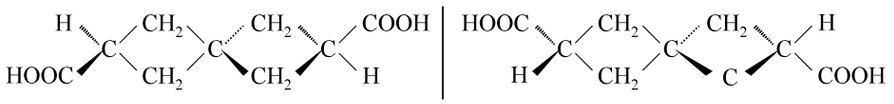
If one of the double bond of allene is replaced by a ring, the geometry of resultant molecule remains identical to that of original allene. Such a molecule is chiral and non- superimposable on its mirror image. Pope *et al.* have resolved 4-methylcyclohexylidene-1-acetic acid (III)



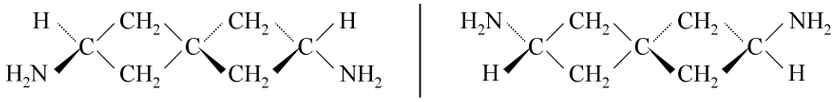
(III)

(*b*) **Spiranes:** These are bicyclic or polycyclic systems having one carbon atom common to two rings. (Spiranes are compounds in which a C-atom, is bound to 4 other C-atoms, in such a way that each belongs to a ring.) Again because of restricted rotation two rings of spirane become perpendicular to each other and consequently there is no element of symmentry in suitably substituted spirane. Such a molecule has no element of symmetry and is chiral and will not be superimposable on its mirror image.

Backer *et al*. (1928) resolved spiro (3.3) cycloheptane carboxylic acid (IV) and Pope *et al*. (1932) resolved 2,6-diamino dispiro (3.3) heptane (V)



(IV) Spiro (3.3) cycloheptane carboxyhc acid

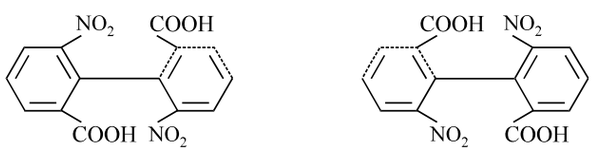


(V) 2,6-Diaminospiro, (3,3)-heptane

These two compounds are non-superimposable on their mirror images and hence show optical activity.

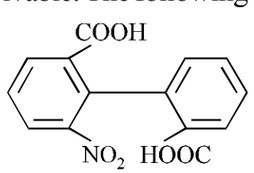
(*c*) **Biphenyls:** It has ben shown by physico-chemical studies that biphenyls are planar and the two rings are coaxial and linear.

However the bulky groups in ortho position of biphenyls prevent free rotation around carbon to carbon bond joining the two benzene rings. This restricted rotation prevents the two rings from acquiring the coplanarity and a situation similar to allenes or spiranes gives rise to optical isomerism in the derivatives of biphenyls. Stereoisomers resulting from hindered rotation around a single bond (where the barrier to rotation is high enough for their isolation) are called atropisomers and the phenonenon as *atropisomerism*. Atropisomers display axial chirality and differ from other chiral compounds in that they can be equilibrated thermally. The most important class of atropisomers is biphenyls. When the two rings are suitably substituted optical activity is observed, for example, Kenner *et al*. (1927) resolved 2,2′-dinitro-6,6′-diphenic acid, which does not have an asymmetric carbon atom but the miolecule as a whole is chiral.

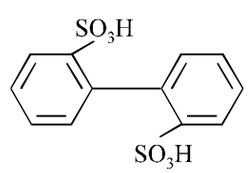


2,2′-Dinitro-6,6′-diphenic acid

Turner *et al*. (1932) have shown that if the groups are sufficiently bulky then even tri-, di-and even monosubstituted biphenyls may have restricted rotation and hence resolvable. The following compounds have been resolved.



2-Nitro-6,6′-diphenic acid



Biphenyl-2,2′-disulphonic acid

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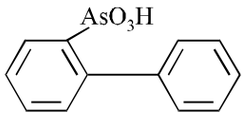
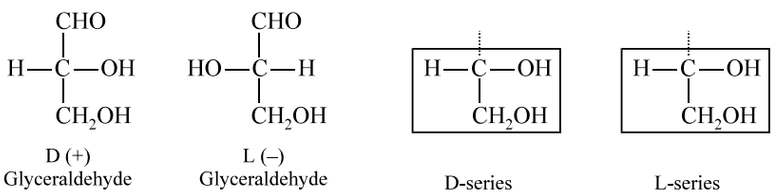


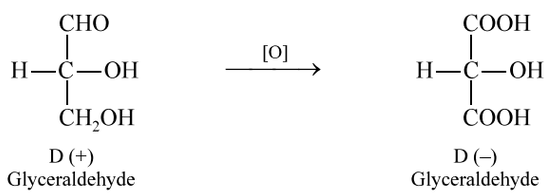
Biphenyl-2-arsonic acid

In these cases bulky, sulphonic acid group or arsonic acid group interact a with H— of the other ring to cause restricted rotation. Hence the two rings become non-coplanar and the molecules becomes non-superimposable on its mirror image and therefore are resolvable.

(*vii*) **Configuration: Relative and Absolute Configuration:** Arrangements of groups or atoms in space in a molecule is referred to as its configuration. It has been seen in the previous section that compounds with asymmetric carbon atoms can have different configurations—each of which belongs to different optical isomer. Thus for lactic acid dextro (*d*) and laevo (*l*) enantiomorphs are known and out of the two possible configurations one is of detro lactic acid and the other of laevo lactic acid. Fischer, however, thought that it is more important to indicate the stereochemical relationship than merely to indicate the actual direction of rotation. To solve this problem of assigining the configuration it was suggested by Rosanoff that glyceraldehyde be chosen as standard and a configuation be assigned to its arbitrarily. Accordingly the two forms of glyceraldehyde were assigned the following congfigurations and labelled as 'D' and 'L' glyceraldehyde respectively.



All those compounds which have genetic relationship with 'D'-glyceraldehyde in configuration belong to D-series. Similarly those which have configurational similarity with standard 'L'-glyceraldehyde molecule must belong to L-series. Hence by prefixing 'D' or 'L' before the name of a compound we can immediately specify its configuration. The configuration of an optical isomer when established in relation to some compound of known configuration (as glyceraldehyde) is termed as its **relative configuration**. For example D-gylceraldehyde can be converted to glyceric acid by simple oxidation and, therefore, the configuration of glyceric acid obtained must be 'D'.

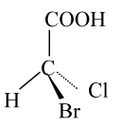


It must be borne in mind that this 'D' or 'L' prefix does not indicate the direction of rotation to be 'dextro' (+) or 'laevo' (–) but only shows the configuration at asymmetric carbon atom. The actual direction of rotation is usually written after D or L, it being (+) for dextro and (–) for laevo. Also it is not necessary that molecules with the same configuration should have the same direction (whether dextro or laevo) of rotation. Thus D-glyceric acid is laevorotatory, whereas D-glyceraldehyde is dextro-rotatory.

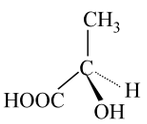
The *absolute configuration* of 'D' and 'L' glyceraldehydes could be verified experimentally only in 1951 by the use of asymmetric X-ray crystallography and other physical techniques. As a result, it has now been established that the arbitrary choice of Rosanoff was correct. The determination of absolute configuration is a very tedious and time-consuming affair. Therefore it is convenient to obtain the configuration of optically active compounds by relating it to known standard configuration. However, this system, of relating the configurations has a basic defect that sometimes the configuration of the same molecule may be related to both 'D' and 'L' series. Also it is difficult to apply it to molecules having complicated structures and more than one asymmetric carbon atoms.

R and S System: To overcome these and such other difficulties of this system Cahn, Ingold and Prelog gave a new convention for specifying the configuration of asymmetric carbon atoms. This is also known as *Rectus* (*Latin*, meaning right) and *Sinister* (*Latin*, meaning left) system, and is often abbreviated as 'R' and 'S' system. In this system the atoms joined to the asymmetric C-atoms directly are arranged in a sequence. The important sequence rules are:

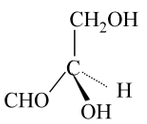
1. The order of priority or sequence is determined on the basis of the atomic numbers of the atoms joined directly to asymmetric C, the greater the atomic number the higher the order.



Chloro bromo acetic acid
(H = 1, C = 6, O = 8, Cl = 17, Br = 35)



Lactic acid



Glyceraldehyde

Thus in chloro bromo acetic acid the priority will be:

$$Br > Cl > COOH > H$$

2. If two or more atoms attached to asymmetric carbon atom are same then the atoms next to those similar atoms are taken into consideration for determination of the priority order. If these are also the same then the third atoms are taken into consideration, and so on, till the ambiguity about preference is resolved. Thus for $— CH_3$ and $—CH_2.CH_3$, the order of priority will be $— CH_2. CH_3 > — CH_3$ because in methyl C— is joined to H, H, H whereas in ethyl it is joined to C, H and H.

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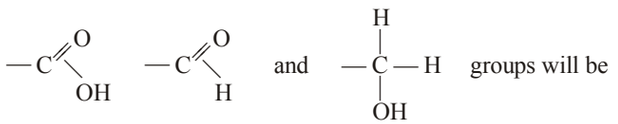
3. For determining order of priority, multiple bonds are treated as separate single bonds. Thus H—C═O is regarded as carbon linked to 2 oxygen and 1 hydrogen. The order or priority of

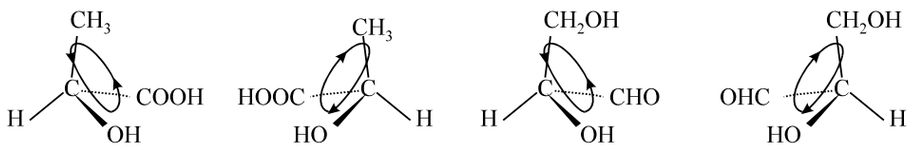


—COOH (2O + 1O) > — CHO (2O + 1H) > — CH_2OH (2H + 1O)

Applying these rules the order of priority of groups and atoms in lactic acid will be OH > COOH > CH_3 > H and in glyceraldehyde OH > CHO > CH_2OH > H.

After fixing the priority order of the groups joining the asymmetric C atoms the tetrahedral perspective formula of the isomer is viewed from the side opposite to the group of lowest priority and the arrangement of rest of the groups is observed. If the arrangement of groups, in going from top priority group to second and then to the third priority group, is in clockwise direction, the configuration is considered as 'R' or rectus configuration. If this arrangement is in anti-clockwise direction, the configuration is termed as 'S' or sinister configuration.

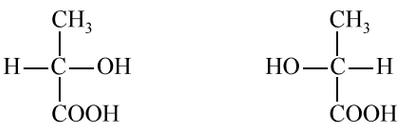
In the figures below the molecule may be visualized as steering wheel of a car with lowest priority group as steering rod and other three groups around the wheel.



d-Lactic acid S-Configuration | *l*-Lactic acid R-Configuration | S-Glyceraldehyde | R-Glyceraldehyde

The racemic modification is termed as RS compound. This system is thus very convenient for writing the absolute configurations of the compounds, however, it does not give any indication of the actual direction of rotation.

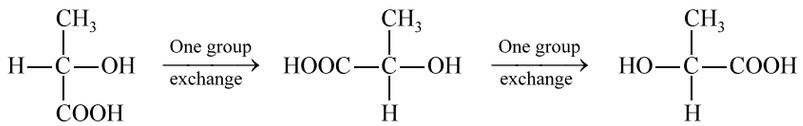
Thus, the optical isomer must be represented by a tetrahedral, perspective, or projection formula as the planar representation will not give a correct idea of the molecule. However for the sake of convenience planar formulae are still extensively used for writing the configurations of optical isomers. In fact, so long as the planar formulae are kept in the plane of paper, they remain non-superimposable. Thus lactic acid may be conveniently represented as:



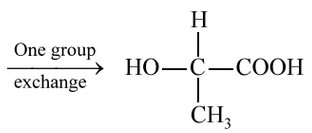
d-Lactic acid | *l*-Lactic acid

Fischer Projection Formulae

The planar configuration of optically active compounds is referred to as Fischer projection formula. So long as these structures are not taken out of the plane of paper they serve the same purpose as perspective formulae. In Fischer projection structures the group on the left and right are considered to be projected above the plane of paper and those on top and bottom are considered to be below the plane of paper. Any odd number of interchanges of groups in these formulae results in isomeric structures while even number of exchange of groups results in the structure of same isomer. For example,

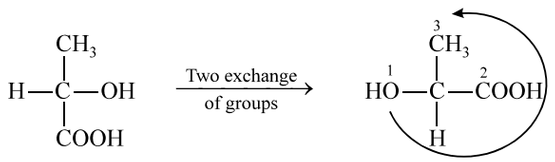


d-Lactic acid *l*-Lactic acid *d*-Lactic acid



l-Lactic acid

To specify RS configuration in a Fischer projection formulae exchange even number of groups to bring least priority group to the bottom and then determine the sequence of remaining groups in usual way to assign R or S configuration.



d-Lactic acid *d*-Lactic acid (Anticlockwise, hence S-configuration)

Erythro and Threo Nomenclature System

Erythro and Threo system of specifying configuration originated from tetraldoses erythrose and threose which are diastereoisomers.

D (–) Erythrose D (–) Threose

Thus any compound having two dissimilar chiral carbon atoms may exist in four isomeric forms. Of these isomers having identical groups on same side are termed as *erythro*-isomer while those having similar group on opposite side are

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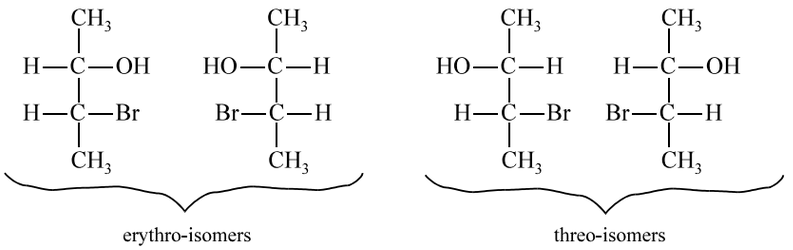
termed as *threo*-isomer. Thus isomers of 3-bromo-2-butanol may be designated as erythro- or threo- as follows:

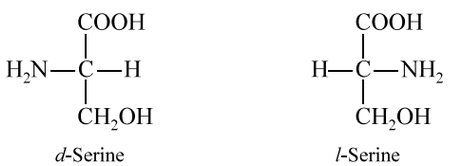


(*viii*) **Compounds with One Asymmetric Carbon Atom**

(*a*) **Stereochemistry of Lactic Acid:** Compounds like lactic acid, malic acid etc., contain one asymetric carbon atom and hence can have two configuration, one of these being dextro and other laevorotatory. These are related to each other as object and mirror image and, therefore, constitute a pair of enantiomorphs. Their configurations have been shown earlier.

Compounds containing one asymmetric carbon also occur in an optically inactive form which in fact is a mixture of equal amounts of '*d*' and '*l*' varieties and is known as *racemic* or *dl* or (±) forms. However this form can be separated into '*d*' and '*l*' forms and such type of optical inactivity is said to be because of *external compensation.*

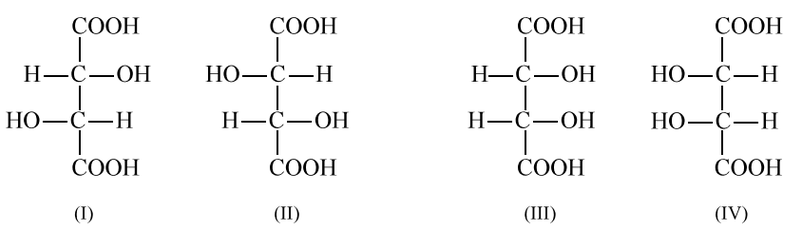
(*b*) ***Stereoch Emistry of Serine:*** Serine is an amino acid which contains an asymmetric carbon atom and hence exists in two forms: *dextro* and *laevo*. These are related to each other as object and its mirror image and are thus enantiomorphs. However naturally occurring serine is laevorotatory.



A third form of serine is a mixture of *d*- and *l*-forms which is optically inactive due to external compensation and is called racemic or *dl*-form.

(*ix*) **Compounds with Two Asymmetric Carbon Atoms**

Stereochemistry of Tartaric Acid: Tartaric acid contains two asymmetric carbon atoms which are similar to each other. Theoretically the number of possible isomers is $2^2 = 4$ and they may be represented as:



Of these Formulae I and II are related to each other as object and mirror image and are thus enantiomorphs. Similarly III and IV are related as object and mirror images but when one of these is rotated through 180° they become identical. Thus for tartaric acid only three different arrangements may be visualised.

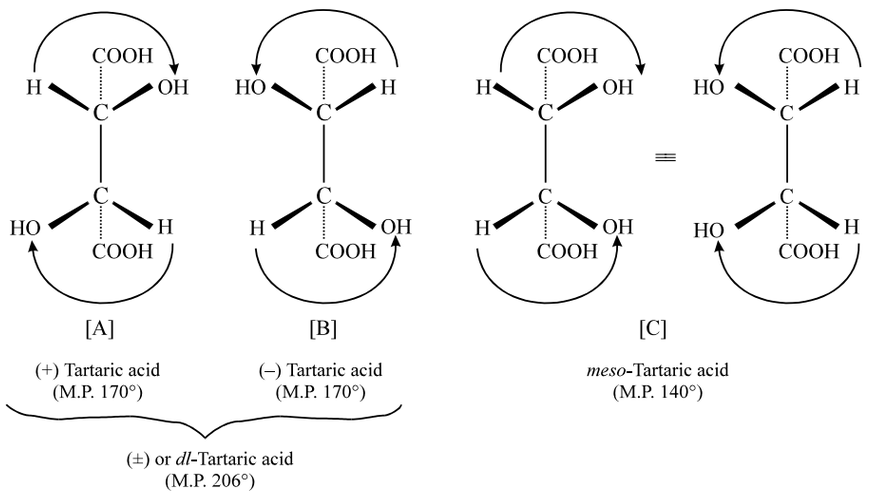


Fig. 5.10 *Different forms of Tartaric Acid*

The Formulae A and B are enantiomorphs to each other whereas A and C or B and C are not related to each other as object and mirror image and so constitute pairs of diastereoisomers. The formula C has a plane of symmetry and is thus optically inactive.

If it is considered that the force which rotates the plane of plane polarised light operates from —H to —OH via — COOH groups (Reger Figure. 5.10), then structure A will rotate it in clockwise directioin and will be *d*-tartaric acid and the structure B will rotate it in anti-clockwise direction and will represent *l*-tartaric acid. However, in case of structure C one asymmetric carbon atom is rotating it in clockwise direction whereas the other equally in an anticlockwise direction and thus the isomer becomes optically inactive.

This optical inactivity in the molecule C has arisen because of equal and opposite rotation by two similar asymmetric C-atoms of the same molecule. In other words, we can say that the dextrorotation of one-half of the molecule is compensated by the laevorotation of the other half. Since this compensation comes from within the molecule itself; the molecule is said to be inactive due to **internal compensation**.

Besides these three forms, tartaric acid also occurs in a racemic or *dl* or (±) form which is inactive because of *external compensation*. Melting points and densities of the meso- and racemic forms differ considerably from those of *d*- and *l*- forms.

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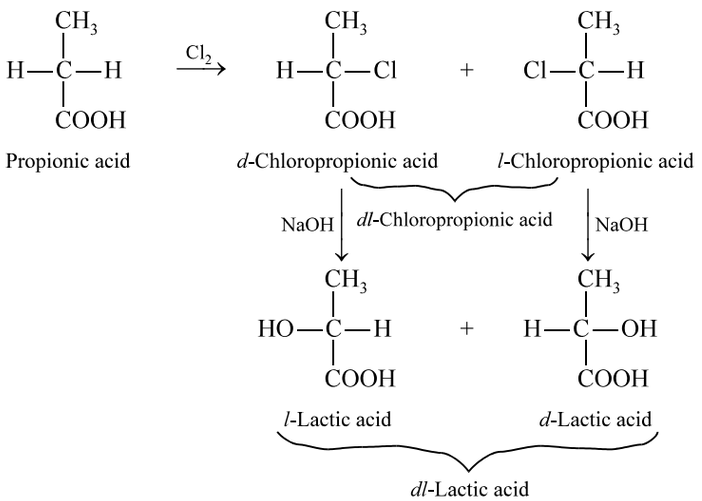
Resolution

In the laboratory synthesis of compounds containing asymmetric carbon atom the product is almost an equal mixture of two enantiomorphs *d* and *l*. Even when the starting material is racemic mixture or an optically active compound, the product obtained is racemic, hence inactive. On the other hand, asymmetric compounds in nature always occur in optically active form.

Thus if propionic acid is converted to chloropropionic acid in the laboratory, it will result in the formation of *dl* or (±) chloropropionic acid. Similarly if (±) chloropropionic acid is hydrolysed to give lactic acid, the later also is obtained in racemic form. The reason for this is that in the conversion of propionic acid to its chloro derivative a hydrogen is replaced by chlorine and there are two such hydrogens identically placed in the molecule. The replacement of one of these hydrogens gives one enantiomorph. Since the chances of the substitution of the two hydrogens are equal, the product is a racemic mixture, for example,



If the hydrolysis of chloropropionic acid proceeds by S_N2 mechanism it is accompanied with inversion of configuration and the *d*-form will be converted to *l*-lactic acid whereas the *l*-form will be converted to *d*-lactic acid. Since the two forms of chloropropionic acid are present in equal amounts the product in this case also is a mixture of equal amounts of the two enantiomorphs and therefore racemic.

The separation of a racemic (dl) mixture into the component d- and l-enantiomorphs is termed as resolution. Since most of the chemical and physical properties of enantiomorphs are same they cannot be separated by general methods of separation like fractional distillation, fractional crystallization etc. The methods commonly used for resolution are:

(*i*) **Mechanical Resolution:** Pasteur in 1848 used this method to demonstrate that racemic tartaric acid was actually a mixture of *d*- and *l*-acid. The method is

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thus of historical importance and can be applied to those solids only which form two types of well defined crystals. These crystals are also related to each other as object and mirror images and can be seen under a magnifying glass and picked mechanically.

However, only a few compounds are known to form such well defined crystals and besides the method is very laborious.

(*ii*) **Biochemical Resolution:** Pasteur in 1858 observed that when certain micro-organisms were allowed to grow in the solution of a racemic mixture of certain compounds, they consumed preferentially only one stereoisomer, leaving the other in the solution. The form left over in solution can be isolated by fractional crystallization. For example, *dl*-tartaric acid, when treated with micro-organism P. glaucum is converted to *l*-tartaric acid because *d*-tartaric acid is consumed by the organism.

However, the method has only limited application because it is not easy to find the proper organism which may consume one of the isomer in preference to the other. Another drawback of the method is that one-half of the compound is consumed. The poisonous enantiomers cannot be separated by this method because no micro-organism can consume poisonous compounds.

(*iii*) **Chemical Method of Conversion to Diastereoisomers:** This method is also due to Pasteur (1858). He noticed that though the enantiomorphs have the same physical properties, diastereoisomers differ significantly in their physical properties. Therefore, racemic mixture may be resolved by converting them to diastereoisomers, by reaction with an asymmetric substrate, and then resolving diastereoisomers by taking advantage of the difference in their physical properties like solubility. The separated diastereoisomers may be converted to optically active compounds. For example (±) lactic acid when treated with *l*-brucine will give two diastereoisomers which may be resolved by taking advantage of differential solubility. Hydrolysis of diastereoisomers yields the optically active product.

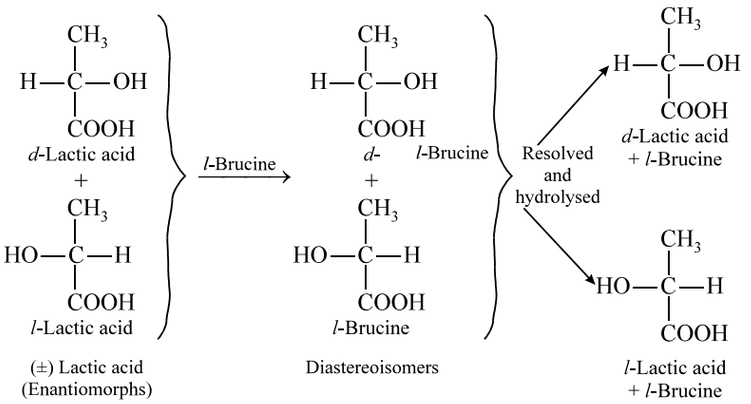
The bases used for the resolution of *dl*-acid mixtures are (–) quinine, (+) cinchonine and (–) strychnine, etc.

Similarly, for the resolution of bases an optically active acid may be used. The acids used are (+) tartaric acid, (–) malic acid, (–) mandelic acid etc. The following scheme will make the point clear.

$$dl\ \text{Base} \xrightarrow{d\text{-Acid}} \left\{\begin{array}{l}(1)\ d\text{-Base-}d\text{-Acid}\\(2)\ l\text{-Base-}d\text{-Acid}\end{array}\right\} \xrightarrow[\text{and hydrolysed}]{\text{Resolved}} \begin{array}{l}d\text{-Base} + d\text{-Acid}\\l\text{-Base} + d\text{-Acid}\end{array}$$

The method is most commonly used but is applicable mainly to acids and bases. Compounds like alcohol and aldehyde may also be resolved by this method by conversion to diastereoisomeric esters and hydrazones respectively.

NOTES



(*iv*) **Differential Adsorption Method:** When a racemic mixture in the solution form is placed on chromatographic column containing optically active substances like starch, quartz etc., then the enantiomorphs will move down the column at different rates and thus can be separated because of the adsorption selectivity of the adsorbent. The *dl*-mandelic acid has been resolved by adsorption over starch. This method eliminates the necessity of converting the *dl*-mixture to diastereoisomer.

(*v*) **Differential Reactivity or Kinetic Method:** The enantiomorphs react with optically active substances at different rates. Therefore, in some cases it is possible to obtain a separation (usually partial) by stopping the reaction before it acquires equilibrium. However, this method results in only partial resolution and is similar to asymmetric synthesis.

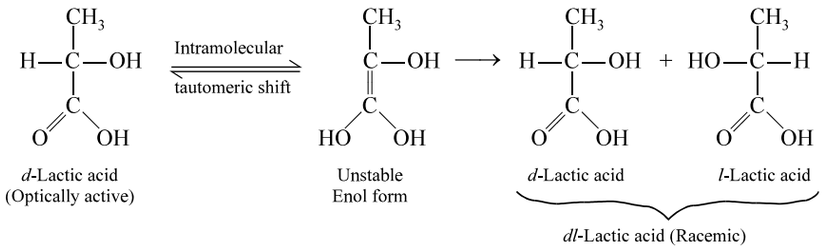
Racemisation

During his researches on stereochemistry Walden observed that many optically active substances when kept for long time tend to become racemic mixtures. Later on it was found that application of heat, light etc., to the optically active compounds, may result in the loss of their optical actrivity. *This conversion of dextro or laevo compounds to their racemic (dl) forms is known as* **Racemisation**.

Racemisation occurs through some intramolecular rearrangement caused by light, heat or catalysts. Because of this rearrangement the optically active compound exists temporarily in equilibrium with this rearranged product. The latter does not have an asymmetric centre so that when it again forms the asymmetric centre, both *d*- and *l*-forms are obtained in equal amounts. For example, lactic acid may recemise as follow:

The tartaric acid on heating is converted to racemic as well as meso form.

It has been observed that compounds having carbonyl group adjacent to asymmetric carbon atom carrying a hydrogen are most easily racemised. Other substances which cannot enolise easily do not under go racemisation ordinarily.

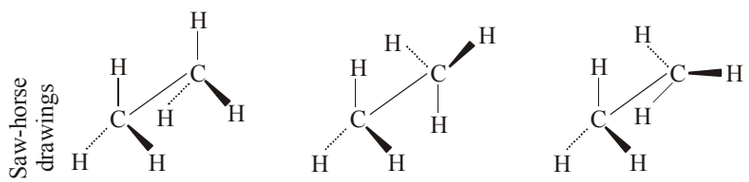


NOTES

Conformations of Alkanes

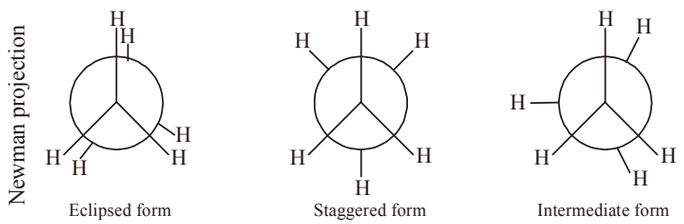
The sigma bond joining the two carbon atoms in ethane is symmetrical about the nuclear axis. This symmetry of the bond permits free rotation of the two carbon atoms with respect to each other, along the bond axis without breaking the bond. Since the two carbon atoms are having tetrahedral arrangement 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 σ (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:



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 parrallel to those of the other and the arrangment is known as *Eclipsed 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.

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 5.11 show 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.

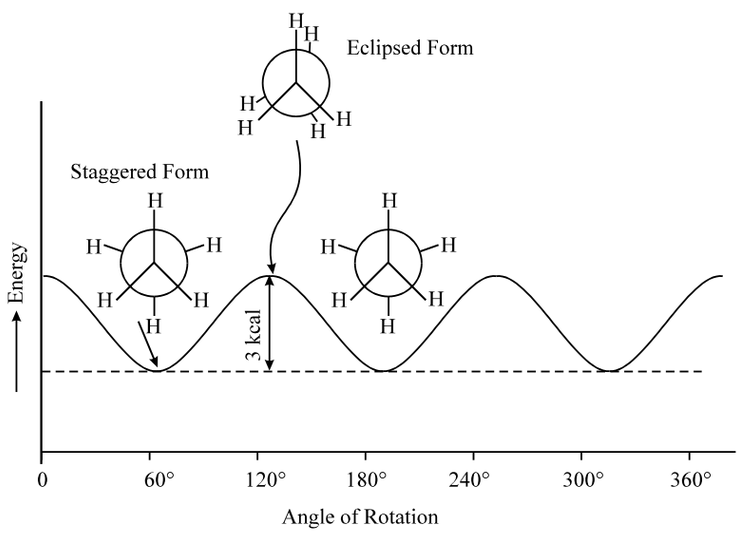
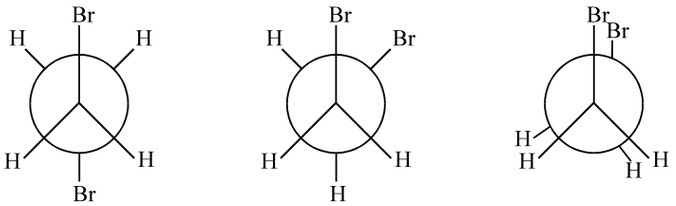


Fig. 5.11 *Energy of Various Conformations of Ethane.*

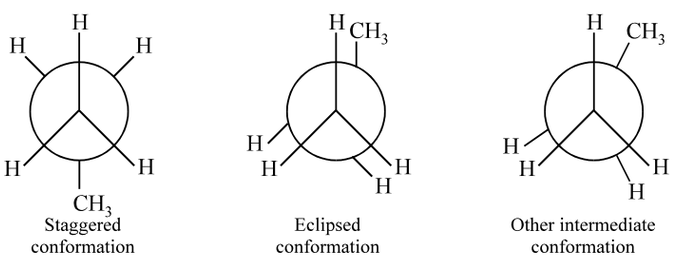
In case of 1,2-dibromoethane the important conformations are:



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— to —CH_3 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

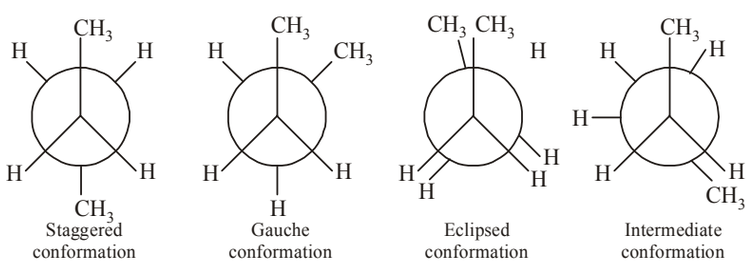


Figure 5.12 represents the potential energy as a function of angle of rotation for *n*-butane.

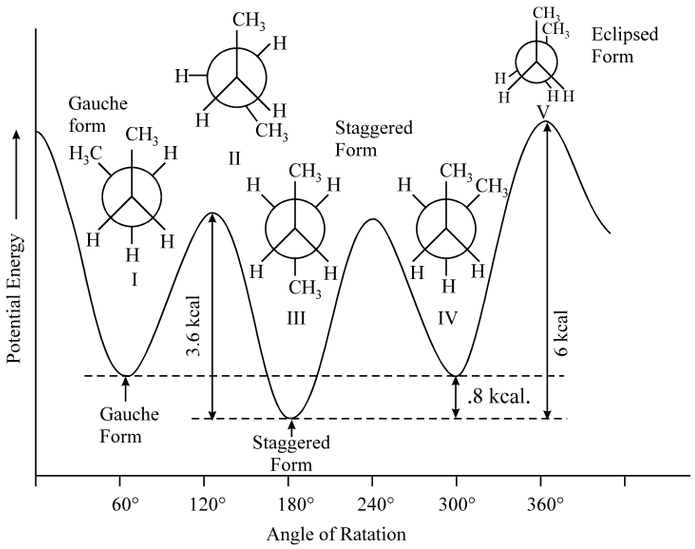


Fig. 5.12 *Energy of Various Conformations of Butane*

Study of the above diagram for the energy of various ecnformations 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. 5.12) 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 **conforma-tional isomers** or **conformers**. Conformations III and I or III and IV are not mirror images of each other and hence are **conformational diastereoisomers**.

Check Your Progress

1. Define isomerism.
2. How many types of isomerism are there? Name them.
3. What is functional isomerism?

NOTES

5.3 CENTER OF CHIRALITY - MOLECULES WITH C, N, S BASED CHIRAL CENTRES

Chirality is a geometric property of some molecules and ions. A chiral molecule/ ion is non-superposable on its mirror image. The presence of an asymmetric carbon center is one of several structural features that induce chirality in organic and inorganic molecules. The term chirality is derived from the Ancient Greek word for hand.

The mirror images of a chiral molecule or ion are called enantiomers or optical isomers. Individual enantiomers are often designated as either right-handed or left-handed. Chirality is an essential consideration when discussing the stereochemistry in organic and inorganic chemistry. The concept is of great practical importance because most biomolecules and pharmaceuticals are chiral. Chiral molecules and ions are described by various ways of designating their absolute configuration, which codify either the entity's geometry or its ability to rotate plane-polarized light. Following example illustrates chirality of (*S*)-Alanine (left) and (*R*)-Alanine (right).

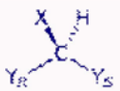
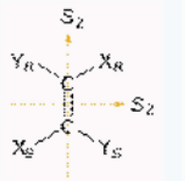
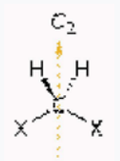
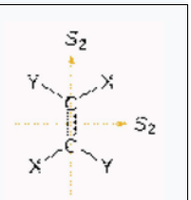
(*S*)-alanine mirror plane (*R*)-alanine

Definition: Chirality is based on molecular symmetry elements. Specifically, a chiral compound can contain no improper axis of rotation (S_n), which includes planes of symmetry and inversion center. Chiral molecules are always dissymmetric (lacking S_n) but not always asymmetric (lacking all symmetry elements except the trivial identity). Asymmetric molecules are always chiral.

NOTES

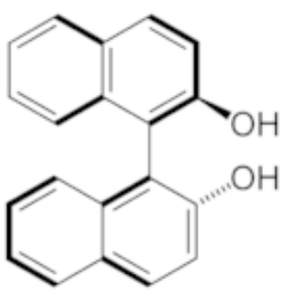
Following Table 5.2 illustrates the molecular symmetry and chirality.

Table 5.2 *Molecular Symmetry and Chirality*

Rotational Axis (C_n)	Improper Rotational Elements (S_n)		
	Chiral No S_n	**Achiral** Mirror Plane $S_1 = \sigma$	**Achiral** Inversion Centre $S_2 = i$
C_1			
C_2			

Stereogenic Centers

In general, chiral molecules have **point chirality** at a single *stereogenic* atom, which has four different substituents. The two enantiomers of such compounds are said to have different **absolute configurations** at this center. This center is thus stereogenic, i.e., a grouping within a molecular entity that may be considered a focus of stereoisomerism. The stereogenic atom, also known as the *stereocenter*, is usually carbon. However a stereocenter can coincide with any atom, including metals, as in many chiral coordination compounds, phosphorus or sulfur. The low barrier of nitrogen inversion make most *N*-chiral amines (NRR2 R3) impossible to resolve, but *P*-chiral phosphines (PRR2 R3) as well as S-chiral sulfoxides (OSRR2) are optically stable. Following is the example of 1,12 -Bi-2-Naphthol of a molecule lacking point chirality.



The presence of a stereogenic atom describes the chiral molecules, though many variations and exceptions exist. For example, it is not necessary for the chiral substance to have a stereogenic atom, such as 1-bromo-3-chloro-5-fluoroadamantane, methylethylphenyltetrahedrane, certain calixarenes and fullerenes, which have inherent chirality. The C_2-symmetric species 1,12 -bi-2-naphthol (BINOL), 1,3-dichloroallene have axial chirality. (*E*)-cyclooctene and many ferrocenes have planar chirality.

When the optical rotation for an enantiomer is too low for practical measurement, the species is said to exhibit cryptochirality.

Even isotopic differences must be considered when examining chirality. The derivative of benzyl alcohol PhCHDOH is chiral.

The *S* enantiomer has $[a]_D = +0.715°$.

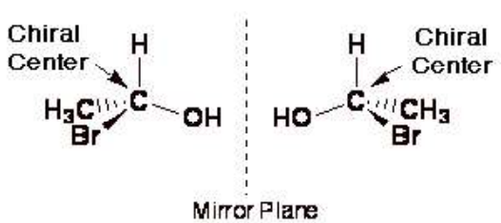
Chirality is a symmetry property, not a characteristic of any part of the periodic table. Thus many inorganic materials, molecules, and ions are chiral. In the coordination chemistry and organometallic chemistry, chirality is pervasive and of practical importance. The example is tris(bipyridine)ruthenium(II) complex in which the three bipyridine ligands adopt a chiral propeller-like arrangement. The two enantiomers of complexes, such as $[Ru (2,22 -bipyridine)_3]^{2+}$ may be designated as Ë (capital lambda, the Greek version of 'L') for a left-handed twist of the propeller described by the ligands, and Ä (capital delta, Greek 'D') for a right-handed twist. Also referred as dextro- and levo- (laevo-).

The term optical activity is derived from the interaction of chiral materials with polarized light. In a solution, the (") form, or levorotatory form, of an optical isomer rotates the plane of a beam of linearly polarized light counter-clockwise. The (+) form, or dextrorotatory form, of an optical isomer does the opposite. The rotation of light is measured using a polarimeter and is expressed as the optical rotation.

Chiral Centre

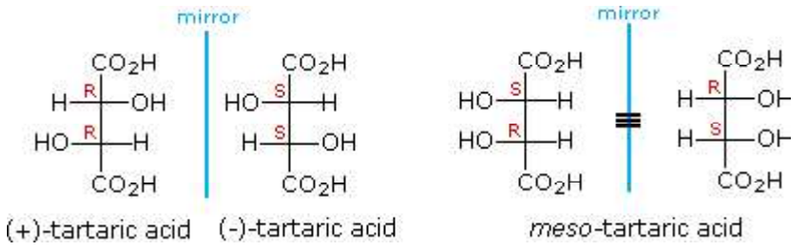
A **chiral centre** is an atom that has four different groups bonded to it in such a manner that it has a non-superimposable mirror image. The term 'Chiral Centre' is also sometimes expressed by the term **chirality centre**.

In the molecule shown below, the carbon atom is a chiral centre or chirality centre. It has four different groups attached, and the two structures are non-superimposable mirror images of each other.



NOTES

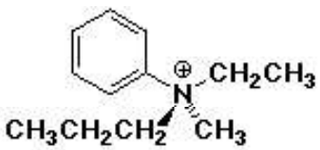
Molecules with a single chirality centre or with more than one chirality centre are termed as 'chiral'. The exceptions are *meso* compounds. For example, tartaric acid has two chirality centres, so it is expected to have $2^2 = 4$ stereoisomers.



But there are only three isomers. The (S, R) and (R, S) isomers are a single *meso* compound because they are superimposable on each other. They are achiral because they have an internal plane of symmetry. The most common chirality centres in organic molecules are sp^3 hybridized carbon atoms, because they can form four bonds.

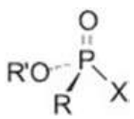
Following are some more types of chirality centre.

Quaternary N Atoms



(or any other four carbon groups)

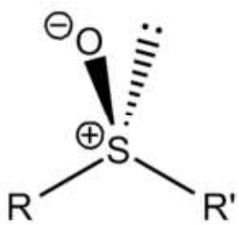
Tetravalent P Atoms



The above chiral tetravalent P atom displays the absolute configuration of the most active nerve agent stereoisomers for AChE inhibition. Many nerve gases contain chiral P atoms.

Sulfoxides

In sulfoxides, the fourth group is a lone pair. Unlike in amines, the energy required to invert this stereocentre is high, so sulfoxides are optically stable.



Principally, the following Cahn-Ingold-Prelog sequence rules assign priorities to the groups that are attached to each chiral centre.

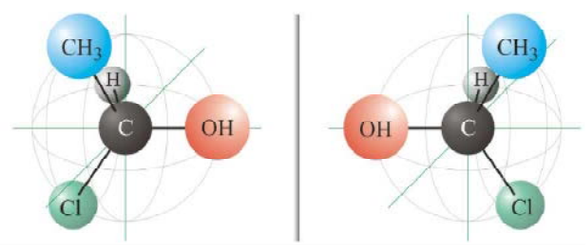
- The atom with higher atomic number receives higher priority.
- If there is a tie, we go one bond further out until we come to the earliest difference.
- If there is still a tie, we keep going further out until we find a difference.
- Double and triple bonds are treated as if they were separate single bonds to the same atom.

Finding Chirality Centers

Chirality means a molecule that is mirrored and would not be superimposable. Typically, a chiral molecule can usually be found if there is no plane of symmetry. The most simple and common example is our hands. They are mirror images but one cannot be put onto the other such that they would appear the same. Same is applicable to molecules. First determine a specific atom whether it be a Carbon or other, where there are four different substituents bonded to the atom.

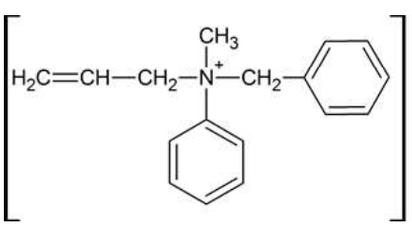
Chiral molecule is, therefore, a molecule which cannot be superimposed on its mirror image. A common example is an organic molecule containing a carbon atom to which four different atoms or groups are attached. Such molecules exhibit optical activity, i.e., they rotate the plane of a polarised light beam.

Following image illustrates four different substituents that are bonded to a chirality center.



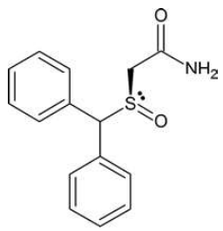
A carbon with four different groups results in a chiral molecule and is referred to as a chiral or asymmetric or stereogenic center.

The example given below shows a resolvable compound containing a chiral nitrogen atom. It was resolved by William Pope and Stanley Peachey in 1899. It had the structure shown below.



NOTES

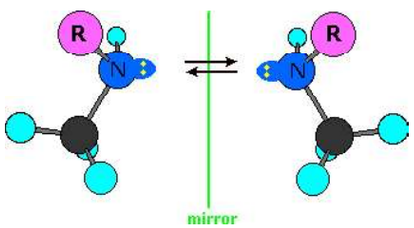
Chiral sulfoxides are used in certain drugs, such as esomeprazole and armodafinil, which exhibit the feature of a stereogenic sulfur center, as shown below.



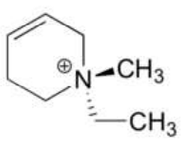
armodafinil

Stereogenic Nitrogen

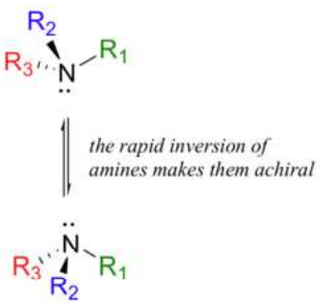
Single-bonded nitrogen is pyramidal in shape, with the non-bonding electron pair pointing to the unoccupied corner of a tetrahedral region. Since the nitrogen in these compounds is bonded to three different groups, its configuration is chiral. The non-identical mirror-image configurations are illustrated in the following diagram, in which the remainder of the molecule is represented by R. If these configurations were stable, there would be four additional stereoisomers of ephedrine and pseudoephedrine. However, pyramidal nitrogen is normally not configurationally stable. It rapidly inverts its configuration, as represented through equilibrium arrows, by passing through a planar, sp^2-hybridized transition state, leading to a mixture of interconverting R and S configurations. If the nitrogen atom were the only chiral center in the molecule, a 50:50 (racemic) mixture of R and S configurations would exist at equilibrium. If other chiral centers are present, as in the ephedrin isomers, a mixture of diastereomers will result. Hence, the nitrogen does not contribute to isolable stereoisomers.



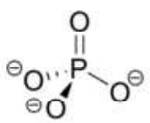
Asymmetric quaternary ammonium groups are also chiral. Amines, however, are not chiral, because they rapidly invert, or turn 'inside out', at room temperature.



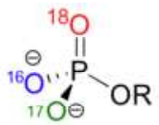
a chiral quaternary ammonium



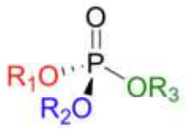
The phosphorus center of phosphate ion and organic phosphate esters, for example, is tetrahedral, and thus is potentially a stereocenter, as shown below.



phosphate (achiral)



labeled phosphate ester (chiral)

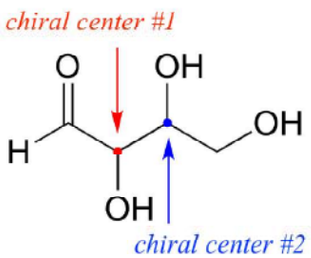


a chiral phosphate triester

In the stereochemistry of reactions at the phosphate center, the incorporated sulfur and/or ^{17}O and ^{18}O isotopes of oxygen (the 'normal' isotope is ^{16}O) to create chiral phosphate groups. Phosphate triesters are chiral if the three substituent groups are different.

Compounds with Multiple Chiral Centers

We have discussed about compounds with a single chiral center. Now let us understand about those compounds which have multiple chiral centers. Following is the stereoisomeric four-carbon sugars with two chiral centers.



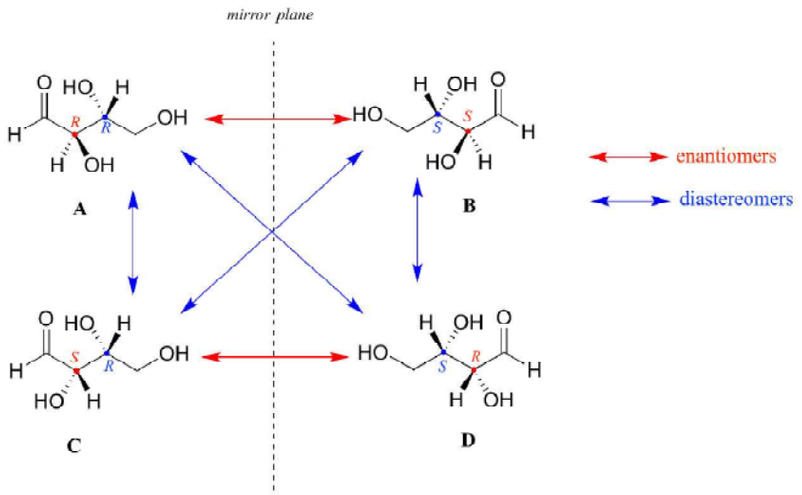
In the following example, in Compound A both chiral centers have the *R* configuration. The mirror image of Compound A is Compound B, which has the *S* configuration at both chiral centers. If we flip the Compound A and put it next to Compound B then it shows that they are not superimposable. Both the Compounds A and B are non-superimposable mirror images, i.e., enantiomers.

In the Compound C, the configuration is 'S' at chiral center 1 and 'R' at chiral center 2. Compounds A and C are stereoisomers since they have the same molecular formula and the same bond connectivity, but a different arrangement of atoms in space, as per the definition of the stereoisomer. Because they are not mirror images of each other and hence they are not enantiomers. By definition, they are diastereomers of each other.

Both the Compounds C and B also have a diastereomeric relationship, according to the same definition.

Therefore, the Compounds A and B are a pair of enantiomers, and Compound C is a diastereomer of both of them. Additionally the Compound D is the mirror image of Compound C, and the two are not superimposable. Therefore,

C and D are a pair of enantiomers. Compound D is also a diastereomer of Compounds A and B.



Check Your Progress

4. On what is chirality based ?
5. Define chiral centre.

5.4 STEREOISOMERISM: ENERGY CRITERIA, CONFIGURATION AND CONFORMATIONAL STEREOISOMERS

In stereochemistry, stereoisomers are isomeric molecules that have the same molecular formula and sequence of bonded atoms (constitution), but differ in the three-dimensional orientations of their atoms in space. This is different to the structural isomers, which share the same molecular formula, but the bond connections or their order differs. By definition, "***Molecules that are stereoisomers of each other represent the same structural isomer***". Therefore, the stereochemistry typically focuses on stereoisomers.

The three C's - Constitution, Configuration and Conformation are significant features of isomerism. The constitutional isomers differ in the nature and sequence of their bonds. But these are not the only kind of isomer. Configurational and conformational isomers differ not in their bonding pattern, i.e., constitution, but in the position or geometric arrangement of their atoms in space, their **stereochemistry**. Isomers with the same constitution are called **stereoisomers**. They can differ either in **configuration** or in **conformation**. The distinction between configurational and conformational isomers is limited.

NOTES

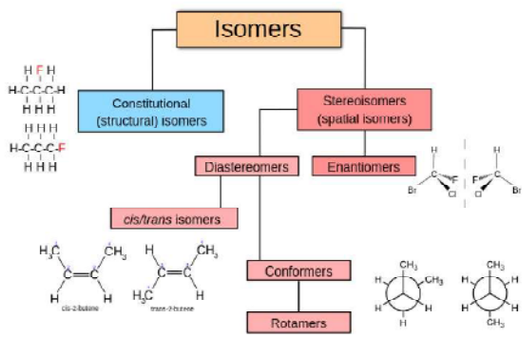
Configurational Isomers: To convert one configurational isomer to another, a bond must be broken and reformed.

Conformational Isomers: Conformational isomers can be interconverted by rotation around single bonds.

Changing configuration is usually much more difficult than changing conformation as it requires more energy in most cases. In other words, it generally takes more **energy** to interconvert configurational isomers than to interconvert conformational isomers. However, there are exception to this rule because some bonds are so easy to break that it is essentially easy to interconvert configurational isomers than conformational isomers.

Characteristically, the 'isomers' represent a structure at a local energy minimum.

Following figure illustrates the different types of isomers.



Conformers or Conformational Isomerism

Conformational isomerism is a form of isomerism that describes the phenomenon of molecules with the same structural formula but with different shapes due to rotations about one or more bonds. Different conformations can have different energies, can usually interconvert, and are very rarely isolatable. For example, cyclohexane can exist in a variety of different conformations including a chair conformation and a boat conformation, but, for cyclohexane itself, these can never be separated. The boat conformation represents the energy maximum on a conformational itinerary between the two equivalent chair forms; however, it does not represent the transition state for this process, because there are lower-energy pathways. There are some molecules that can be isolated in several conformations, due to the large energy barriers between different conformations.

Conformational Analysis of Alicyclic 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 alicyclic compounds, due to distortion of valency angle (Baeyer's strain), the molecule tends to take up non-

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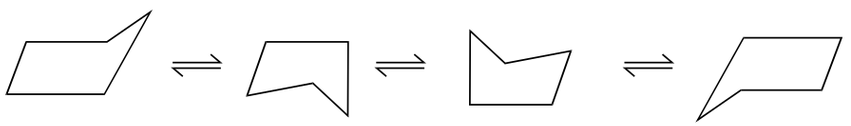
planar configuration forming **strainless rings**. Apart from Baeyer's strain there exist other types of strain in the molecule. Thus in cyclopropane every hydrogen atom is almost in contact with the neighbouring hydrogen atoms thus producing strain due to mutual repulsion of three pairs of hydrogen 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.



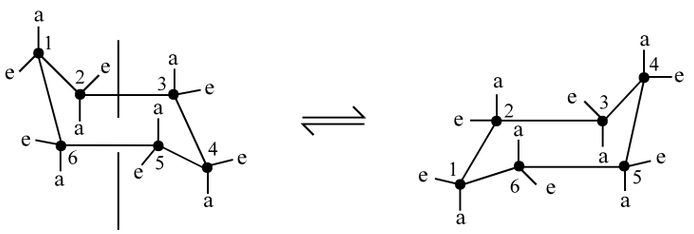
Conformation of Cyclohexane

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. Bowspirit-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 orginally become equatorial and *vice versa*.



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 Fig. 5.13.

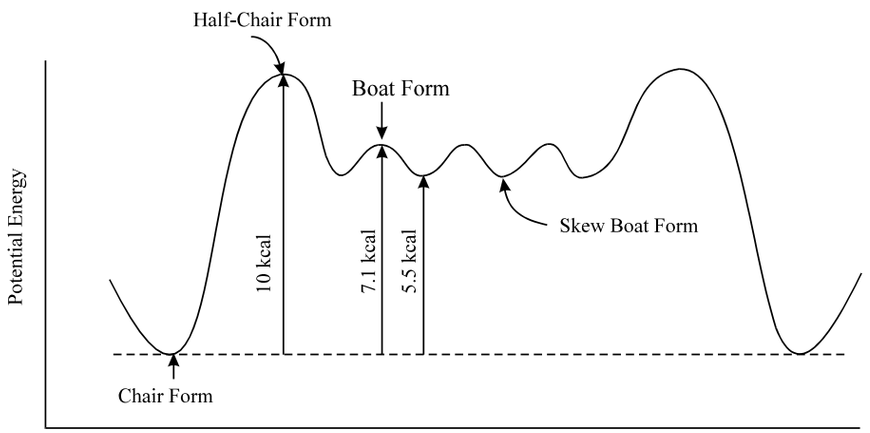


Fig. 5.13 *Interconversion of Conformations of Cyclohexane.*

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.

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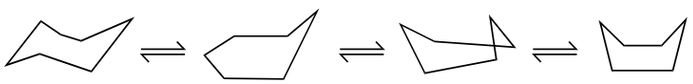
In the boat form also there is no angle strain but there is bond opposition or eclipsing strain of four pairs of hydrogen of bottom carbon atoms and also strain due to interaction of pairs of hydrogen at the top carbon atoms known as **bowspirit flagpole** interaction.



Chair form Half-chair form Skew boat form Boat form

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.

trans-1, 3-*di*-*t*-Butylcyclohexane

Check Your Progress

6. What is torsional strain?
7. What does configuration mean?
8. What does triad system involve?

5.5 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. The compounds having same molecular formula but different physical characteristics or chemical properties are known as isomers and this phenomenon is known as isomerism.
2. There are two types of isomerism, i.e., structural isomerism, stereroisomerism.
3. Isomerism exhibited by compounds differing in functional groups is known as functional isomerism.
4. Chirality is based on molecular symmetry elements.
5. A **chiral centre** is an atom that has four different groups bonded to it in such a manner that it has a non-superimposable mirror image. The term 'Chiral Centre' is also sometimes expressed by the term **chirality centre**.

6. The stains which twists one or more atoms of the ring out of plane is termed as torsional strain.
7. The term configuration refers to the arrangement of groups or atoms in space around dissymmetric part of molecule.
8. Triad system involve the oscillation of hydrogen between first and third of the three polyvalent atoms linked together.

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5.6 SUMMARY

- The compounds having same molecular formula but differing at least in some physical characteristics or chemical properties are known as isomers and the phenomenon is known as isomerism.
- Obviously this difference in properties must be due to some difference in the arrangement of atoms within the molecules of the isomers. Depending on the type of this difference in arrangement of atoms, there can be two types of isomerism.
- Structural isomerism arises from the difference in the arrangement of atoms within the molecule resulting in two or more different structural formulae, and the isomers are known as structural isomers. Thus, the structural isomers have same molecular formula but different structures.
- When the isomers have the same structural formulae but they differ in relative arrangement of atoms or groups in space, the phenomenon is termed as stereoisomerism and the isomers are known as stereoisomers.
- The spatial arrangement (or arrangement in space) of atoms or groups is also referred to as configuration of the molecule.
- Isomers differing in the structure of carbon chains are known as skeletal or chain isomers and the phenomenon as skeletal or chain isomerism.
- The simplest compound exhibiting this type of isomerism is of molecular formula C4H10 (butane). There are two compounds corresponding to this formula which differ only in the nature of carbon skeleton.
- Similarly, pentane (C5H12) exists in three isomeric forms because the five carbon atoms can be linked in three different forms of chains.
- The number of chain isomers goes on increasing with increase in the number of carbon atoms (cf. Alkanes) in the chain.It is also possible that one of the isomer may have an open chain skeleton while the other may have a closed chain or ring (cyclic) skeleton.
- Isomerism exhibited by compounds differing in functional groups is known as functional isomerism.
- As the functional group largely determines the properties of a compound, such compounds differ in their physical and chemical properties. Compounds exhibiting this type of isomerism are called functional isomers.

NOTES

- Compounds of the same homologous series show this type of isomerism because of unequal distribution of carbon atoms (or difference in size of alkyl groups) on either side of the functional group in the molecules. Only those compounds which have a polyvalent functional group can exhibit metamerims.
- Thus diethyl ether and methyl propyl ether, both having the same molecular formula and the same functional group (i.e., ether linkage) are metamers because of difference in alkyl groups on either side of ether linkage.
- Compounds having the same atoms or groups with a different spatial arrangement are called stereoisomers.
- In modern concept a single bond is considered to be an axially symmetrical bond permitting free rotation about its axis. The double bond is considered to be consisting of a and a bond.
- If the carbon atoms are rotated with respect to each othermolecular orbital is distorted. The two 'p' atomic orbitals remain no longer parallel and no orbital overlap can occur. It is this energy barrier which prevents the rotation and substituents are held in a rigid planar geometrical conformation.
- The compounds having a carbon to nitrogen double bond (as in oximes) and nitrogen to nitrogen double bond (as in azo compounds) also exhibit geometrical isomerism because nitrogen too has the same hybridization state—as carbon, i.e., sp2 in doubly bonded nitrogen.
- Geometrical isomerism in inorganic compounds in this the coordination compounds usually exhibit geometrical isomerism. In such compounds if the geometry is square planar or octahedral the cis-trans isomerism is observed.
- The geometrical isomers are generally two different compounds having appreciable difference in their physical and chemical properties—though the differences in the latter are few. Thus cis-isomer, in general have lower m.p. and higher values for density, refractive index, dipole moment, etc., as compared to trans-isomers.

5.7 KEY WORDS

- **Stereochemistry:** Stereochemistry is defined as a sub-discipline of chemistry which involves the study of the relative spatial arrangement of atoms that together forms the structure of molecules and their manipulation.
- **Isomerism:** The compounds having same molecular formula but different physical characteristics or chemical properties are known as isomers and this phenomenon is known as isomerism.
- **Torsional strain:** The stains which twists one or more atoms of the ring out of plane is termed as torsional strain.

- **Configuration:** The term configuration refers to the arrangement of groups or atoms in space around dis-symmetric part of molecule.
- **Functional isomerism:** Isomerism exhibited by compounds differing in functional groups is known as functional isomerism.
- **Configurational isomers:** To convert one configurational isomer to another, a bond must be broken and reformed.
- **Conformational isomers:** Conformational isomers can be interconverted by rotation around single bonds.

5.8 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. What is structural isomerism?
2. What is stereoisomerism ?
3. Define chain isomerism.
4. Write short note on metamerism.
5. Write a short note on compounds with one asymmetric carbon atom.
6. What are monosubtitutes cyclohexanes?

Long Answer Questions

1. Give a descriptive note on stereochemistry, isomerism and its types in detail.
2. What is structural isomerism and how many types of structural isomerism are there? Explain in detail.
3. Explain the E-Z system for designating isomeric alkenes with examples.
4. Elaborate a note on optical isomerism and its related terms.
5. Expalin Fischer projection formulae.
6. Give a detailed note on molecules with C.N.S based Chiral centres.
7. Explain stereoisomerism, also give its definition based on energy criteria.

5.9 FURTHER READINGS

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UNIT 6 NOMENCLATURE

NOTES

Structure

6.0 INTRODUCTION

The method of unambiguously assigning the handedness of molecules was originated by three chemists: R.S. Cahn, C. Ingold, and V. Prelog and, as such, is also often called the Cahn-Ingold-Prelog rules. The purpose of the Cahn-Ingold-Prelog priority rules (CIP priority rules) is so that chemists can correctly and unambiguously name a specific stereoisomer of a molecule. Stereoisomers are compounds that have the same chemical formula, the same atom connectivity, but differ in their three-dimensional orientation.

By using the CIP priority rules, it's possible to correctly prioritize each atom or group of atoms bonded to a specific carbon atom (stereocenter) within a molecule so that chemists can assign a designator to that specific carbon. Something that's important for us to realize, however, is that in order for a carbon to be a stereocenter within a compound it has to have four different atoms or groups of atoms bonded to it.

In this unit, you will learn the rules of R and S nomenclature using CIP system. You have already studied about chirality in the previous unit, this unit discusses about molecules with one or more than chiral centre. You will also understand the concept of diastereoisomers.

6.1 OBJECTIVES

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

- Understand the R and S nomenclature using CAHN-INGOLD-PRELOG rules

- Know about molecules with one and more than one chiral centres
- Discuss diastereoisomers
- Know about erythro and threo nomenclature
- Know about E and Z nomenclature

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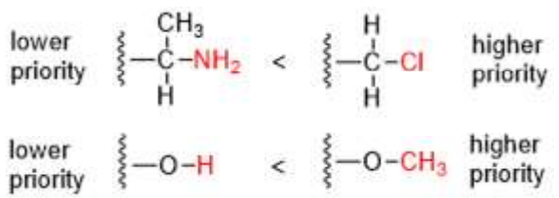
6.2 R AND S NOMENCLATURE USING CAHN-INGOLD-PRELOG RULES

Cahn–Ingold–Prelog (CIP) priority rules or the Cahn–Ingold–Prelog sequence rules, named for organic chemists Robert Sidney Cahn, Christopher Kelk Ingold and Vladimir Prelog alternatively also termed the CIP priority rules, system or conventions are a standard process used in organic chemistry to completely and unequivocally name a stereoisomer of a molecule. The purpose of the CIP system is to assign an R or S descriptor to each stereocenter and an E or Z descriptor to each double bond so that the configuration of the entire molecule can be specified uniquely by including the descriptors in its systematic name. A molecule may contain any number of stereocenters and any number of double bonds, and each usually gives rise to two possible isomers. A molecule with an integer n describing the number of its stereogenic centers will usually have 2n stereoisomers, and 2n–1 diastereomers each having an associated pair of enantiomers. The CIP sequence rules contribute to the precise naming of every stereoisomer of every organic and organometallic molecule with all atoms of ligancy of fewer than 4, but including ligancy of 6 as well, this term referring to the 'number of neighboring atoms' bonded to a center.

The key article setting out the CIP sequence rules was published in 1966, and was followed by further refinements, before it was incorporated into the rules of the International Union of Pure and Applied Chemistry (IUPAC), the official body that defines organic nomenclature.

Following example illustrates the prioritisation of structure within the CIP system. Priority is assigned according to the substitution of elements with higher atomic numbers, or other attached groups. The NH_2, Cl, H and CH_3 substituents determines the final priority.



The steps for naming molecules using the CIP system are as follows:

- Identification of stereocenters and double bonds.

- Assignment of priorities to the groups attached to each stereocenter or double-bonded atom.
- Assignment of R/S and E/Z descriptors.

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Assignment of Priorities

R/S and E/Z descriptors are assigned by using a system for ranking priority of the groups attached to each stereocenter. This procedure, often known as the sequence rules, is the core of the CIP system.

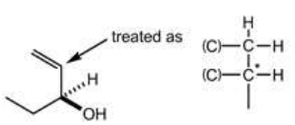
- Compare the atomic number (Z) of the atoms directly attached to the stereocenter; the group having the atom of higher atomic number receives higher priority.
- If there is a tie, then consider the atoms at distance 2 from the stereocenter as a list is made for each group of the atoms bonded to the one directly attached to the stereocenter. Each list is arranged in order of decreasing atomic number. Then the lists are compared atom by atom; at the earliest difference, the group containing the atom of higher atomic number receives higher priority.
- If there is still a tie, each atom in each of the two lists is replaced with a sublist of the other atoms bonded to it (at distance 3 from the stereocenter), the sublists are arranged in decreasing order of atomic number, and the entire structure is again compared atom by atom. This process is repeated recursively, each time with atoms one bond farther from the stereocenter, until the tie is broken.

Isotopes

If two groups differ only in isotopes, atomic masses are used at each step to break ties in atomic number.

Double and Triple Bonds

If an atom A is double-bonded to an atom B, then atom A is treated as being singly bonded to two atoms, atom B and a 'ghost atom' that is a duplicate of atom B and has the same atomic number but is not attached to any other except atom A. When atom B is replaced with a list of attached atoms, then atom A itself, but not its 'ghost' is excluded in accordance with the general principle of not doubling back along a bond that has just been followed. A triple bond is handled the same way except that atom A and atom B are each connected to two ghost atoms of the other. The following example illustrates the 'divide and duplicate rule' feature for double bonds. The vinyl group (C=C) or alkene portion has a higher priority over the alkane (C–C) portion.



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Geometric Isomers

If two substituents on an atom are geometric isomers of each other, the *Z*-isomer has higher priority than the *E*-isomer.

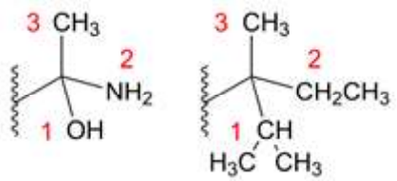
Cyclic Molecules

To handle a molecule containing one or more cycles, it must be first expanded into a tree, termed as **hierarchical digraph**, by traversing bonds in all possible paths starting at the stereocenter. When the traversal encounters an atom through which the current path has already passed, a ghost atom is generated in order to keep the tree finite. A single atom of the original molecule may appear in many places, some as ghosts and some not as ghosts in the tree.

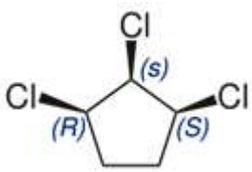
Assigning Descriptors

The descriptors can be assigned in the following way.

Stereocenters R/S: After the substituents of a stereocenter have been assigned their priorities, the molecule is oriented in space so that the group with the lowest priority is pointed away from the observer. If the substituents are numbered from 1 (highest priority) to 4 (lowest priority), then the sense of rotation of a curve passing through 1, 2 and 3 distinguishes the stereoisomers. A center with a clockwise sense of rotation is an R (Rectus) center and a center with a counterclockwise sense of rotation is an S (Sinister) center. The names are derived from the Latin for 'Right' and 'Left', respectively. The following two examples are of stereocenters. The lowest substituent (number 4) is shown only by a wavy line, and is assumed to be behind the rest of the molecule. Both centers are S isomers.



Following is an example of a (S) descriptor for (1R,2s,3S)-1,2,3-trichloro-cyclopentane.



A practical method used for of determining whether an enantiomer is R or S is by using the right-hand rule. The molecule is assumed to be wrapped with the fingers in the direction $1 \rightarrow 2 \rightarrow 3$. If the thumb points in the direction of the fourth substituent, the enantiomer is R otherwise it is S. In rare cases it is possible that

two substituents on an atom differ only in their absolute configuration (R or S). If the relative priorities of these substituents need to be established, R takes priority over S. When this happens, the descriptor of the stereocenter is a lowercase letter 'r' or 's' instead of the uppercase letters that are normally used.

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Double Bonds E/Z: For alkenes and similar double bonded molecules, the same prioritizing process is followed for the substituents. In this case, it is the placing of the two highest priority substituents with respect to the double bond which matters. If both high priority substituents are on the same side of the double bond, i.e., in the **cis** configuration, then the stereoisomer is assigned a **Z** (Zusammen). If by contrast they are in a **trans** configuration, then the stereoisomer is assigned an **E** (Entgegen). In this case the identifying letters are derived from German for 'together' and 'opposite', respectively.

6.3 CHIRAL CENTRE

A chiral centre is an atom that has four different groups bonded to it in such a manner that it has a non-superimposable mirror image.

The Cahn Ingold Prelog (CIP) System for Naming Chiral Centers

The CIP protocol for naming chiral centers works as follows:

1. Prioritize the four groups around a chiral center **according to atomic number**. The highest atomic number is assigned priority #1, and the lowest atomic number is assigned priority #4.
2. Orient the chiral centre such that the #4 priority substituent is pointing **away** from the viewer. It is merely to be attached to a 'dashed' bond.
3. Trace the path of priorities #1, #2 and #3. (For this part you ignore #4).
   - If the path traced from 1-2-3 is **clockwise**, the chiral center is assigned (*R*) (from Latin, *Rectus*).
   - If the path traced is **counter clockwise**, the chiral center is assigned (*S*) (from the Latin *Sinister).*

Thus the designations (R) and (S) bear no relationship to whether a molecule rotates plane-polarized light clockwise (+) or counter-clockwise (-). For example, the most common naturally occurring configuration of the amino acid alanine is (S), but its optical rotation (in aqueous acid solution) is (+).

The designations (R) and (S) strategy has been specifically developed for distinguishing between a pair of enantiomers as follows.

- Arrange the four substituents in order of *decreasing* atomic number of the atoms attached to the stereocenter. The substituent with the highest atomic number gets the highest priority. For example, the substituents in

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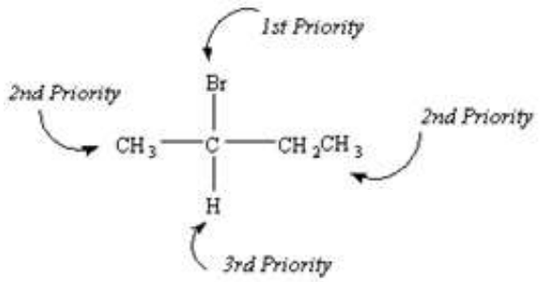
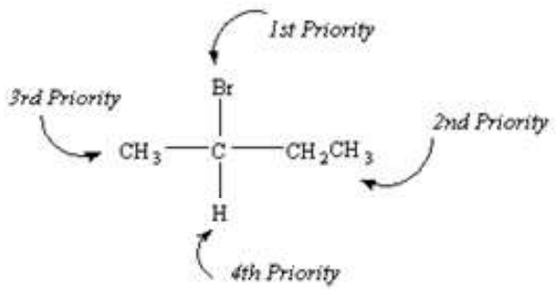
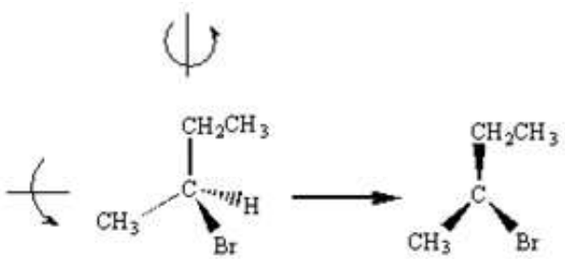
2-bromobutane would be listed in the order: Br > CH_3 = CH_2CH_3 > H.



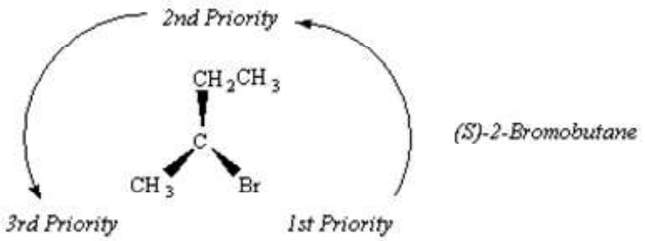
- When two or more substituents have the same priority, such as the CH_3 and CH_2CH_3 groups in 2-bromobutane then continue working with the substituent chain until you find a difference. In 2-bromobutane, we give the CH_2CH_3 group a higher priority than the CH_3 group because the next point in the chain is a CH_3 group in the CH_2CH_3 substituent and an H atom in the CH_3 group. Thus, the four substituents on 2-bromobutane would be listed in the order: Br > CH_2CH_3 > CH_3 > H.



- View the enantiomer from the direction that places the substituent with the lowest priority. In the following example, this involves rotating the molecule counter-clockwise around the C–CH_2CH_3 bond and tilting it slightly around an axis that lies in the plane of the paper. When this is done, the substituent that has the lowest priority is not visible.



- Trace a path that links the substituents in *decreasing* order of priority. If the path curves to the right, i.e., clockwise then the molecule is the *R* enantiomer. If it curves to the left, i.e., counter-clockwise then it is the *S* enantiomer.



(S)-2-Bromobutane

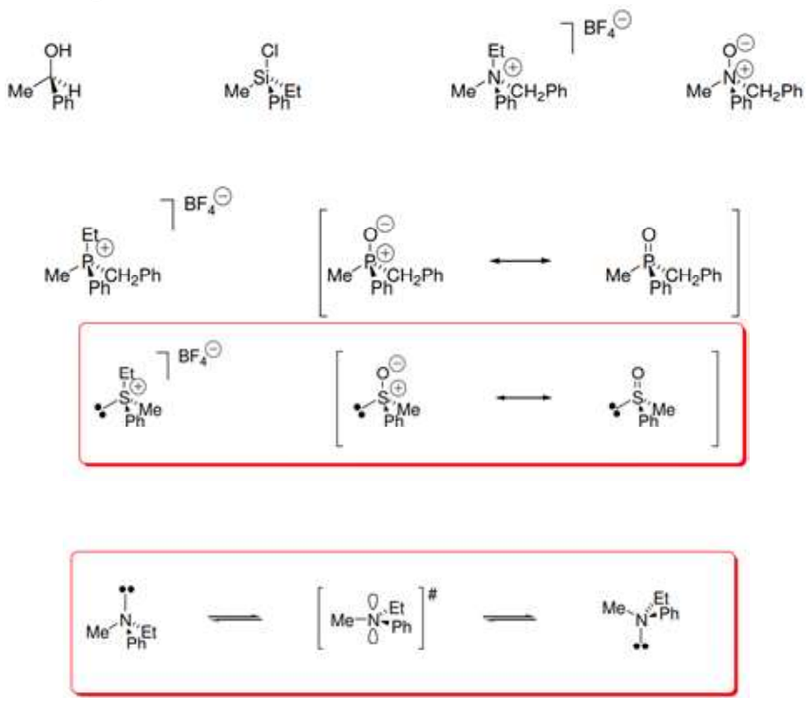
In this example, the path curves to the left, so this enantiomer is the (*S*)-2-bromobutane stereoisomer.

It is important to recognize that the (*R*)/(*S*) system is based on the structure of an individual molecule and the (+)/(-) system is based on the macroscopic behaviour of a large collection of molecules. The most complete description of an enantiomer combines aspects of both systems. The enantiomer analyzed in this section is best described as (*S*)-(-)-2-bromobutane. It is the (*S*) enantiomer because of its structure and the (-) enantiomer because samples of the enantiomer with this structure are levorotatory, they rotate plane-polarized light clockwise. The sign of the optical rotation is not correlated to the absolute configuration.

6.3.1 Molecules with a Chiral Center and C_n

Such molecules are asymmetric and have only a C_n (n = 1, i.e., C_1) proper rotation axis. Dissymmetric molecules, which have C_1 and C_n (n = integer > 1) proper rotation axes only, are also chiral.

Following is the example of asymmetric chiral molecules (C_1) with a single chiral/stereogenic centre.



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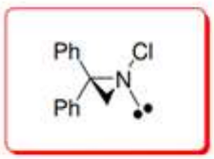
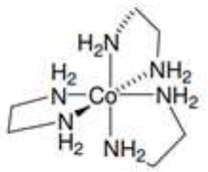
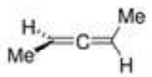
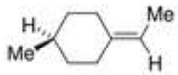
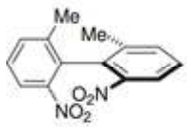


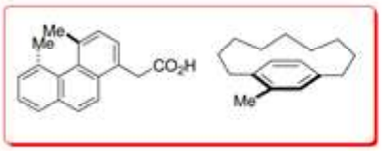


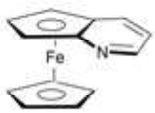
Following is the example of asymmetric chiral molecules (C_1) without a chiral/ stereogenic centre.



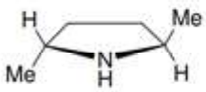


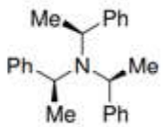






Following is the example of dissymmetric molecules (C_n).





6.3.2 Molecules with More than One Chiral Center

If there are two chiral centers in a single molecule, then there are four possible stereoisomers, because each carbon atom can be in one of two possible forms (R or S) hence there are 2 x 2 = 4 possible combinations. The **enantiomers** must be mirror images of each other. **Diastereomers** is the chemistry term that describes the relationship between the pairs of molecules that are not even mirror images of each other. In other words, each pair of molecules must be related because they are all stereoisomers of each other, so they are either enantiomers (mirror images) or diastereomers (not mirror images). Thus, diastereomers are stereoisomers that are not enantiomers. If a molecule happens to be symmetric so that two of the four possible stereoisomers are identical, i.e., the S, R is identical to the R,S then the S,S and R,R will always be enantiomers. This form of the molecule is called the **meso form**. Since this situation requires some special symmetry (usually a plane of symmetry) to be present, it is the unusual exception, not the rule.

Check Your Progress

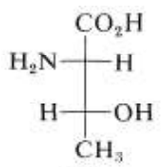
1. What does IUPAC stand for?
2. What are sequence rules?
3. What are isotopes?
4. What is chiral centre?
5. What is the meso form of molecules?

NOTES

6.4 DIASTEREOISOMERS

Diastereomers, also sometimes termed as diastereoisomers, are specific type of a stereoisomer. Typically, the diastereomerism occurs when two or more stereoisomers of a compound have different configurations at one or more (but not all) of the equivalent (related) stereocenters and are not mirror images of each other. When two diastereoisomers differ from each other at only one stereocenter they are epimers. Each stereocenter gives rise to two different configurations and thus typically increases the number of stereoisomers by a factor of two.

Consider the stereoisomers of the important amino acid, threonine, (2-amino-3-hydroxybutanoic acid). For this, if we write all of the possible configurations of its *two* chiral carbons, we have *four* different projection formulas, as shown below from 19-22, corresponding to four different stereoisomers:



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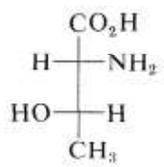

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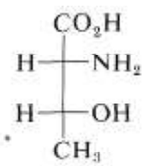

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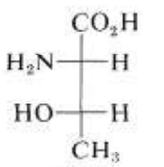


22

Such substances, related to each other in this way and which can be converted one into the other only by changing the configurations at one or more chiral centers, are called **diastereomers**.

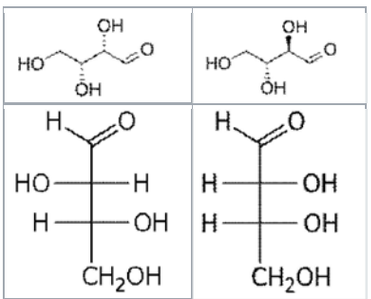
Diastereomers differ from enantiomers in that the latter are pairs of stereoisomers that differ in all stereocenters and are therefore mirror images of one another. Enantiomers of a compound with more than one stereocenter are also diastereomers of the other stereoisomers of that compound that are not their mirror image (that is, excluding the opposing enantiomer). Diastereomers have different physical properties (unlike most aspects of enantiomers) and often different chemical reactivity.

Diastereomerism can also occur at a double bond, where the **cis** vs. **trans** relative positions of substituents give two non-superposable isomers. Many conformational isomers are diastereomeric as well. Diastereoselectivity is the

preference for the formation of one or more than one diastereomer over the other in an organic reaction.

Following are the examples of the diastereomers that are also epimers.

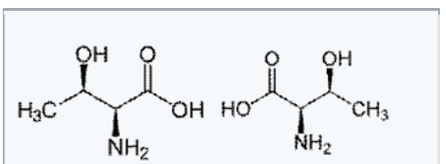
NOTES



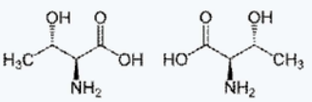
D-Threose | D-Erythrose

6.5 ERYTHRO AND THREO NOMENCLATURE

Two older prefixes still commonly used to distinguish diastereomers are **threo** and **erythro**. In the case of saccharides, when drawn in the Fischer projection the erythro isomer has two identical substituents on the same side and the threo isomer has them on opposite sides. When drawn as a zig-zag chain, the erythro isomer has two identical substituents on different sides of the plane (anti). The names are derived from the diastereomeric aldoses erythrose (a syrup) and threose (melting point 126 °C). These prefixes are not recommended for use outside of the realm of saccharides because their definitions can lead to conflicting interpretations. Another threo compound is threonine, one of the essential amino acids. The *erythro* diastereomer is called allothreonine.



L-Threonine (2*S*,3*R*) and D-Threonine (2*R*,3*S*)



L-Allothreonine (2*S*,3*S*) and D-Allothreonine (2*R*,3*R*)

Check Your Progress

6. When does diastereomerism occur?
7. What is allothreonine?

NOTES

6.6 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. International Union of Pure and Applied Chemistry.
2. R/S and E/Z descriptors are assigned by using a system for ranking priority of the groups attached to each stereocenter. This procedure, often known as the sequence rules, is the core of the CIP system.
3. If two groups differ only in isotopes, atomic masses are used at each step to break ties in atomic number.
4. A chiral centre is an atom that has four different groups bonded to it in such a manner that it has a non-superimposable mirror image.
5. If a molecule happens to be symmetric so that two of the four possible stereoisomers are identical, i.e., the S, R is identical to the R,S then the S,S and R,R will always be enantiomers. This form of the molecule is called the meso form.
6. The diastereomerism occurs when two or more stereoisomers of a compound have different configurations at one or more (but not all) of the equivalent (related) stereocenters and are not mirror images of each other.
7. The erythro diastereomer is called allothreonine.

6.7 SUMMARY

- Cahn–Ingold–Prelog (CIP) priority rules or the Cahn–Ingold–Prelog sequence rules, named for organic chemists Robert Sidney Cahn, Christopher Kelk Ingold and Vladimir Prelog alternatively also termed the CIP priority rules, system or conventions are a standard process used in organic chemistry to completely and unequivocally name a stereoisomer of a molecule.
- R/S and E/Z descriptors are assigned by using a system for ranking priority of the groups attached to each stereocenter. This procedure, often known as the sequence rules, is the core of the CIP system.
- If two substituents on an atom are geometric isomers of each other, the *Z*-isomer has higher priority than the *E*-isomer.

NOTES

- A chiral centre is an atom that has four different groups bonded to it in such a manner that it has a non-superimposable mirror image.
- Such molecules are asymmetric and have only a C_n (n = 1, i.e., C_1) proper rotation axis. Dissymmetric molecules, which have C_1 and C_n (n = integer > 1) proper rotation axes only, are also chiral.
- If there are two chiral centers in a single molecule, then there are four possible stereoisomers, because each carbon atom can be in one of two possible forms (R or S) hence there are 2 x 2 = 4 possible combinations.
- When two diastereoisomers differ from each other at only one stereocenter they are epimers.
- Diastereomers differ from enantiomers in that the latter are pairs of stereoisomers that differ in all stereocenters and are therefore mirror images of one another.
- Two older prefixes still commonly used to distinguish diastereomers are threo and erythro.

6.8 KEY WORDS

- **Stereocenter:** A stereocenter or stereogenic center is any point in a molecule, though not necessarily an atom, bearing groups, such that an interchanging of any two groups leads to a stereoisomer.
- **Isomer:** Each of two or more compounds with the same formula but a different arrangement of atoms in the molecule and different properties.
- **Chiral:** Asymmetric in such a way that the structure and its mirror image are not superimposable.
- **Enantiomers:** Each of a pair of molecules that are mirror images of each other.

6.9 SELF ASSESSEMNT QUESTIONS AND EXERCISES

Short Answer Questions

1. What are double and triple bonds?
2. What are Double Bonds E/Z?
3. What are the molecules with more than one chiral center?
4. Write a short note on erythro and threo nomenclature.

Long Answer Questions

1. Explain R and S nomenclature using CAHN-INGOLD-PRELOG RULES.
2. Discuss the Cahn Ingold Prelog (CIP) system for naming chiral centers
3. Discuss molecules with a chiral center.
4. What are diastereoisomers? Also give examples of diastereoisomers.

NOTES

6.10 FURTHER READINGS

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Mukherji, S.M. and S.P. Singh. 1984. *Reaction Mechanism in Organic Chemistry*, 3rd Edition. London: MacMillan.

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Pine, S.H., J.B. Hendrickson, D.J. Cram and G.S. Hammond. 1980. *Organic Chemistry*, 4th Edition. New York: McGraw-Hill Company.

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UNIT 7 STEREOCHEMISTRY AND ABSOLUTE CONFIGURATION

Structure

7.0 INTRODUCTION

Stereochemistry is defined as a subdiscipline of chemistry which involves the study of the relative spatial arrangement of atoms that together forms the structure of molecules and their manipulation. The study of chiral molecules which is one of the elements of symmetry is an important branch of stereochemistry. In other words, stereochemistry belongs to that department of chemistry which take care of the three-dimensional structures of molecules and how they are an impact on the chemical and the physical properties of the substance.

An absolute configuration refers to the spatial arrangement of the atoms of a chiral molecular entity (or group) and its stereochemical description, for example, R or S, referring to Rectus, or Sinister, respectively. Absolute configurations for a chiral molecule (in pure form) are most often obtained by X-ray crystallography. All enantiomerically pure chiral molecules crystallise in one of the 65 Sohncke groups (chiral space groups). Alternative techniques are optical rotatory dispersion, vibrational circular dichroism, use of chiral shift reagents in proton NMR and Coulomb explosion imaging When the absolute configuration is obtained the assignment of R or S is based on the Cahn–Ingold–Prelog priority rules. Absolute configurations are also relevant to characterization of crystals

In this unit, you will study about axial, planar and helical chirality, stereochemistry and absolute configuration of allenes, biphenyls and binaphthyls, ansa and cyclophanic compounds, spiranes, exo-cyclic alkylidenecycloalkanes in detail.

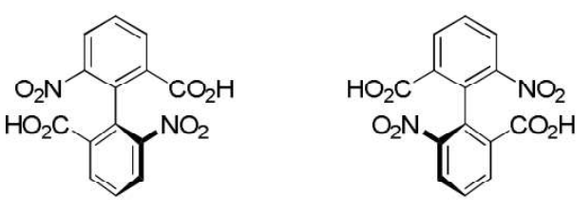
7.1 OBJECTIVES

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

- Understand about axial, planar and helical chirality
- Explain stereochemistry and absolute configuration of allenes, biphenyls and binaphthyls, ansa and cyclophanic compounds
- Discuss about spiranes, exo-cyclic alkylidene cycloalkanes

7.2 AXIAL, PLANAR AND HELICAL CHIRALITY

Chirality plays a crucial role in life-sustaining processes and therefore asymmetric synthesis has become a central research theme in the field of organic chemistry. Although a lot of research has been focussed earlier on the chemistry of molecules with sp^3 chiral center, other features such as axial chirality, helical chirality, and planar chirality have been recently investigated for their potential use in synthesis, in asymmetric catalysis, and as chiral perturbers. Axially chiral compounds, unlike molecules that feature central chirality (point chirality), lack stereogenic center(s) yet exist as enantiomers. Atropisomers belong to this class of chiral compounds; however, in this case the enantiomers exist due to the restricted rotation around a single bond. Following in an example of isolated atropisomeric molecules.



7.2.1 Axial Chirality

Axial chirality is a special case of chirality in which a molecule does not possess a stereogenic center (the most common form of chirality in organic compounds) but an axis of chirality – an axis about which a set of substituents is held in a spatial arrangement that is not superposable on its mirror image. Axial chirality is most commonly observed in atropisomeric substituted biarylcompounds wherein the rotation about the aryl–aryl bond is restricted, for example, various biphenyls, binaphthyls such as BINAP, and certain dihydroanthracenone compounds. Certain allenecompounds and spirans also display axial chirality. The enantiomers of axially chiral compounds are usually given the stereochemical labels Ra and Sa.

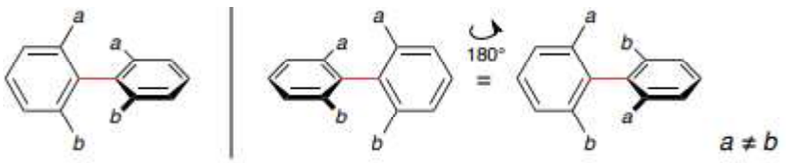
The designations are based on the same Cahn–Ingold–Prelog priority rules used for tetrahedral stereocenters. The chiral axis is viewed end-on and the two 'near' and two 'far' substituents on the axial unit are ranked, but with the additional rule that the near substituents have higher priority than the far ones.

Axial chirality takes two forms:

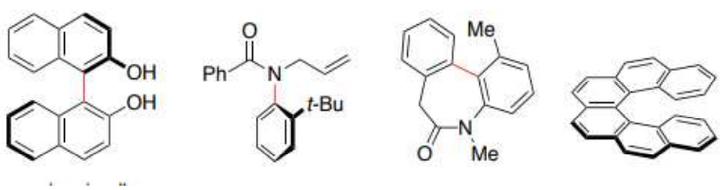
- Atropisomerism
- Isomerism in Allenes

Atropisomerism

- Atropisomerism is caused by inhibition of free rotation of a single bond. The inhibition of free rotation is often observed in the biaryl compounds bearing four ortho-substituents or some sterically hindered carboxamides.



- A racemate of axially chiral compound can be resolved into each enantiomer when the rotation barrier is over 20 kcal/mol.
- Axial chirality will be stable at room temperature when the rotation barrier is over 30 kcal/mol.
- Herical chirality is originated from the accumulation of axial chirality.



Types of Atropisomers

Atropisomers are stereoisomers that can be interconverted by rotation about single bonds but for which the barrier to rotation is large enough that the stereoisomers do not interconvert readily at room temperature and can be separated. Atropisomers are often broken down into several classes based on the type of hybridisation of the atom involved in the hindered rotation or by the type of bonds around which rotation is blocked (Refer Figure 7.1).

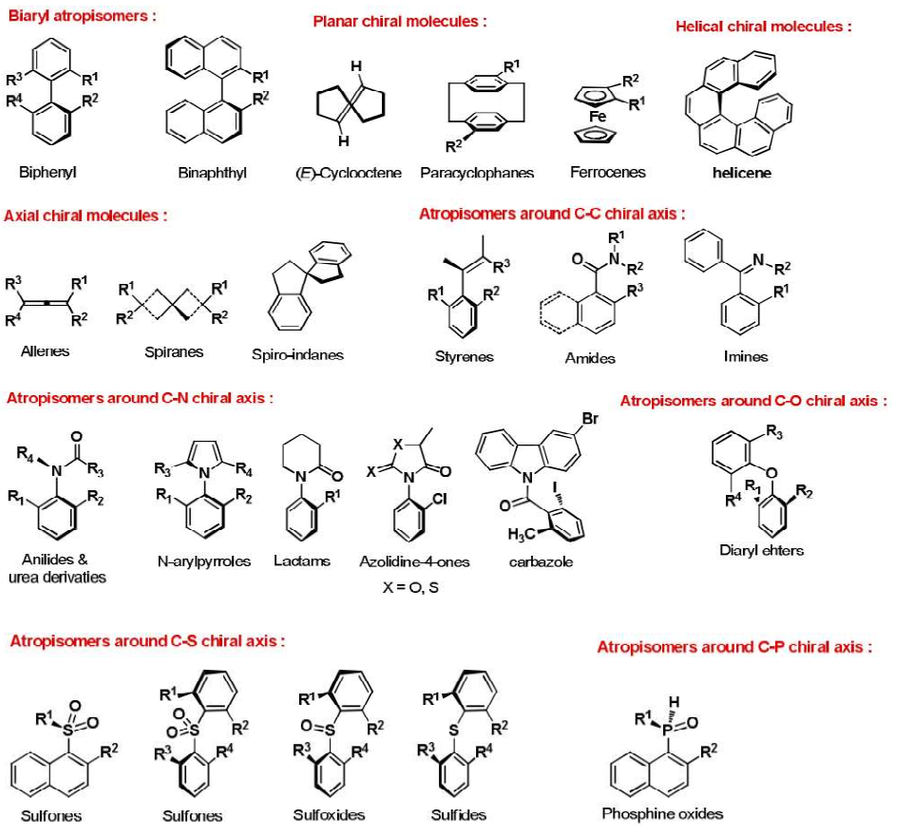
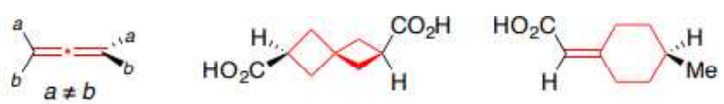


Fig. 7.1 *Various forms of Chiralities*

Isomerism in Allenes

- Each terminal carbon in C=C=C is plane because it is sp^2 -hybridized. One of the planes is perpendicular to another because the internal carbon in C=C=C is linear and hybridized in sp manner to form two C–C double bonds. Therefore, substituted allenes are possible to be chiral as with biaryls.
- The chirality is seen in some spiro bicyclic compounds and alkylidene cycloalkanes.



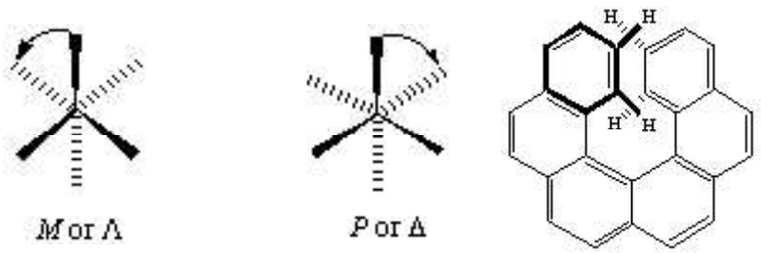
7.2.2 Planar Chirality

- Planar chirality appears when a planar molecule loses its symmetry plane by bridging with short tether or forming π-complex.
- The chirality is seen in some cyclophanes, metallocenes, and trans-cycloalkenes.

NOTES

7.2.3 Helical Chirality

The chirality of a helical, propeller or screw-shaped molecular entity can be defined as a right-handed helix as P (or plus), a left-handed one as M (or minus).



(M)-Hexahelicene

The application of this system to the description of conformations considers the torsion angle between two specified (fiducial) groups that are attached to the atoms linked by that bond. Helicity in a molecule arises when the molecule contains a stereogenic axis instead of a stereogenic centre. In a molecule that is not inherently helically chiral, helicity can be induced by designing the molecule such that an unfavourable steric interaction, or strain, is present in its planar conformation. The release of this strain forces the molecule to adopt a helical twist against the cost of the torsional strain induced in the backbone, an interplay of forces, which must be balanced in favour of the helical conformation over the planar one.

7.3 STEREOCHEMISTRY AND ABSOLUTE CONFIGURATION

Stereochemistry

Stereochemistry, a subdiscipline of chemistry, involves the study of the relative spatial arrangement of atoms that form the structure of molecules and their manipulation. The study of stereochemistry focuses on stereoisomers, which by definition have the same molecular formula and sequence of bonded atoms (constitution), but differ in the three-dimensional orientations of their atoms in space. For this reason, it is also known as 3D chemistry—the prefix stereo-means three-dimensionality (Refer Figure 7.2).

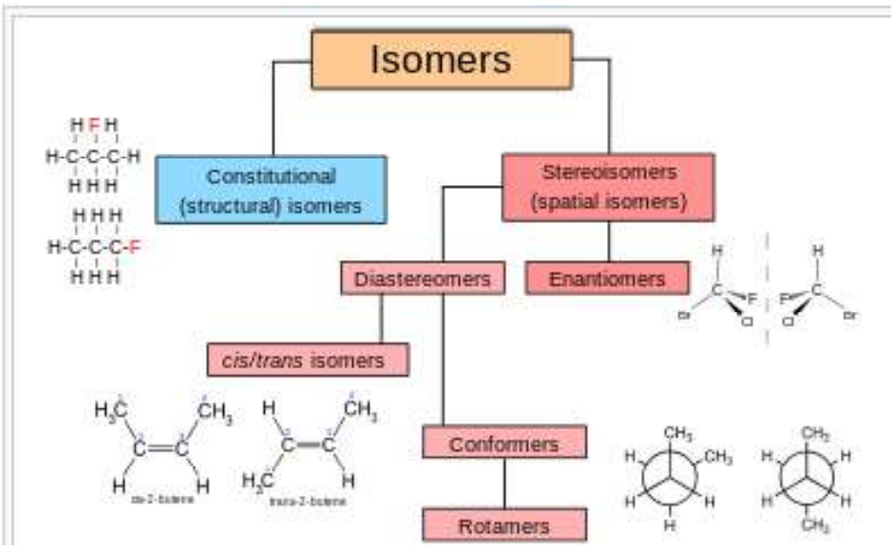
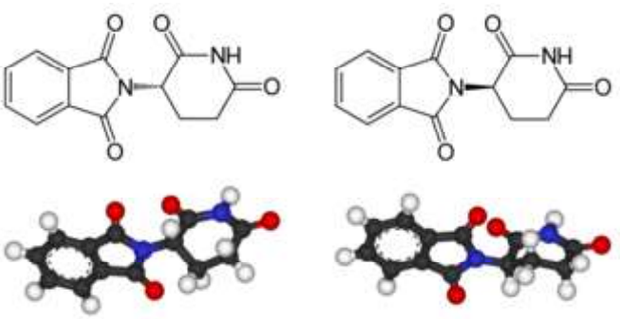


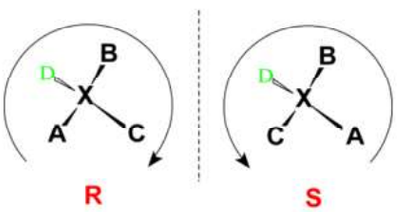
Fig. 7.2 *The Different Types of Isomers, Stereochemistry Focuses on Stereoisomers*



Thalidomide

Absolute Configuration

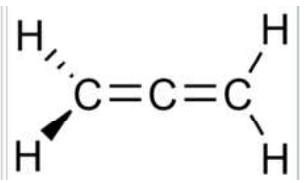
An absolute configuration refers to the spatial arrangement of the atoms of a chiral molecular entity (or group) and its stereochemicaldescription, for example, R or S,referring to Rectus, or Sinister, respectively.



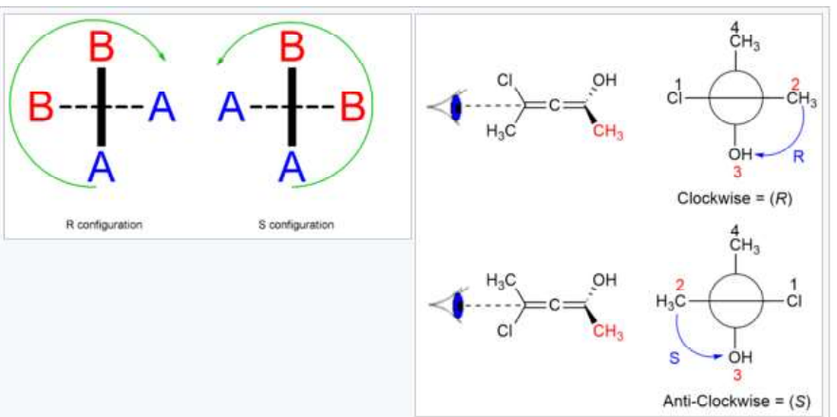
7.2.1 Allene

An allene is a compound in which one carbon atom has double bonds with each of its two adjacent carbon centres. Allenes are classified as polyeneswith cumulated

dienes. The parent compound of allene is propadiene. Compounds with an allene-type structure but with more than three carbon atoms are called cumulenes. Allenes are much more reactive than most other alkenes. For example, their reactivity with gaseous chlorine is more like the reactivity of alkynes than that of alkenes.



Propadiene, the Simplest Allene

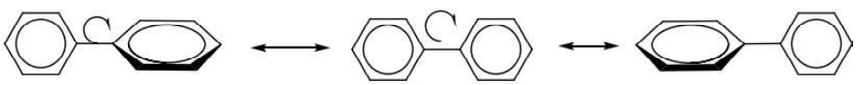


R and S configurations are determined by precedences of the groups attached to the axial section of the molecule when viewed along that axis. The front plane is given higher priority over the other and the final assignment is given from priority 2 to 3 (i.e.,the relationship between the two planes).

7.3.2 Biphenyls and Binaphthyls

Biphenyl Systems

Biphenyls are compounds whereby a phenyl ring is connected to another through a central σ bond.



In unsubstituted biphenyl, there is sufficient amount of freedom of rotation around the central single bond to allow for free interconversion between the various conformers or rotamers so that the various rotamers can not exist independently.

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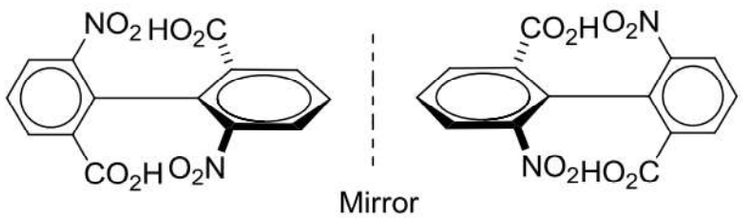
Biphenyl Systems (Atropisomerism)

However, biphenyls with large substituents at the ortho positions on either side of the central ó bond experience restricted rotation along this bond due to steric hindrance. If the substituents are different, a chiral molecule existing as a pair of enantiomers called atropisomers is obtained. The enantiomers can be made racemic by heating. The free energy required is in the range of 42 - 210 kJ/mole.



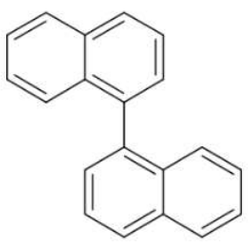
Binaphthyls

Binaphthyl

Molecular Formula: C20H14

Average Mass: 254.325 Da

Monoisotopic Mass: 254.109543 Da



The two symmetric binaphthyls (1,13 - and 2,23 -binaphthyl) were synthesized by Grignard coupling reactions of 1-bromonaphthalene and 2-bromonaphthalene, respectively, using two different promoters (Ni(acac)2 and 1,4-dichloro-2-butene). The non-symmetric 1,23 -binaphthyl was prepared via two methods:

- Coupling of 2-naphthylmagnesium bromide with 1-tetralone, followed by dehydration, then sulfur-catalyzed dehydrogenation.
- A Kharash-type Grignard coupling between 1-naphthylmagnesium bromide and 2-bromonaphthalene, with Ni(acac)2 as the promoter. The binaphthyls were exposed to room-and high-temperature tetrachloro-aluminate molten salts of differing composition.

1,13 -Binaphthyl and 1,23 -binaphthyl isomerized to 2,23 -binaphthyl in the room temperature molten salts, whereas 2,23 -binaphthyl was unchanged. In molten salts at temperatures in excess of 75æ, each of the binaphthyls underwent cyclodehydrogenation to form perylene and small amounts of benzofluoranthenes.

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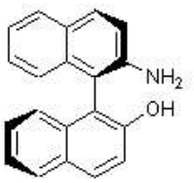
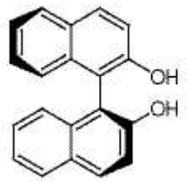
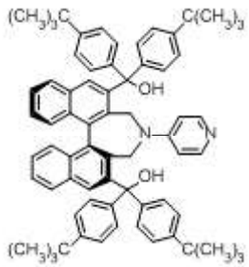


(R)-(+)-2-Amino-2'-hydroxy-1,1'-binaphthyl



(S)-(-)-1,1'-Bi-2-naphthol

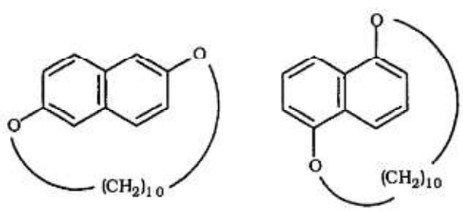


(S)-[4-(Pyridin-4-yl)-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepine-2,6-diyl]bis[bis[4-(tert-butyl)phenyl]methanol]

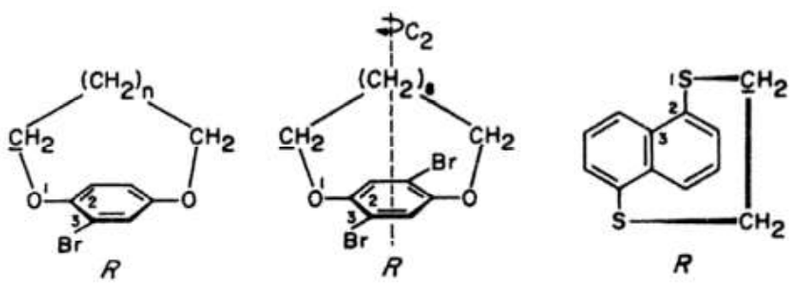
7.3.3 Ansa and Cyclophanic Compounds

Ansa Compounds

Ansa compounds are the derevatives of hydroquinone. It two para-position of an aromatic ring are attached to hetero atom and they are connected through a polymethylene chain.



The First Ansa Compounds



Ansa Compounds

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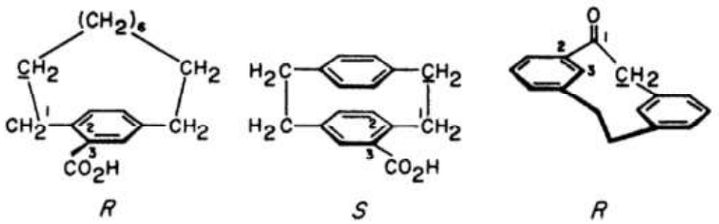
Cyclophane Compounds

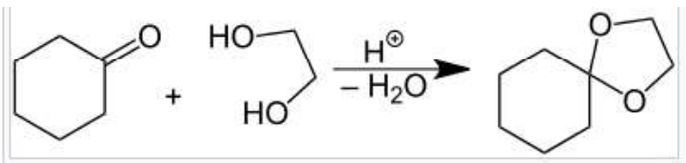
A cyclophane is a hydrocarbon consisting of an aromatic unit (typically a benzene ring) and an aliphatic chain that forms a bridge between two non-adjacent positions of the aromatic ring. More complex derivatives with multiple aromatic units and bridges forming cagelike structures are also known. Cyclophanes are well-studied in organic chemistry because they adopt unusual chemical conformations due to build-up of strain.



Cyclophanes Compounds: Simple, Para and Meta

7.3.4 SPIRANES

A spiro compound, or spirane, from the Latin spîra, meaning a twist or coil, is a chemical compound, typically an organic compound, that presents a twisted structure of two or more rings (a ring system), in which 2 or 3 rings are linked together by one common atom, SP-0 examples of which are shown at right.

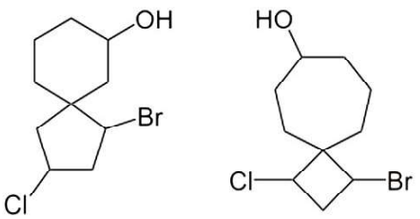


Preparation of a Heterocyclic Spiro Compound

A spiro compound is a bicyclic organic compound with rings connected through just one atom. The rings can be different in nature or identical. The connecting atom is also called the spiroatom, most often aquaternary carbon (spiro carbon). All spiro compounds have the infix spiro followed by square brackets containing the number of atoms in the smaller ring and the number of atoms in the larger ring excluding the spiroatom itself; the numbers being separated by a dot. For example,

- Compound A is called: 1-bromo-3-chlorospiro decan-7-ol
- Compound B is called: 1-bromo-3-chlorospiro decan-7-ol

The spiro compound consisting of a cyclohexane ring and a cyclopentane ring is called spiro decane. This nomenclature was proposed by Adolf von Baeyer in 1900. An example of a spiro compound with a trivial name: spiropentadiene.



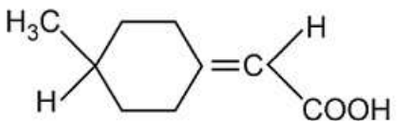
A **B**

Above is an example of Spiro Compound with a Trivial Name: Spiropentadiene

7.3.5 Exo-Cyclic Alkylidene Cycloalkanes

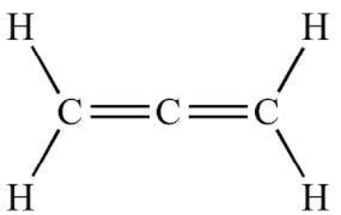
The 1,3 Dienes has two exocyclic double bonds and includes alkenation reactions, alkene metathesis, metal mediated coupling reactions and cycloisomerizations. Examples include the metal mediated transformations of acyclic diynes or enzymes into 1, 2 – bis (alkylidene) cycloalkanes.

Following is an 'Alkylidene Cycloalkane'. Its structure closely resembles that of allenes.



1-Methylcyclohexylidene-4-acetic acid (Alkylidene cycloalkane)

The allenes are non-planar molecules due to the two ðð-bonds being formed on almost perpendicular planes as shown below:



Check Your Progress

1. What is axial chirality?
2. How many types of axial chirality are there?
3. Define atropisomers.

7.4 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

NOTES

1. Axial chirality is most commonly observed in atropisomeric substituted biaryl compounds wherein the rotation about the aryl–aryl bond is restricted, for example, various biphenyls, binaphthyls such as BINAP, and certain dihydroanthracenone compounds.
2. Axial chirality takes two forms:
   - Atropisomerism
   - Isomerism in Allenes
3. Atropisomers are stereoisomers that can be interconverted by rotation about single bonds but for which the barrier to rotation is large enough that the stereoisomers do not interconvert readily at room temperature and can be separated.
4. Stereochemistry, a subdiscipline of chemistry, involves the study of the relative spatial arrangement of atoms that form the structure of molecules and their manipulation. The study of stereochemistry focuses on stereoisomers, which by definition have the same molecular formula and sequence of bonded atoms (constitution), but differ in the three-dimensional orientations of their atoms in space.
5. An absolute configuration refers to the spatial arrangement of the atoms of a chiral molecular entity (or group) and its stereochemicaldescription, for example, R or S,referring to Rectus, or Sinister, respectively.
6. An allene is a compound in which one carbon atom has double bonds with each of its two adjacent carbon centres.
7. Biphenyls are compounds whereby a phenyl ring is connected to another through a central ó bond.

7.5 SUMMARY

- Chirality plays a crucial role in life-sustaining processes and therefore asymmetric synthesis has become a central research theme in the field of organic chemistry.
- Although a lot of research has been focussed earlier on the chemistry of molecules with sp^3 chiral center, other features such as axial chirality, helical chirality, and planar chirality have been recently investigated for their potential use in synthesis, in asymmetric catalysis, and as chiral perturbers.
- Axially chiral compounds, unlike molecules that feature central chirality (point chirality), lack stereogenic center(s) yet exist as enantiomers. Atropisomers

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belong to this class of chiral compounds; however, in this case the enantiomers exist due to the restricted rotation around a single bond.

- Axial chirality is a special case of chirality in which a molecule does not possess a stereogenic center (the most common form of chirality in organic compounds) but an axis of chirality – an axis about which a set of substituents is held in a spatial arrangement that is not superposable on its mirror image.
- Axial chirality is most commonly observed in atropisomeric substituted biaryl compounds wherein the rotation about the aryl–aryl bond is restricted, for example, various biphenyls, binaphthyls such as BINAP, and certain dihydroanthracenone compounds.
- Certain allenecompounds and spirans also display axial chirality. The enantiomers of axially chiral compounds are usually given the stereochemical labels Ra and Sa. The designations are based on the same Cahn–Ingold–Prelog priority rules used for tetrahedral stereocenters.
- The chiral axis is viewed end-on and the two 'near' and two 'far' substituents on the axial unit are ranked, but with the additional rule that the near substituents have higher priority than the far ones.
- Atropisomerism is caused by inhibition of free rotation of a single bond. The inhibition of free rotation is often observed in the biaryl compounds bearing four ortho-substituents or some sterically hindered carboxamides.
- Atropisomers are stereoisomers that can be interconverted by rotation about single bonds but for which the barrier to rotation is large enough that the stereoisomers do not interconvert readily at room temperature and can be separated.
- Atropisomers are often broken down into several classes based on the type of hybridisation of the atom involved in the hindered rotation or by the type of bonds around which rotation is blocked Each terminal carbon in C=C=C is plane because it is sp^2 -hybridized.
- One of the planes is perpendicular to another because the internal carbon in C=C=C is linear and hybridized in sp manner to form two C–C double bonds. Therefore, substituted allenes are possible to be chiral as with biaryls.
- Stereochemistry, a subdiscipline of chemistry, involves the study of the relative spatial arrangement of atoms that form the structure of molecules and their manipulation.
- The study of stereochemistry focuses on stereoisomers, which by definition have the same molecular formula and sequence of bonded atoms (constitution), but differ in the three-dimensional orientations of their atoms in space.
- An absolute configuration refers to the spatial arrangement of the atoms of a chiral molecular entity (or group) and its stereochemicaldescription, for example, R or S,referring to Rectus, or Sinister, respectively.

NOTES

- An allene is a compound in which one carbon atom has double bonds with each of its two adjacent carbon centres. Allenes are classified as polyenes with cumulated dienes.
- The parent compound of allene is propadiene. Compounds with an allene-type structure but with more than three carbon atoms are called cumulenes.
- Allenes are much more reactive than most other alkenes.
- Biphenyls are compounds whereby a phenyl ring is connected to another through a central ó bond.
- Ansa compounds are the derevatives of hydroquinone. It two para-position of an aromatic ring are attached to hetero atom and they are connected through a polymethylene chain.
- A cyclophane is a hydrocarbon consisting of an aromatic unit (typically a benzene ring) and an aliphatic chain that forms a bridge between two non-adjacent positions of the aromatic ring.

7.6 KEY WORDS

- **Absolute configuration:** A description of the precise 3-dimensional topography of the molecule.
- **Ansa compounds:** Ansa compounds are the derevatives of hydroquinone.
- **Cyclophane:** A cyclophane is a hydrocarbon consisting of an aromatic unit (typically a benzene ring) and an aliphatic chain that forms a bridge between two non-adjacent positions of the aromatic ring.
- **Biphenyls:** Biphenyls are compounds whereby a phenyl ring is connected to another through a central ó bond.
- **Allene:** An allene is a compound in which one carbon atom has double bonds with each of its two adjacent carbon centres.
- **Stereochemistry:** Stereochemistry, a sub-discipline of chemistry, involves the study of the relative spatial arrangement of atoms that form the structure of molecules and their manipulation.

7.7 SELF ASSESSMENT QUESTIONS AND EXERCICES

Short Answer Questions

1. Write a brief note on chirality.
2. What is axial chirality ?
3. What is planar chirality ?

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4. Define Stereochemistry ?
5. Brief a note on allene .
6. Give short note on ansa compounds.

Long Answer Questions

1. Define chirality. Explain about axial, planar and helical chirality in detail.
2. Explain stereochemistry and absolute configuration.
3. Write a descriptive note on allenes.
4. Explain biphenyls and binaphthyls.
5. Discuss about ansa and cyclophanic compounds.
6. Elaborate a note on spiranes and exo-cyclic alkyldenecycloalkanes.

7.8 FURTHER READINGS

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Pine, S.H., J.B. Hendrickson, D.J. Cram and G.S. Hammond. 1980. *Organic Chemistry*, 4th Edition. New York: McGraw-Hill Company.

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NOTES

BLOCK - III
REACTION MECHNAISM AND
MOLECULAR REARRANGEMENT

UNIT 8 KINETICS OF REACTION MECHANISM

Structure

8.0 INTRODUCTION

Organic reactions are chemical reactions involving organic compounds. The number of possible organic reactions is basically infinite. However, certain general patterns are observed that can be used to describe many common or useful reactions. Organic reactions can be categorized based on the type of functional group involved in the reaction as a reactant and the functional group that is formed as a result of this reaction.

The basic organic chemistry reaction types are addition reactions, elimination reactions, substitution reactions, pericyclic reactions, rearrangement reactions, photochemical reactions and redox reactions. In organic synthesis, organic reactions are used in the construction of new organic molecules. The production of many man-made chemicals such as drugs, plastics, food additives, fabrics depend on organic reactions.

Chemical kinetics, also known as reaction kinetics, is the study of rates of chemical processes. Chemical kinetics includes investigations of how different experimental conditions can influence the speed of a chemical reaction and yield information about the reaction's mechanism and transition states, as well as the construction of mathematical models that can describe the characteristics of a chemical reaction.

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In this unit, you will study four major organic reactions i.e., substitution reaction, addition reaction, elimination reaction and rearrangement reaction. After going through the types of reactions, you will study and understand the kinetics of reaction mechanism.

8.1 OBJECTIVES

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

- Understand the classification of organic reactions
- Know about principle of microscopic reversibility
- Discuss kinetic and thermodynamic control of chemical reactions
- Discuss kinetic and non-kinetic methods for determining organic reaction mechanism

8.2 CLASSIFICATION OF ORGANIC REACTIONS

Most organic reactions involve conversion of one functional group into another by the attack of a reagent. Usually the saturated hydrocarbon residue of the molecule remains unaffected during the reaction. An organic compound which is attacked by a reagent is known as **substrate** or **reactant**. The reagent is generally a simple inorganic or organic substance which is used to create a desired transformation in the compound. Thus an organic reaction may be represented as:

$$\text{Substrate} + \text{Attacking reagent} \rightarrow [\text{Intermediate(s)}] \rightarrow \text{Product(s)}$$

Any classification of organic reactions must emphasize the changes that occur in the carbon bondings of the substrate at the site of the reaction. Thus a large variety of organic reactions may be placed in four major groups: (1) *Substitution reactions* (2) *Addition reactions* (3) *Elimination reactions*, and (4) *Rearrangements*.

The acid base reactions may be considered as a separate class because this type of reaction does not change the structure of substrate fundamentally.

1. **Substitution reactions.** Reactions in which an atom or a group is replaced by another atom or group, are called substitution reactions. In such reactions the bonds are broken and formed at the same atom which is considered as the reactive site of the substrate. The substitution may be initiated by an electrophile, nucleophile or a free radical resulting in three categories shown below:

1. Free radical substitution at saturated carbon

$$\text{R—H} \xrightarrow[h\nu]{\text{Cl}_2} \text{R—Cl} + \text{HCl}$$

2. Electrophilic substitution at unsaturated carbon

$$\text{C}_6\text{H}_3\text{—H} + \text{Cl}_2 \xrightarrow{\text{FeCl}_3} \text{C}_6\text{H}_5\text{Cl} + \text{HCl}$$

3. Nucleophilic substitution

(i) at saturated carbon $C_2H_5—Br + NaOH \rightarrow C_2H_5—OH + NaBr$

(ii) at unsaturated carbon $C_6H_5—Cl + NaOH \xrightarrow[\text{High P}]{\Delta} C_6H_5ONa + HCl$

Each of these types of substitution reaction may be unimolecular or biomolecular depending on the kinetics of the reaction.

In the first reaction a chlorine has been substituted by hydroxyl group. In the second all the hydrogens have been substituted by chlorine atoms; in the third hydroxyl group has been replaced by bromine and in the last reaction a hydrogen of benzene has been substituted by chlorine.

2. **Addition reactions**. 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 π bond of the molecule two σ 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:

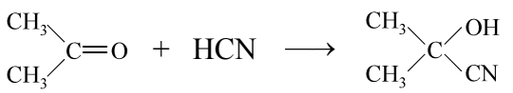
1. Free radical addition

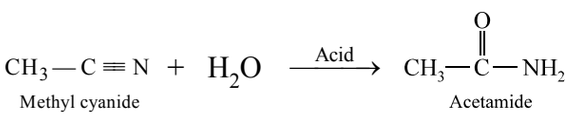
$$CH \equiv CH + H_2 \xrightarrow[140°]{Ni} CH_2 = CH_2 \xrightarrow[200°]{H_2/Ni} CH_3 — CH_3$$

2. Electrophilic addition

$$CH_2 = CH_2 + Br_2 \longrightarrow CH_2Br — CH_2Br$$

3. Nucleophilic addition





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 π bond of sp^2 hybridized carbon is converted to two σ bond of sp^3 hybridized carbon by addition of two atoms of bromine. In the third reaction $\rangle C = O$ adds up a molecule of HCN resulting in corresponding cyanohydrin. The π bond of sp^2 carbon is changed to sp^3 carbon σ 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.

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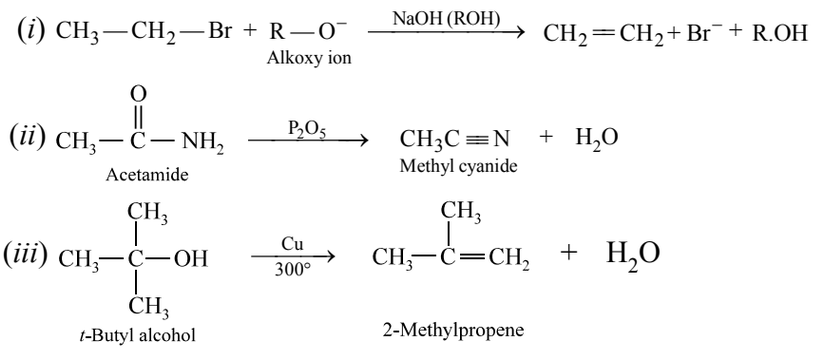
3. **Elimination reactions**. The reverse of addition reactions are eliminations. In elimination reactions the number of groups or atoms attached to carbon decrease and the degree of unsaturation in the molecule increases. In essence σ bonds are converted to π bonds. State of hybridization of carbon changes from sp^3 to sp^2 and sp^2 to sp. Unlike other reactions the elimination reactions are not categorized depending on the nature of attacking reagent but are generally classified on the basis of molecularity of the reaction. Some examples of elimination reactions are given below:

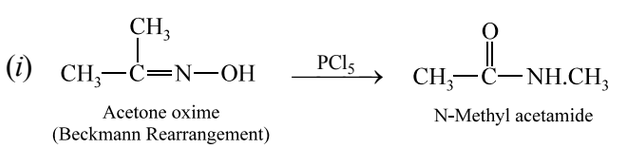


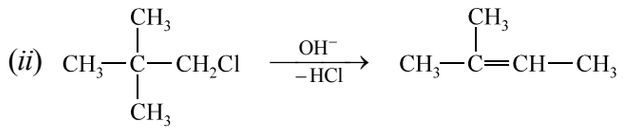
In the first reaction a molecule of HBr is eliminated and two sp^3 carbons are converted to sp^2 carbons and two σ bonds are changed to one π bond. In second reaction a water molecule is eliminated to yield a triple bond (sp carbon) starting from a double bond (sp^2 carbon). In the last reaction a water molecule is eliminated from saturated sp^3 carbon to form unsaturated sp^2 carbon linkage.

Fragmentation reactions involving cleavage of carbon-carbon bonds and decomposition of molecules to smaller molecules or fragments, can also be considered as a type of elimination reaction.

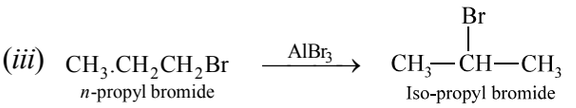
4. **Rearrangement reactions**. *The reactions in which the carbon skeleton of the molecule is rearranged to give a structural isomer of the original molecule are known as rearrangement reactions.* These rearrangements can also be considered as a sequence of steps involving substitution, additions or elimination reactions. Usually in such reactions atoms or groups shift from one position to another within the molecule resulting in a new molecular structure.

The rearrangements vary in their types depending on the atoms or groups migrating in the molecule. The migrating groups are anions or carbanions, cation or carbocations and free radicals. Examples of some rearrangement reactions are given below:





(*Elimination followed by rearrangement*)



8.3 MICROSCOPIC REVERSIBILITY

In the course of a reaction, the nuclei and electrons assume positions that at each point correspond to the lowest free energies possible. If the reaction is reversible, these positions must be the same in the reverse process, too. This means that the forward and reverse reactions (run under the same conditions) must proceed by the same mechanism. This is called the principle of microscopic reversibility. For example, if in a reaction A '! B there is an intermediate C, then C must also be an intermediate in the reaction B '! A. This is a useful principle since it enables one to know the mechanism of reactions in which the equilibrium lies far over to one side. Reversible photochemical reactions are an exception, since a molecule that has been excited photochemically does not have to lose its energy in the same way.

The Principle of Microscopic Reversibility can be stated in several different ways:

- If a certain series of steps constitutes the mechanism of a forward reaction, the mechanism of the reverse reaction (under the same conditions) is given by the same steps traversed backwards. (Note: The phrase "under the same conditions" means that this applies only to thermal reactions, not photochemical ones.)
- The sequence of transition states and reactive intermediates in the mechanism of a reversible reaction must be the same, but in reverse order, for the backward reaction as for the forward reaction
- If the mechanism in one direction is known, then the mechanism in the opposite direction is known.
- The lowest-energy pathway in the forward direction will be the lowest-energy pathway in the reverse direction.

Let's illustrate this with an example of a generic organometallic complex, $L_nM(A)(B)$ undergoing reductive elimination of AB:

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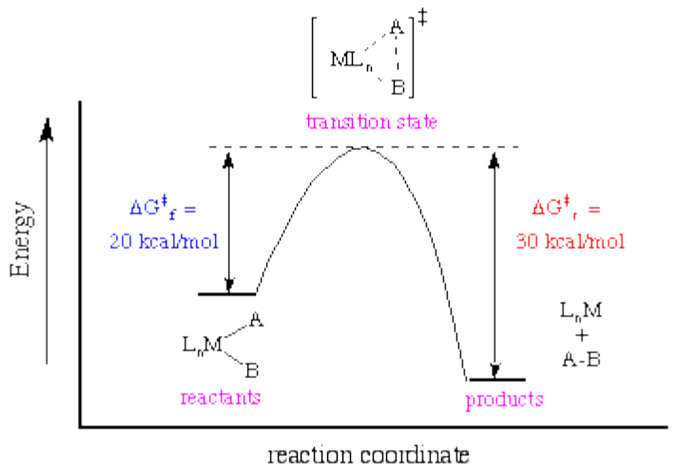

Fig. 8.1

In the example shown above, the activation energy, Ä-G^t_f in the forward direction is 20 kcal/mol. If we wish to do the reverse reaction, oxidative addition of AB to L_nM, then we have to surmount a higher barrier with a Ä-G^t_f of 30 kcal/mol. This does not mean that the reverse reaction does not or cannot occur, only that it is thermodynamically disfavored.

In other cases, the relative energies of the products and reactants might make the forward activation barrier higher in energy or even equal to that of the reverse reaction:

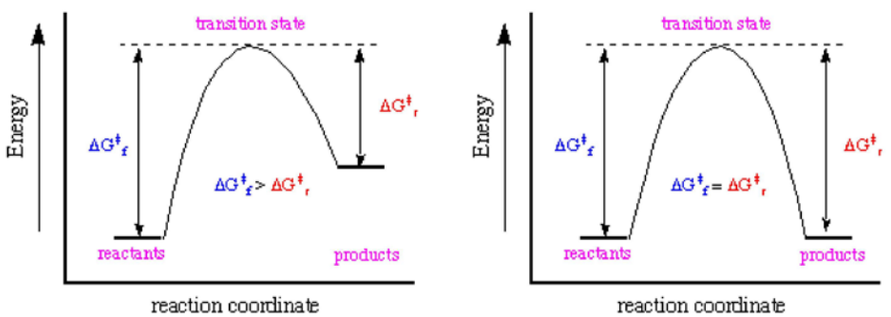

Fig. 8.2

Check Your Progress

1. What are fragmentation reactions?
2. What is the reverse of addition reactions?
3. Which reactions are considered as a sequence steps involving substitution, addition or elimination reactions?

8.4 KINETIC AND THERMODYNAMIC CONTROL OF CHEMICAL REACTIONS

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The feasibility of a particular reaction is based on the energetics (energy considerations) for that reaction. Thermodynamics is the study of the energy flow in a system. If thermodynamics predicts that a reaction will not occur under certain conditions—then it is no use trying it, because it would not occur. However if a reaction is predicted by thermodynamics, then though theoretically it may take place but unless its reaction rate is fast enough, it will be of no use. The energetics of a system can be interpreted in terms of heat content of the system termed as **Enthalpy** (H) in thermodynamics.

Usually, all reactions have an equilibrium which is characterized by an equilibrium constant (K). Equilibrium constant for a reaction depends on Gibb's free energy (G) change of the system. To understand the concept of Gibb's free energy, it may be applied to a hypothetical equilibrium.

$$\underset{\text{Reactants}}{A + B} \rightleftharpoons \underset{\text{Products}}{C + D}$$

Equilibrium constant $K = \frac{[C][D]}{[A][B]}$.

The relation of free energy with equilibrium constant is given by the equation:

$$\Delta G \text{ (Change in free energy)} = -2.3\ R T \log K$$

where R is gas constant, T is temperature, in absolute scale.

Thus both A and B possess certain amount of energies and in order that the reactions may proceed some existing bonds in these reactants must be broken. Breaking of bond requires energy. So for the reaction to occur a certain amount of energy must be provided to the reactants. Similarly when C and D are formed new bonds must be created. Formation of bonds releases energy—which may be greater or less depending upon individual bond energies involoved. Thus the energy of a chemical reaction is equal to the difference in energy between reactants and products. If in formation of products, the energy is released the reaction is said to be **exothermic** whereas if the energy is absorbed the reaction is known as **endothermic**. In exothermic reactions the total energy of the system is lowered and it thus becomes more stable after the reaction i.e. the products are more stable than the reactants. In endothermic reactions the system goes to a higher energy level and products are less stable than reactants. This difference of energy is also referred to as change in free energy. The idea has been illustrated in Figure. 8.3.

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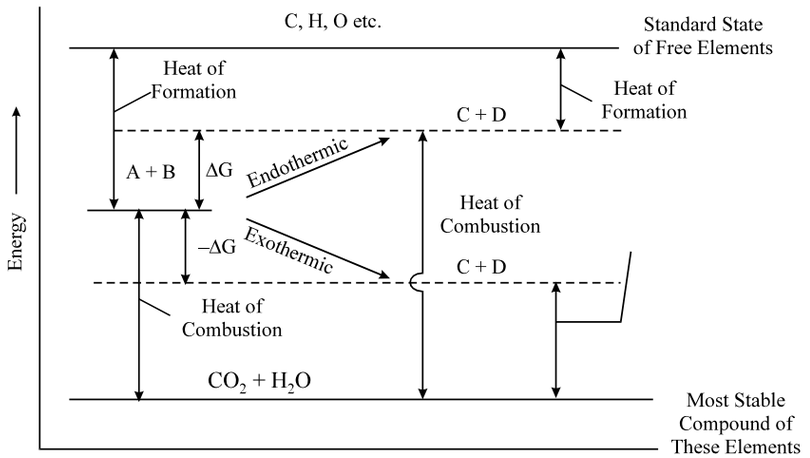

Fig. 8.3 *Energy relations between elements, compounds, reactants and products.*

The change in free energy (ΔG) is related to the change in enthalpy (ΔH) or heat content and change in entropy (ΔS) of the system by the equation.

$$\Delta G = \Delta H - T\Delta S \text{ where } T \text{ is absolute temp.}$$

The entropy is a measure of randomness or disorder or probability of a system. The greater the disorder the greater is the entropy. For example molecules in gaseous state are much more disorderly as compared to the liquid state. Again in the liquid state molecules are more disorderly as compared to solid state. So the entropy of such a system decreases as we go from gaseous to solid state via liquid state. For a reaction of the type $A + B \rightarrow C + D$ usually the entropy change is small or negligible because the number of molecules before and after the reaction is same and molecules are distributed with same randomness. Entropy is negative for the reactions of the type $A + B \rightarrow C$ and positive for the reaction $A \rightarrow C + D$. In case entropy changes are negligible the value of ΔG is obtained from change in enthalpy directly. A negative value of ΔG indicates the thermodynamic probability of a reaction.

Kinetic Versus Thermodynamic Control of Reactions

Product distribution in a chemical reaction is generally influenced by two factors:

1. Relative stability of the product (thermodynamic factor)
2. Rate of formation of the product (kinetic factor)

Suppose in a reaction two products 'A' and 'B' are formed, of which 'B' is more stable. It the activation energy for the formation of 'A' is lower than that of formation of 'B' it will be formed faster (kinetic control), otherwise the product 'B' will be formed as it is more stable (thermodynamic control). Thus the kinetic product distribution is derived from the energy difference between the transition states leading to the two products while the thermodynamic product distribution is derived from the free energy difference between the two products. In both cases it is the lower energy species which predominates over the other one.

Consider a case where a starting material (R) gives rise to two different products (A) and (B) via different pathways. Reaction forming (A) via T.S. (A) will be factor since at has a more stable transition state. Hence it is a kinetic product.

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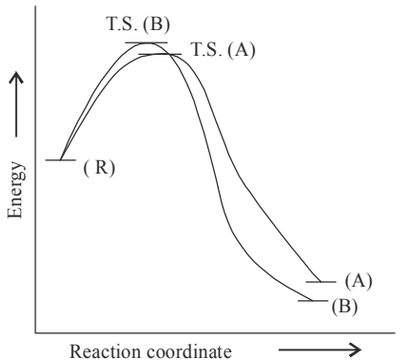

Fig. 5.4

On the other hand (B) in more stable since it is has a lower energy. Hence it is a thermodynamic product.

The conditions of the reaction, such as temperature, pressure and solvent, decide upon the favoured pathway.

In the above reaction at low temperatures, (A) will be formed predominantly and stop as it has not got the energy to revert to (R), i.e., the reaction is irreversible. Hence the product ratio will depend on the rates of formation of (A) and (B).

On the other hand, at higher temperature the reaction forming (A) becomes reversible and hence though (A) may be formed initially it reverts to (R) and then reacts to give the more stable (B).

At still higher temperatures both the reactions become reversible and the product ratio is decided by the equilibrium constants of the two reactions.

In conclusion it may be stated that:

(i) At low temperatures the reaction is kinetically controlled and the major product is (A).

(ii) At higher temperatures the reaction is thermodynamically controlled and the major product is more stable (B).

(iii) In every reaction the first product formed is kinetically controlled.

(iv) An essential condition for thermodynamic control is the reversibility of the reactions permitting equilibration of products.

(v) Short reaction times favour kinetic control while longer reaction times favour thermodynamic control.

(vi) If a reaction is under kinetic control, at a given temperature it will always be under kinetic control at any lover temperature.

(vii) If a reaction is under thermodynamic control at a given temperature it will also be under thermodynamic control at any higher temperature.

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During addition of HBr to 1, 3-butadiene a mixture of 3-bromo-1-butene and 1-bromo-2-butene is formed. At –80°C, 3-bromo-1-butene is the major product (kinetic control) while at 40°C, 1-bromo-2-butene is the major product (thermodynamic control).

In sulphonation of naphthalene with oleum at 80°C the product is 1-naphthalene sulphonic acid (kinetic control) whereas at 160°C the product is 2-naphthalene sulphonic acid (thermodynamic control).

Kinetics of Reaction and Reaction Rates

Kinetics deals with the rate of reaction and factors affecting the rate. For the type of reaction $A + B \rightarrow C + D$ if the rate is expressed as Rate = K. [A][B], where K is the rate constant. The reaction is dependent on two concentrations, that of A and B and is a second order reaction. Since two molecules are involved in collision and are undergoing valency change it is **Bimolecular reaction**.

Alternatively the reaction may occur in two steps such as

$$(i)\ A \xrightarrow{\text{Slow}} \underset{\text{Intermediate}}{Z} \qquad \text{and} \qquad (ii)\ Z + B \xrightarrow{\text{Fast}} \underset{\text{Product}}{C + D}$$

In this case Rate = K[A] as only A is involved in rate determining slow step.

For a reaction of the type $A \rightarrow C + D$, the rate = K[A], is dependent on the concentration of A only and is a first order reaction. Since only one molecule is undergoing valency change it is a **Unimolecular reaction**.

The above two types of reactions may proceed as

$$(i)\ \underset{\text{Reactants}}{A + B} \xrightarrow{\text{Slow}} \underset{\text{Intermediates}}{Z} \xrightarrow{\text{Fast}} \underset{\text{Products}}{C + D;} \qquad \text{Rate} = K[A][B]$$

$$(ii)\ \underset{\text{Reactants}}{A} \xrightarrow{\text{Slow}} \underset{\text{Intermediates}}{Z} \xrightarrow{\text{Fast}} \underset{\text{Products}}{C + D;} \qquad \text{Rate} = K[A]$$

Both are two-step reactions involving formation of intermediate Z. When more than one step is involved in a reaction it is known as multi-step reaction. The rate of such a reaction is equal to the rate of the slowest step known as the **rate determining step** and the kinetics of the reaction is the kinetics of the slowest or the rate determining step.

In contrast to this, in a single step reaction all the molecules are undergoing valency change simultaneously and hence such a reaction is known as synchronous or concerted reaction.

The two general theories commonly used to explain reactions, their rates, order etc. are (*i*) *Collision Theory*, and (*ii*) *Transition State Theory.*

Curtin – Hammett Principle. According to this principle if for a chemical reaction there is a pair of reactive intermediates or reactants that interconvert rapidly and each forming different products irreversibly then the product ratio will depend only on the difference in the free energy of the transition state forming each product

and not on the equilibrium constant between the intermediates. For example, in a reaction where A and B are in equilibrium and A changes into C and B into D both irreversibly, K is the equilibrium constant between A and B and K_1 and K_2 are rate constants for the formation of C and D respectively. If the rate of interconversion between A and B is much faster than either rate constants than Curtin-Hammett Principle prodicts then the C : D product ratio will not be decided by K but by the relative energies of the transition states.

$$C \xleftarrow{K_1} A \rightleftharpoons B \xrightarrow{K_2} D$$

Curin-Hammett Principle is important in explaining the selectivity ratios in stereoselective reactions.

Hammond's Postulates. Also known as Hammond-Leffler postulate it concerns the transition state of organic chemical reactions. It states that if a transition state and an intermediate occur consecutively in a reaction and have nearly the same energy their interconversion will involve only a small reorganization of the molecular structure.

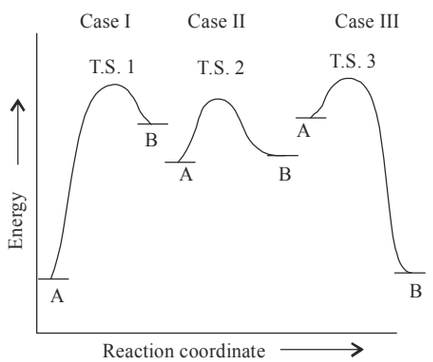

Fig. 5.5

In essence the postulate states that the structure of a transition state resembles that of the species nearest to it in free energy. Since due to the very nature of transition state it is not possible to observe them and deduce their structure, Hammond's postulate allows us to make assumption about the structure of transition state. Consider the following three cases.

Case I. In such a highly endothermic reaction TS_1 resembles the structure of B being closer to it in energy.

Case II. Here neither A nor B has a structure similar to TS_2.

Case III. In a highly exathermic reaction the structure of TS_3 resembles reactant A is the transition state is much closer to the reactant in energy.

In order to predict the effect of substituents on the energy of the transition state and hence on the rates of reaction, **Polanyi-Hammond postulate** states that *mutual conversion between two species which are adjacent to each other on the reaction coordinate requires only a minor change in the structure provided they have nearly the same energy.*

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If an energy-rich intermediate is formed after the transition state on the reaction coordinate, then the structure of the transition state has only a minor difference as compared to that of the reaction intermediate. Thus the effect of substituents on the energy of the transition state can be estimated by noting the effect these substituents have on the energy of the reaction intermediate. Such energy-rich reaction intermediates are often observed in electrophilic aromatic substitution as sigma (σ) complexes or as carbonium ion in addition of hydrogen halide to olefins.

Polanyi-Hammond postulate helps not only in the prediction of the structure of transition state but also in predicting the effect of substituents on the energy of activation and rates of reactions.

8.5 KINETIC AND NON-KINETIC METHODS FOR DETERMINIG ORGANIC REACTION MECHANISMS

A number of methods besides the study of thermodynamics and kinetics are used to study the course of a reaction. Some of these are:

1. Identification of products and by-products.
2. Determination of the presence of intermediate(s) by isolation or detection or trapping.
3. Study of catalyst action.
4. Isotopic labelling of reactive sites to distinguish two identical atoms.
5. Relative reactivities of various reagents and substrates.
6. Variation in rate of reaction or other parameters with different solvents.
7. Stereochemical evidences—effect of reaction on asymmetric centres in the molecules.

1. **Identification of products and by-products.** Any proposed mechanism for a reaction must account for the formation of all the products, by-products as well as their ratios. Thus the halogenation of methane in presence of sunlight must account for the formation of ethane as a by-product,

$$Cl\!-\!Cl \xrightarrow{h\nu} Cl\cdot + \cdot Cl$$

$$H\!-\!CH_3 \xrightarrow{\cdot Cl} H-Cl + \cdot CH_3$$

$$Cl\!-\!Cl + \cdot CH_3 \longrightarrow CH_3-Cl + \cdot Cl$$

The formation of ethane occurs due to combination of two methyl radicals.

$$\cdot CH_3 + \cdot CH_3 \longrightarrow CH_3-CH_3$$

In epoxidation reaction of alkene with peracids which is an electrophilic attack on the alkene and is of first order with respect to olefin as well as to peracid, the product is stereo- specific suggesting it to have concerted mechanism.

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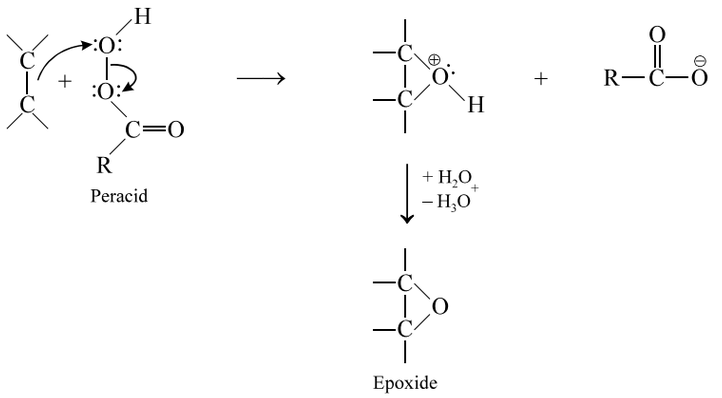


cis-alkene forms *cis*-epoxide while *trans*-alkene forms *trans*-epoxide excluding the possibility of formation of an intermediate carbocation.

2. **Determination of the presence of an Intermediate**

(*a*) *Isolation of intermediate.* An intermediate believed to be formed in a proposed mechanism, may sometimes be isolated by carrying out the reaction under mild conditions.

Thus in Hofmann degradation of an amide using halogen and alkali, an isocyanate intermediate has been isolated supporting the proposed mechanism.

(*b*) *Detection of intermediate.* Sometimes an intermediate cannot be isolated but its presence may be indicated by IR, NMR spectra etc. or some other technique.

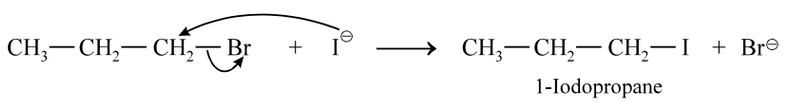
In the nitration of benzene which is an electrophilic substitution, involvement of NO_2^+ (nitronium ion), was shown with the help of Raman spectra.

(*c*) *Trapping of an intermediate.* The formation of an intermediate may be confirmed by carrying out the reaction in presence of a substance known to react with intermediate and analysing the product for adduct.

Thus benzyne intermediate is known to undergo Diels Alder reaction with dienes. In a reaction where benzyne is suspected to be an intermediate, a little diene is added to the reaction mixture. Formation of adduct with diene (thus trapping it) confirms the involvement of benzyne as intermediate.

(*d*) *Indirect evidence.* Indirect evidence also helps in deciding the mechanism of reaction.

For example, the reaction of 1-bromopropane with sodium iodide forms exclusively 1-iodopropane. Obviously the reaction cannot occur via the formation of a carbocation, because if 1° carbocation is formed, it will rearrange to 2° carbocation and the product will be 2-iodopropane. Since no 2-iodopropane is formed reaction must be proceeding through a concerted mechanism



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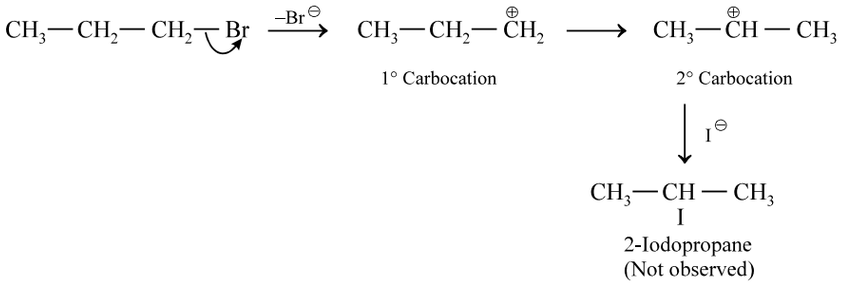
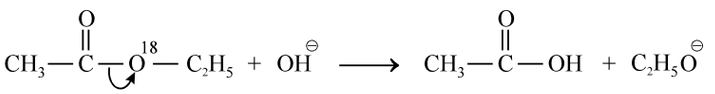
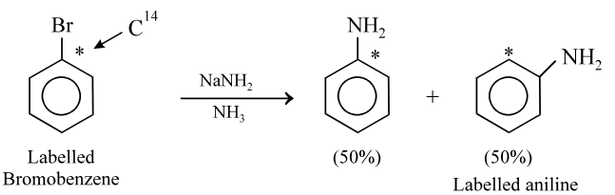


3. **Isotopic labelling**. A lot of information regarding reaction mechanism has been obtained using isotopically labelled molecule and tracing the path of the reaction.

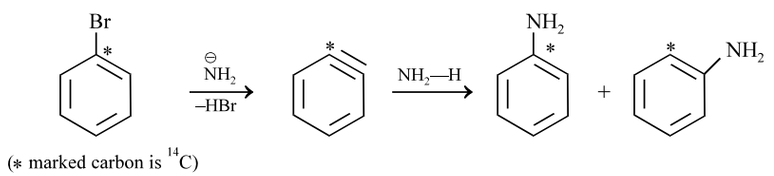
For example, the alkaline hydrolysis of esters labelled with O^{18} helped to prove that the reaction involves bond cleavage between oxygen and acyl group.



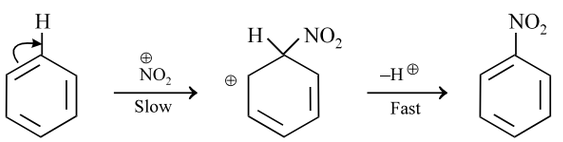
Similarly the benzyne mechanism for nucleophilic aromatic substitution was established by isotopic labelling experiments.



The reaction must proceed via the formation of benzyne intermediate to account for the formation of two products



Rate of nitration of benzene and deuterobenzene are same suggesting that loss of proton or deutron is not the rate determining step but the fast step.



4. **Kinetic evidence**. The rate of a reaction is the rate of disappearance of a reactant or formation of a product. In some cases change in concentration of a reactant results in no change in the rate of reaction.

If the rate is proportional to the change in the concentration of only one reactant, it is first order with respect to that reactant.

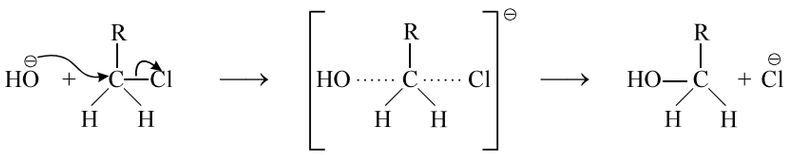
If the rate of reaction is proportional to the change in the concentration of two reactants, it is second order.

The rate law of a reaction is experimentally determined. From this we derive information about the molecularity of the reaction and which reactants are involved in rate determining step. This tells us about reaction mechanism. Thus nucleophilic substitution of alkyl halides may be of two types dpending on kinetic studies.

For primary and secondary alkyl halides the kinetic data tells us that

$$\text{Rate} \propto [\text{Alkyl halide}]\,[\text{Nucleophile}]$$

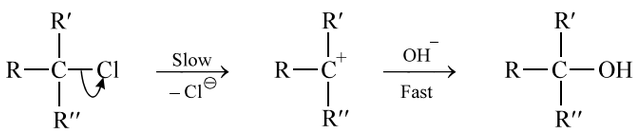
Thus we may write the mechanism as



For tertiary alkyl halides

$$\text{Rate} \propto [\text{Alkyl halide}]$$

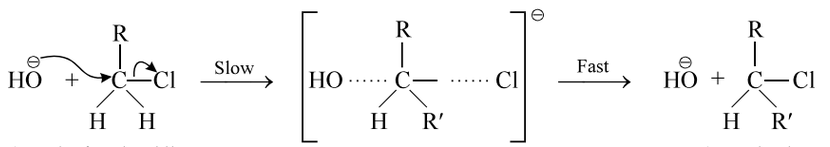
so the mechanism is



5. **Stereochemical evidence.** Information about reaction mechanism can also be obtained by following correlation in the stereochemistry of reactants and products.

Mechanisms of nucleophilic substitution reactions of alkyl halides have been investigated by carrying out experiments with optically active compounds and then checking optical activity of the products.

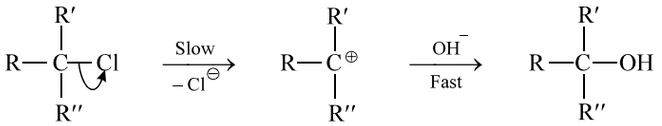
Thus nucleophilic substitution of optically active secondary alkyl halides lead to formation of optically active products with inversion in configuration. This results in following mechanism for the reaction:



(Attack of nucleophile from side opposite to that occupied by leaving group)

(Inversion in configuration known as Walden inversion)

In case of tertiary alkyl halide the product is always a racemic product starting from an optically active halide visualising formation of a planar carbocation.



Optically active Carbocation Racemic product

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In rearrangement reaction it is often necessary to find out if the rearrangement is intramolecular or intermolecular. To ascertain this advantage is taken of stereochemical evidence. The migrating group having an asymmetric centre (and optically active) directly attached to migration origin is allowed to undergo rearrangement.

If the migrating group retains its asymmetric nature (optical activity) in the product then it never got detached completely from the migration origin, suggesting the rearrangement to be intramolecular.

Intramolecular nature of many rearrangements for example, Beckmann, Hofmann etc. has been established using stereochemical evidence of this kind.

Check Your Progress

4. What is enthalpy?
5. What is an exothermic reaction?
6. What is a bimolecular reaction?
7. What does Hammond's postulate state?

8.6 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Fragmentation reactions involving cleavage of carbon-carbon bonds and decomposition of molecules to smaller molecules or fragments, can also be considered as a type of elimination reaction.
2. The reverse of addition reactions are eliminations.
3. Rearrangement reactions.
4. The energetics of a system can be interpreted in terms of heat content of the system termed as Enthalpy (H) in thermodynamics.
5. If in formation of products, energy is released the reaction is said to be exothermic.
6. When two molecules are involved in collision and are undergoing valency change it is bimolecular reaction.
7. It states that mutual conversion between two species which are adjacent to each other on the reaction coordinate requires only a minor change in the structure provided they have nearly the same energy.

8.7 SUMMARY

NOTES

- An organic compound which is attacked by a reagent is known as substrate or reactant.
- A large variety of organic reactions may be placed in four major groups: (1) Substitution reactions (2) Addition reactions (3) Elimination reactions, and (4) Rearrangements.
- Reactions in which an atom or a group is replaced by another atom or group, are called substitution reactions.
- 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.
- The reverse of addition reactions are eliminations. In elimination reactions the number of groups or atoms attached to carbon decrease and the degree of unsaturation in the molecule increases.
- The reactions in which the carbon skeleton of the molecule is rearranged to give a structural isomer of the original molecule are known as rearrangement reactions.
- In the course of a reaction, the nuclei and electrons assume positions that at each point correspond to the lowest free energies possible. If the reaction is reversible, these positions must be the same in the reverse process, too. This means that the forward and reverse reactions (run under the same conditions) must proceed by the same mechanism. This is called the principle of microscopic reversibility.
- The feasibility of a particular reaction is based on the energetics (energy considerations) for that reaction. Thermodynamics is the study of the energy flow in a system.
- Product distribution in a chemical reaction in generally reaction is generally influenced by two factors: 1. Relative stability of the product (thermodynamic factor) 2. Rate of formation of the product (kinetic factor).
- Kinetics deals with the rate of reaction and factors affecting the rate.
- Polanyi-Hammond postulate states that mutual conversion between two species which are adjacent to each other on the reaction coordinate requires only a minor change in the structure provided they have nearly the same energy.
- A number of methods besides the study of thermodynamics and kinetics are used to study the course of a reaction. Some of these are: 1. Identification of products and by-products. 2. Determination of the presence of

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intermediate(s) by isolation or detection or trapping. 3. Study of catalyst action. 4. Isotopic labelling of reactive sites to distinguish two identical atoms. 5. Relative reactivities of various reagents and substrates. 6. Variation in rate of reaction or other parameters with different solvents. 7. Stereochemical evidences—effect of reaction on asymmetric centres in the molecules.

8.8 KEY WORDS

- **Kinetics:** The branch of chemistry or biochemistry concerned with measuring and studying the rates of reactions.
- **Thermodynamics:** It is the study of the interrelation of heat and work with chemical reactions or with physical changes of state within the confines of the laws of thermodynamics.
- **Organic reaction:** Organic reactions are chemical reactions involving organic compounds.

8.9 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. Write a short note on principle of microscopic reversibility.
2. What do you understand by kinetics of reactions and reaction rates?
3. Discuss Hammond's postulate.
4. Write a short note on Curtin-Hammett Principle.
5. Write a short note on rearrangement reaction?

Long Answer Questions

1. What do you understand by substitution reaction? Explain with help of examples.
2. What do you understand by addition reaction? Explain with help of examples.
3. What do you understand by elimination reaction? Explain with help of examples.
4. What thermodynamic factors do influence the product distribution in a chemical reaction?
5. What kinetic factors do influence the product distribution in a chemical reaction?
6. What are the kinetics and non-kinetics methods for determining organic reaction mechanisms?

8.10 FURTHER READINGS

NOTES

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UNIT 9 CARBOCATION

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Structure

9.0 INTRODUCTION

A carbocation is an ion with a positively charged carbon atom. Among the simplest examples are the methenium CH_3^+, methanium CH_5^+ and vinyl $C_2H_3^+$ cations. Occasionally, carbocations that bear more than one positively charged carbon atom are also encountered (for example, ethylene dication $C_2H_4^{2+}$).

Until the early 1970s, all carbocations were called carbonium ions. In present-day chemistry, a carbocation is any ion with a positively charged carbon atom, classified in two main categories according to the coordination number of the charged carbon: three in the carbenium ions and five in the carbonium ions. This nomenclature was proposed by G. A. Olah. Carbonium ions, as originally defined by Olah, are characterized by a three-center two-electron delocalized bonding scheme and are essentially synonymous with so-called 'nonclassical carbocations', which are carbocations that contain bridging C–C or C–H σ-bonds. However, others have more narrowly defined the term 'carbonium ion' as formally protonated or alkylated alkanes (i.e., CR_5^+, where R is hydrogen or alkyl), to the exclusion of nonclassical carbocations like the 2-norbornyl cation.

In this unit, you will get an overview of the concept of carbocation in detail. You will know about the structure and stability of carbocations. The notion of neighbouring group participation has been taken in this unit to enhance your knowledge about carbocations. In the end of this unit, rearrangement of carbocations has been discussed.

9.1 OBJECTIVES

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

- Understand the meaning, structure and stability of carbocations

- Discuss classical and non-classical carbocations
- Get an overview of neighbouring group participation
- Describe rearrangement of carbocations

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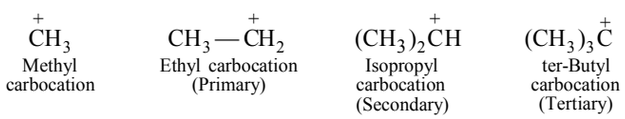
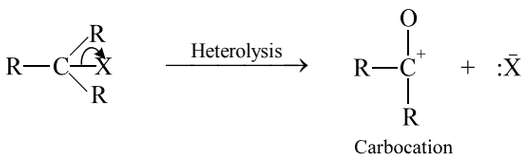
9.2 STRUCTURE AND STABILITY OF CARBOCATIONS

If a covalent bond, in which carbon is attached to a more electronegative atom or group, breaks up by heterolytic fission, the more electronegative atom will take away the electron pair and become negatively charged while the carbon will lose its electron and thus acquire a positive charge. Such cationic species carrying a positive charge on carbon are known as carbocations. These carbocations are called primary, secondary and tertiary depending upon the nature of the carbon atom bearing the charge.

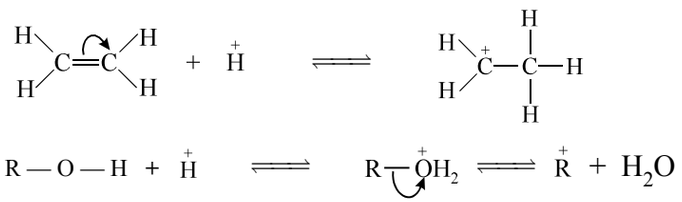


Carbocations may be obtained by heterolysis, protonation of olefins or by decomposition of compounds like the diazo.

(*i*) **Heterolysis**



(*ii*) **Protonation**



(*iii*) **Decomposition**

Stability. The carbocations like cycloheptatrienyl cation (tropylium cation) are so stable that they can be isolated and studied whereas methyl or ethyl cabocations are so unstable that it is normally not possible to detect them in a chemical reaction. Usually they are very reactive and combine readily with any molecule that can give a pair of electrons for sharing with them which accounts for their instability in

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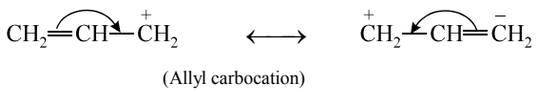
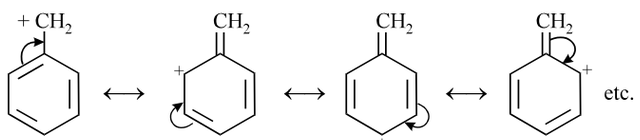
general. *If the groups having electron repelling (+I) effect like $-CH_3$ are attached to the carbon carrying the positive charge then some of this positive charge or electron deficiency is compensated by this push of the electrons towards the positive carbon and this stabilises the carbocation somewhat.*

An alkyl group is electron releasing (hyperconjugation effect) and larger the number of akyl groups attached to carbon bearing the positive charge the greater will be the stability of the carbocation. Thus a tertiary carbocation will be more stable than a secondary carbocation which in turn will be more stable than a primary carbocation. *In contrast the groups with electron withdrawing (–I) effect like $-NO_2$ will decrease the stability of the carbocation. If the positive charge can be delocalized over adjacent atoms then it results in greater stability of the carbocation. Thus carbocations showing resonance are far more stable than those in which the resonance is not playing any part.* For example allyl and benzyl cabocations are more stable than propyl carbocation.



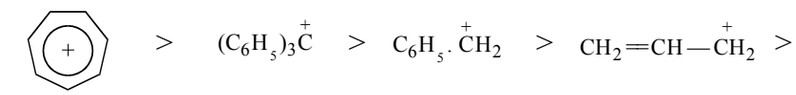
(Allyl carbocation)



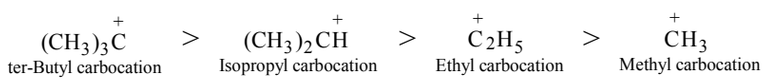
(Benzyl carbocation)

(Methoxymethyl carbocation)

Some of the carbocations in their order of stability are given below:

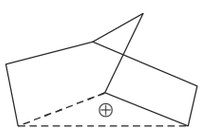


Tropylium cation > Triphenylmethyl carbocation > Benzyl carbocation > Allyl carbocation >



ter-Butyl carbocation > Isopropyl carbocation > Ethyl carbocation > Methyl carbocation

Some carbocations like norbornyl cation exhibit a symmetrical bridged two electron three centre bonding which has been termed as a **nonclassical carbocation** (J.D. Roberts 1951). The existence of such ions as reaction intermediates was demonstrated conclusively by G.A. Olah (1964).



In these cations the carbocation centre is always surrounded by eight electrons but is overall electron deficient due to sharing of two electrons between three or more atoms.

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According to Brown and Schleyer (1977) a nonclassical carbocation in a positively charged species which cannot be represented by a single Lewis structure because it contains one or more carbon or hydrogen bridges joining the two electron defficient centres. The bridging atoms have coordination numbers higher than usual which may be five or more for carbon and two or more for hydrogen. Thus they have two-electron, three (or multiple) centre bonds including a carbon or hydrogen bridge.

The carbocations are sp^2 hybridised and therefore planar in configuration. In the formation of carbocation intermediate from saturated compounds a tetrahedral carbon atom collapses to a planar arrangement. Thus if an asymmetric carbon atom (*cf.* Isomerism and optical activity) is converted to a carbocation during the course of reaction then, because of the planarity of the latter, the optical activity of the asymmetric carbon atoms will be lost and the resulting product will be optically inactive.

Carbocations undergo three types of reactions:

1. **Combination with a nucleophile or base** to form a neutral molecule. Thus:

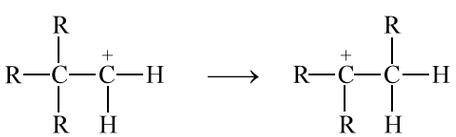
$$\underset{\text{Ethyl cation}}{C_2H_5^+} + \underset{\text{Halide ion}}{:X^-} \longrightarrow \underset{\text{Ethyl halide}}{C_2H_5X}$$

$$\underset{\text{Isopropyl cation}}{(CH_3)_2\overset{+}{C}H} + \underset{\text{Water}}{H_2O:} \longrightarrow (CH_3)_2CH\overset{+}{O}H_2 \xrightleftharpoons{-H^+} \underset{\text{Isopropyl alcohol}}{(CH_3)_2CHOH}$$

2. **Elimination of a proton.** This results in the formation of an olefin, for example,

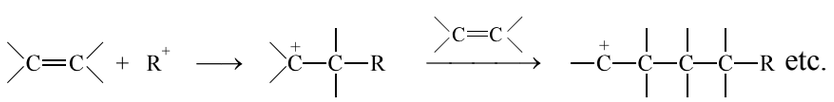
$$\underset{\text{Ethyl cation}}{CH_3-\overset{+}{C}H_2} \xrightarrow{-\overset{+}{H}} \underset{\text{Ethylene}}{CH_2=CH_2}$$

3. **Rearrangement.** In this another carbocation, usually of greater stability, is formed. Thus a primary carbocation will tend to rearrange so as to form a secondary or tertiary carbocation even if it involves the cleavage of C—H or C—C bonds. Thus:



(A schematic rearrangement reaction)

The carbocations may also combine with olefins to propagate cationic polymerisation.



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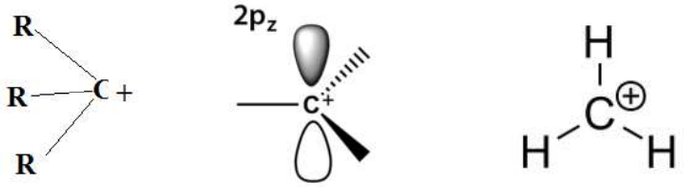
Check Your Progress

1. Give an example of primary carbocation.
2. Give an example of secondary carbocation.
3. Why tertiary carbocation is more stable than secondary carbocation?
4. What is classical carbocation?

9.3 CLASSICAL AND NON CLASSICAL CARBOCATIONS

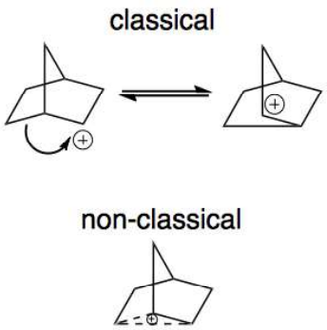
The 'classical' carbocation, in which an electron deficient carbon bearing a positive charge. It means the carbon atom have deficiency of electron, due to this deficiency the carbon have +ve charge on it.



Non-Classical Carbocation

A carbocation the ground state of which has delocalized (bridged) bonding ð- or ó-electrons.

There are many examples of 'non-classical' carbocations, like- 2-norbornyl carbocation.



Labeling experiments have shown that the positive charge resides on more than one carbon in the 2-norbornyl ion. Early on, the data was explained by equilibrating classical ions, but soon another possibility emerged - one involving a single non-classical ion.

The problem comes down to: are the equilibrating classical ions ground state structures with the non-classical ion serving as the transition state, or is the

non-classical ion the ground state? This debate went on for a very long period of time, but now most agree that the non-classical structure is the ground state in the 2-norbornyl system. In fact, a recent, and difficult to obtain, crystal structure for the 2-norbornyl cation has been published proving that the ion exists with the non-classical geometry.

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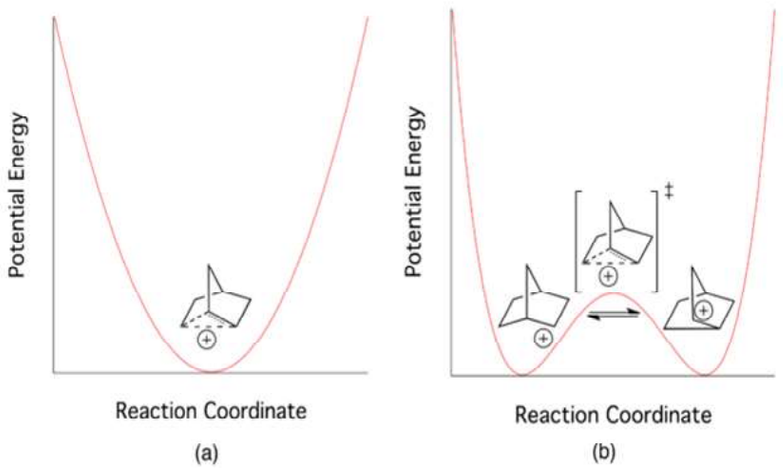
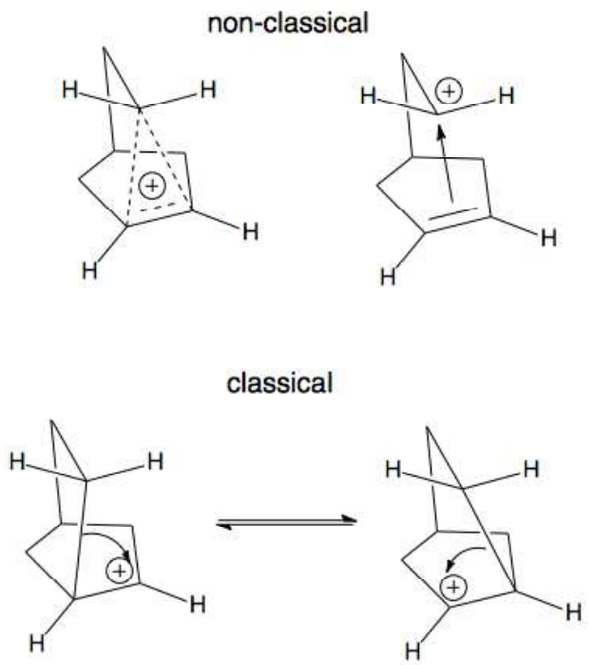


A key difference between classical and non-classical structures is the bonding. As illustrated above, a classical ion has a carbon with a sextet of electrons and 3 other bonds. The non-classical ion, on the other hand, involves 3 carbons with 2 electrons spread over them. This is called a 3-center 2-electron bond (hypercoordinate bonding) and is **a clear marker for a non-classical ion.**



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9.4 NEIGHBOURING GROUP PARTICIPATION ANSD REARRANGEMENT OF CARBOCATIONS

Neighbouring group participation (NGP)

The interaction of a reaction centre with a lone pair of electrons in an atom or the electrons present in a sigma bond or pi bond contained within the parent molecule but not conjugated with the reaction centre. At the point when NGP is in activity it is typical for the response rate to be expanded. It is also possible for the stereochemistry of the reaction to be abnormal (or unexpected) when compared with a *normal* reaction. While it is possible for neighbouring groups to influence many reactions in organic chemistry (*e.g.* the reaction of a diene such as 1,3-cyclohexadiene with maleic anhydride normally gives the endo isomer because of a secondary effect.

NGP by Heteroatom lone Pairs

The reaction of a sulfur or nitrogen mustard with a nucleophile, the rate of reaction is much higher for the sulfur mustard and a nucleophile than it would be for a primary alkyl chloride without a heteroatom.

NGP by an Alkene

The ð orbitals of an alkene can stabilize a transition state by helping to delocalize the positive charge of the carbocation. For instance the unsaturated tosylate will react more quickly with a nucleophile than the saturated tosylate.

NGP by a Cyclopropane, Cyclobutane or a Homoallyl Group

When Cyclopropylmethyl chloride is reacted with ethanol and water then a mixture of 48% cyclopropylmethyl alcohol, 47% cyclobutanol and 5% homoallyl alcohol (but-3-enol) is obtained. This is because the carbocationic intermediate is delocalised onto many different carbons through a reversible ring opening.

NGP by an aromatic ring

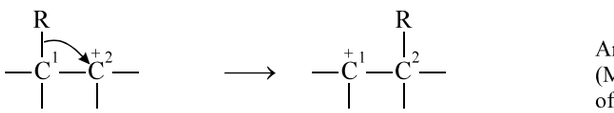
An aromatic ring can assist in the formation of a carbocationic intermediate called a phenonium ion by delocalising the positive charge.

9.4.1 Rearrange of Carbocations

In a rearrangement reaction the atoms or groups within a molecule move from one atom to another, thus giving rise to structural isomer of the starting compound or the reactant. The product is the rearranged molecule. It is difficult to visualize these reactions separately from the addition, substitution or eliminate type because most of the rearrangements involve one or more than one of these processes. The atom or group which migrates is known as **migrating group**, the atom to which it

was initially attached is known as **migration origin** and the atom which it finally joins is known as **migration terminus**. If the migrating group gets completely detached from the molecule during the rearrangement then it may as well go to the migration terminus of other molecules of the compound. Such rearrangements in which the migrating group actually becomes free even for a small fraction of time, are known as **Intermolecular rearrangements**. However if the migrating group remains attached to the molecule in some or the other way throughout the process of rearrangement then this type is known as **Intramolecular rearrangements**.

The migration of atoms or groups may occur with the pair of electrons through which it is attached to migration origin (known as **anionotropic migration**), or without this pair of electrons (**cationotropic migration**), or with just one unpaired electron (**free radical migration**).

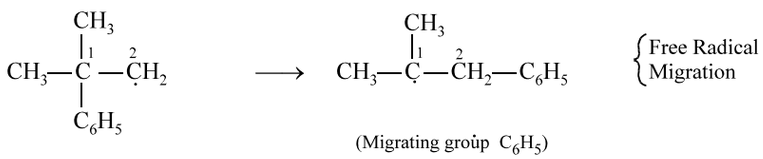


Anionotropic Migration (Migration with the pair of the electrons)

Carbocation

Rearranged carbocation

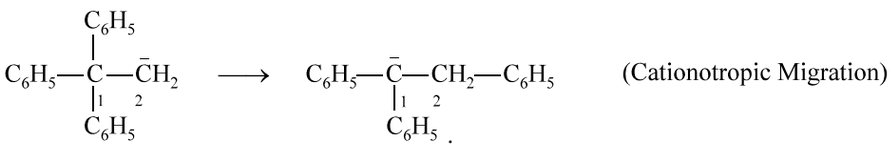
(R = Migrating group; C1 = Migration origin; C2 = Migration terminus)



Free Radical Migration

(Migrating group C_6H_5)

Examples of cationotropic rearrangements are few and these involve the formation of a carbanion which then may rearrange as follows:



(Cationotropic Migration)

(Migrating group $\overset{+}{C}_6H_5$)

The most common type of rearrangements involve migration of the group with its pair of electrons (anionotropic) and these involve the formation of a carbocation in most cases. The carbocations in order to acquire greater stability tend to rearrange by the migration of hydrogen or alkyl group with its pair of electrons. Allylic and pinacol-pinacolone rearrangements are given here as examples of rearrangement by migration of a multiple bond or an alkyl or allyl group as a carbanion respectively.

Allylic rearrangement. Substitution reactions at allylic positions usually occur by S_N1 mechanism forming an allylic carbocation which is resonance stabilised. This results in a mixture of two isomers in the product due to the migration of a double bond from its original position to an adjacent site. Such rearrangement reactions in which the carbon skeleton remains unchanged but multiple bonds rearrange are known as *allylic rearrangements*.

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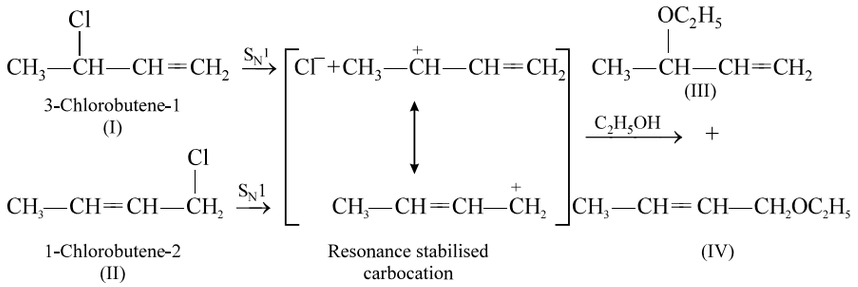
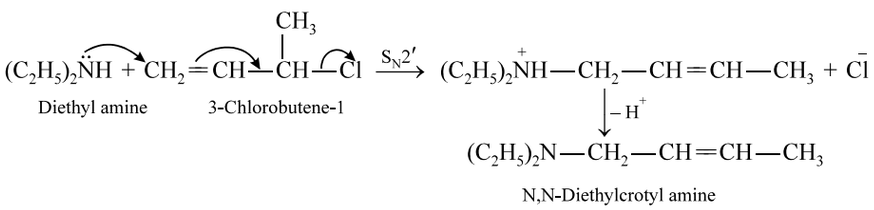


Whether the starting material is (I) or (II), in either case it is always a mixture of (III) and (IV) which is obtained obviously due to two important resonance contributing structures of intermediate carbocation. Such substitution reaction occurring by S_N1 mechanism resulting in a rearranged product are S_N1' reactions.

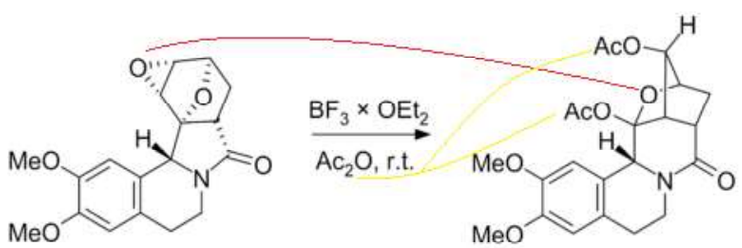
Bernard David de la Mare and coworkers (1953) have shown that allylic rearrangements are also possible in S_N2 reaction which are designated as S_N2' reactions. These reactions occur as follows:



Wagner-Meerwein rearrangement

A Wagner–Meerwein rearrangement is a class of carbocation 1,2-rearrangement reactions in which a hydrogen, alkyl or aryl group migrates from one carbon to a neighboring carbon.

Example: In the synthesis of bridged azaheterocycles.



Wagner–Meerwein Rearrangement in the synthesis of bridged azaheterocycles

Wagner-Meerwein rearrangement mechanism used to convert an alcohol to an olefin using an acid catalyst.

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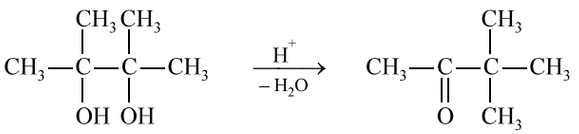
Mechanism: Protonation of the alcohol by the acid which is then released as water to forms a carbocation. A 1,2-shift then occurs to form a more substituted and stabilized carbocation. A final deprotonation with water produces the final olefin product and regenerates the acid catalyst.

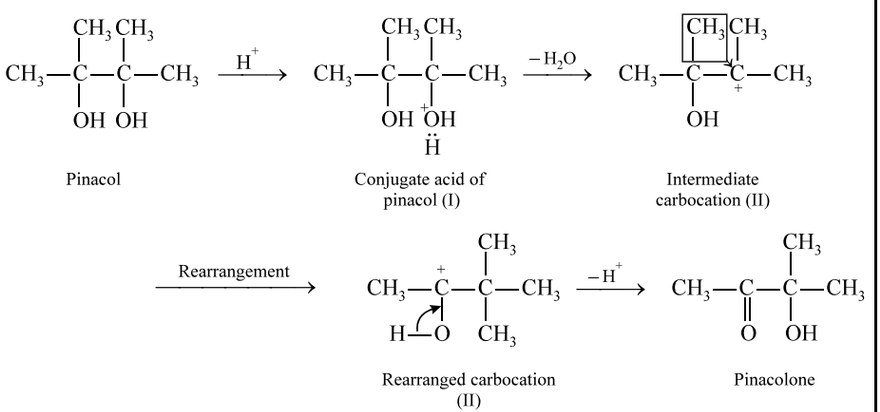
Pinacol-pinacolone rearrangement. Transformations of 1,2-glycols to aldehydes or ketones, involving the migration of an alkyl or aryl group, under acidic conditions are known as Pinacol-pinacolone rearrangement. Originally the term was applied to the conversion of pinacol to pinacolone



Pinacol (1,2-glycol) Pinacolone

This is an intramolecular rearrangement in which alkyl group migrates to an electron deficient adjacent carbon atom.

Mechanism: Under acidic conditions pinacol forms its conjugate acid (I) which loses a molecule of water to form a carbocation (II). An alkyl group from adjacent carbon atom then migrates with its pair of electrons to the electron deficient carbocation carbon forming the rearranged carbocation (III) of pinacolone. This loses a proton to form the rearranged pinacolone (IV).



Pinacol | Conjugate acid of pinacol (I) | Intermediate carbocation (II)

Rearranged carbocation (II) | Pinacolone

Semi-Pinacol Rearrangement

The **semipinacol rearrangement** is a rearrangement reaction in organic chemistry involving a heterosubstituted alcohol of the type $R_1R_2(HO)C–C(X)R_3R_4$. The hetero substituent can be a halogen (Cl, Br, I), a tosylate, a mesylate or a thiol group. This reaction proceeds by removal of the leaving group X forming a carbocation as electron deficient center. One of the adjacent alkyl groups then migrates to the positive carbon in a 1,2-shift. Simultaneously with the shift, a pi bond forms from the oxygen to carbon, assisting in driving the migrating group off its position. The result is a ketone or aldehyde. In another definition all semipinacol

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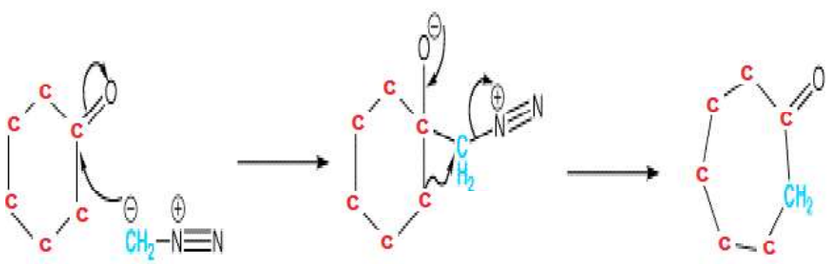
rearrangements "*share a common reactive species in which an electrophilic carbon center, including but not limited to carbocations, is vicinal to an oxygen-containing carbon and can drive the 1,2-migration of a C–C or C–H bond to terminate the process, generating a carbonyl group* ".

The rearrangement reaction can be classified into 4 types. Type 1 concerns all 2-heterosubstituted alcohols. Substrates in type 2 rearrangements are allyl alcohols. The carbocation is formed by electrophilic addition to the alkene group with electrophiles such as halonium ions, Brønsted acids and Lewis acids. In type 3 the substrates are epoxides, notably 2,3-epoxy-alcohols and type 4 concerns the reactions of alpha hydroxyketones and alpha hydroxy imines. Reactions of type 4 are also called acyloin rearrangements.

While similar to the pinacol rearrangement, the semipinacol rearrangement differs from the pinacol rearrangement in that the cation is not formed from a vicinal 1,2-diol. With diazoalcohols the reaction is known as the Tiffeneau–Demjanov rearrangement.

Example: When diazomethane mix in to ketone, the product undergoes a ring extension by rearrangement of the intermediate. Cyclohexanone is more reactive as an electrophile than either cyclopentanone or cycloheptanone, so it ring expands cleanly to cycloheptanone.



Check Your Progress

5. What are intermolecular rearrangements?
6. What are allylic rearrangements?
7. Give an example of intramolecular rearrangement.
8. Give an example of Semi-Pinacol rearrangement.

9.5 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Ethyl carbocation.
2. Isopropyl carbocation.

3. An alkyl group is electron releasing (hyperconjugation effect) and larger the number of akyl groups attached to carbon bearing the positive charge the greater will be the stability of the carbocation. Thus a tertiary carbocation will be more stable than a secondary carbocation.
4. In classical carbocation, an electron deficient carbon bears a positive charge.
5. If the migrating group remains attached to the molecule in some or the other way throughout the process of rearrangement then this type is known as Intramolecular rearrangements.
6. Rearrangement reactions in which the carbon skeleton remains unchanged but multiple bonds rearrange are known as allylic rearrangements.
7. Pinacol-Pinacolone rearrangement.
8. When diazomethane mix in to ketone, the product undergoes a ring extension by rearrangement of the intermediate. Cyclohexanone is more reactive as an electrophile than either cyclopentanone or cycloheptanone, so it ring expands cleanly to cycloheptanone.

9.6 SUMMARY

- If a covalent bond, in which carbon is attached to a more electronegative atom or group, breaks up by heterolytic fission, the more electronegative atom will take away the electron pair and become negatively charged while the carbon will lose its electron and thus acquire a positive charge. Such cationic species carrying a positive charge on carbon are known as carbocations.
- The carbocations like cycloheptatrienyl cation (tropylium cation) are so stable that they can be isolated and studied whereas methyl or ethyl cabocations are so unstable that it is normally not possible to detect them in a chemical reaction.
- Carbocations showing resonance are far more stable than those in which the resonance is not playing any part.
- Carbocations undergo three types of reactions: 1.Combination with a nucleophile or base to form a neutral molecule 2. Elimination of a proton. This results in the formation of an olefin 3. Rearrangement
- In classical carbocation, an electron deficient carbon bears a positive charge.
- In non-classical carbocation, the ground state has delocalized (bridged) bonding ð- or ó-electrons.
- The interaction of a reaction centre with a lone pair of electrons in an atom or the electrons present in a sigma bond or pi bond contained within the parent molecule but not conjugated with the reaction centre. At the point when NGP is in activity it is typical for the response rate to be expanded.

NOTES

- In a rearrangement reaction the atoms or groups within a molecule move from one atom to another, thus giving rise to structural isomer of the starting compound or the reactant. The product is the rearranged molecule.
- A Wagner–Meerwein rearrangement is a class of carbocation 1,2-rearrangement reactions in which a hydrogen, alkyl or aryl group migrates from one carbon to a neighboring carbon.
- Transformations of 1,2-glycols to aldehydes or ketones, involving the migration of an alkyl or aryl group, under acidic conditions are known as Pinacol-pinacolone rearrangement.
- All semipinacol rearrangements share a common reactive species in which an electrophilic carbon center, including but not limited to carbocations, is vicinal to an oxygen-containing carbon and can drive the 1,2-migration of a C–C or C–H bond to terminate the process, generating a carbonyl group.

9.7 KEY WORDS

- **Carbocation:** An ion that has a positively charged carbon atom.
- **Rearrangement reaction:** A rearrangement reaction is a broad class of organic reactions where the carbon skeleton of a molecule is rearranged to give a structural isomer of the original molecule.

9.8 SELF ASSESSEMNT QUESTIONS AND EXERCISES

Short Answer Questions

1. Write a short note on carbocations.
2. How do carbocations undergo rearrangement reaction?
3. Discuss Wagner-Meerwein rearrangement.
4. Describe neighboring group participation by a cyclopropane, cyclobutane or a homoallyl group.

Long Answer Questions

1. Discuss the stability of carbocations.
2. Discuss the structure of carbocations.
3. What are classical and non-classical carbocations?
4. Explain neighbouring group participation.
5. Explain Pinacol-Pinacolone rearrangement.
6. Explain Semi-Pinacol rearrangement.

9.9 FURTHER READINGS

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UNIT 10 MOLECULAR REARRANGEMENTS

Structure

10.0 INTRODUCTION

Rearrangement reactions are an interesting class of reactions wherein a group or an atom migration during the course of the reaction. While most of the rearrangements are designed in that fashion, it can also be undesirable in some cases. Depending on the reaction conditions, the nature of rearrangement (and the product) could also change. Rearrangements are divided into intramolecular and intermolecular processes. In intramolecular process, the group that migrates is not completely detached from the system in which rearrangement is taking place. In contrast, in intermolecular process, the migrating group is first detached and later re-attached at another site.

In this unit, various rearrangement reactions are presented.

10.1 OBJECTIVES

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

- Discuss molecular rearrangement
- Understand mechanism of various rearrangement reactions

10.2 MOLECULAR REARRANGEMENT

A rearrangement reaction is a broad class of organic reactions where the carbon skeleton of a molecule is rearranged to give a structural isomer of the original

molecule. Often a substituent moves from one atom to another atom in the same molecule. In the example below the substituent R moves from carbon atom 1 to carbon atom 2:

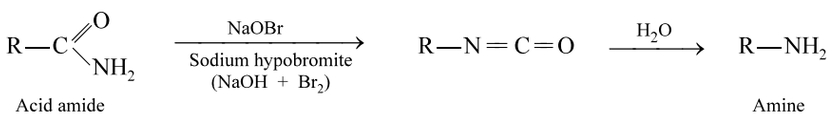
Intermolecular rearrangements also take place.

A rearrangement is not well represented by simple and discrete electron transfers. The actual mechanism of alkyl groups moving, as in Wagner-Meerwein rearrangement, probably involves transfer of the moving alkyl group fluidly along a bond, not ionic bond-breaking and forming. In pericyclic reactions, explanation by orbital interactions give a better picture than simple discrete electron transfers. It is, nevertheless, possible to draw the curved arrows for a sequence of discrete electron transfers that give the same result as a rearrangement reaction, although these are not necessarily realistic. In allylic rearrangement, the reaction is indeed ionic. Three key rearrangement reactions are 1,2-rearrangements, pericyclic reactions and olefin metathesis.

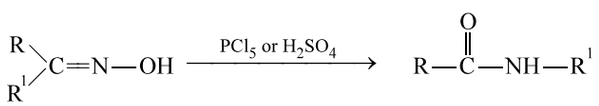
10.2.1 Beckmann and Favorskii Rearrangements

Hofmann and Beckmann rearrangement reaction are examples of rearrangements with nitrogen as migration terminus.

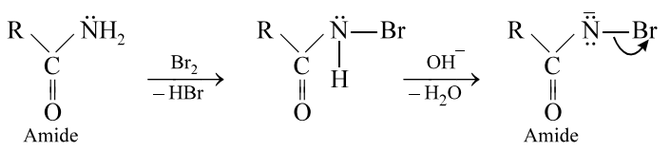
Hofmann Rearrangement



Beckman Rearrangement



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 CO_2 gives the amine with one less carbon atom.



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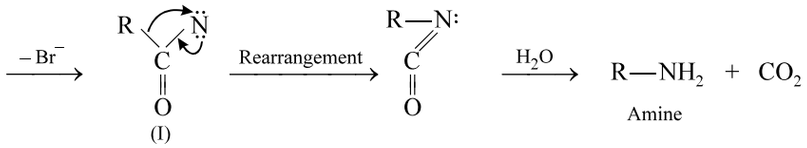
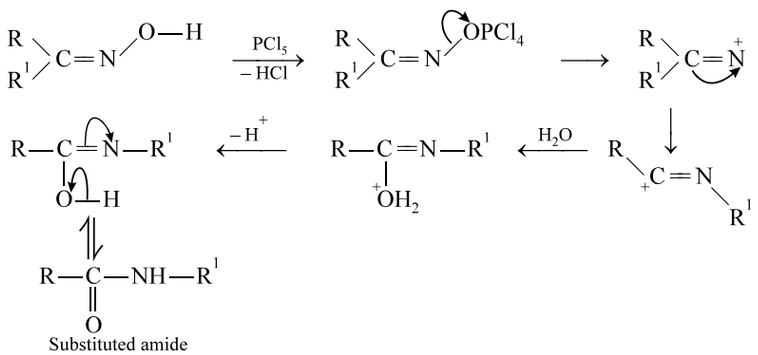


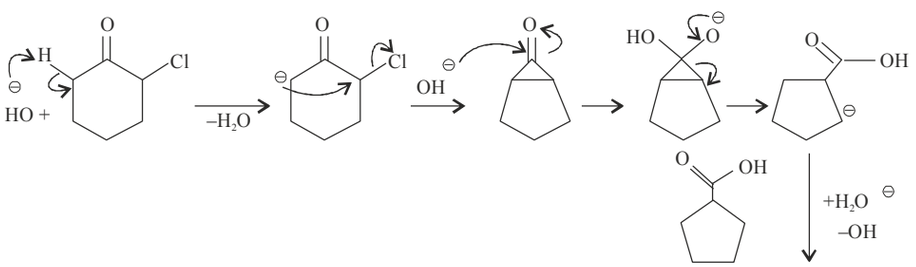
In the Beckmann rearrangement the oxime is converted to its O-ester (—OH group is converted to ester group). This group is then eliminated and the resulting ion carries a positive charge at nitrogen which then neutralizes its charge by inducing the migration of a group with its electron pair to it. Finally addition of a OH^- ion or H_2O 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.

Favorskii Rearrangement

Rearrangement of cyclic α-haloketones in the presence of bases to form a carboxylic acid accompanied by ring contraction is known as Favorskii rearrangement.

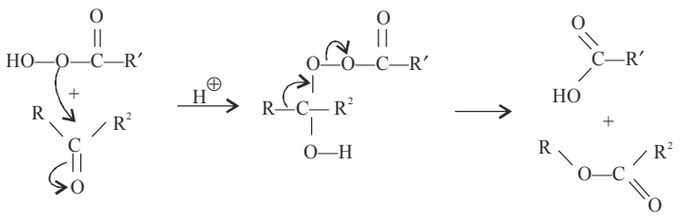


The cyclic carbanion produced by the loss of a proton undergoes ring contraction losing $Cl^{\ominus}$. The rearrangement then results in ring contraction.

10.2.2 Baeyer-Villiger Oxidation

Oxidation of ketones to esters on treatment with peracids in known as Baeyer-Villiger oxidation.

Addition of peroxyacid to ketone forms a tetrahedral intermediate (known as Criegee intermediate). This is followed by concerted migration of adjacent alkyl group with retention of configuration to oxygen with the loss of carboxylic acid.

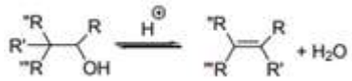


Ester

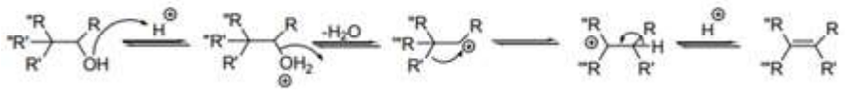
In unsymmetrical keters the migrating group is the one which can best stailize the positive charge in the transition state.

10.2.3 Wagner-Meerwein Rearrangement

It is one of the simplest systems where an alkyl group migrates, with its bonding pair, to an electron-deficient carbon atom.



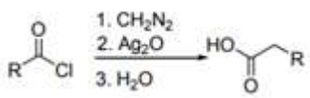
Mechanism



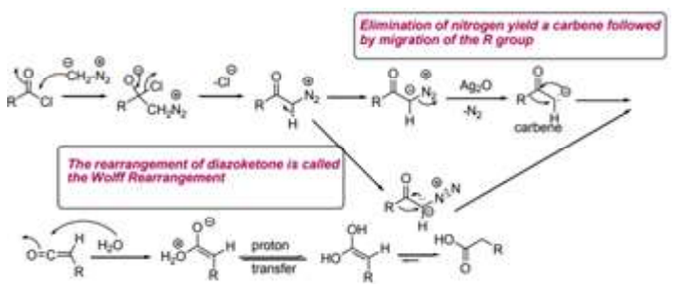
The driving force for the rearrangement resides in the greater stability of a tertiary carbocation compared to that of primary carbocation.

10.2.4 Wolff Rearrangement

The reaction of acid chloride with diazomethane gives a diazoketone which is in the presence of silver oxide under heating proceeds the Wolff rearrangement to yield a ketene that is directly converted into an acid in the presence of water.



Mechanism



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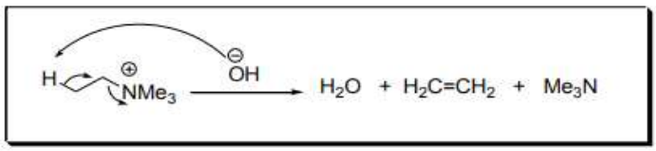
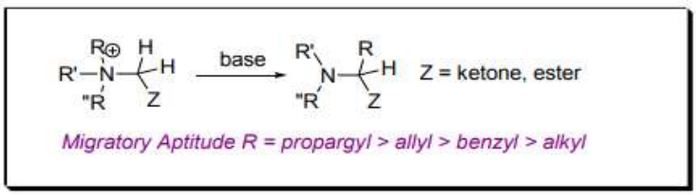
10.2.5 Steven Rearrangement

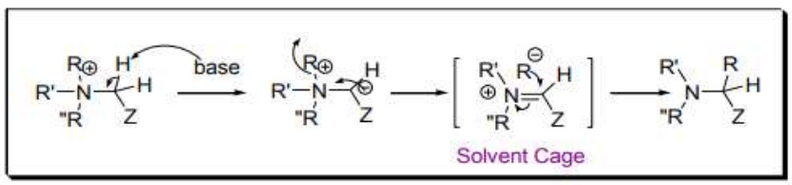
Quaternary ammonium salt which has β-hydrogen proceeds E_2 (Hofmann) elimination with base.



In case of quaternary ammonium salts containing β-ketone or ester or aryl group, an α-hydrogen is removed by base to give an ylide and then the rearrangement occurs.



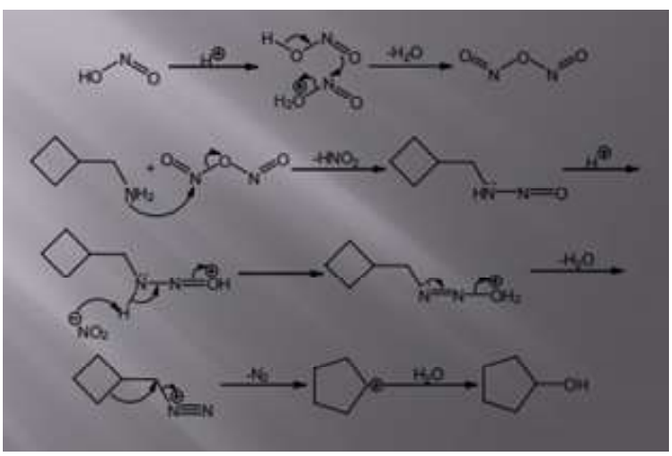
Mechanism



10.2.6 Demjanov Rearrangement

The reactions in which a carbocation is generated by diazotization is called Demjanov reaction.

Mechanism



Check Your Progress

1. In Beckman rearrangement reaction, the oxime is converted to which group?
2. What is Criegee intermediate?
3. In which reaction a carbocation is generated by diazotization?

NOTES

10.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. In the Beckmann rearrangement the oxime is converted to its O-ester (—OH group is converted to ester group).
2. Tetrahedral intermediate is also known as Criegee intermediate.
3. The reactions in which a carbocation is generated by diazotization is called Demjanov reaction.

10.4 SUMMARY

- Rearrangement reactions are an interesting class of reactions wherein a group or an atom migration during the course of the reaction.
- Hofmann and Beckmann rearrangement reactions are examples of rearrangement with nitrogen as migration terminus.
- Beckmann rearrangement is an 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.
- Rearrangement of cyclic α-haloketones in the presence of bases to form a carboxylic acid accompanied by ring contraction is known as Favorskii rearrangement.
- The reactions in which a carbocation is generated by diazotization is called Demjanov reaction.

10.5 KEY WORDS

- **Rearrangement reaction**: A rearrangement reaction is a broad class of organic reactions where the carbon skeleton of a molecule is rearranged to give a structural isomer of the original molecule.
- **Intramolecular:** Existing or taking place within a molecule.

NOTES

10.6 SELF ASSESSEMNT QUESTIONS AND EXERCISES

Short Answer Questions

1. Write a short note on molecular rearrangement.
2. What is the Wolff rearrangement?
3. What is Demjanov rearrangement?

Long Answer Questions

1. Discuss the mechanism of Beckman rearrangement.
2. Discuss the mechanism of Baeyer-Villiger rearrangement.
3. Discuss the mechanism of Steven rearrangement.

10.7 FURTHER READINGS

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BLOCK - IV

SUBSTITUTIONS REACTION

NOTES

UNIT 11 ALIPHATIC NUCLEOPHILIC SUBSTITUTIONS

Structure

11.0 INTRODUCTION

In organic and inorganic chemistry, nucleophilic substitution is a fundamental class of reactions in which an electron rich nucleophile selectively bonds with or attacks the positive or partially positive charge of an atom or a group of atoms to replace a leaving group; the positive or partially positive atom is referred to as an electrophile. The whole molecular entity of which the electrophile and the leaving group are part is usually called the substrate. The nucleophile essentially attempts to replace the leaving group as the primary substituent in the reaction itself, as a part of another molecule.

Nucleophilic substitution reactions are commonplace in organic chemistry, and they can be broadly categorised as taking place at a saturated aliphatic carbon or at (less often) an aromatic or other unsaturated carbon centre. Aliphatic systems involve chains of saturated hydrocarbons, in which carbons are attached to each other only through single bonds. Aliphatic nucleophilic substitution is the substitution of a nucleophile at a tetrahedral or sp^3 carbon.

In this unit, details of different types of nucleophilic substitution reactions are described. These reactions are a useful class of reactions for carbon-carbon and carbon-heteroatom bond formation reactions. The approach is also widely used for synthetic transformations (for example, leaving groups such as tosylates). Depending on the nature of the nucleophiles and reaction conditions, different mechanisms are possible. These reactions typically occur on a saturated carbon atom, attached to a leaving group.

NOTES

11.1 OBJECTIVES

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

- Discuss nucleophiles and nucleofuge
- Get an overview of aliphatic nucleophilic substitution reactions
- Discuss the mechanism of aliphatic nucleophilic substitution reactions

11.2 NUCLEOPHILES AND NUCLEOFUGE

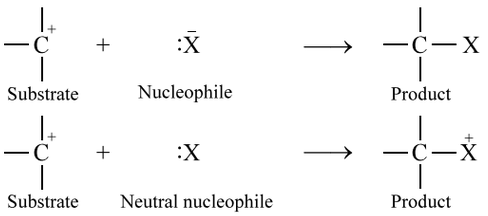
Nucleophilic Reagents Or Nucleophiles

Reagents having an unshared pair of electrons are known as *nucleophilic reagents* or *nucleophiles* because they have a tendency to share this pair of electrons with electron deficient substrate. They can also be classified into two groups (*i*) **negative nucleophiles**, and (*ii*) **neutral nucleophiles**. Negative nucleophiles are those which carry an electron pair and are negatively charged because of one extra electron. If a negative charge is present at carbon, such nucleophiles are known as *carbanions*. Some simple examples of such nucleophiles are given in Table 11.1.

Table 11.1 *Some Common Nucleophiles*

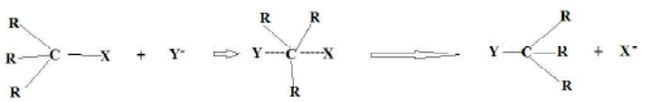
Negative nucleophile		*Neutral nucleophile*	
Halide ion (X = Cl, Br, I)	$:\ddot{\underset{\cdot\cdot}{X}}:^-$	Trialkyl amine	$R_3N:$
		Ammonia	$:NH_3$
Alkoxy ion	$R-\ddot{\underset{\cdot\cdot}{O}}:^-$	Water	$H-\ddot{\underset{\cdot\cdot}{O}}-H$
Amino ion	$:\bar{\ddot{N}}H_2$	Alcohol	$H-\ddot{\underset{\cdot\cdot}{O}}-C_2H_5$
Hydroxyl ion	$:\bar{\ddot{\underset{\cdot\cdot}{O}}}H$	Dialkyl sulphide	$R_2\ddot{\underset{\cdot\cdot}{S}}$
Cyanide ion	$:\bar{C}\equiv\ddot{N}$	Alkyl hydrosulphide	$R-\ddot{\underset{\cdot\cdot}{S}}-H$
Carbanion	$-\underset{\vert}{\overset{\vert}{C}}:^-$		

The neutral nucleophiles are rich in electrons because of the presence of unshared electron pair, but are not charged and are electrically neutral for example, H_2O: and $:NH_3$. The addition of negative nucleophile to a positively charged substrate results in a neutral molecule whereas the addition of a neutral nucleophile to a positively charged substrate will give a positively charged product. Thus:



11.2.1 Nucleofuge

A **nucleofuge** - This term is the combination of two term Nucleo and Fugetake (*nucleo*- nucleus means the positive charge part in an atom and fuge, *fugitive mean* to escape) is a leaving group which retains the lone pair from its previous bond with another species. For example, in the SN^2 mechanism a nucleophile attacks an organic compound containing the nucleofuge which simultaneously breaks the bond with the nucleofugeo (in given reaction X^-) and make this a leave group or atom (*A leaving group that carries away the bonding electron pair).*



In this reaction the leaving group is X^-.

11.3 KINETICS OF ALIPHATIC NUCLEOPHILIC SUBSTITUTIONS: S_N1, S_N2, AND S_Ni MECHANISM

Substitution reactions by nucleophilic reagents are known as nucleophilic substitution (S_N) reactions. Nucleophiles generally react at sites that are deficient in electrons. Consequently such reaction will be most important for compounds where a carbon is linked to greater electronegative atom or group (like halogen) and is thus deficient in electrons because of unequal sharing of bonding electrons. Like electrophilic substitution these can also be of two types—nucleophilic substitution at saturated or aliphatic carbon and at unsaturated or aromatic carbon. Unlike electrophilic substitution which predominates in aromatics and unsaturated compounds the nucleophilic substitution is more common in aliphatic compounds and has been extensively studied. Kinetic investigations of conversions of alkyl halides to alcohols by the action of alkali shows that there are two extreme types of reaction. In one type the reaction rate is proportional to the concentration of alkyl halide only and it is designated as S_N1 reaction. Here S stands for substitution, N for nucleophile and 1 for unimolecular. The term unimolecular is used here since the rate determining step involves only one molecule. In general S_N1 reactions follow *first order kinetics.* In the other type the rate of reaction is proportional to the concentrations of alkyl halide and alkali or hydroxyl ions and is a bimolecular reaction designated as S_N2 reaction. S_N2 reactions follow second order kinetics.

NOTES

For S_N1: Rate $\propto$ [R—X] Independent of $[O\bar{H}]$.

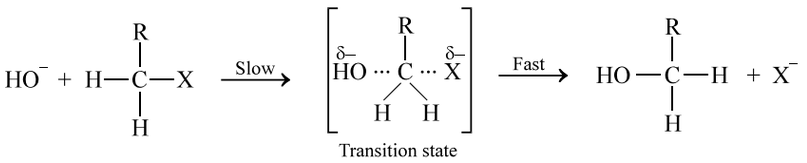
(Stepwise mechanism)

(*i*) $R—X \xrightarrow{\text{Slow}} \overset{+}{R} + \bar{X}$

(*ii*) $\overset{+}{R} + O\bar{H} \xrightarrow{\text{Fast}} R—OH$

For S_N2: Rate $\propto$ [R—X][OH^-]

(Concerted mechanism)



Some examples of the nucleophilic substitution reaction are hydrolysis of alkyl halides, acyl halides; cleavage of ethers with HI (Ziesel reaction and alkylation with alkyl halides (Williamson's synthesis).

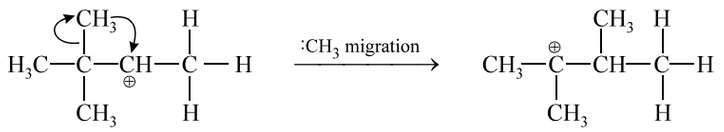
The various factors guiding the reaction to follow S_N1 or S_N2 mechanism have been discussed below.

Structure of the substrate: Alkyl halides have been extensively used as substrate for studying nucleophilic substitution reactions. It has been observed that the hydrolysis of primary and tertiary alkyl halides are fast although the former follows S_N2 and the latter S_N1 mechanism. The rate of hydrolysis of secondary alkyl halides is slow and they follow both S_N1 and S_N2 mechanism of hydrolysis. The rate of reactivity of various alkyl halides is iodide > bromides > chlorides for a particular alkyl group and tertiary > secondary > primary > CH_3 alkyl halides for a particular halogen. Amongst the primary alkyl halide the order of reactivity is $CH_3X > C_2H_5X > n\text{-}C_3H_7X > n\text{-}C_4H_9X$ etc.

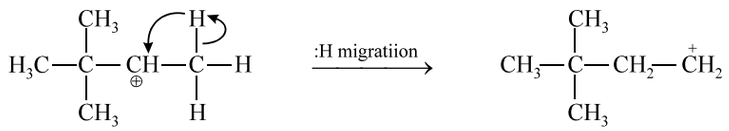
The reason from this transformation from S_N2 to S_N1 type mechanism in going from primary to tertiary is the structural difference in their molecules. Tertiary alkyl halides have three alkyl groups attached to the carbon atom joined to halogen. The (+I) effect of the three alkyl groups increases the electron density on the carbon to which they are joined and this increases the repulsion towards halogen thereby increasing the chance of formation of carbocation. Thus in tertiary alkyl halides the tendency to follow the path of S_N1 mechanism increases. Primary alkyl halides follow S_N2 mechanism.

Steric effect: S_N2 mechanism involves the attack by a nucleophile from the side opposite to that of the leaving group. Now if the carbon atom has bulky alkyl group(s) attached to it then it will be difficult for nucleophile to reach the carbon atom hence the reaction will be slowed down. Since S_N2 mechanism operates better in primary alkyl halides therefore with the increase in the size of alkyl group the rate of reaction decreases i.e., $CH_3X > n\text{-}C_4H_9X$. Tertiary alkyl halides are not affected much because they follow S_N1 mechanism.

Rearrangement of carbocations: Sometimes it is found that the attacking nucleophile joins a carbon atom other than that of the leaving group. This happens due to the rearrangement of the carbocation in S_N1 mechanism to a more stable cation. This is due to 1,2 alkyl or hydrogen shift which results in the formation of stabler cation. The formation of stabler



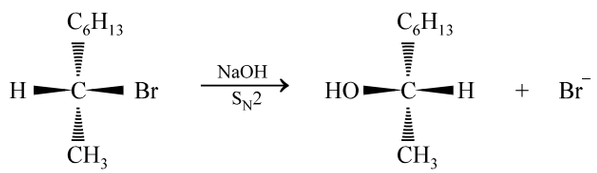
[2° Carbocation] [3° Carbocation]



[2° Carbocation] [1° Carbocation] (This rearrangement not possible forming less stable carbocation)

cation decides the shift. In the above example of hydrolysis of 3-bromo- 2,2-dimethylbutane the carbocation formed rearranges to stable (3°) cation and therefore the alcohol obtained will be 2,3-dimethyl- butanol-2 and not 3,3-dimethylbutanol-2. It is also clear that in single step S_N2 mechanism such a rearrangement is not possible.

Stereochemistry of S_N2 and S_N1 reactions: In S_N2 reaction of hydrolysis of 2-bromo-octane, having a chiral centre, it is found that the laevorotatory 2-bromo-octane gives dextro-rotatory 2-octanol. This clearly means that there has been an inversion of rotation. Hence it shows that S_N2 reaction proceeds with complete inversion of configuration accompanied by inversion in rotation.



(–) 2-Bromo-octane (–) 2-Octanol

To explain this it is assumed that the nucleophile —OH attacks the carbon from the opposite side of the leaving group so as to avoid over crowding and starts forming a bond by sharing of its pair of electrons. At approximately the same time, the group which is leaving the molecule starts acquiring the bonding electron pair. Thus a negative charge spreads in the transition state from the nucleophile at one end to the departing group at the other end. The configuration of transition state is perhaps that of a triangular bipyramid with all the other groups in the same plane. Since the nucleophile enter the molecule from the opposite end of the departing group, the configuration of the molecule is turned upside down like an

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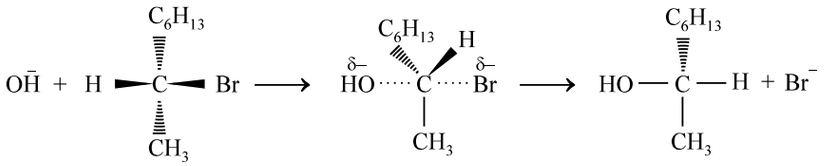
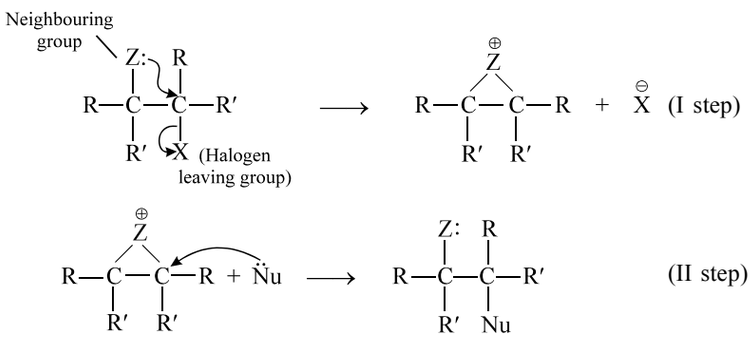
inverted umbrella. This therefore results in the inversion of configuration known as *Walden inversion*, when bromide ion is expelled and tetrahedral arrangement reverts back with arrangement opposite to that of the original molecule.



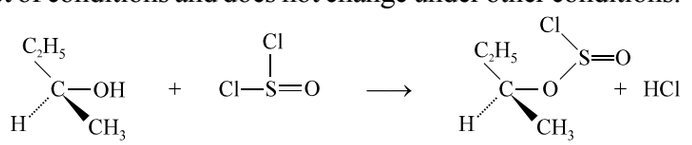
Transition state

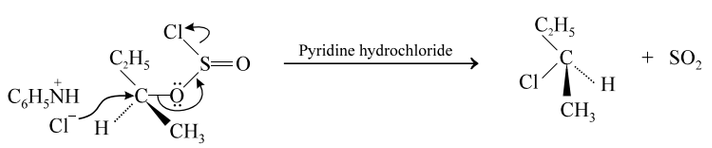
Neighbouring Group Participation: The neighbouring group participation is defined as the interaction of the reaction centre either with a lone pair of electrons as adjacent atom or with electrons present in a sigma or pi-bonds (as in a double bond). It generally leads to increased reaction rates and sometimes results in unexpected stereochemical nature of the product.

If the neighbouring group (the group attached to the carbon which is next to carbon having leaving group) is an electron-rich substituent at a proper place then the configuration is retained. This is a two-step process.



S_Ni. Substitution nucleophilic internal (S_Ni) are those substitution reactions in which substitution takes place by intramolecular process. In these reactions the configuration of the product may or may not change; depending upon the conditions employed in the reaction. Conversion of an alcohol (S)-2-butanol to corresponding chloride using thionyl chloride, is a reaction where the configuration changes only under a set of conditions and does not change under other conditions.





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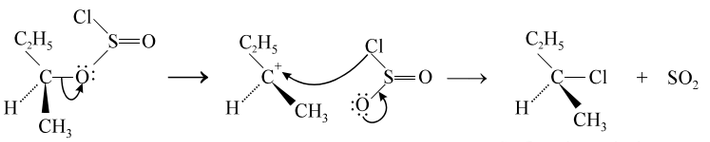
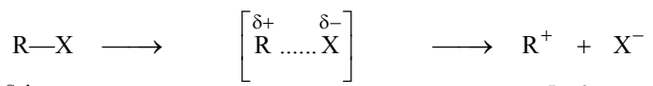
However, in the absence of pyridine the chlorosulphite ester decomposes to give the chloride having the same configuration.



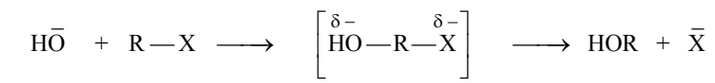
Configuration retained

Solvent Effect: In S_N1 substitution reaction the bond breaking between carbon and halogen requires energy. The ions generated during heterolysis of the bond are surrounded by polar solvent molecules oriented with their negative end towards the carbocation and positive end towards anion. The substrate molecule is then pulled apart as solvated ions. Individually these ion-dipole bonds are weak but altogether they provide a great deal of energy. The transition state has a stretched carbon-halogen bond with well developed charges. Thesolvent thus stabilizes transition state more than the reactant, thereby lowering the energy of activation and speeding up the reaction. This lowering of energy compensates for the energy required for breaking the bond.



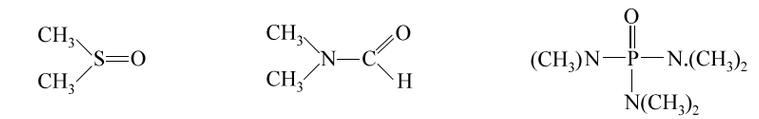
Substrate — Transition state (More polar than reactants stabilized by solvation) — Products

In S_N2 mechanism the solvent stabilizes the reactants specially the nucleophiles, more than it does the transition state and thus raises the energy of activation and slows down the reaction (stabilization deactivates the nucleophile)



Stabilized — Transition state (Dispersed charge stabilized to small-extent)

Here we must understand that cations are solvated through unshared pair of electrons but the anions are chiefly solvated through hydrogen bonding. Hence protic solvents like water and alcohol are good for S_N1 mechanism but they slow down S_N2 reaction. (CF_3CH_2OH, HCOOH and CF_3COOH are other solvents which form strong H-bond with the leaving group and are better solvents for S_N1 mechanism.) In aprotic solvents like DMSO, DMF and HMPT, S_N2 reactions go 10^6 times as fast as in polar solvents like water and alcohol.

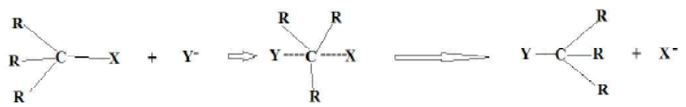


Dimethyl sulphoxide (DMSO) — Dimethyl formamide (DMF) — Hexamethyl phosphorotriamide (HMPT)

Leaving Group: Most of the leaving groups leave as negative ion and if they stabilize this charge most effectively as they will be considered as good leaving groups. Weak bases which are conjugate bases of strong acids do this best. The anions of strong acids like Cl^-, Br^-, I^- and $HS\bar{O}_4$ are good leaving groups in S_N2 reactions. Amongst the halogens Iodide ion is the best leaving group and fluoride is the poorest of the lot $I^- > Br^- > Cl^- > F^-$.

Kinetics of a Reaction

The rate of nucleophilic substitution in a reactions depends on the concentration of both the haloalkane and the nucleophile.



(a) If we double the concentration of either the haloalkane or the nucleophile, then the rate of the reaction would proceed twice as fast as the initial rate.

(b) If we double the concentration of both the haloalkane and the nucleophile,then that the rate of the reaction would proceed four times as fast as the initial rate.

Let as assume the initial reaction is:

$$HO^- + CH_3-I \longrightarrow CH_3OH + I^-$$

$$\text{Rate} = k[CH_3-I][HO^-]$$

Changing of Concentration:

$$\text{Rate}_1 = k[CH_3-I][HO^-]$$
$$\text{Rate}_2 = 2k[CH_3-I][HO^-]$$
$$\text{Rate}_2 = 2\,\text{Rate}_1$$

$$\text{Rate}_1 = k[CH_3-I][HO^-]$$
$$\text{Rate}_2 = 4k[CH_3-I][HO^-]$$
$$\text{Rate}_2 = 4\,\text{Rate}_1$$

Check Your Progress

1. What are the two groups of nucleophiles?
2. What are carbanions?
3. Give two examples of nucleophilic substitution reaction.
4. What is neighbouring group participation?

11.4 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Negative nucleophiles and positive nucleophiles.
2. If a negative charge is present at carbon, such nucleophiles are known as

carbanions.

3. Examples of the nucleophilic substitution reaction are hydrolysis of alkyl halides, acyl halides; cleavage of ethers with HI (Ziesel reaction and alkylation with alkyl halides (Williamson's synthesis).
4. The neighbouring group participation is defined as the interaction of the reaction centre either with a lone pair of electrons as adjacent atom or with electrons present in a sigma or pi-bonds (as in a double bond).

11.5 SUMMARY

- Reagents having an unshared pair of electrons are known as nucleophilic reagents or nucleophiles because they have a tendency to share this pair of electrons with electron deficient substrate.
- A nucleofuge - This term is the combination of two term Nucleo and Fugetake (*nucleo*- nucleus means the positive charge part in an atom and fuge, *fugitive mean* to escape) is a leaving group which retains the lone pair from its previous bond with another species.
- Substitution reactions by nucleophilic reagents are known as nucleophilic substitution (S_N) reactions.
- S_N1 reactions follow first order kinetics.
- S_N2 reactions follow second order kinetics.
- The various factors guiding the reaction to follow S_N1 or S_N2 mechanism are structure of the substrate, steric effect, rearrangement of carbocations, solvent effect and leaving group.

11.6 KEYWORDS

- **Rate of reaction:** It is the speed at which reactants are converted into products.
- **Substrate:** A substrate is typically the chemical species being observed in a chemical reaction, which reacts with a reagent to generate a product.
- **Leaving group:** A leaving group is a molecular fragment that departs with a pair of electrons in heterolytic bond cleavage.
- **Nucleophile:** It is a chemical species that donates an electron pair to an electrophile to form a chemical bond in relation to a reaction.

11.7 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. Write a short note on nucleophiles.
2. Write a short note on nucleofuge.
3. What do you understand by steric effect?

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Long Answer Questions

1. Discuss the mechanism of S_N1 reaction.
2. Discuss the mechanism of S_N2 reaction.
3. What do you understand by kinetics of aliphatic nucleophilic substitutions?
4. Discuss the factors that guide the reactions to follow S_N1 or S_N2 mechanism.

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UNIT 12 ALIPHATIC ELECTROPHILIC SUBSTITUTIONS

Structure

12.0 INTRODUCTION

In electrophilic substitution reactions, an electrophile displaces a functional group in a compound, which is typically, but not always, a hydrogen atom.

In aliphatic electrophilic substitution, an electrophile displaces a functional group. The four possible electrophilic aliphatic substitution reaction mechanisms are S_E1, S_E2 (front), S_E2 (back) and S_Ei (Substitution Electrophilic), which are also similar to the nucleophile counterparts S_N1 and S_N2. In the S_E1 course of action the substrate first ionizes into a carbanion and a positively charged organic residue. The carbanion then quickly recombines with the electrophile. The S_E2 reaction mechanism has a single transition state in which the old bond and the newly formed bond are both present.

In this unit, you will study the reactivity, structure and mechanism of aliphatic electrophilic substitution reactions.

12.1 OBJECTIVES

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

- Understand aliphatic electrophilic substitution reactions
- Know about S_E1, S_E2 and S_Ei reactions

12.2 ALIPHATIC ELECTROPHILIC SUBSTITUTIONS

Substitution reactions initiated by electrophilic reagents are known as electrophilic substitution reactions. Obviously for such reactions the reactive site in the substrate

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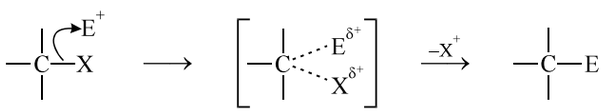
must be rich in electrons. Two types of such reactions are electrophilic substitutions at saturated or aliphatic carbon atoms and at unsaturated or aromatic carbon atoms. The latter type is important. Electrophilic substitution reactions are designated as S_E reactions. If the reaction is unimolecular it is written as S_E1 and if it is bimolecular it is then written as S_E2 type of reaction. Usually the S_E1 reactions involve two steps—a slow ionization to give a carbanion and then a fast combination of this carbanion with electrophile. Thus:

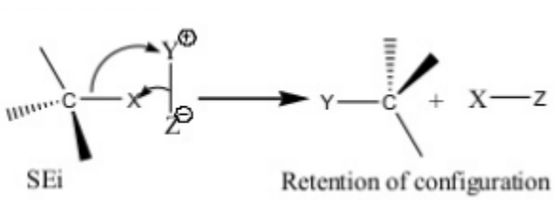
Step 1. $R—X \xrightarrow{\text{Slow}} R^- + X^+$ Step 2. $R^- + E^+ \xrightarrow{\text{Fast}} R—E$

The S_E2 reactions take place by a concerted mechanism. The incoming group approaches the reactive site from the front side and starts the formation of bond by overlapping with the orbital of carbon on the reactive site. At the same time the departing group is loosening its grip on the bonding pair of electrons. Thus:



This reaction will therefore proceed with the retention of configuration at reactive site whereas S_E1 reactions will result in racemic products because of the probability of attack of E^+ on carbanion from either side.

In S_Ei Mechanism, the final product forms with the same stereochemistry of a starting material i.e. S_Ei results in retention of configuration. S_Ei is also a bimolecular reaction.



Reactivity and Structure: Electrophilic substitutions at aliphatic carbon atom are usually observed in organometallic compounds where the metal is less electronegative than carbon. In such reaction the chances for S_E1 type will decrease with the presence of electron donating groups and increase with the presence of electron withdrawing groups. The stability of the resulting carbanion also influences the course of reaction. The greater the polarity of bond C—X, the greater will be the S_E1 reaction rate. Similarly increase in the polarity of solvent favours S_E1 reactions. For S_E2 reactions the electron donating and withdrawing group do not have such rationalized influence. The solvent of greater polarity enhances the S_E2 reaction but lesser than the S_E1 reaction.

The reactivities in substitution at aromatic carbon atoms are strongly influenced by the nature of the substituents present in the ring.

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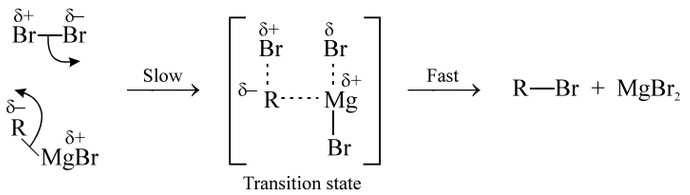
Applications: Some examples of typical electrophilic substitution reactions are given below together with their mechanisms.

(1) ***Substitution at aliphatic or Saturated carbon atom***

(*i*) Reaction of Grignard reagent with halogen:

$$\underset{\text{Alkyl magnesium bromide}}{R—Mg—Br} + Br_2 \longrightarrow \underset{\text{Alkyl bromide}}{R—Br} + MgBr_2$$

The reaction proceeds by a S_E2 type mechanism



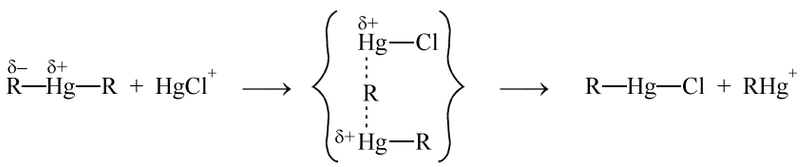
The replacement of —MgBr group by the electrophilic attack of bromonium ion (Br^+) occurs through a transition state resulting in the formation of alkyl bromide.

(*ii*) Reaction of dialkyl mercury with mercuric chloride:

$$\underset{\text{Dialkyl mercury}}{R—Hg—R} + HgCl_2 \longrightarrow \underset{\text{Alkyl mercuric chloride}}{2R—Hg—Cl}$$

This is another example similar to one described above.

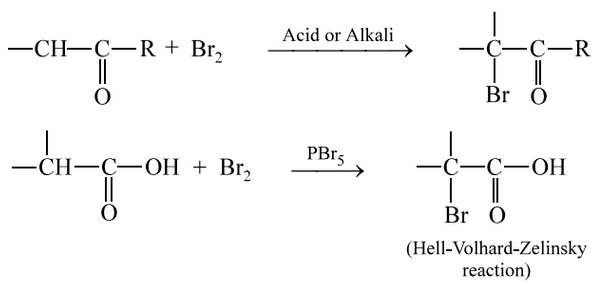
$$HgCl_2 \longrightarrow HgCl^+ + Cl^-$$



$$R—Hg^+ + Cl^- \longrightarrow R—Hg—Cl$$

Here the Hg^+Cl electrophile replaces the Hg^+R group from the molecule by S_E2 mechanism.

(*iii*) Halogenation of aldehydes, ketones, and acids—The reaction may be represented as



The mechanisms for these reactions too is explained by the application of electrophilic substitution.

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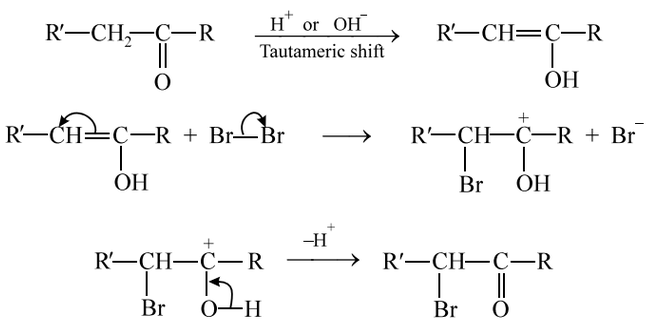


Thus a bromonium ion has been substituted in place of a hydrogen ion.

(2) ***Mechanism of haloform reaction:*** When methyl carbonyl compounds (CH_3CHO, $CH_3CO.CH_3$ etc.) react with halogens in presence of alkali, haloform (CHX_3) is formed. The reaction is known as *haloform reaction.*

The reaction is given by all compounds containing the acetyl group attached to either carbon or hydrogen, or by compounds which are oxidised under the conditions of the reaction to derivatives containing the acetyl group for example, ethyl alcohol, isopropyl alcohol, lactic acid etc. (Booth and Saunders in 1950 have shown that certain quinones and dihydric phenols also give haloform reaction.) Thus with ethyl alcohol the following steps are involved in preparation of chloroform.

(*i*) Oxidation of ethyl alcohol by chlorine to acetaldehyde

$$CH_3.CH_2OH + Cl_2 \longrightarrow CH_3CHO + 2HCl$$

(*ii*) Chlorination of acetaldehyde to chloral (trichloroacetaldehyde)

$$CH_3CHO + 3Cl_2 \longrightarrow \underset{\text{Chloral}}{CCl_3.CHO} + 3HCl$$

(*iii*) Hydrolysis of chloral by calcium hydroxide yielding chloroform

$$2CCl_3.CHO + Ca(OH)_2 \longrightarrow \underset{\text{Chloroform}}{2CHCl_3} + \underset{\text{Calcium formate}}{(H.COO)_2Ca}$$

In case of acetone the following steps are involved:

(*i*) Chlorination of acetone to trichloroacetone

$$CH_3.CO.CH_3 + 3Cl_2 \longrightarrow \underset{\text{Trichloroacetone}}{C.Cl_3.CO.CH_3} + 3HCl$$

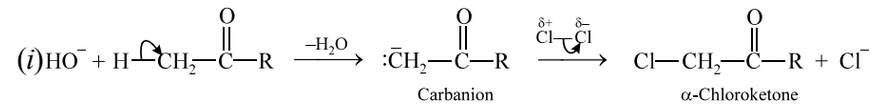
(*ii*) Hydrolysis of trichloroacetone by calcium hydroxide yielding chloroform

$$2CCl_3.CO.CH_3 + Ca(OH)_2 \longrightarrow \underset{\text{Chloroform}}{2CHCl_3} + \underset{\text{Calcium acetate}}{(CH_3.COO)_2Ca}$$

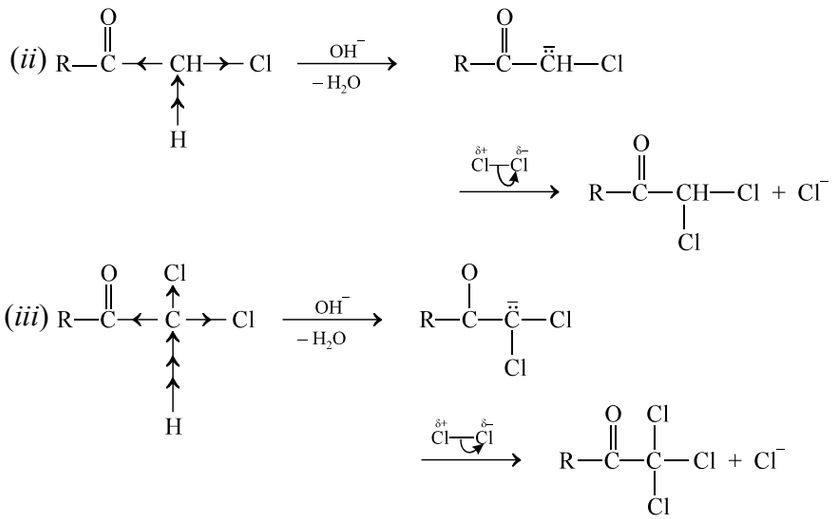
The mechanism is as given below:

The hydrogen atoms at α-carbon to the carbonyl group are slightly acidic in nature due to the electron withdrawing effect of the carbonyl group.

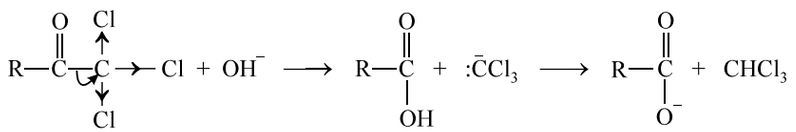
In presence of base $(O\bar{H})$ these hydrogen atoms become still more reactive and are replaced easily by chlorine attacking as chloronium ion.



Once α-chloroketone is formed the other H atoms of the carbon having chlorine become more reactive on account of –I effect caused by chlorine and are replaced successively yielding trichloromethyl carbonyl compound.



Trihalocarbonyl compound is then cleaved by alkali giving chloroform



(Replacing R with H or CH_3, the reaction with CH_3CHO or CH_3COCH_3 can be written.)

Check Your Progress

1. What are electrophilic reactions?
2. What are the two types of electrophilic reactions?
3. How unimolecular electrophilic substitution reactions are represented?

12.3 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Substitution reactions initiated by electrophilic reagents are known as electrophilic substitution reactions.
2. Saturated or aliphatic reaction and at unsaturated or aromatic reaction.
3. If the reaction is unimolecular it is written as S_E1.

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12.4 SUMMARY

- Substitution reactions initiated by electrophilic reagents are known as electrophilic substitution reactions.
- Electrophilic substitution reactions are designated as S_E reactions.
- If the reaction is unimolecular it is written as S_E1 and if it is bimolecular it is then written as S_E2 type of reaction.
- The reactivities in substitution at aromatic carbon atoms are strongly influenced by the nature of the substituents present in the ring.
- When methyl carbonyl compounds (CH_3CHO, $CH_3CO.CH_3$ etc.) react with halogens in presence of alkali, haloform (CHX_3) is formed. The reaction is known as haloform reaction.

12.5 KEY WORDS

- **Aliphatic:** Relating to or denoting organic compounds in which carbon atoms form open chains (as in the alkanes), not aromatic rings.
- **Electrophilic:** (of a molecule or group) having a tendency to attract or acquire electrons.
- **Substitution reaction:** Substitution reaction is a chemical reaction during which one functional group in a chemical com pound is replaced by another functional group.

12.6 SELF ASSESSEMNT QUESTIONS AND EXERCISES

Short Answer Questions

1. Write a short note on S_E1 reaction.
2. Write a short note on S_E2 reaction.
3. What are S_Ei reactions?

Long Answer Questions

1. Explain the aliphatic substitution reaction of Grignard with halogen.
2. Explain the aliphatic substitution reaction of dialkyl mercury with mercuric chloride.
3. Represent the halogenation of aldehydes, ketones and acids.
4. Discuss the mechanism of haloform reaction.

12.7 FURTHER READINGS

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UNIT 13 AROMATIC ELECTROPHILIC SUBSTITUTIONS

Structure

13.0 INTRODUCTION

Although aromatic compounds have multiple double bonds, these compounds do not undergo addition reactions. Their lack of reactivity toward addition reactions is due to the great stability of the ring systems that result from complete π electron delocalization (resonance). Aromatic compounds react by electrophilic aromatic substitution reactions, in which the aromaticity of the ring system is preserved. For example, benzene reacts with bromine to form bromobenzene.

Substitution at aromatic or unsaturated carbon atoms. The most important reactions of the aromatic compounds are the electrophilic substitution reactions like nitration, halogenation, sulphonation etc. Nitration is introduction of a nitro group (—NO_2) in place of hydrogen by electrophile (nitronium ion). Sulphonation is the replacement of a hydrogen by —SO_3H group and takes place by electrophilic attack of SO_3 on aromatic carbon.

In this unit, you will study about aromatic electrophilic substitution reaction, electrophilic substitution reaction, activation and deactivation of benzene nucleus, Vilsmeier–Haack reaction in detail.

13.1 OBJECTIVES

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

- Explain aromatic electrophilic substitution reaction
- Discuss about electrophilic substitution reaction

- Understand what is activation and deactivation of benzene nucleus
- Explain about Vilsmeier–Haack reaction

13.2 AROMATIC ELECTROPHILIC SUBSTITUTION REACTION

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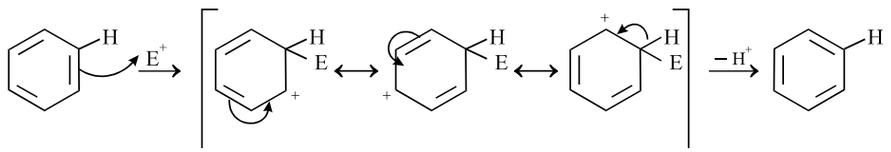
***Substitution at Aromatic or Unsaturated Carbon Atoms*:** The most important reactions of the aromatic compounds are the electrophilic substitution reactions like nitration, halogenation, sulphonation etc. Nitration is introduction of a nitro group (—NO_2) in place of hydrogen by electrophile $\overset{+}{N}O_2$ (nitronium ion). Sulphonation is the replacement of a hydrogen by —SO_3H group and takes place by electrophilic attack of SO_3 on aromatic carbon. These reactions are dealt at length in the chapter on aromatic hydrocarbons. However the mechanism of a general electrophilic substitution in benzene by electrophile (E^+) is given below:



(Carbocation stabilised by resonance)

$\overset{+}{E}$ can be

- $\overset{+}{N}O_2$ for nitration $(HNO_3 + 2H_2SO_4 \rightarrow NO_2^+ + H_3\overset{+}{O} + 2HSO_4^-)$
- Cl^+ for chlorination $(Cl_2 + FeCl_3 \rightarrow Cl^+ + FeCl_4^-)$
- Br^+ for bromination $(Br_2 + FeCl_3 \rightarrow Br^+ + \bar{F}eCl_3Br)$

The carbocation formed as intermediate in an aromatic electrophilic substitution is an arenium ion, also known as *Wheland intermediate* or a sigma (σ) complex. The smallest arenium ion is a protonated benzene $C_6H_7^{\oplus}$ called *benzenium ion* which can be isolated as a stable compound when benzene is protonated by the carborane super acid.

Electrophilic substitution of a monorsubstituted benzene derivative can give rise to three *regioisomeric* products in which the new substitutent is placed at C–2 (ortho), C–3 (meta) or C–4 (para) position. There are two ortho- and two meta positions available but a statistical distribution of products is not observed and the actual proportion is dependent upon whether the group present is activating or deactivating.

A vast majority of electrophilic substitution reactions proceed under kinetic control where the rate- and product-determining step is the formation of a Wheland intermediate which is a highly endothemic process. Hammond's postulate states that the factors stabilizing the transition state should also operate in Wheland intermediate. Hence the stabler the intermediate faster is its formation.

When *o*-, *p*-directing and activating groups (for example, —NH_2, —OH etc.) are attached to benzene then the wheland intermediate resulting from *o*- or *p*-

NOTES

attack is more stabilized by resonance. In case of *o*-, *p*-directing but deactivating group (like —Cl) the Wheland intermediate from *o*- or *p*-attack are stabilized by resonance involving lone pair of chlorine, whereas when *m*-directing and deactivating groups (for example, —NO_2, —CN etc.) are attached to benzene then Wheland intermediate from *m*-attack is less destabilized as compared to their *o*- or *p*-counterparts.

Check Your Progress

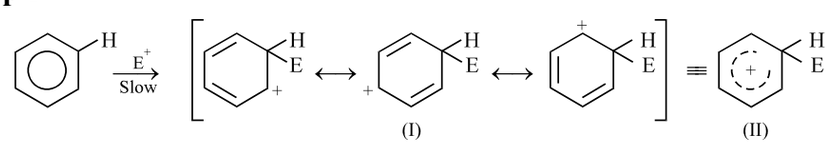
1. What is Wheland intermediate ?
2. What does Hammond's postulate states?
3. What happens when o-, p-directing and activating groups are attached to benzene ?

13.3 ELECTROPHILIC SUBSTITUTION REACTIONS

The π electrons of benzene ring are losely held and are available to an electrophilic reagent seeking electrons *hence typical reactions of benzene are electrophilic substitution reactions. In the reactions the attacking electrophile may be produced in different ways but what happens to the aromatic ring is basically same in all the cases*.

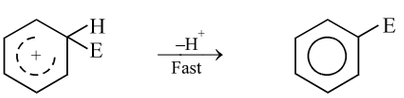
The attacking electrophile may be a positive ion or a dipole. If it is a positive ion it attacks the ring removing a pair of electron from the sextet to give a carbocation which gets resonance stabilized as shown in (I) and is represented as shown in (II).

Step 1



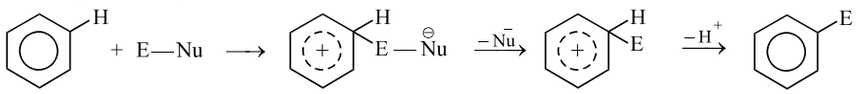
Ions of the type (II) are called *carbocation*, *Wheland intermediates*, σ-*complex* or *arenium ions* see also reaction mechanism chapter 5 section 5.20. In case of benzenoid system they are called cyclohexadienyl cations. The arenium ion has been isolated and is quite stable but it stabilizes itself by the loss of either E^+ or H^+. The aromatic sextet is then restored. This is the second step of the mechanism in which the proton is accepted by a proton acceptor (base) to revert the system to stable benzenoid structure. The second step is faster than the first step. Lars Melander (1949, 1950) while studying the nitration of a variety of aromatic compounds established that first step is slower.

Step 2

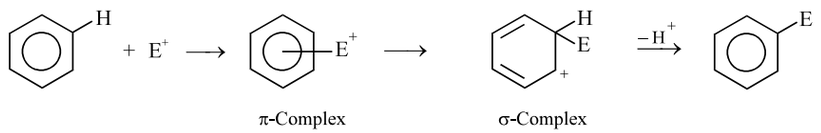


NOTES

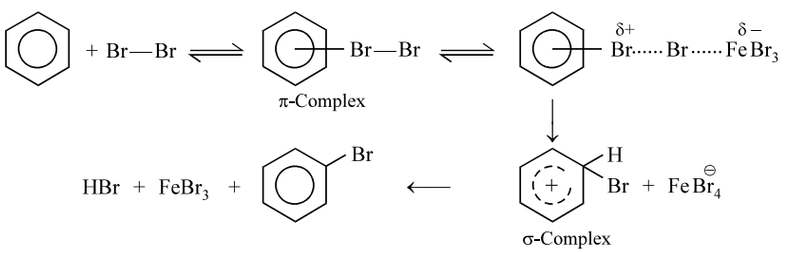
If the attacking species is not an ion but a dipole, the product must have a negative charge, unless part of the dipole with its electron pair, is broken off at some stage in the process.



The arenium ion formed and isolated is commonly called σ-*complex*. However, it was found that the relative reactivity and the percentage of *o*, *m* and *p* products formed depended not only a particular reaction but also on the nature of the reagent employed. This led some chemists to believe that a π-complex is formed during the electrophilic *substitution* between the substrate and the electrophile before the formation of arenium ion (σ-complex) and that influences the reaction rate.



In the electrophilic substitution of bromine, kinetic data has shown that the rate of bromination depends on the concentration of catalyst $FeBr_3$ also besides halogen and benzene. The positive end of the dipole attacks the aromatic ring forming π-complex and the negative end is complexed with the catalyst. The formation of σ-complex (arenium ion) between Br^+ and carbon of the benzene ring is the slow step of the reaction. The reaction may be represented as given below:

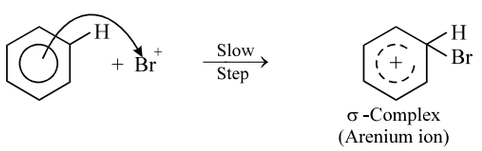


However, since σ-complex is formed, substitution can also be represented by the steps given below.

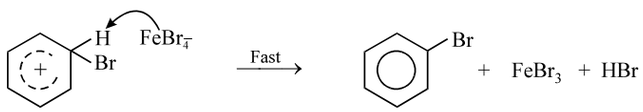
(*i*) $Br—Br + FeBr_3 \rightleftharpoons Br^+ + FeBr_4^-$

Lewis base — Lewis acid — Electrophile

(*ii*)



(*iii*)



In the substitution reactions given below there are three steps in the reactions. First step is the production of electrophile, the second step is the formation of arenium ion or σ complex and the third step is the removal of the proton to form the substitution product.

NOTES

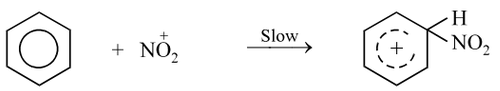
1. **Nitration:** Nitration of benzene is carried out with a mixture of conc. nitric and conc. sulphuric acid.

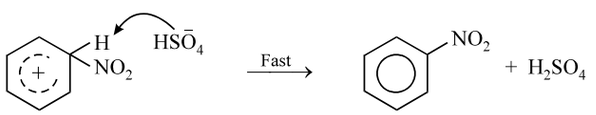
$$C_6H_6 + HNO_3 \xrightarrow{H_2SO_4} C_6H_5NO_2 + H_2O$$

Mechanism: In the first step of the reaction $\overset{+}{N}O_2$ is produced (strong sulphuric acid causes nitric acid to ionise as $\overset{-}{O}H + \overset{+}{N}O_2$) which reacts with benzene in the second step to give the arenium ion. The arenium ion transfers a proton to some base in the mixture *e.g.*, $H\overset{-}{S}O_4$ to give nitrobenzene.

(*i*) $2H^+ \; H\overset{-}{S}O_4 + HO{-}N(=O)(\rightarrow O) \longrightarrow O{=}\overset{+}{N}{=}O + 2H\overset{-}{S}O_4 + H_3\overset{+}{O}$

Nitronium ion

(*ii*) 

(*iii*) 

The energy changes taking place have been shown in the energy profile Figure. 11.1.

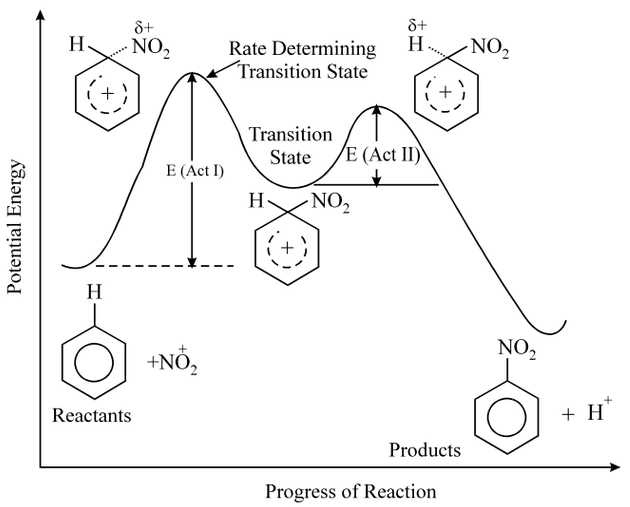
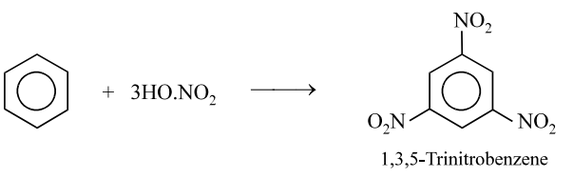


***Fig. 11.1** Energy Changes*

If fuming nitric acid is used for the reaction it is possible to introduce two or three nitro groups.



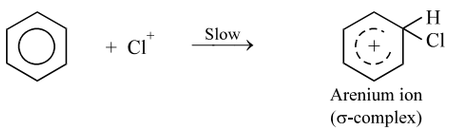
1,3,5-Trinitrobenzene

2. **Halogenation:** Benzene undergoes chlorination and bromination forming monochloro or monobromobenzene. The reaction takes place in presence of $FeCl_3$ or $AlCl_3$ at room temperature.

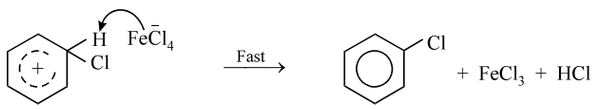
$$C_6H_6 + Cl_2 \xrightarrow{FeCl_3} C_6H_5Cl + HCl$$

Mechanism: In the first step the electrophile is formed which in the second step attacks the π electrons to form arenium ion (σ-complex). The arenium ion loses the proton to the base in the last step to give monohalo substituted benzene.

(*i*) $Cl — Cl + FeCl_3 \longrightarrow Cl^+ + \bar{F}eCl_4$

(*ii*) 

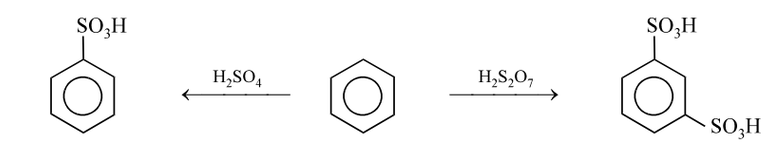
Arenium ion
(σ-complex)

(*iii*) 

The reaction with bromine is given just above. Reaction with iodine presents some difficulty since iodine is the least active among the halogens but if carried out in presence of some oxidising agent *e.g.*, nitric acid or mercuric oxide, the reaction takes place with good yield of iodo-compound.

$$2C_6H_6 + I_2 \xrightarrow[[O]]{HNO_3} 2C_6H_5I + H_2O$$

3. **Sulphonation:** With hot and concentrated sulphuric acid benzene forms benzene sulphonic acid. If fuming sulphuric acid is used *m*-benzene disulphonic acid is formed.

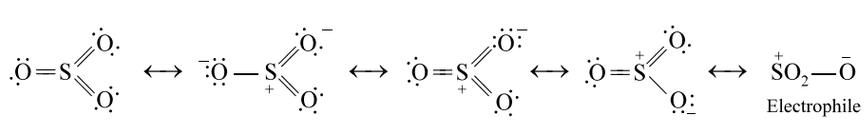


Benzene sulphonic acid

m-Benzene disulphonic acid

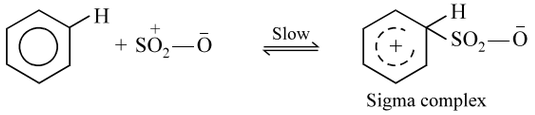
Mechanism: In the first step of reaction H_2SO_4 acts both as an acid and a base to produce the electrophile SO_3 which is a resonance hybrid of many forms in which the following dipolar form predominates.

(*i*) $2H_2SO_4 \rightleftharpoons H_3\overset{+}{O} + H\bar{S}O_4 + SO_3$



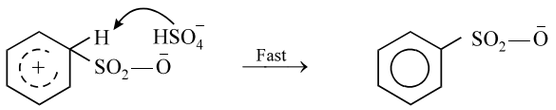
NOTES

The electrophile SO_3 attacks π electrons of the ring to form arenium ion.

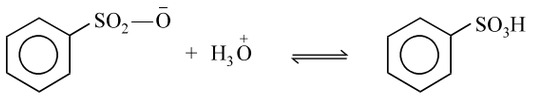
(*ii*) 

Sigma complex

Sigma complex loses a proton to base $H\bar{S}O_4$ to give resonance stabilized substitution product.

(*iii*) 

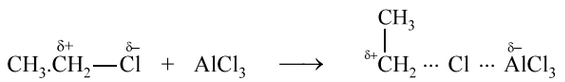
The product in step (*iii*) accepts a proton to give the acid which remains dissociated.

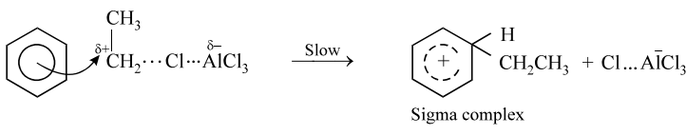


4. **Friedel-Crafts alkylation of benzene:** Benzene on being treated with alkyl halide in presence of $AlCl_3$ form alkyl benzenes in which the alkyl group comes from alkyl halide.

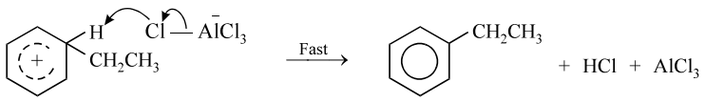
$$C_6H_6 + CH_3Cl \xrightarrow{AlCl_3} \underset{\text{Toluene}}{C_6H_5.CH_3} + HCl$$

Mechanism: In Friedel-Crafts alkylation, the electrophile is a carbocation which is easily formed if the alkyl halide is secondary or tertiary. The available evidence suggests that the alkyl halide (say on alkyl chloride) reacts with the $AlCl_3$ used to form a ion-pair type complex. This complex attacks the benzene ring in step II to form sigma complex.

(*i*) 

(*ii*) 

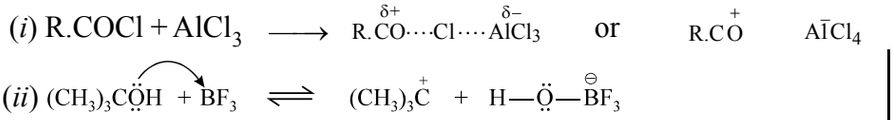
Sigma complex

(*iii*) 

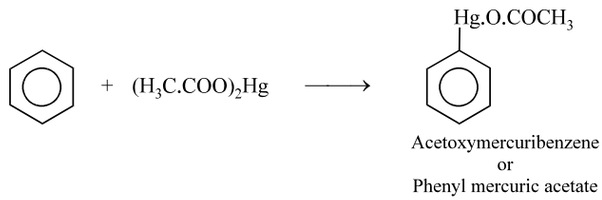
In the last step sigma complex loses a proton to base $Cl—\bar{A}lCl_3$ to give the alkyl benzene.

Friedel-Crafts reaction is also used to introduce groups like R.CO— or $(CH_3)_3C$— in benzene nucleus. In each case the electrophile is produced which

then reacts in the manner indicated above. Production of electrophile has been indicated in a rather simplified manner here. For details see Sec. 6.22.



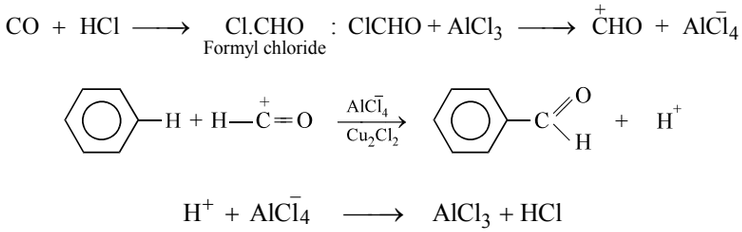
5. **Mercuration:** When benzene is heated to (90–160°C) with mercuric acetate for about an hour, one hydrogen atom is replaced by acetoxy-mercuric group. *Conditions of the reaction are such that electrophile* $H_3C.COOHg^+$ *is created for the reaction*.



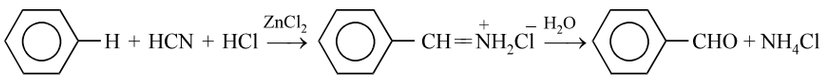
Mercurated compounds are of great medicinal value.

6. **Formylation:** During some reactions given below an aldehydic group gets introduced into the nucleus. This is called *formylation.*

- **Gattermann Koch Reaction:** When a mixture of carbon monoxide and hydrogen chloride is passed in an ethereal solution of benzene in presence of anhydrous $AlCl_3$ and cuprous chloride, an aldehyde is obtained.



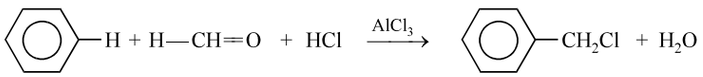
- **Gattermann Aldehyde Synthesis:** When benzene is treated with liquid hydrogen cyanide and dry hydrogen chloride in presence of anhydrous $AlCl_3$ or $ZnCl_2$ then an aldimine is formed which on being hydrolysed give an aldehyde.



This is also an electrophilic substitution reaction and the attacking electrophile is $\overset{+}{C}H=NH$.

The reaction can also be applied to toluene, xylene etc.

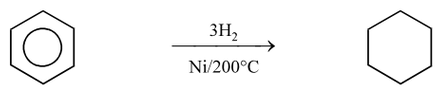
7. **Chloromethylation:** Introduction of the chloromethyl group (— CH_2Cl) in the benzene nucleus is also an electrophilic substitution reaction and is known as chloromethylation. This can be done by heating benzene or its homologues with formaldehyde and HCl in presence of anhydrous $AlCl_3$ or $ZnCl_2$.



Benzyl chloride

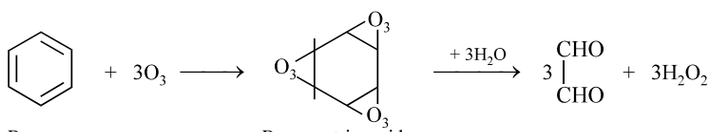
(B) Addition Reactions

8. **Hydrogenation:** Benzene undergoes hydrogenation in presence of finely divided metal catalyst like nickel, platinum etc., at about 200°C and form corresponding saturated cyclohexane.



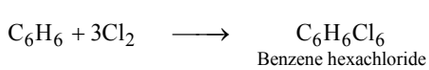
Benzene Cyclohexane

9. **Ozonide Formation:** Benzene adds up one ozone molecule at each one of the three double bonds to form a triozonide.



Benzene Benzene triozonide

10. **Addition of Halogen:** In bright sunlight and absence of halogen carrier, benzene react with chlorine and bromine to form hexahalides *e.g.*,

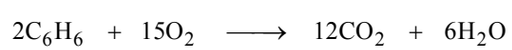


Benzene hexachloride

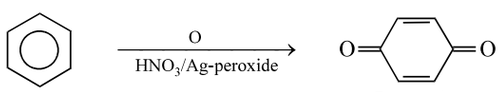
Benzene hexachloride (BHC) exists in several isomeric form. Its γ-isomer is a powerful insecticide sold under the name Gammexane (or 666).

(C) Miscellaneous Reactions

11. **Combustion:** Benzene is highly inflammable liquid and burns with a sooty (smoky) flame forming carbon dioxide and water vapour.

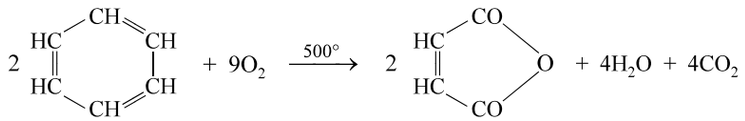


12. **Oxidation:** Benzene is very stable to oxidising agents like chromic acid, alkaline potassium permanganate or dilute nitric acid. Thus benzene does not decolourise potassium permanganate. However, when oxidised with nitric acid in presence of silver peroxide, it forms *p*-quinone.



p-Benzoquinone

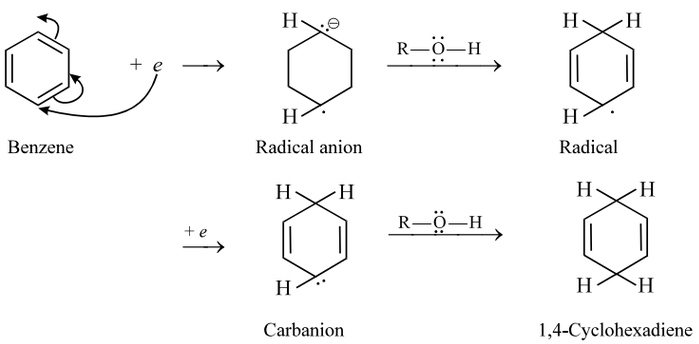
Vapours of benzene mixed with air, when passed over heated vanadium pentoxide form maleic anhydride by oxidation.



13. **Birch Reduction:** Partial reduction of aromatic ring can be achieved by dissolving lithium, sodium or potassium in liquid ammonia or amine in presence of ethyl, isopropyl or isobutyl alcohol.

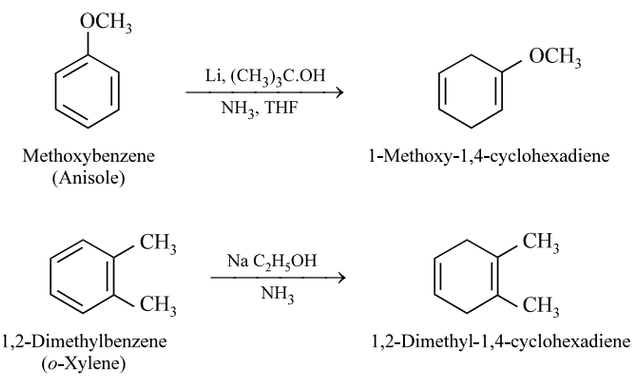
$$Na + (x+y)NH_3 \longrightarrow [Na(NH_3)_x]^+ + [e(NH_3)_y]^-$$

The mechanism of Birch reduction involves solvated electron which are transferred from metal to solvent and then to the ring. The reaction begins with addition of an electron to form a radical anion which is resonance stabilized. Protonation of the radical ion gives neutral radical. Addition of electron and protonation repeats itself to yield 1,4-cyclohexadiene.



The double bonds in 1,4-cyclohexadiene are isolated and are much less reducible, hence the reaction steps. The presence of electron releasing groups like alkyl or alkoxy retard the electron transfer hence retard the reaction whereas the presence of electron withdrawing group like —COONa facilitates reduction.

Electron **releasing** groups present in benzene nucleus and Birch reduction



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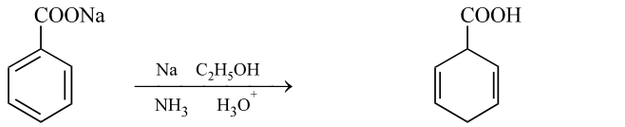
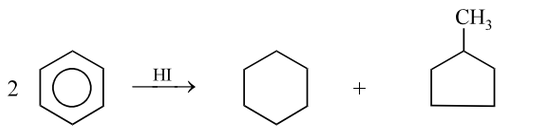
Electron **withdrawing** group present in benzene nucleus and Birch reduction



2,5-Cyclohexadiene-1-carboxylic acid

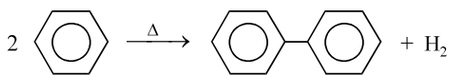
It is to be noted that electron releasing groups remain on the unsaturated carbon atom whereas electron withdrawing groups remain on the saturated carbon atom in the product.

14. **Action of HI:** Benzene on prolonged heating with HI forms a mixture of cyclohexane and methylcyclopentane.

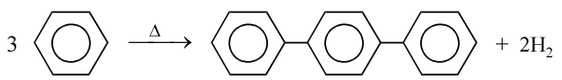


Cyclohexane Methylcyclopentane

15. **Formation of Polynuclear Hydrocarbons:** Vapour of benzene when passed through a red hot tube form a mixture of polynuclear hydrocarbons e.g., biphenyl and terphenyl.



Biphenyl



Terphenyl

Uses of Benzene

- As a solvent for extraction of fats and oils
- As a motor fuel along with petrol
- As a starting material for synthesis of various substances to be used for the preparation of dyes, drugs, plastics, perfumes, explosives etc.
- In the manufacture of maleic acid by catalytic oxidation.

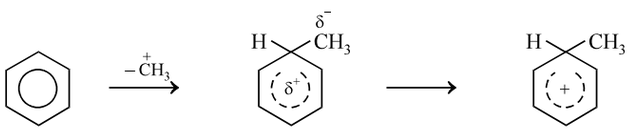
Check Your Progress

4. How is nitration of benzene is carried out?
5. What is Gattermann Koch reaction?
6. What happens in ozonide formation benzene ?

13.4 ACTIVATION AND DEACTIVATION OF BENZENE NUCLEUS

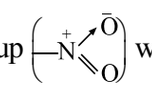
NOTES

In benzene ring the electron density is uniform at all the carbon atoms, hence the attacking electrophile has no preferential choice and may occupy any position. However in presence of a substituent the uniform electron density of benzene ring is disturbed and the nucleus is either activated or deactivated for further substitution. For example if a —CH_3 group is present in the nucleus of benzene (it is toluene) the sulphonation becomes twenty to twentyfive times faster under identical conditions. In other words we can say that the presence of



Developing +ve charge Arenium ion (σ-Complex) full +ve charge

methyl group has activated the nucleus. Methyl group has +I effect and at the time when methyl group is joining the nucleus +I effect stabilizes the developing positive charge and this lowers the activation energy in the rate determining step resulting in the faster reaction and the nucleus is said to be activated. Such groups which can release electrons into the nucleus by inductive or resonance effect, activate the nucleus. Halogens exert resonance effect, due to non-bonding lone pair of electrons and thus release the electrons to the nucleus but their strong –I effect more than neutralises this effect and thus they deactivate the nucleus. Such groups which activate the nucleus are *ortho* and *para*-directing and halogens though they deactivate the nucleus yet they are also *ortho-para*-directing.

Again consider the nitro group  which has a positive charge at nitrogen.

If this group is joined to the nucleus through nitrogen then it will try to withdraw electrons from the nucleus and thus intensify the positive charge and thus destabilize the carbocation because of the rise in the activation energy of the rate determining step. This will deactivate the nucleus. Such groups which withdraw electrons from the nucleus and deactivate it are *meta*-directing.

Table 13.1 *Reactivity and Orientation of the Groups*

Groups	*Polar Character*			
	Inductive	*Resonance*	*Hyperconjugation*	*Orientation and activity*
— C_6H_5— CH_3 and other alkyl groups	+ I	—	— CH_3 group shows hyper-conjugation	*o* and *p*-directing and weakly activating
—NH_2, —NHR, —NR_2 —OH	– I	+R	–	*o* and *p*-directing and strongly activating

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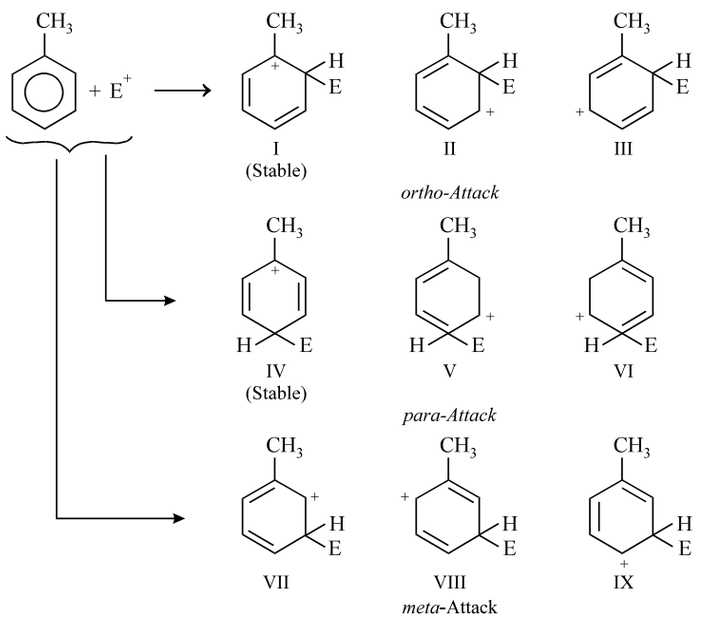
OR (—OCH_3, —OC_2H_5 etc.), —NHCOR, —O.CO.R	– I	+R	–	*o* and *p*-directing and moderately activating
— F, — Cl,	– I	+R	–	*o* and *p*-directing but moderately deactivating
— Br, — I	– I	+R		*o* and *p*-directing and activating
—$\overset{+}{N}H_3$, —$\overset{+}{N}R_3$, —$C.Cl_3$	– I	—	—	*meta*-directing and deactivating
—NO_2, —CN, —SO_3H, —COR, —CHO, —COOH, —COOR	– I	– R	—	*meta*-directing and strongly deactivating

Theory of Orientation

When we say that a particular group activates the nucleus and is *ortho* and *para*-directing then it does not mean that it will direct the new entrant only to *ortho* and *para* and that there will be no *meta* substituted compound formed. In fact the groups activating the nucleus form *ortho* and *para* compounds in greater proportion than *meta*. Sometimes the proportion of *o* and *p* is very high and *meta*-compound formation is very low. The presence of *o*, *p*-directing group gives a stable cation only when the substituents enter the *ortho* and *para* position with respect to the substituent already present. Let us examine the *ortho*, *para* and *meta* substitutions in case of toluene.



Out of the three hybrid structures for *ortho* attack (I to III) we can see that structure I has the positive charge on the tertiary carbon atom to which —CH_3 group is joined. Although —CH_3 group releases electrons uniformly to all the six positions of the hexagon but it does so most effectively to carbon atom nearest to

NOTES

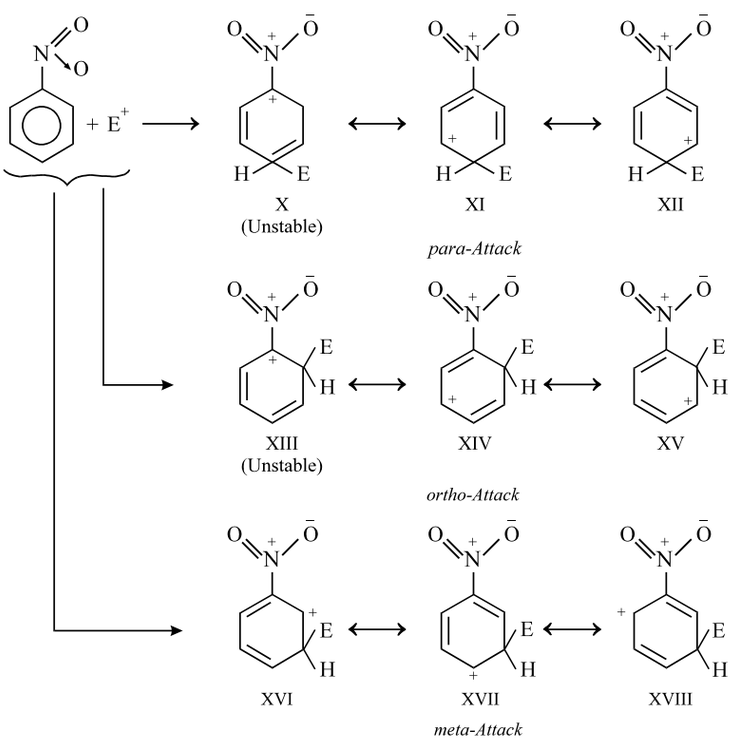
it (I) at *ortho* position. Thus structure I provides stability to the hybrid carbocation resulting form the *ortho* attack on toluene.

Similarly it can be seen that the attack at the *para* position yield a stable carbocation IV which provides stability to the hybrid carbocation resulting from the *para*-attack on toluene.

Attack at *meta* position by the substituent does not provide a stabler carbocation hence methyl group gives a poor yield of the *meta* product. It can be seen from VII to IX structure that only secondary carbocation is formed in each case as against the tertiary carbocation formed in case of *ortho* and *para* substitution.

Next let us take an example of electron withdrawing group joining the nucleus. Nitro group is such a group which has a positive charge on nitrogen and when joined to nucleus will withdraw electrons. When a new substituent joins nitrobenzene at *ortho*, *para* or *meta* positions the resonance structures associated with the intermediates are as given below.

In these structures we can see that in X and XIII the positive charges are located on the adjacent atoms and therefore they have very high energy as compared to other intermediates where the positive charges are separated by one or more atoms. This results in the destabilization of intermediates leading to *ortho* and *para*-substitution of nitrobenzene. The positive ions produced by *meta* substitution are more stable and all the three intermediate structures (XIV to XVI) contribute equally to the stability of resonance structure. Hence *meta* substitution is more favoured in comparison to *ortho* and *para* substitution in cases where electron withdrawing group is attached to the nucleus.



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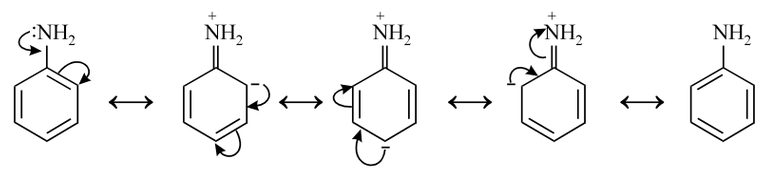
On the basis of similar arguments it can be shown that all groups which release electrons through I or R effect will have *ortho* and *para*-directing influence and those with electron withdrawing effect through I and R effect will prefer *meta* orientation.

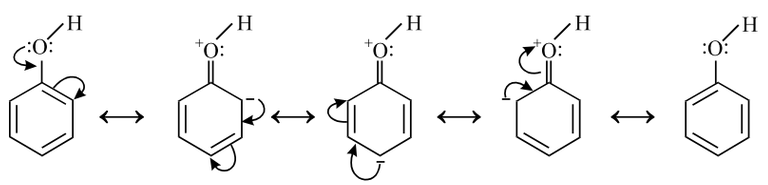
Electronic Explanation of *O*- and *P*-directive Influences

From an examination of the electronic structure and polar characteristics of *o*- and *p*-directing groups it is evident that with the exception of alkyl groups all of them posses at least one lone pair of electrons at the atom adjacent to the benzene ring known as *key atom.* Also that their polar characteristics are –I and +R type, except alkyl group which is +I type and halogens which have strong +E effect in addition (Table 12.3). This lone pair of electrons is in conjugation with the π electrons of the ring and exhibits a strong +R effect, thus increasing the overall electron density in the benzene ring. Although the –I effect opposes the +R effect but latter predominates. Such groups, for example, —OH, —OR, —NH_2, —NHR, —NR_2 etc., therefore activate the benzene ring towards electrophilic substitution. However, the *relative increase of electron density is greater at o- and p-positions* due to the nature of conjugation and hence the substitution occurs at these positions.

The resonance contributing structures of such substituted benzene derivatives make it clear as to how the electron density is increased at these positions. The molecule being a hybrid of the contributing structures, the actual state of the molecule is having a small negative charge at the *o*- and the *p*-positions. Thus:



Resonance in aniline



Resonance in phenol

The *o*- and *p*-directing effect of halogens is somewhat anomalous in that they exert strong –I effect and thus deactivate the ring. According to Ingold (1933) the +R effect of chlorine is too small to be of any significance. In presence of an attacking reagent the +E (electromeric) effect is brought into play and the *o*- and *p*-positions are raised in electron density above *m*-position. However, there is an overall decrease in the electron density as compared to benzene. Hence, although chlorine is *o*- and *p*-directing, it is weakly deactivating.

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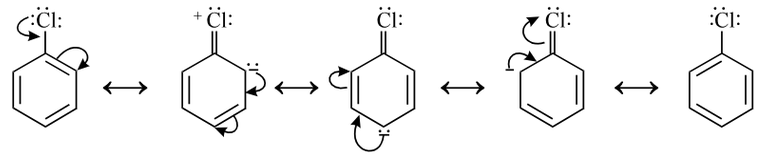
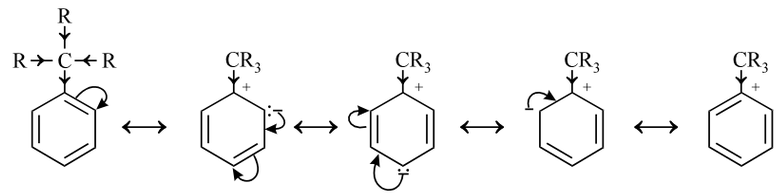


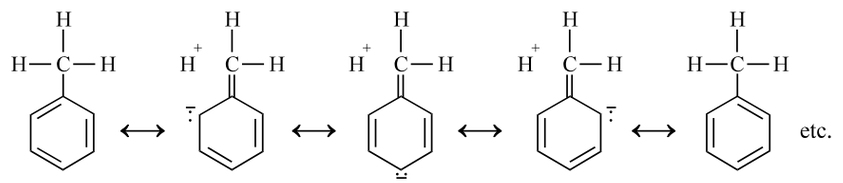
Resonance in chlorobenzene

Methyl or other alkyl groups repel electrons towards the ring by inductive and hyperconjugation effects and hence activate the ring moderately. For example, toluene is 25 times and *t*-butylbenzene is 16 times as reactive as benzene.



Activation and increase of electron density at o- and p-positions due to +I effect

For toluene consideration of hyperconjugation contributing structures is also important.



Hyperconjugation in toluene

Although the alkyl substituent increases the electron density in the ring as a whole, but more so at *o*- and *p*-positions with respect to alkyl group. Therefore, further electrophilic substitution occurs at these positions and not at *m*-position.

Electronic Explanation of *M*-directive Influence

The polar characteristics of these groups are –I and –R with the exception of $—\overset{+}{N}R_3$ and —CCl_3 groups which exhibit only –I effect. Hence $—\overset{+}{N}R_3$ and —CCl_3 groups *deactivate* the benzene ring in general by decreasing electron density due to –I effect. However, the withdrawal of electrons from *o*- and *p*-positions is much greater as compared to *m*-position. Thus *m-position remains the point of comparatively high electron density* and electrophilic substitution occurs preferentially at *m*-position.

The groups like —NO_2, —CN, —SO_3H, —CHO, —COOH etc., have a multiple bond conjugated to the benzene ring and a strongly electron attracting atom linked through this multiple bond. Due to conjugation the electron attracting atom causes withdrawal of electrons away from the ring and towards the group by a –R effect, thus deactivating the nucleus. However the effect is more pronounced at *o*- and *p*-positions leaving the *m*-position as point of relatively high electron density. The –I effect assists the –R effect.

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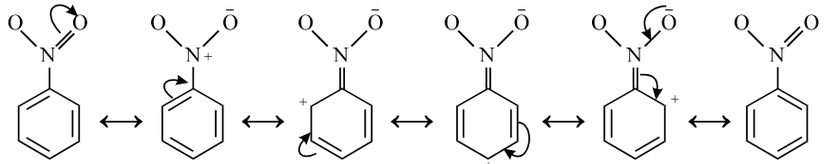
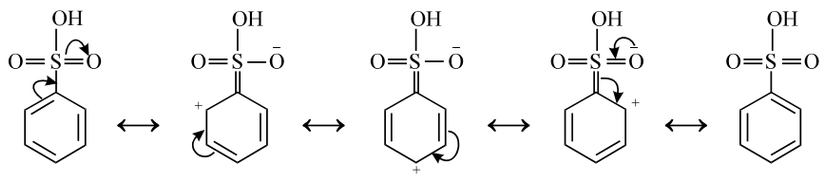
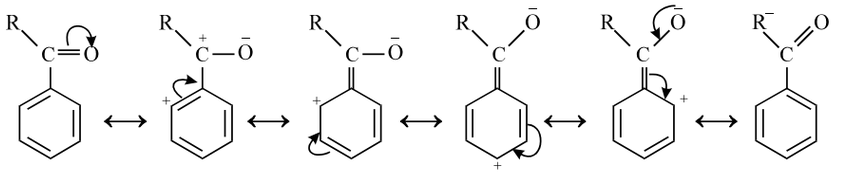
As the molecule is a resonance hybrid of various contributing structures there is a small positive charge at the two *o*- and the *p*-positions. The *m*-position remains the position of relatively high electron density and is attacked by electrophiles resulting in *m*-substitution.



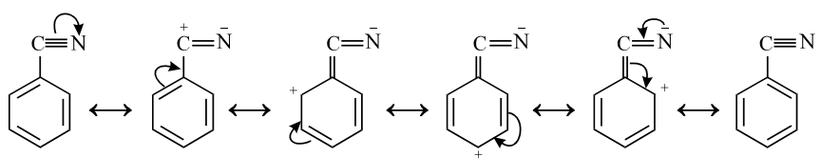
Resonance in nitrobenzene



Resonance in benzene sulphonic acid



[For substituent —CHO, R = H; for —COOH, R = OH etc.]



Resonance in phenyl cyanide

Other Factors Affecting Aromatic Substitution

Other factors like nature of incoming substituent and reaction conditions *e.g.*, temperature, concentration, solvent used etc., also affect the orientation in a substitution reaction. However, these factors are of only minor importance.

Ortho-para Ratio: Since there are two *ortho*- and only one *para*-position in a monosubstituted benzene derivative, it might be expected that the ratio of *o*- and *p*-isomers formed should be 2 : 1. In actual practice, however, the ratio is seldom 2 : 1, indeed for some reactions *o*-substitution is favoured and for the others *p*-substitution.

As the electron density both at *o*- and *p*-positions are same, the abnormal behaviour is explained on the basis of *steric hinderance.* Thus it had been observed that as the size of the substituent already present in the ring increases, the amount of *o*-isomer decreases.

Similarly, greater the size of incoming substituent, the smaller is the proportion of *o*-isomer formed. Besides these the nature of solvent also affects the *ortho-para* ratio.

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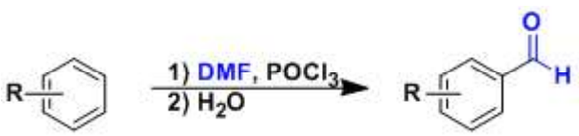
Check Your Progress

7. What position does electrophile occupy in benzene ring?
8. What happens when the size of incoming subsitute is greater?

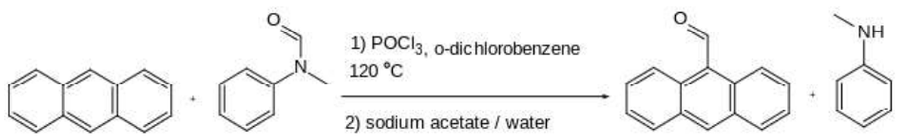
13.5 VILSMEIER–HAACK REACTION

The Vilsmeier–Haack reaction, also termed as the Vilsmeier reaction, is the chemical reaction of a substituted amide with phosphorus oxychloride and an electron-rich arene to produce an aryl aldehyde or ketone. The reaction is named after Anton Vilsmeier and Albrecht Haack.

The Vilsmeier-Haack reaction is a common method used for introducing a formyl group into electron rich aromatic compounds and can also be applicable to electron rich alkenes. The process and the reaction conditions are simple. In chemistry, the addition of a formyl functional group is termed formylation. A formyl functional group consists of a carbonyl bonded to hydrogen. When attached to an R group, a formyl group is called an aldehyde.



For example, benzanilide and dimethylaniline react with phosphorus oxychloride to produce an unsymmetrical diaryl ketone. Similarly, anthracene is formylated at the 9-position. The reaction of anthracene with N-Methylformanilide, using the phosphorus oxychloride, is shown below.



Reaction Mechanism

The reaction of a substituted amide with phosphorus oxychloride gives a substituted chloroiminium ion (2), also termed as the Vilsmeier Reagent. The initial product is an iminium ion (4b), which is hydrolyzed to the corresponding aldehyde.

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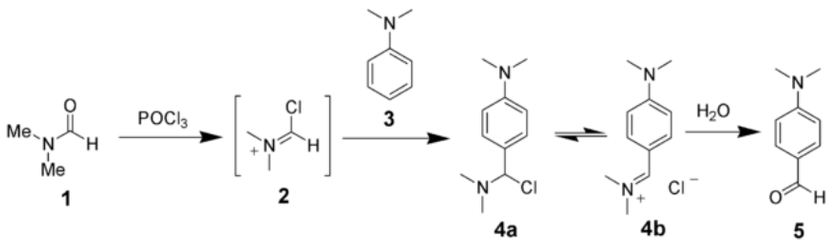
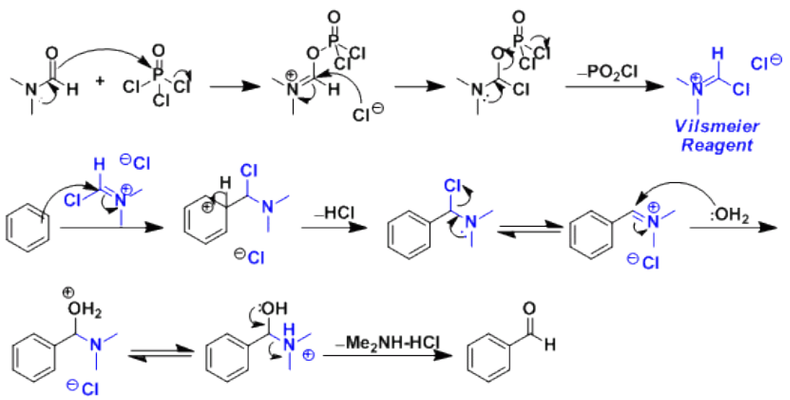
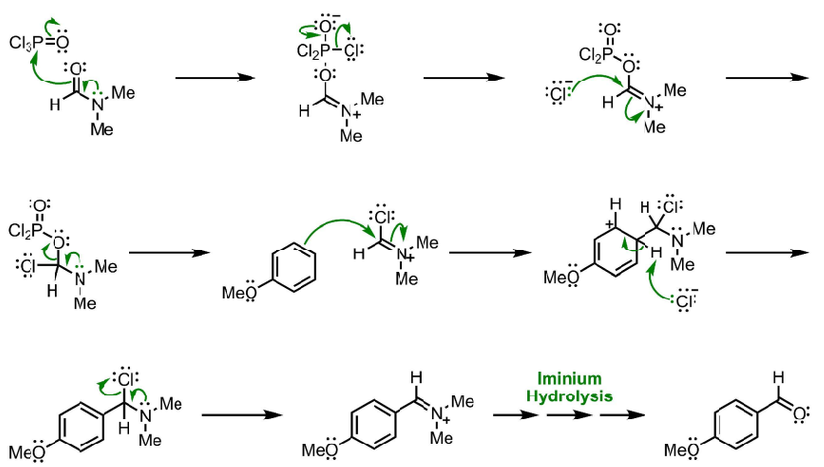


Following is the detailed reaction mechanism of N, N-Dimethylformamide (DMF) and phosphorus oxychloride ($POCl_3$) oxychloride reaction which react to form the Vilsmeier Reagent or Vilsmeyer-Haack Reagent or Formylating Agent, which further undergoes S_EAr reaction.

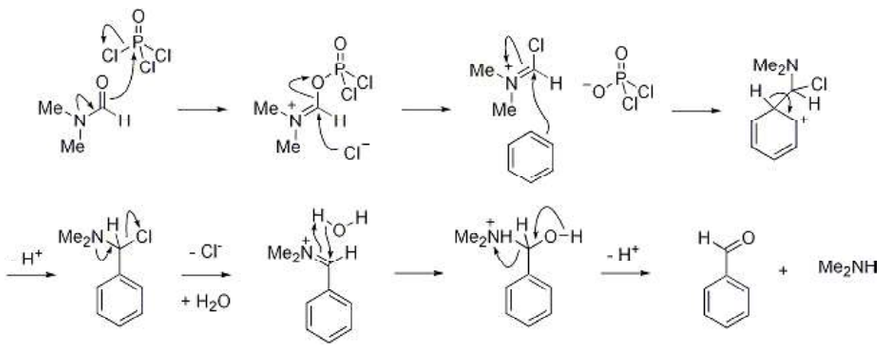


Typically, the formylating agent or the Vilsmeyer-Haack Reagent is formed from DMF and phosphorus oxychlorid due to an electrophilic aromatic substitution which leads to α-chloro amines, which are rapidly hydrolyzed during the reaction process to give the aldehyde.

Hydrolysis of the iminium intermediate gives the formylated product. Mechanism of the Vilsmeier-Haack Formylation reaction is shown below.



The Vilsmeier reaction allows the formylation of electron-rich arenes. The reaction of the amide with phosphorus oxychloride produces an electrophilic iminium cation. The subsequent electrophilic aromatic substitution produces an iminium ion intermediate, which is hydrolyzed to give the desired aryl ketone or aryl aldehyde.



Check Your Progress

9. What is Vilsmeier-Haack reaction?
10. What is Vilsmeier Reagent.

13.6 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. The carbocation formed as intermediate in an aromatic electrophilic substitution is an arenium ion, also known as *Wheland intermediate* or a sigma (σ) complex.
2. Hammond's postulate states that the factors stabilizing the transition state should also operate in Wheland intermediate. Hence the stabler the intermediate faster is its formation.
3. When *o*-, *p*-directing and activating groups (for example., —NH_2, —OH etc.) are attached to benzene then the Wheland intermediate resulting from *o*- or *p*-attack is more stabilized by resonance.
4. Nitration of benzene is carried out with a mixture of conc. nitric and conc. sulphuric acid.
5. Gattermann Koch reaction: when a mixture of carbon monoxide and hydrogen chloride is passed in an ethereal solution of benzene in presence of anhydrous $AlCl_3$ and cuprous chloride, an aldehyde is obtained.
6. In ozonide formation benzene adds up one ozone molecule at each one of the three double bonds to form a triozonide.

NOTES

7. In benzene ring the electron density is uniform at all the carbon atoms, hence the attacking electrophile has no preferential choice and may occupy any position.
8. Greater the size of incoming substituent, the smaller is the proportion of *o*-isomer formed.
9. The Vilsmeier–Haack reaction, also termed as the Vilsmeier reaction, is the chemical reaction of a substituted amide with phosphorus oxychloride and an electron-rich arene to produce an aryl aldehyde or ketone. The reaction is named after Anton Vilsmeier and Albrecht Haack.
10. The reaction of a substituted amide with phosphorus oxychloride gives a substituted chloroiminium ion (2), also termed as the Vilsmeier Reagent.

13.7 SUMMARY

- Substitution at aromatic or unsaturated carbon atoms. The most important reactions of the aromatic compounds are the electrophilic substitution reactions like nitration, halogenation, sulphonation etc. Nitration is introduction of a nitro group (—NO_2) in place of hydrogen by electrophile (nitronium ion). Sulphonation is the replacement of a hydrogen by —SO_3H group and takes place by electrophilic attack of SO_3 on aromatic carbon.
- The carbocation formed as intermediate in an aromatic electrophilic substitution is an arenium ion, also known as Wheland intermediate or a sigma (s) complex. The smallest arenium ion is a protonated benzene $C_6H_7Å$ called benzenium ion which can be isolated as a stable compound when benzene is protonated by the carborane super acid.
- Electrophilic substitution of a monorsubstituted benzene derivative can give rise to three regioisomeric products in which the new substitutent is placed at C–2 (ortho), C–3 (meta) or C–4 (para) position. There are two ortho- and two meta positions available but a statistical distribution of products is not observed and the actual proportion is dependent upon whether the group present is activating or deactivating.
- A vast majority of electrophilic substitution reactions proceed under kinetic control where the rate- and product-determining step is the formation of a Wheland intermediate which is a highly endothemic process. Hammond's postulate states that the factors stabilizing the transition state should also operate in Wheland intermediate. Hence the stabler the intermediate faster is its formation.
- When o-, p-directing and activating groups (e.g., —NH_2, —OH etc.) are attached to benzene then the wheland intermediate resulting from o- or p-attack is more stabilized by resonance.

- In case of o-, p-directing but deactivating group (like —Cl) the Wheland intermediate from o- or p-attack are stabilized by resonance involving lone pair of chlorine, whereas when m-directing and deactivating groups (for example, —NO_2, —CN etc.) are attached to benzene then Wheland intermediate from m-attack is less destabilized as compared to their o- or p-counterparts.
- The p electrons of benzene ring are losely held and are available to an electrophilic reagent seeking electrons hence typical reactions of benzene are electrophilic substitution reactions. In the reactions the attacking electrophile may be produced in different ways but what happens to the aromatic ring is basically same in all the cases.
- The arenium ion formed and isolated is commonly called s-complex. However, it was found that the relative reactivity and the percentage of o, m and p products formed depended not only a particular reaction but also on the nature of the reagent employed. This led some chemists to believe that a p-complex is formed during the electrophilic substitution between the substrate and the electrophile before the formation of arenium ion (s-complex) and that influences the reaction rate.
- In the electrophilic substitution of bromine, kinetic data has shown that the rate of bromination depends on the concentration of catalyst FeBr3 also besides halogen and benzene. The positive end of the dipole attacks the aromatic ring forming p-complex and the negative end is complexed with the catalyst.
- When benzene is heated to (90–160°C) with mercuric acetate for about an hour, one hydrogen atom is replaced by acetoxy-mercuric group. Conditions of the reaction are such that electrophile $H_3C.COOHg^+$ is created for the reaction.
- Introduction of the chloromethyl group (—CH_2Cl) in the benzene nucleus is also an electrophilic substitution reaction and is known as chloromethylation. This can be done by heating benzene or its homologues with formaldehyde and HCl in presence of anhydrous $AlCl_3$ or $ZnCl_2$.
- Benzene undergoes hydrogenation in presence of finely divided metal catalyst like nickel, platinum etc., at about 200°C and form corresponding saturated cyclohexane.
- Benzene adds up one ozone molecule at each one of the three double bonds to form a triozonide.
- In benzene ring the electron density is uniform at all the carbon atoms, hence the attacking electrophile has no preferential choice and may occupy any position. However in presence of a substituent the uniform electron density of benzene ring is disturbed and the nucleus is either activated or deactivated for further substitution.

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- The resonance contributing structures of such substituted benzene derivatives make it clear as to how the electron density is increased at these positions. The molecule being a hybrid of the contributing structures, the actual state of the molecule is having a small negative charge at the o- and the p-positions.
- The o- and p-directing effect of halogens is somewhat anomalous in that they exert strong –I effect and thus deactivate the ring. According to Ingold (1933) the +R effect of chlorine is too small to be of any significance. In presence of an attacking reagent the +E (electromeric) effect is brought into play and the o- and p-positions are raised in electron density above m-position.

13.8 KEY WORDS

- **Electrophilic Aromatic Substitution:** A reaction in which the hydrogen atom of an aromatic ring is replaced as a result of an electrophilic attack on the aromatic ring.
- **Gattermann Koch reaction:** When a mixture of carbon monoxide and hydrogen chloride is passed in an ethereal solution of benzene in presence of anhydrous $AlCl_3$ and cuprous chloride, an aldehyde is obtained.
- **Vilsmeier–Haack reaction:** The Vilsmeier–Haack reaction, also termed as the Vilsmeier reaction, is the chemical reaction of a substituted amide with phosphorus oxychloride and an electron-rich arene to produce an aryl aldehyde or ketone. The reaction is named after Anton Vilsmeier and Albrecht Haack.
- **Vilsmeier Reagent:** The reaction of a substituted amide with phosphorus oxychloride gives a substituted chloroiminium ion (2), also termed as the Vilsmeier Reagent.

13.9 SELF ASSESSMENT QUESTIONS AND EXERCISES

Short Answer Questions

1. What is nitration?
2. Define sulphonation.
3. What is chloromethylation?
4. What is hydrogenation?
5. List some uses of benzene.

Long Answer Questions

1. Give a detailed note on aromatic electrophilic substitution reaction.
2. Explain about electrophilic substitution reaction in detail.
3. Write a detailed note on nitration, halogenation, sulphonation, mercuration, hydrogenation in detail also mentioning its mechanism.
4. Write about activation and deactivation of benzene nucleus.
5. List the factors that affect aromatic substitution.
6. Discuss about Vilsmeier-Haack reaction.

13.10 FURTHER READINGS

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UNIT 14 AROMATIC NUCLEOPHILIC SUBSTITUTIONS

Structure

14.0 INTRODUCTION

A nucleophilic aromatic substitution is a substitution reaction in organic chemistry in which the nucleophile displaces a good leaving group, such as a halide, on an aromatic ring.The discovery of nucleophilic aromatic substitution (SNAr) pathways dates back to the early 20th century, yet, despite all the extraordinary advances in cross-coupling and related reactions, SNAr remains by some measures the second most frequently used reaction class in medicinal chemistry. This may occur in several ways, including aromatic SN1 mechanism, involving benzyne intermediate and SNAr mechanism involving addition and elimination.

The Von-Richter reaction, also termed as the Von-Richter rearrangement, is a name reaction in the organic chemistry. It is named after Victor von Richter, who discovered this reaction in year 1871. It is the chemical reaction of aromatic nitro compounds with potassium cyanide giving carboxylation 'ortho' to the position of the former nitro group.

In this unit, you will study about nucleophilic aromatic substitution, benzyne mechanism, Von-Richter reaction in detail.

14.1 OBJECTIVES

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

- Understand what nucleophilic aromatic substitution is
- Discuss about benzyne mechanism
- Explain Von-Richter reaction

14.2 NUCLEOPHILIC AROMATIC SUBSTITUTION

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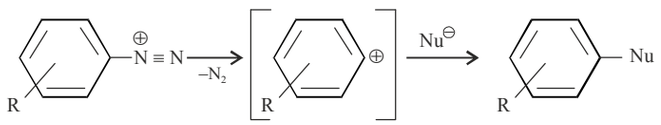
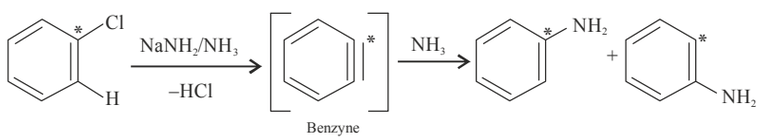
Nucleophilic Aromatic Substitution

This may occur in several ways, including (i) aromatic S_N1 mechanism, (ii) involving benzyne intermediate and (iii) S_NAr mechanism involving addition and elimination.

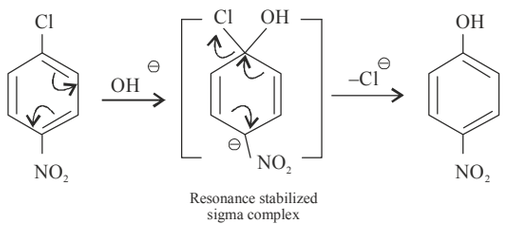
(i) Aromatic S_N1 mechanism is observed in diazonium salts



(ii) Benzyne mechanism is observed in reaction of chlorobenzene with $NaNH_2$.



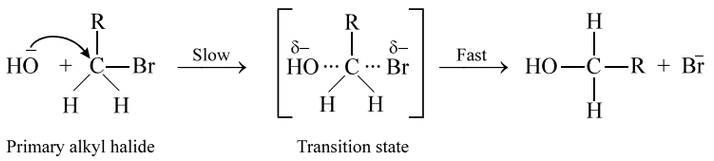
(iii) S_NAR mechanism is observed when an electron withdrawing group like $–NO_2$ activates the ring towards nucleophilic attack.



Applications: The mechanisms of the hydrolysis of alkyl halides have been successfully explained by nucleophilic substitution. Some examples are given below:

(1) ***Hydrolysis of Alkyl Halide (Primary and Secondary)***

S_N2 mechanism



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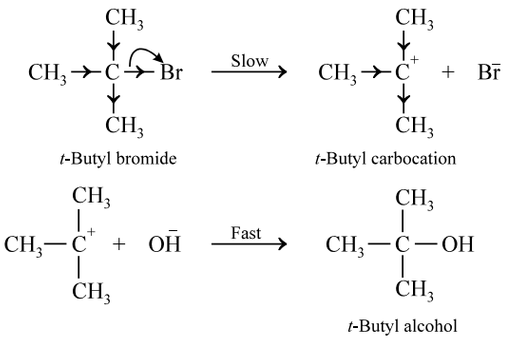
Hydrolysis of t-butyl Bromide

S_N1 Mechanism



In the S_N2 mechanism the nucleophile hydroxide ion approaches the alkyl halide molecule preferably from the side opposite to that occupied by the departing group. As the carbon atom involved in carbon to halogen bond is slightly deficient in electron density because of greater electronegativity of halogen (bromine in above example) the hydroxide ion offers a pair of electrons for the formation of bond with this carbon. Simultaneously bromine starts taking hold of the electron pair through which it is bonded to carbon and a transition state or activated complex is visualized for such reactions in which five groups are linked to carbon. Finally bromine leaves the molecules as a bromide ion and hydroxide ion forms a covalent bond with the carbon giving alcohol as the reaction product.

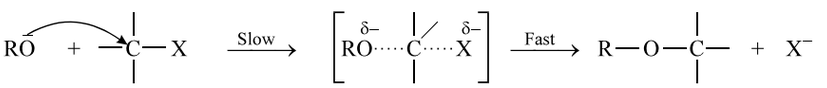
In the hydrolysis of *t*-butyl bromide which occurs by S_N1 mechanism, the first step is the slow dissociation of alkyl halide to give a bromide ion and tertiary butyl carbocation, which is stabilised due to hyperconjugation. The tertiary butyl carbocation then combines with a hydroxide ion to form the tertiary butyl alcohol.

(2) ***Alkylation with Alkyl Halides (Williamson Synthesis of Ethers)***

$$R—X + R'—ONa \longrightarrow R—O—R' + NaX$$

S_N2 mechanism for the reaction is given below:

$$R'—ONa \longrightarrow R—O^- + Na^+$$

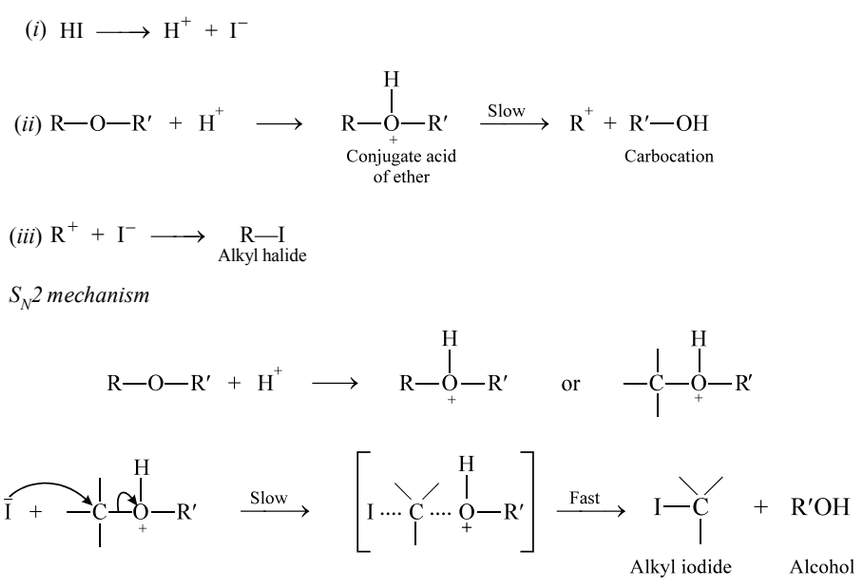


(3) ***Cleavage of Ethers (Ziesel's Method for Determining Alkoxy Groups)***

$$R—O—R' + HI \longrightarrow RI + R'—OH$$

The mechanism is similar to above reaction and may be S_N1 or S_N2

S_{NI} mechanism



Addition Reactions

The addition reactions are the reactions of the double or triple bonds. In a >C═C< or —C≡C— the π electrons are most readily available. These π 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≡N, the π electron density is slightly shifted towards the more electronegative elements O and N, and at the approach of a reagent electromeric shift results in complete transfer of this π electron pair to O or N (hetero atoms 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 >C═O or —C≡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.

Addition reactions are, therefore, dealt in two parts: additions to >C═C< and additions to >C═O groups. The free radical addition reactions have not been dealt separately but a reference to them is made wherever considered necessary in the text (*viz.* Peroxide effect).

1. **Additions at Carbon to Carbon Multiple Bonds:** 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

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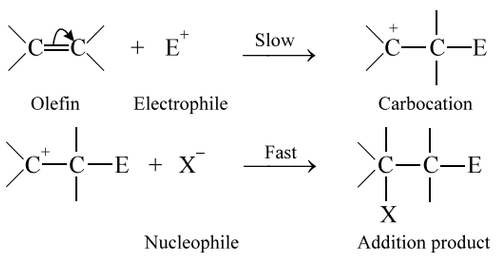
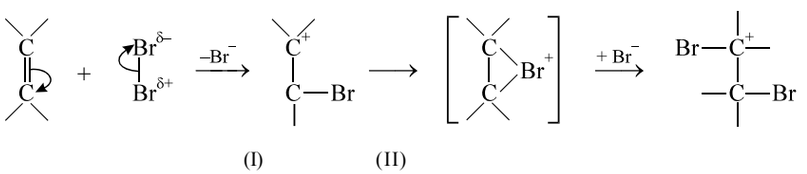
followed by the addition of nucleophile which is a fast reaction. In all addition reactions π bonds are converted to σ bonds or the hybridization state of carbon changes from sp^1 to sp^2 or sp^3 and from sp^2 to sp^3. The examples of such reactions are hydration and hydrogenation of olefins, additions of halogens and halogen acids to olefins and ozonolysis.

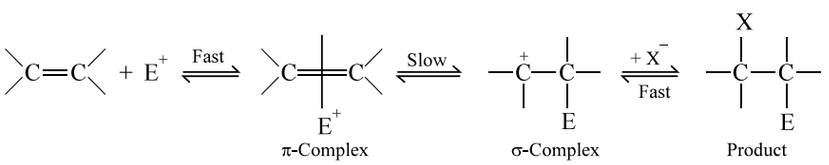
In electrophilic addition reactions an electrophile approaches the double or triple bond and in the first step forms a covalent bond with one of the carbon by converting π bond into a pair of σ bonds, resulting in the formation of a carbocation which then takes up a nucleophile to result in addition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



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



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 π electrons to form a π complex which later changes to a σ complex or carbocation, exemplified as follows:

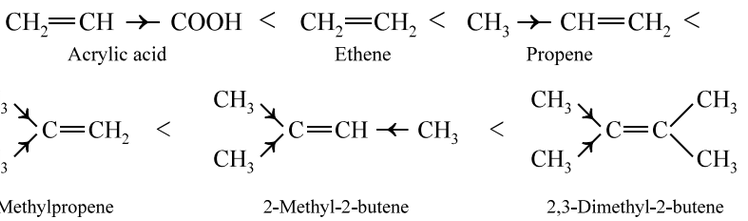


The π complex or the three membered ring cation is roughly on one side of the double bond and therefore the attack of nucleophile must occur from the other side of the double bond. Thus the two groups are added on opposite sides of the double bond—such additions are known as **trans-additions**. On the 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

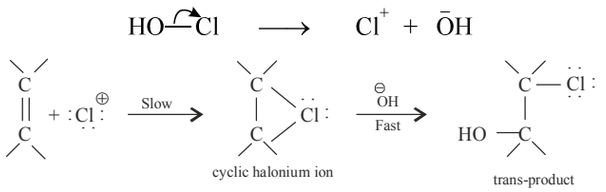
electrophile at either of these will yield the same product but in unsymmetrical olefins like propylene the two carbon atoms involved in double bond are not identical and hence the addition of electrophile to each one of these respectively should result in two isomeric products. Since the addition of 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.



Applications

(*i*) **Addition of Halogens and Hypohalous Acids to Olefins:** When a halogen molecule or hypohalous acid reacts with olefin the π 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 whihc 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



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-

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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 Cl^-, NO_2^-, RO^- etc. then these are also incorporated in some of the substrate molecules. Thus:

$$CH_2{=}CH_2 + Br_2 \longrightarrow Br^- + Br{-}CH_2{-}\overset{+}{C}H_2$$

$$\xrightarrow{Br^-} Br.CH_2.CH_2.Br \quad (1)$$

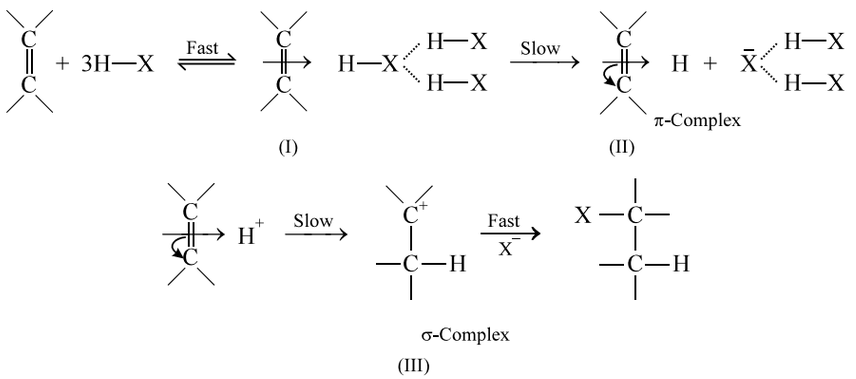
$$\xrightarrow{Cl^-} Br.CH_2.CH_2.Cl \quad (2)$$

$$\xrightarrow{NO_2^-} Br.CH_2.CH_2.NO_2 \quad (3)$$

$$\xrightarrow[ROH/Na]{RO^-} Br.CH_2.CH_2.OR \quad (4)$$

These products (2) to (4) are not the products of substitution of (1) but are formed as a result of competition between various anions for reaction with carbocation intermediate.

(*ii*) **Addition of Halogen Acids to Olefins:** The addition of halogen acid (HX) to olefins may be shown as follows:

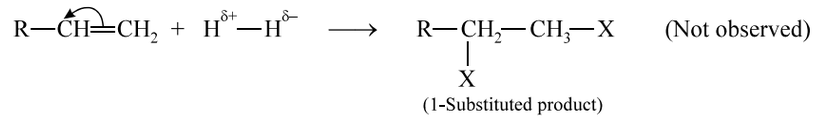


The addition of halogen acids to olefins is first order in olefin and indefinite (or third) order in halogen acid. The purpose of the other HX molecules is to polarise a HX molecule and to remove halide ion as shown in (I) and (II). Combination of a proton with π electrons gives a π complex which polarizes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

$$R{-}CH{=}CH_2 + H^{\delta+}{-}H^{\delta-} \longrightarrow R{-}\underset{\displaystyle X}{\underset{|}{CH}}{-}CH_3 \qquad \text{(Observed)}$$

(2-Substituted product)



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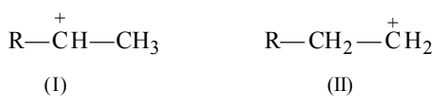
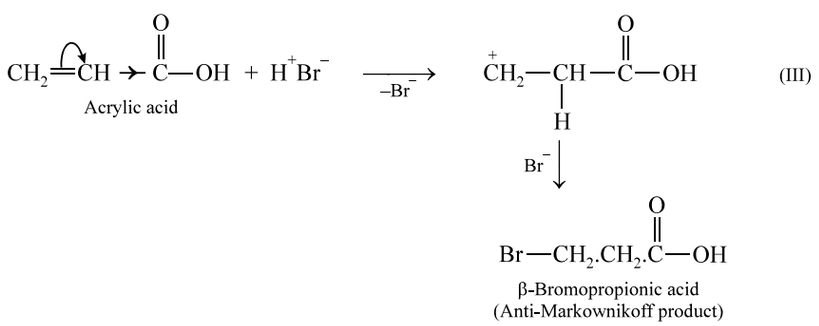
But in such reactions it is the first type which predominates. To explain this Markovnikov in 1869 gave a generalization which is known as **Markovnikov's rule. According to this rule** "*the negative part of the addendum (reagent which is adding) goes to the carbon atom, constituting the double bond,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

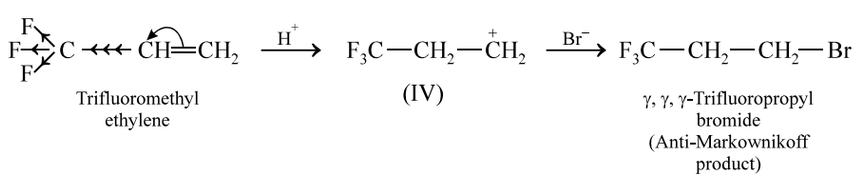
Obviously in such cases the direction of polarization of bond by electromeric shift is determined by the inductive effect (+I effect) of the alkyl group and thus it polarizes in such a manner that the electron pair shifts to carbon which is farthest from the alkyl substituent. Also the predominant direction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



the (I) will be more stable as it is a secondary carbocation whereas (II) is a primary carbocation. Thus the stability of carbocation 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 carbocations derived from one olefin. Thus addition of HBr to olefinic acids like acrylic acid proceeds as follows:



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



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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.

$$\underset{\text{Dibenzoyl peroxide}}{C_6H_5CO.O.O.OC.C_6H_5} \longrightarrow \underset{\text{Benzoyloxy radical}}{2C_6H_5CO.O^{\cdot}}$$

$$C_6H_5CO.O^{\cdot} + H{-}Br \longrightarrow C_6H_5COOH + Br^{\cdot}$$

$$Br^{\cdot} + R{\rightarrow}CH{=}CH_2 \longrightarrow R{-}\dot{C}H{-}CH_2{-}Br \quad \text{or} \quad R{-}\overset{Br^{\cdot}}{\underset{\diagdown\,\diagup}{CH}}{-}CH_2$$

$$R{-}\dot{C}H{-}CH_2{-}Br \xrightarrow{HBr} R{-}CH_2{-}CH_2{-}Br + Br^{\cdot}$$

n-Alkyl bromide

That 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.

(*iii*) **Hydroboration of Olefins:** Reaction of diborane (B_2H_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)

$$\underset{\text{Olefin}}{R{-}CH{=}CH_2} \xrightarrow{B_2H_6} \underset{\text{Alkylborane}}{R{-}CH_2{-}CH_2BH_2} \xrightarrow{R{-}CH{=}CH_2} \underset{\text{Dialkylborane}}{(R{-}CH_2{-}CH_2)_2BH}$$

$$(R{-}CH_2{-}CH_2)BH \xrightarrow{R{-}CH{=}CH_2} \underset{\text{Trialkyl borane}}{(R{-}CH_2{-}CH_2)_3B}$$

The addition of diborane is an electrophilic attack by diborane on π 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.

$$\underset{\text{Olefin}}{R{-}CH{=}CH_2} + \underset{\text{Boron hydride}}{BH_3} \longrightarrow \underset{\text{Transition state}}{\left[\begin{array}{l} \overset{\delta-}{H}\cdots\overset{H}{\overset{|}{\overset{\delta+}{B}}}{-}H \\ R{-}\underset{\delta+}{CH}\cdots\underset{\delta-}{CH_2} \end{array}\right]} \longrightarrow \underset{\text{Alkyl borane}}{R.CH_2{-}CH_2{-}BH_2}$$

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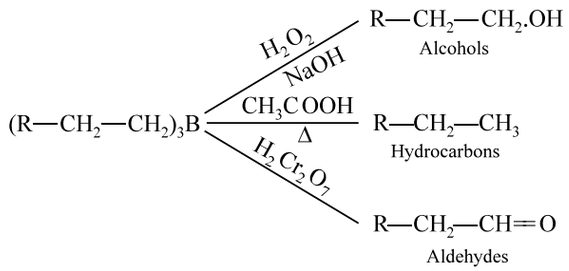
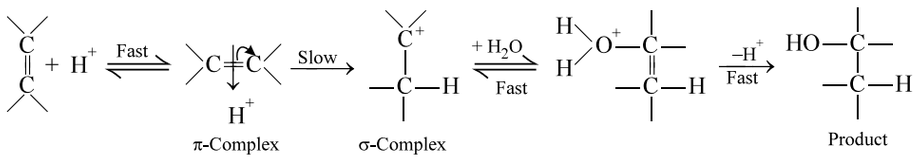
Hydroboration is an important synthetic method because alkyl-boranes can be transformed into a number of useful products.

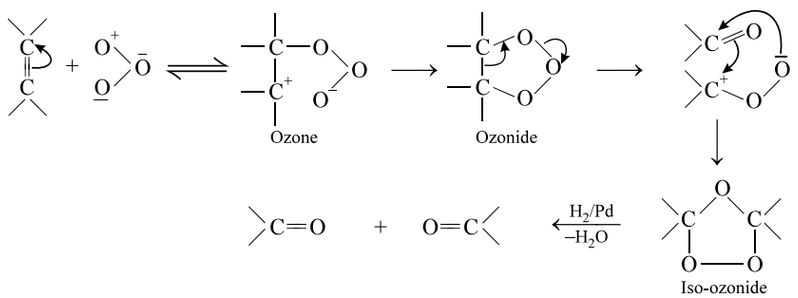


(*iv*) **Hydration of Olefins:** Addition of a molecule of water to olefins is known as hydration reaction. Hydration of olefins in acidic media results in the formation of alcohols. The mechanism for hydration is the electrophilic addition at $>C=C<$



Initially, a proton adds up at double bond to form a π complex which then changes to σ 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*) **Ozonolysis:** Addition of ozone to olefinic linkage resulting in the formation of ozonide, which on subsequent hydrogenation gives carbonyl compounds, is known as ozonolysis. The reaction follows the electrophilic addition reaction mechanism.



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 π 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 >C=O compounds.

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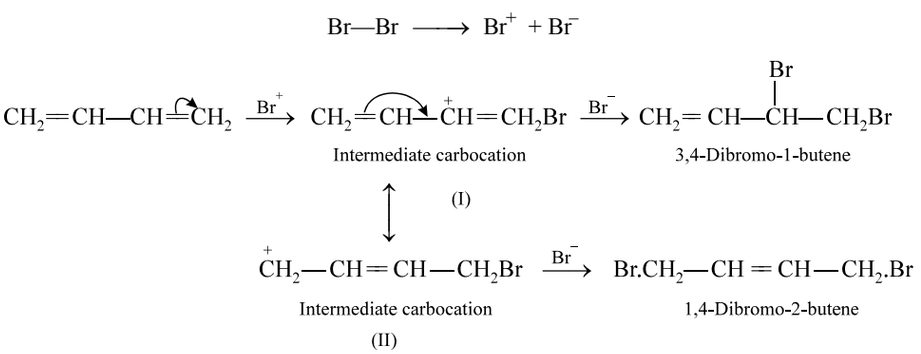
Ozonolysis is used to locate the position of double bonds in olefins.

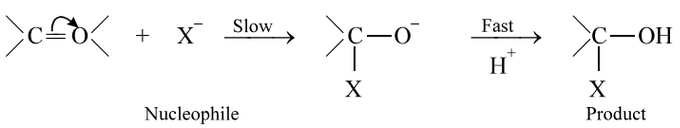
(*vi*) **Addition to Conjugated Dienes:** Although conjugated dienes are considered to be more stabilized, because of resonance, than simple olefins, yet they undergo electrophilic additions readily. However, in butadiene such a reaction with bromine results in two products 3,4-dibromo-1-butene and 1,4-dibromo-2-butene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



The addition of bromonium ion to butadiene gives an intermediate carbocation 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.*

Additions at Carbon to Oxygen Double Bonds

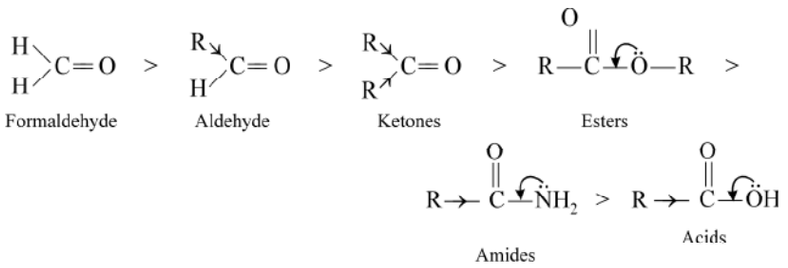
Unlike the carbon to carbon multiple bonds, the carbon to oxygen double bonds are highly polarized because of greater electronegativity of oxygen atom. The π electrons are shifted towards oxygen atom by simple electromeric effect at the requirement of the attacking reagent. The carbon thus acquires a 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.



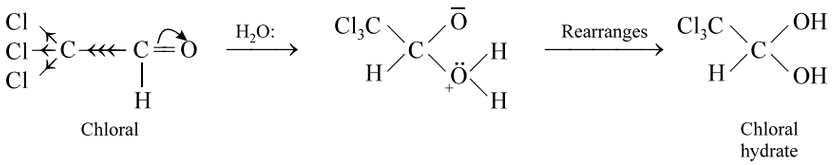
The above scheme shows a simple nucleophilic addition of a nucleophile X^- to > C═O groups. At the approach of X^- the π electrons are shifted towards oxygen by electromeric shift. The nucleophile combines with the positively charged carbon to yield anion which then takes up a proton or electrophile 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:



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 ($CCl_3.CHO$) 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:

Hydration %	HCHO	CH_3CHO	CH_3COCH_3
	99	58	0

Polar solvents, acids and bases catalyze nucleophilic addition reactions.

Applications

(1) **Addition of HCN and $NaHSO_3$ (Sodium Bisulphite) to Carbonyl Group:** The addition of HCN and $NaHSO_3$ to >C═O group is a simple nucleophilic addition. HCN combines with >C═O group in the presence of basic catalysts to give corresponding cyanohydrin. 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 cyanohydrin.

$$HCN \rightleftharpoons H^+ + CN^-$$

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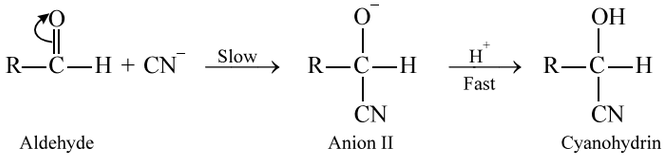
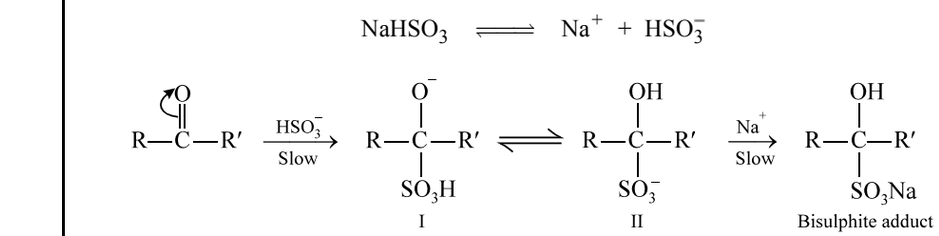
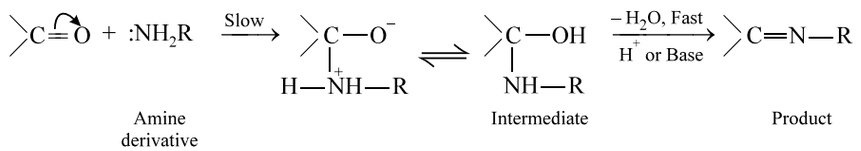


Addition of sodium bisulphite to carbonyl group occurs in the absence of acids or bases because sodium bisulphite readily ionises to give bisulphite anion nucleophile which then adds to carbon of carbonyl group resulting in anion (I). The (I) then rearranges by migration of a hydrogen from —SO_3H group to negatively charged oxygen to give anion (II) which then combines with sodium ion to give bisulphite addition product.



(2) **Addition of Ammonia and Amine Derivatives to Carbonyl Group:** Ammonia and its derivatives like R—NH_2 (amines), NH_2OH (hydroxylamine), $NH_2.CO.NH.NH_2$ (semicarbazide), and $NH_2.NH_2$ (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.

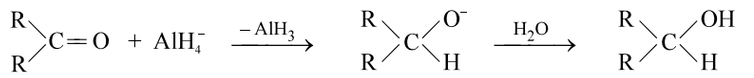


Amine derivatives act as nucleophiles because of the presence of the lone pair of electrons at nigrogen. At the approach of these reagents, π electron pair is shifted to oxygen by electromeric effect and the lone pair of nitrogen co-ordinates with electron deficient carbon to give a dipolar intermediate. 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.

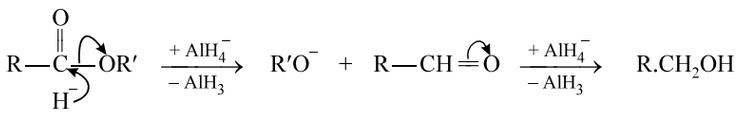
The reaction of ammonia is different with different carbonyl compounds. Thus formaldehyde with ammonia gives hexamethylene tetramine $(CH_2)_6N_4$; acetaldehyde and other aldehydes give aldehyde ammonia $RCH(OH)NH_2$; whereas ketones usually undergo condensation reaction to give complex products.

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 $LiAlH_4$ (lithium aluminium hydride) or $NaBH_4$ (sodium borohydride) are in essence nucleophilic additions of a hydride ion to the carbon atom. $LiAlH_4$ dissociates to give AlH_4^- which acts as a carrier of hydride ion. The reduction of ketones and esters may be represented as given below:



Ketone — Secondary alcohol



Ester — Aldehyde — Primary alcohol

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 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.* Essentially this is a nucleophilic addition of a carbanion, generated by the abstraction of a proton from α-position of an aldehyde or ketone by a base, to the carbonyl 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*) $CH_3CHO + CH_3CHO \xrightarrow{OH^-} CH_3—\underset{\displaystyle OH}{\underset{|}{CH}}—CH_2CHO$

Acetaldehyde (2 moles) — β-Hydroxy butyraldehyde (Aldol)

(*ii*) $CH_3.CO.CH_3 + CH_3.COCH_3 \xrightarrow{OH^-} CH_3—\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle OH}{\overset{|}{C}}}}—CH_2.CO.CH_3$

Diacetone alcohol
(4-Hydroxy-4-methyl-2-pentanone)

(*iii*) $CH_3.CHO + CH_3.CO.CH_3 \xrightarrow{OH^-} CH_3—\underset{\displaystyle H}{\underset{|}{\overset{\displaystyle OH}{\overset{|}{C}}}}—CH_2—CO.CH_3$

Acetaldehyde — Acetone — 4-Hydroxyl-2-pentanone

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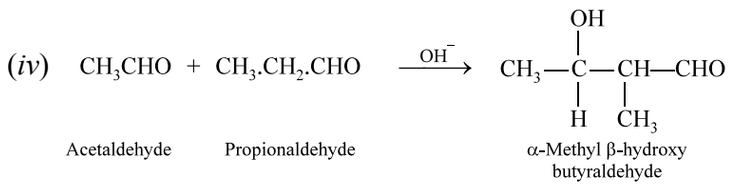
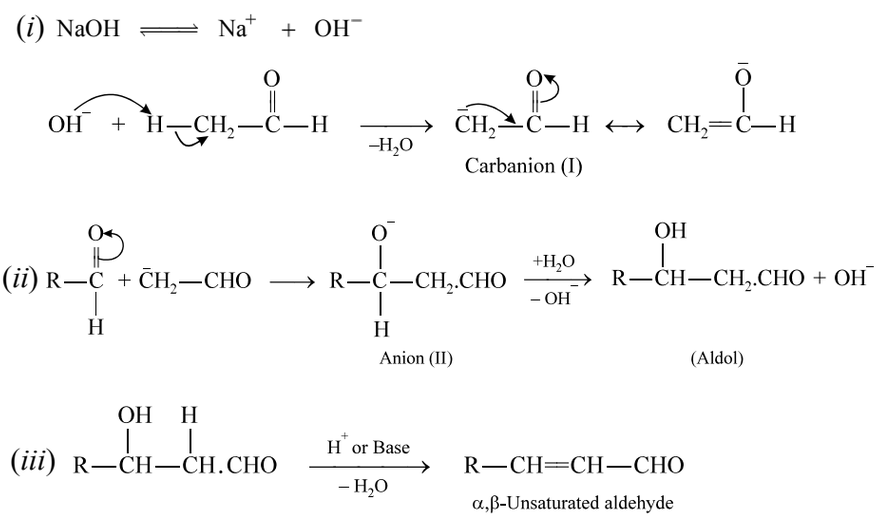


As seen in the above examples, in crossed aldol condensations the carbonyl group of aldehydes is more reactive than carbonyl group of ketones. Thus the aldol formation involves carbonyl group of aldehyde and α-hydrogen of ketone. Similarly when condensation is between two aldehydes the α-hydrogen comes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

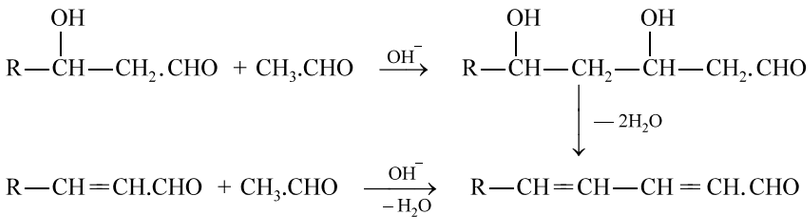
Reaction between two molecules of an aldehyde, not having α-hydrogen atoms, in presence of alkali, results in Cannizzaro's reaction. Thus formaldehyde reacts with NaOH to form a mixture of methyl alcohol and sodium formate.

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



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



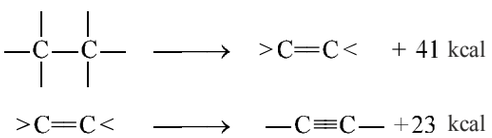
NOTES

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

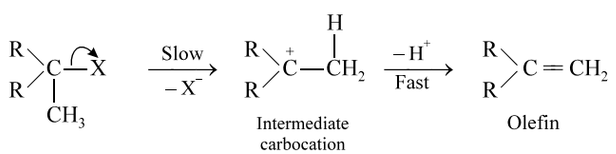
$$>C=C<,\ -C\equiv C-,\ -C\equiv N,\ >C=N-,\ >C=O \quad \text{etc.}$$

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), OH^-, $RCOO^-$ etc. The adjacent atoms of substrate molecule from which these groups are removed, are designated as α- and β-atoms and the type of elimination is referred to as β-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.

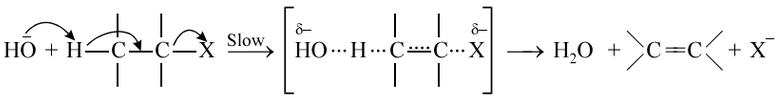


Elimination reactions usually compete with nucleophilic substitution reactions at saturated carbon atoms (S_N reactions). By analogy to S_N reactions, in elimination also there are two extreme types of reactions. With nucleophile which are strong bases a concerted reaction involving a transition state 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:

E_1 mechanism



E_2 mechanism



Transition state

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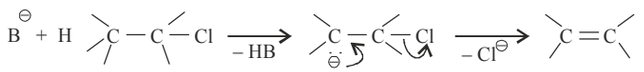
The E_2 reaction theoretically can involve the formation of a carbanion of the type $-\bar{C}-C-X$ but evidence has been obtained that such an intermediate is not formed in elimination reaction.

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 $E_{1C}B$ (Elimination 1st order conjugate base).

The reaction take place around sp^3–sp^3 covalent bond with an α-acidic hydrogen and a β-leaving group (like halide or tosyl etc.). A strong base abstracts the α-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 $(E_1cB)_r$ but when the first step is forming carbanium is slow and second step fast then the reaction is irreversible and is called $E_1(cB)_i$.

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

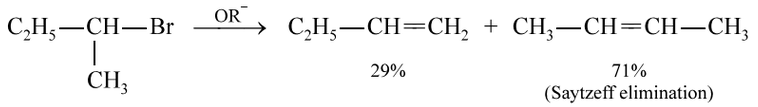
Structure and Reactivity: The nature of the substrate, solvent and the catalyst (usually a nucleophile) determine whether the reaction will proceed by E_1 or E_2 mechanism. It has also been observed that conditions favouring S_N1 reactions will lead to E_1 reactions as well. Similarly conditions favourable to S_N2 reactions also lead to E_2 reactions. The ratios of E_1 to S_N1 and E_2 to S_N2 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. Two simple rules have been given to govern the direction of elimination in such cases.

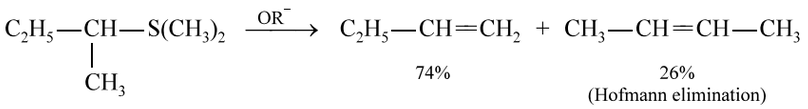
(1) **Saytzeff Rule (1875):** According to this rule the neutral substrates (like alkyl halides) in elimination reaction predominantly yield the olefin bearing the larger number of alkyl groups around >C═C<.

NOTES

(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:





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 that transition state in which larger number of such groups are present around carbon stoms 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 β-atom. So the effect is more pronounced if these groups are attached to β-atom. Presence of phenyl group at β-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 contract to S_N2 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 sp^3 carbons to 120° in sp^2 carbons.

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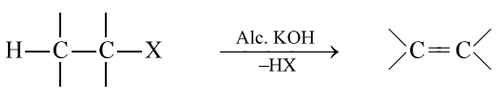
Change of attacking reagent does not alter the rate of E_1 reaction significantly but the rate of E_2 reaction increases with increase in the basicity of the reagent. Again the nature of departing group does not influence E_1 reaction whereas the rate of E_2 reaction increases in the following order 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.

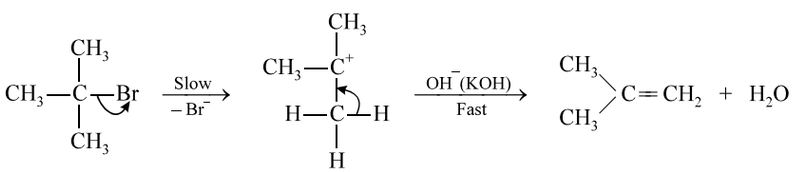
(1) **Dehydrohalogenation of Alkyl Halides:** Alkyl halides when treated with alcoholic KOH or NaOH undergo elimination of a molecule of hydrogen halide resulting in the formation of olefins. This elimination of hydrogen and halogen from the same molecule is known as dehydrohalogenation reaction.



Alkyl halide Olefin

Tertiary alkyl halides undergo the reaction most readily preferably by a E_1 mechanism. For other types of alkyl halides (secondary and primary) usually the E_2 mechanism is favoured. For example:

E_1 mechanism



t-Butyl bromide *t*-Butyl carbocation 2-Methyl-2-propene

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.

E_2 mechanism

$$KOH \rightleftharpoons K^+ + OH^-$$

$$OH^- + H{-}CH_2{-}CH_2{-}Br \xrightarrow{\text{Slow}} \underset{\text{Transition state}}{\left[HO^{\delta-}\ldots H\ldots CH_2\ldots CH_2\ldots Br^{\delta-}\right]}$$

$$\xrightarrow{\text{Fast}} H_2O + CH_2{=}CH_2 + Br^-$$

The mechanism involves the formation of a transition state in which nucleophile OH^- or 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 Cl < Br < 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. H_2SO_4 and H_3PO_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°, the *catalytic dehydration* of alcohols takes place. Other dehydrating agents which have been used frequently are $ZnCl_2$ and P_2O_5. Dehydration with acids gives side products like ethers whereas catalytic dehydration usually givers pure olefins. The ease of dehydration increases in the order—primary > secondary > tertiary alcohols. The reactions are given below:

Primary alcohol

$$\underset{\text{Ethyl alcohol}}{CH_3{-}CH_2{-}OH} \xrightarrow[\text{or } H_2SO_4]{Al_2O_3/400^\circ} \underset{\text{Ethylene}}{H_2C{=}CH_2} + H_2O$$

Secondary alcohol

$$\underset{\text{Isopropyl alcohol}}{\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!\!CH{-}OH} \xrightarrow[\text{or } H_2SO_4]{AlO_3/400^\circ} \underset{\text{Propylene}}{CH_2{-}CH{=}CH_2} + H_2O$$

Tertiary alcohol

$$\begin{matrix}CH_3\\CH_3\\CH_3\end{matrix}\!\!>\!\!C{-}OH \xrightarrow[\text{or } H_2SO_4]{Al_2O_3/400^\circ} \underset{\text{Isobutene (2-Methyl-2-propene)}}{CH_3{-}\overset{\displaystyle CH_3}{\overset{|}{C}}{=}CH_2} + H_2O$$

NOTES

Mechanism of Dehydration: When acids like H_2SO_4 or H_3PO_4 are used as dehydrating agents the mechanism is E_1. The alcohol by taking up a proton is converted to its conjugate acid ($R.OH + H^+ \rightarrow RO^+H_2$) which then cleaves into H_2O and R^+ (alkyl carbocation). This carbocation then eliminates a proton to yield olefins. Side reactions result in the formation of ethers also.

$$H_2SO_4 \rightleftharpoons H^+ + HSO_4^-$$

$$\underset{\text{Ethyl alcohol}}{CH_3-CH_2-OH} + \underset{\text{(from acid)}}{H^+} \rightleftharpoons \underset{\substack{\text{Conjugate acid of alochol}\\ \text{(Protonated alcohol)}}}{CH_3-CH_2-\overset{+}{O}H_2}$$

$$CH_3-CH_2-\overset{+}{O}H_2 \xrightleftharpoons{\text{Slow}} CH_3-\overset{+}{C}H_2 + H_2O$$

$$H-CH_2-\overset{+}{C}H_2 \xrightleftharpoons{\text{Fast}} \underset{\text{Ethylene}}{CH_2=CH_2} + H^+$$

Side reactions

$$\underset{\text{Ethyl carbocation}}{CH_3-\overset{+}{C}H_2} \xrightarrow{HSO_4^-} \underset{\text{Ethyl hydrogen sulphate}}{CH_3-CH_2-O-SO_3H}$$

$$\xrightarrow[-H^+]{CH_3.CH_2.OH} \underset{\text{Diethyl ether}}{CH_3.CH_2.O.CH_2CH_3}$$

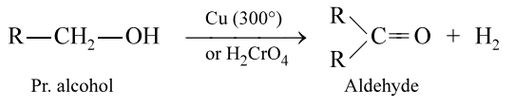
During dehydration in the presence of Al_2O_3, it is believed that alcohol is converted to some kind of aluminate ester which then decomposes to alkyl carbocation. Alternatively the acidic impurities in alumina convert the alcohol to protonated alcohol and the dehydration proceeds by E_1 mechanism as above.

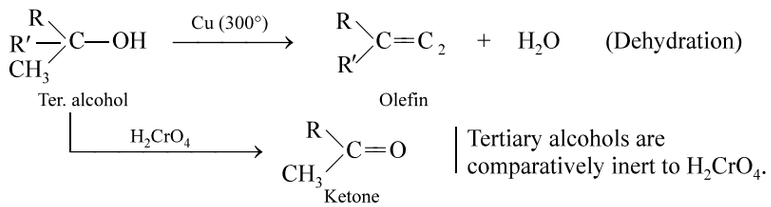
$$\underset{\text{Isopropyl alcohol}}{\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CH-OH} + Al_2O_3 \xrightarrow{\text{Fast}} \underset{\text{Aluminate ester}}{\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CH-\overset{H}{\overset{|}{\overset{+}{O}}}-\bar{A}l_2O_3}$$

$$\xrightarrow{\text{Slow}} \underset{\text{Isopropyl carbocation}}{\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CH^+} + \bar{A}l_2O_3(OH)$$

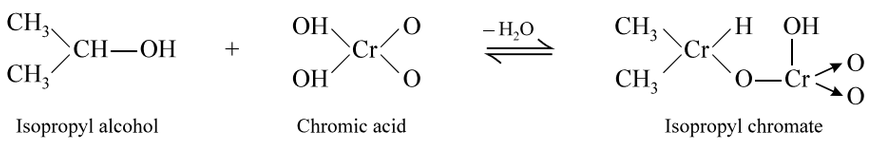
$$CH_3-\overset{+}{C}H-CH_2-H \xrightarrow[\text{Fast}]{-H^+} \underset{\text{Propylene}}{CH_3-CH=CH_2}$$

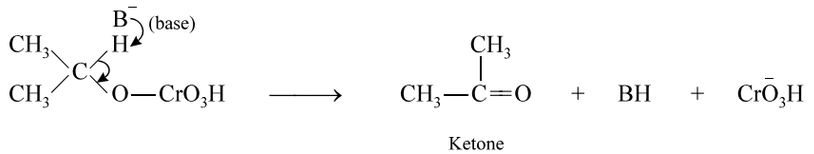
(3) **Dehydrogenation of Alcohols:** Dehydrogenation of alcohols to aldehydes and ketones may be considered as elimination reaction occurring by the loss of a molecule of hydrogen and resulting in the formation of carbon to oxygen double bond. The dehydrogenation can thus be carried out by using chromic acid (H_2CrO_4) or a mixture of Na_2CrO_4 with H_2SO_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.





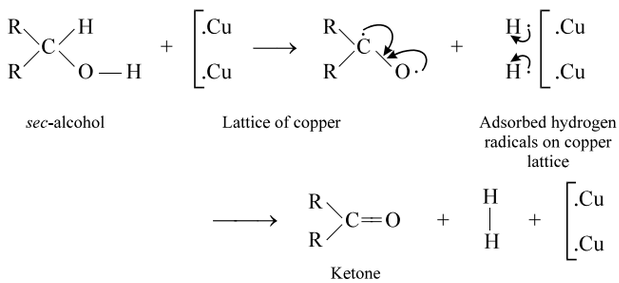
The mechanism for chromic acid dehydrogenation in presence of a base like pyridine is:





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



NOTES

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

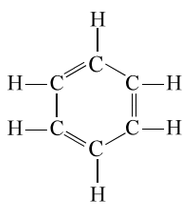
The copper is able to break carbon-hydrogen and oxygen-hydrogen bonds by homolysis at high temperatures; it then adsorbs atomic hydrogen (or radicals) and finally gives them up as molecular hydrogen at high temperatures. The removal of hydrogen leaves an unpaired electron, each on carbon and oxygen which 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.

Check Your Progress

1. Where is aromatic SN1 mechanism seen?
2. Where is benzyne mechanism observed?
3. Where is SNAR mechanism is observed ?

14.3 BENZYNE MECHANISM

Benzene is the parent aromatic hydrocarbon. Though its structural problem will be dealt with later in the unit, it is represented in anyone of the following different manners.



I

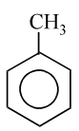
II

III

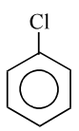
IV

Formula I shows six carbon atoms connected by alternate single and double bonds forming a hexagon. This is the structural formula of benzene, which for the sake of convenience is represented by formulae II, III or IV also. In benzene, as we will see later, each carbon-carbon single bond has somewhat double bond character, so formula IV is a better representation of the molecule, which represents the equivalence of the six carbon-carbon bonds in benzene. However, it is seen that Kekule's formulae is a very convenient in explaining many reactions, hence we shall be using both forms, as and when needed.

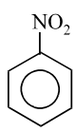
The benzene derivatives are represented, as shown below:



Methylbenzene



Chlorobenzene



Nitrobenzene

Benzene Nucleus and Side Chain

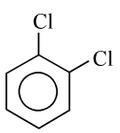
The six carbon atoms of the benzene ring constitute what is known as benzene nucleus. The characteristic properties of aromatic compounds are, truly speaking, the properties of this nucleus. In the nucleus all the six carbon atoms are equivalent.

A carbon chain connected to one of the carbon atoms of the nucleus through a carbon atom, other than of the simple functional groups like —CHO, —COOH, >CO, is called a side chain. Thus $—CH_3$, $—CH_2.CH_3$, $—CH=CH_2$, $—CH_2Cl$, $—CH_2NH_2$ etc., when attached to carbon atom of the benzene nucleus constitute a side chain. The groups like $—NO_2.NH_2$, —Cl (and also —CHO, —COOH, >C=O etc.) when attached to carbon of the benzene nucleus do not constitute a side chain. The side chain shows reactions characteristics of aliphatic compounds and irrespective of its nature, i.e., whether saturated or unsaturated, substituted or otherwise; on oxidation changes to —COOH group ultimately.

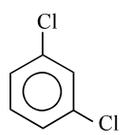
Position Isomerism of Benzene Derivatives

In benzene all the six hydrogen atoms are equivalent, hence the replacement of any one of them by a monovalent atom or group always results in a single monosubstitution product, for example, there can be only one monochlorobenzene.

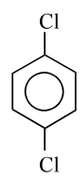
When two hydrogen atoms of benzene are replaced by two similar or dissimilar groups, three isomeric disubstitution products are possible. The position of the substituents are mentioned as *ortho, meta* or *para* depending on the fact, whether substituents are attached to adjacent, alternate or diagonal carbon atoms. Abbreviation *o*, *m* and *p* are used for *ortho*, *meta* and *para* prefixed to the name of the compound, as is shown in the following examples:



o-Dichlorobenzene

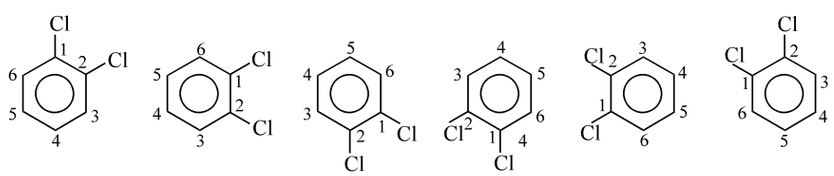


m-Dichlorobenzene



p-Dichlorobenzene

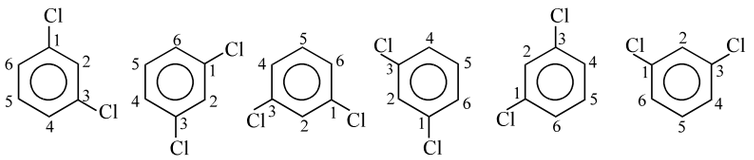
Ortho, meta and para positions can also be indicated by the using numbers. As the six carbon atoms are equivalent in the benzene ring the numbering of the carbon atoms can start from anyone of the substituent carrying carbon atom and then proceeding in the clockwise direction. However, this has to be kept in mind that the sum of locants indicating the position of the substituent should be least considering all possible combinations. Thus ortho-dichlorobenzene can be represented by any one of the following structures:



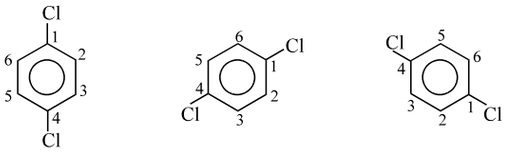
All are *o*-Dichlorobenzene or 1,2-Dichlorobenzene.

NOTES

Similarly the following different structures represent *meta* and *para* dichlorobenzenes as mentioned:



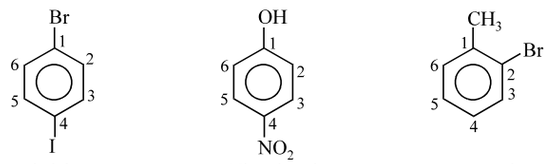
All are *m*-Dichlorobenzene or 1,3-Dichlorobenzene



All are *p*-Dichlorobenzene or 1,4-Dichlorobenzene

For convenience of fixing the orientation (position of the substituent) the ring should be oriented with position 1 at the top.

If the two groups are different and the molecule has no special name, the two groups are successively named in alphabetical order and the name ends with suffix benzene, as for example, bromoiodobenzene, bromonitrobenzene etc. However, if one of the groups is such that it gives a special name to the molecule, then the compound is named as a derivative of that special compound, as for example, *p*-nitrophenol, *o*-bromotoluene etc. The special group or substituent is given number 1 in naming the compound.

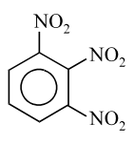


p-Bromoiodobenzene or 1-Bromo-4-iodobenzene

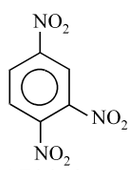
p-Nitrophenol or 4-Nitrophenol

o-Bromotoluene or 2-Bromotoluene

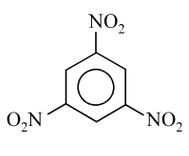
In case of tri or polysubstitution products the number of isomers depend on the fact, whether the substituents are same or different. If three hydrogen atoms of benzene are to be replaced by same monovalent atom or group, the number of isomers will be three but if two substituents are same and the third one different, the number will be six and the number of isomers will be ten when all are different. In such cases the name of the compound can easily be written by numbering the carbon atoms in the above discussed manner.



1,2,3-Trinitrobenzene or (*vic*-Trinitrobenzene)



1,2,4-Trinitrobenzene or (*asym*-Trinitrobenzene)



1,3,5-Trinitrobenzene or (*sym*-Trinitrobenzene)

The trisubstitution products of benzene with three similar groups are termed *vicinal* or 1,2,3- , *asymmetrical* or 1,2,4 and *symmetrical* or 1,3,5 depending upon their relative positions. Abbreviation '*vic*' for *vicinal*, '*as*' for *asymmetrical* and '*s*' or '*sym*' for *symmetrical* are prefixed to the name of the compound as given above.

Classification and Nomenclature

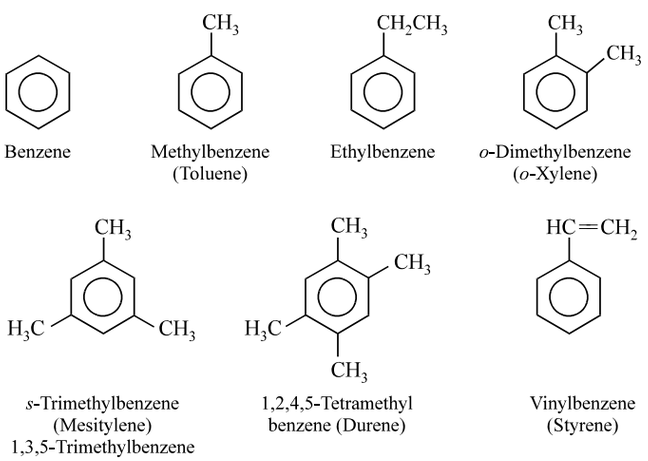
Like aliphatic compounds, aromatic compounds are also classified as hydrocarbons, aryl- halides, hydroxy compounds, aldehydes, ketones etc. For naming the compounds the carbon atoms of benzene are numbered as discussed in Section 11.5. The sequence of numbers should be one which gives the lowest sum to the locants of the substituents. If some special group which gives a special name to the compound is present it is given number 1 or number 1 is given to the functional group if present. If more than one functional group is present then the principal functional group is given number 1. In many cases, however, it is found more convenient to name the aromatic compound using *trivial* or *parent hydrocarbon* name as suffix and in such cases *the root name decides where from the numbering should start*.

The names of the following *aryl radicals* or *groups* are used in nomenclature and one is expected to be familiar with them.

C_6H_5—	C_6H_4<	$H_3C.C_6H_4$—
Phenyl	(*o*, *m*, *p*) Phenylene	Tolyl
$C_6H_5.CH_2$—	C_6H_5CH<	C_6H_5C<
Benzyl	Benzal or Benzylidene	Benzo

Names of various classes of aromatic compounds

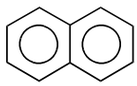
Hydrocarbons



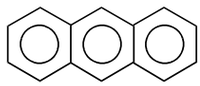
Benzene | Methylbenzene (Toluene) | Ethylbenzene | *o*-Dimethylbenzene (*o*-Xylene)

s-Trimethylbenzene (Mesitylene) 1,3,5-Trimethylbenzene | 1,2,4,5-Tetramethyl benzene (Durene) | Vinylbenzene (Styrene)

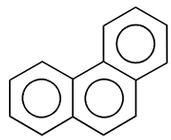
NOTES



Naphthalene

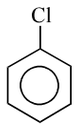


Anthracene

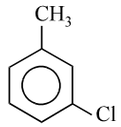


Phenanthrene

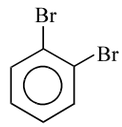
Aryl and Arylalkyl Halides



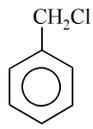
Chlorobenzene
(Phenyl chloride)



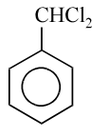
m-Chlorotoluene
(*m*-Tolyl chloride)
or
3-Chlorotoluene



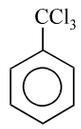
o-Dibromobenzene
o-Phenylenechloride
1,2-Dibromobenzene



Chloromethylbenzene
(Benzyl chloride)

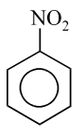


Dichloromethylbenzene
(Benzal chloride)

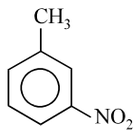


Trichloromethylbenzene
(Benzo trichloride)

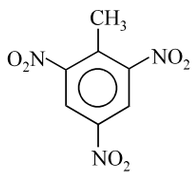
Nitro Compounds



Nitrobenzene

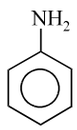


m-Nitrotoluene
or
3-Nitrotoluene

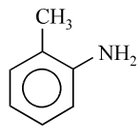


2,4,6-Trinitrotoluene
(TNT)

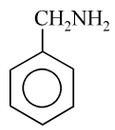
Amino Compounds



Aminobenzene
(Aniline)

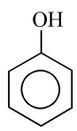


o-Aminotoluene
(*o*-Toluidine)
or
2-Aminotoluene

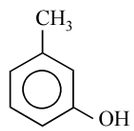


Aminomethylbenzene
(Benzylamine)

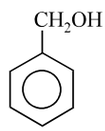
Hydroxy Compounds



Hydroxybenzene
(Phenol)

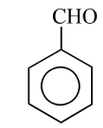


m-Hydroxytoluene
(*m*-Cresol)
or
3-Hydroxytoluene

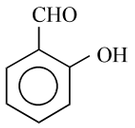


Hydroxymethylbenzene
(Benzyl alcohol)

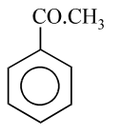
Aldehydes and Ketones



Benzaldehyde

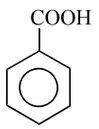


o-Hydroxybenzaldehyde
(Salicylaldehyde)
or
2-Hydroxybenzaldehyde

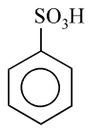


Methylphenyl ketone
(Acetophenone)

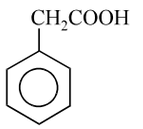
Acids



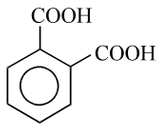
Benzoic acid



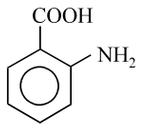
Benzenesulphonic acid



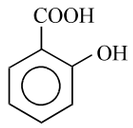
Phenylacetic acid



o-Benzenedicarboxylic
acid
(Phthalic acid)

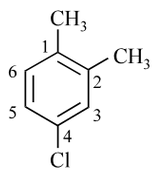


o-Aminobenzoic acid
(Anthranilic acid)

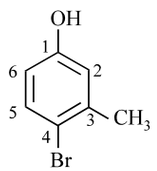


o-Hydroxybenzoic acid
(Salicylic acid)

Some more examples are given below to illustrate the method of nomenclature.



4-Chloro-1,2-dimethylbenzene
or
4-Chloro-*o*-xylene
(I)



4-Bromo-3-methylphenol
or
p-Bromo-*m*-cresol
(II)

Compound (I) is a derivative of benzene or it can be regarded as a derivative of 1,2-dimethylbenzene (special name *o*-xylene). It can, therefore, be named as a derivative of any of the two hydrocarbons. In compound (II) the numbering will start from the principal function group —OH (phenolic) which should be orientated at the top and given number 1. The compound (II) has a methyl group at *meta*-position with respect to —OH hence its special name is *m*-cresol. The compound (II) can be named as a derivative of phenol or cresol. Since both names end in '*ole*', —OH group is given no. 1.

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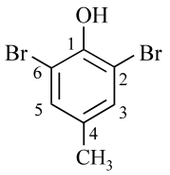
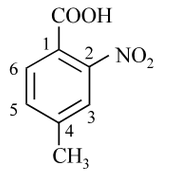


2,6-Dibromo-4-methylphenol
or
2,6-Dibromo-*p*-cresol
(III)

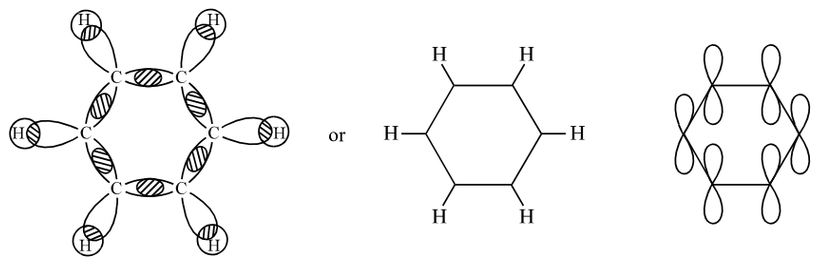


4-Methyl-2-nitrobenzoic acid
or
2-Nitro-*p*-toluic acid
(IV)

Compound (III) is similar to (II) hence will be named similarly. Compound (IV) can be named as a derivative of benzoic or toluic acid.

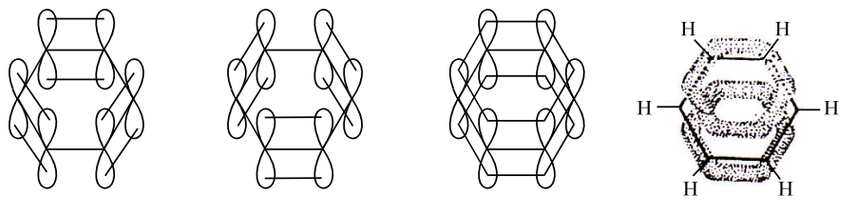
With above basic knowledge and more practice the students will become familiar with nomenclature of aromatic compounds.

Molecular Orbital Structure of Benzene: Modern approach to the benzene structure is on the basis of M.O. theory. Usually a carbon involved in the double bond formation is in sp^2 hybridized state. Thus if we try to write Kekule structure on the basis of M.O. theory then each of the carbon atom in benzene must be in sp^2 hybridized state. The three hybrid orbitals of each of such a carbon atom are in the same plane and form two σ bonds with two other such carbon atoms on either side by coaxial overlap of hybrid orbitals and one σ bond with *s*-orbital of hydrogen. The usual valency angle among the sp^2 hybrid orbitals is 120° which is also the observed bond angle is benzene. This gives rise to a total of 12σ bonds and carbon skeleton acquires a hexagonal shape with all the C and H in the same plane. At each of the sp^2 hybridised carbon atom there is still an unhybridised *p*-orbital that lies perpendicular to the plane of the hybrid orbitals. The sidewise or parallel overlap of these *p*-orbitals with those on adjacent carbon atoms results in the formation of π bonds as shown in two Kekule's structures above. However since *p*-orbital at any carbon atom can overlap with either of the *p*-orbitals on the carbon at its left or right, and the probability of both types of overlapping being equal, this results in the continuous overlapping as shown in structure (III). This leads to the formation of two continuous or delocalised π electron clouds, one above and the other below the plane of the hexagon of 6 carbon atoms—sandwiching the hexagon between them (IV). The six π electrons are delocalised over all the six carbon atoms and the molecular orbital is polycentric. The energy of these six delocalised π electrons is less than that of three pairs of localised or isolated π electrons and therefore the molecule is stabilised. This difference of energy due to which the molecule is stabilised is known as delocalisation energy.



σ-Framework of benzene

Unpaired *p*-orbital at each carbon



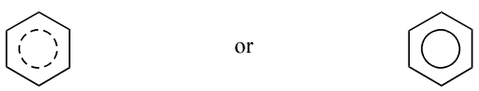
The two Kekule structures

Delocalised π electrons cloud of benzene

The molecular orbital picture explains all the known facts about the benzene i.e., planarity of the molecule, bond angles of 120°, equal C—C bond lengths and stabilisation of molecule as compared to Kekule structure.

Since the π electrons are delocalised and form electron clouds on either side of the plane of carbon atoms, benzene will act as a source of electrons. Electrophilic reagents will therefore attack the molecule much more readily, particularly as the π electrons are loosely held (as compared to σ electrons) and easily polarizable. However to preserve the delocalisation and the corresponding stability (or aromatic character) the molecule will tend to undergo substitution rather than addition reactions with these electrophilic reagents. This explains the tendency of benzene to under electrophilic substitution reaction.

To show the delocalisation of 6 π electrons benzene is represented by drawing a dotted line or continuous inscribed circle as shown below:



Nucleophilic Substitution

Benzene itself does not undergo nucleophilic substitution reactions because of the 6 π electron cloud but some of its derivatives, under suitable conditions, exhibit such reaction. There are three different types of mechanism for such reactions.

Unimolecular Mechanism

In some cases the nucleophilic substitution in aromatic compounds follows a unimolecular mechanism. An example of such a reaction is the replacement of diazo group of the diazonium salts by a nucleophile involving an aryl cation. The

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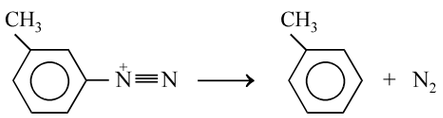
slow rate determining step is the rupture of carbon-nitrogen bond.

$$Ar—\overset{+}{N}\equiv N \xrightarrow{\text{Slow}} \overset{+}{Ar} + N_2$$

The second step, in which the aryl cation reacts with the nucleophile, is a fast reaction leading to the end substitution product.

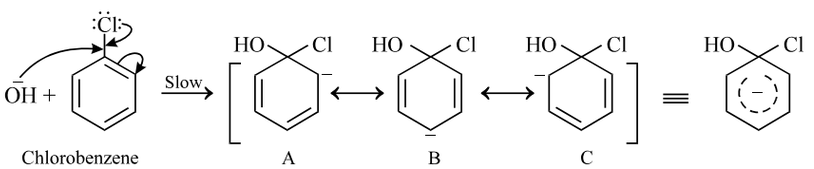
$$\overset{+}{Ar} + (C\bar{l}, O\bar{H}, O\bar{H}, \bar{O}R) \longrightarrow \begin{matrix} Ar\,OH \\ Ar\,OR \\ Ar\,Cl \end{matrix}$$

It is to be noted that the electron donor substituents facilitate the decomposition of aryl diazonium cation into aryl cation.

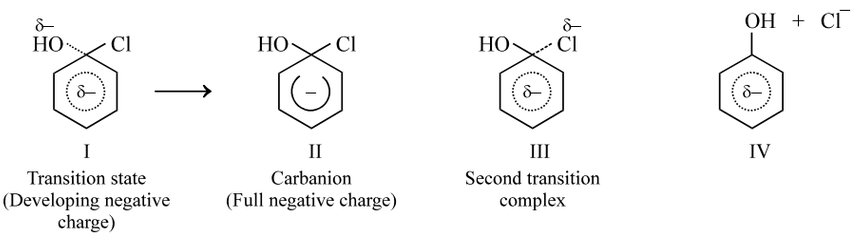


Bimolecular Mechanism

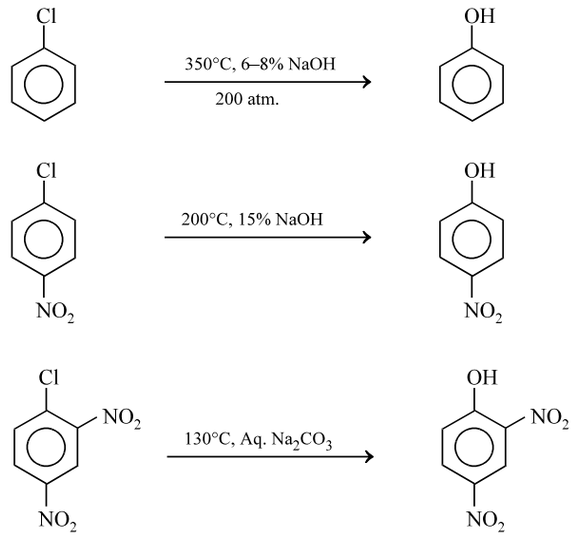
The most common nucleophilic substitution mechanism in benzene derivatives is the bimolecular mechanism. It is generally believed that the reaction proceeds through an intermediate α-complex called benzonium carbanion or pentadienyl anion. Carbanion with a full negative charge is the resonance hybrid of the three canonical froms A, B and C.



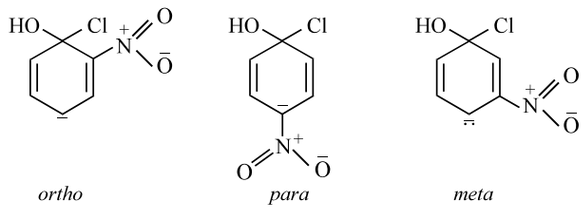
Nucleophilic attack produces a transition complex I with a developing negative charge which changes to resonance hybrid carbanion II. This then change to product IV through a second transition complex III.



The presence of an electron withdrawing group like —NO_2, —CN, —CHO, —COR etc., facilitates the substitution because it stabilises the carbanion and the electron releasing groups like —NH_2, —OH, —OR, —R etc., create an opposite effect.



Electron withdrawing group at ortho and para positions facilitate the substitution because the intermediate canonical structures produced involve extended conjugation resulting in spreading of the negative charge which exists on the most negative electronegative atom.

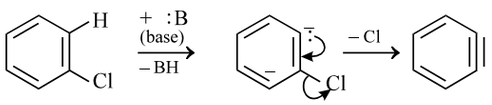


(The figure shows one contributing canonical structure for each one of the ortho, para and meta positions of nitro substituted chlorobenzene. Note the conjugation.)

On the other hand no such extended conjugation exists if the nitro group is present in the meta position.

Elimination-Addition Mechanism

The mechanism for a number of nucleophilic aromatic substitution reactions are believed to proceed through the formation of benzyne (1,2-dehydrobenzene) intermediate. Generally accepted view is that the first step in such reaction is the formation of benzyne by stepwise elimination of the E_2 type. Consider an aryl halide being treated by a strong base. The elimination of H and halogen leaves behind a pair of electrons. This results in the formation of a π type molecular orbital formed by the sideways overlap of the sp^2 hybrid orbitals initially used in bonding of hydrogen and halogen. Since the sideways overlapping is not very efficient, the new C—C bond is very weak and benzyne intermediate is highly reactive,



Benzyne intermediate
(1,2-Dehydrobenzene)

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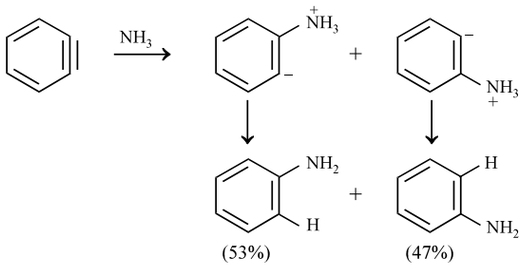
symmetrical and neutral species. Moreover this pair of electron occupies a M.O. that lies in the plane of the ring atoms and therefore is perpendicular to the π electron cloud. Thus no interaction with these π electrons is possible. Usually the benzyne intermediate is represented as having a triple bond but it differs from the normal triple bond of alkynes in the sense that whereas one pair of π electrons is localised and the other pair of π electron is delocalised.

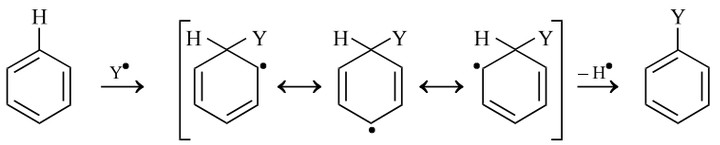
In the second step of the reaction benzyne tends to stabilise itself by addition to complete the reaction. The entering group in many reactions, does not occupy the position vacated



by expelled group. This view has been confirmed by taking chlorobenzene labelled with ^{14}C at the carbon of C—Cl group and reacting it with potassium in liq. ammonia.

Free Radical Substitution

Free radical substitution in benzene or its derivative occur by the following general mechanism. $Y^{\bullet}$ is a free radical having unpaired electron. Reactions like Wurtz Fittig, Ullmann, etc., involve a free radical substitution.



Check Your Progress

4. What is benzene nucleus?
5. What is side chain?
6. What results in monosubstitution product?

14.4 VON-RICHTER REACTION

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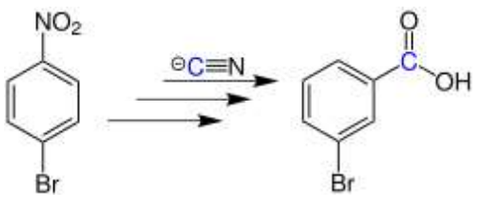
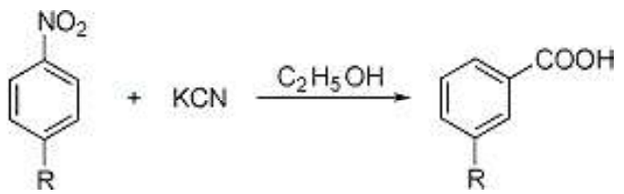
The Von-Richter reaction, also termed as the Von-Richter rearrangement, is a name reaction in the organic chemistry. It is named after Victor von Richter, who discovered this reaction in year 1871. It is the chemical reaction of aromatic nitro compounds with potassium cyanide giving carboxylation 'ortho' to the position of the former nitro group.

The reaction below shows the conversion of bromonitrobenzene into bromobenzoic acid.



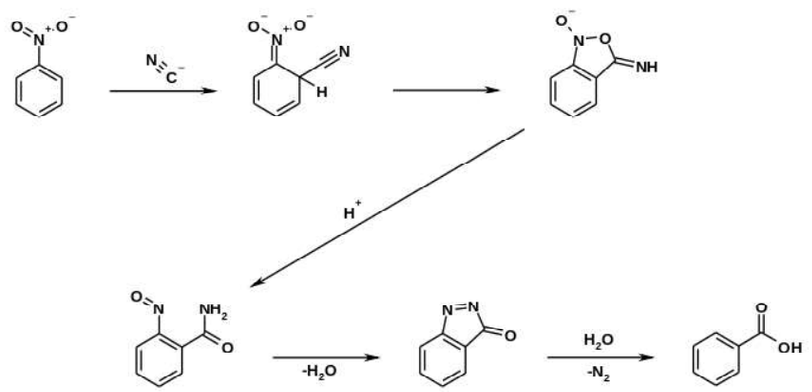
The reaction is an aromatic nucleophilic substitution. Chlorine can be substituted instead of bromine. The following example shows the Von Richter rearrangement reaction.



The above reaction shows the Carboxylation of para- or meta-substituted aromatic nitro compounds with cyanate which takes place at 120-270°. The carboxyl group enters with cine substitution in a position ortho to the eliminated nitro group.

Reaction Mechanism

The cyanide reacts with the carbon atom in ortho-position to the nitro group.



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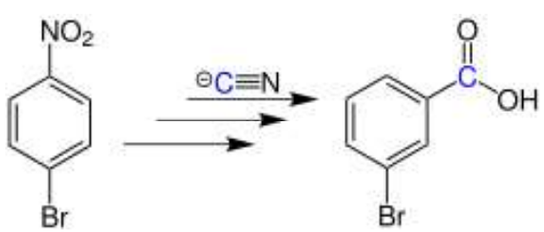
The negative charged oxygen atom reacts with the neighbouring carbon atom to build a five-membered ring which on condensation forms a double bond between the two nitrogen atoms, as shown in the reaction. In the last step, the compound is protonated and the 3-halogenbenzoic acid is built.

Check Your Progress

7. What is Von-Richter reaction?
8. Give a exaample to show the conversion of bromonitrobenzene into bromobenzoic acid.

14.5 ANSWERS TO CHECK YOUR PROGRESS QUESTIONS

1. Aromatic SN_1 mechanism is observed in diazonium salts
2. Benzyne mechanism is observed in reaction of chlorobenzene with $NaNH_2$.
3. SNAR mechanism is observed when an electron withdrawing group like $–NO_2$ activate the ring towards nucleophilic attack.
4. The six carbon atoms of the benzene ring constitute what is known as benzene nucleus.
5. A carbon chain connected to one of the carbon atoms of the nucleus through a carbon atom, other than of the simple functional groups like —CHO, —COOH, >CO, is called a side chain.
6. In benzene all the six hydrogen atoms are equivalent, hence the replacement of any one of them by a monovalent atom or group always results in a single monosubstitution product, for example, there can be only one monochlorobenzene.
7. The Von-Richter reaction, also termed as the Von-Richter rearrangement, is a name reaction in the organic chemistry. It is named after Victor von Richter, who discovered this reaction in year 1871. It is the chemical reaction of aromatic nitro compounds with potassium cyanide giving carboxylation 'ortho' to the position of the former nitro group.
8. The reaction for the conversion of bromonitrobenzene into bromobenzoic acid is:



14.6 SUMMARY

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- Nucleophilic aromatic substitution occur in several ways, including (i) aromatic SN1 mechanism, (ii) involving benzyne intermediate and (iii) SNAr mechanism involving addition and elimination.
- In the SN2 mechanism the nucleophile hydroxide ion approaches the alkyl halide molecule preferably from the side opposite to that occupied by the departing group.
- As the carbon atom involved in carbon to halogen bond is slightly deficient in electron density because of greater electronegativity of halogen (bromine in above example) the hydroxide ion offers a pair of electrons for the formation of bond with this carbon.
- Simultaneously bromine starts taking hold of the electron pair through which it is bonded to carbon and a transition state or activated complex is visualized for such reactions in which five groups are linked to carbon. Finally bromine leaves the molecules as a bromide ion and hydroxide ion forms a covalent bond with the carbon giving alcohol as the reaction product.
- In the hydrolysis of t-butyl bromide which occurs by SN1 mechanism, the first step is the slow dissociation of alkyl halide to give a bromide ion and tertiary butyl carbocation, which is stabilised due to hyperconjugation. The tertiary butyl carbocation then combines with a hydroxide ion to form the tertiary butyl alcohol.
- The addition reactions are the reactions of the double or triple bonds. In a >C==C< or —C^{oo}C— the p electrons are most readily available. These 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^{oo}N, the p electron density is slightly shifted towards the more electronegative elements O and N, and at the approach of a reagent electromeric shift results in complete transfer of this p electron pair to O or N (hetero atoms in general).
- Additions at carbon to carbon multiple bonds. 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.
- 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.

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- In all addition reactions bonds are converted to bonds or the hybridization state of carbon changes from sp^1 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.
- 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.
- 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 whihc prevents cis-addition of OH–. Then the completion of addition occurs by a trans combination of a bromide or hydroxide ion.
- 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_3.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.
- When aldehydes and ketones having a-hydrogen atoms are treated with alkali, they undergo self-addition between two molecules to form a b-hydroxy aldehyde or b-hydroxy ketone (known as aldols). This addition is usually followed by elimination of a water molecule resulting in overall condensation reaction.
- 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.

- Elimination reactions usually compete with nucleophilic substitution reactions at saturated carbon atoms (SN reactions). By analogy to SN reactions, in elimination also there are two extreme types of reactions.
- 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.

14.7 KEY WORDS

- **Nucleophilic aromatic substitution:** A nucleophilic aromatic substitution is a substitution reaction in organic chemistry in which the nucleophile displaces a good leaving group, such as a halide, on an aromatic ring.
- **Benzene nucleus:** The six carbon atoms of the benzene ring constitute what is known as benzene nucleus.
- **Side chain:** A carbon chain connected to one of the carbon atoms of the nucleus through a carbon atom, other than of the simple functional groups like —CHO, —COOH, >CO, is called a side chain.
- **Von-Richter reaction:** It is the chemical reaction of aromatic nitro compounds with potassium cyanide giving carboxylation 'ortho' to the position of the former nitro group.

14.8 SELF ASSESSEMENT QUESTIONS AND EXERCICES

Short Answer Questions

1. What is nucleophilic aromatic substitution ?
2. What is addition reaction?
3. What is ozonolysis?
4. Write short note on aldol condensation.
5. Brief a note on dehydration of alcohol.
6. Give a short note on resonance structure of benzene.

Long Answer Questions

1. Give a detailed note on nucleophilic aromatic substitution and its application?
2. Elaborate a note on addition reaction also mentioning its structure, reactivity and applications.
3. Discuss in detail about elimination reaction also mentioning its structure, reactivity and applications.

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4. Explian in detail about the benzyne mechanism.
5. Discuss about benzene nucleus and side chain in detail.
6. Explain the molecular orbital structure of benzene.
7. Give a detailed description of Von-Richter reaction.

14.9 FURTHER READINGS

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