# PREFACE

With its grounding in the "guiding pillars of Access, Equity, Equality, Affordability and Accountability," the New Education Policy (NEP 2020) envisions flexible curricular structures and creative combinations for studies across disciplines. Accordingly, the UGC has revised the CBCS with a new Curriculum and Credit Framework for Undergraduate Programmes (CCFUP) to further empower the flexible choice based credit system with a multidisciplinary approach and multiple/ lateral entry-exit options. It is held that this entire exercise shall leverage the potential of higher education in three-fold ways – learner's personal enlightenment; her/his constructive public engagement; productive social contribution. Cumulatively therefore, all academic endeavours taken up under the NEP 2020 framework are aimed at synergising individual attainments towards the enhancement of our national goals.

In this epochal moment of a paradigmatic transformation in the higher education scenario, the role of an Open University is crucial, not just in terms of improving the Gross Enrolment Ratio (GER) but also in upholding the qualitative parameters. It is time to acknowledge that the implementation of the National Higher Education Qualifications Framework (NHEQF), National Credit Framework (NCrF) and its syncing with the National Skills Qualification Framework (NSQF) are best optimised in the arena of Open and Distance Learning that is truly seamless in its horizons. As one of the largest Open Universities in Eastern India that has been accredited with 'A' grade by NAAC in 2021, has ranked second among Open Universities in the NIRF in 2024, and attained the much required UGC 12B status, Netaji Subhas Open University is committed to both quantity and quality in its mission to spread higher education. It was therefore imperative upon us to embrace NEP 2020, bring in dynamic revisions to our Undergraduate syllabi, and formulate these Self Learning Materials anew. Our new offering is synchronised with the CCFUP in integrating domain specific knowledge with multidisciplinary fields, honing of skills that are relevant to each domain, enhancement of abilities, and of course deep-diving into Indian Knowledge Systems.

Self Learning Materials (SLM's) are the mainstay of Student Support Services (SSS) of an Open University. It is with a futuristic thought that we now offer our learners the choice of print or e-slm's. From our mandate of offering quality higher education in the mother tongue, and from the logistic viewpoint of balancing scholastic needs, we strive to bring out learning materials in Bengali and English. All our faculty members are constantly engaged in this academic exercise that combines subject specific academic research with educational pedagogy.We are privileged in that the expertise of academics across institutions on a national level also comes together to augment our own faculty strength in developing these learning materials. We look forward to proactive feedback from all stakeholders whose participatory zeal in the teaching-learning process based on these study materials will enable us to only get better. On the whole it has been a very challenging task, and I congratulate everyone in the preparation of these SLM's.

I wish the venture all success.

**Professor Indrajit Lahiri**
Vice-Chancellor

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NETAJI SUBHAS OPEN UNIVERSITY

Four Year Undergraduate Degree Programme

Under National Higher Education Qualifications Framework (NHEQF) &

Curriculum and Credit Framework for Undergraduate Programmes

Course Type: Discipline Specific Course (DSC)

Course Title: Organic Chemistry - I

Course Code: - 6CC-CH- 06

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**: Editing:**
Dr. Puspal Mukherjee & Dr. Sintu Ganai
*Assistant Professor of Chemistry, NSOU*

**: Course Writing :**
Dr. Sintu Ganai
*Assistant Professor of Chemistry, NSOU*

**: Format Editor :**
Dr. Sintu Ganai
*Assistant Professor of Chemistry, NSOU*


## Notification



**Ananya Mitra**
*Registrar* (Additional Charge)


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Netaji Subhas Open University

UG : Chemistry (NCH)

**Course Title: Organic Chemistry - I**

**Course Code: - 6CC-CH- 06**

## Module 1: Bonding and Physical Properties



## Module 2:General Treatment of Reaction Mechanism



## Module 3:Stereochemistry



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# Module-1
# Bonding and Physical Properties

# Unit 1 ❐ Bonding, Structure and Properties

**Structure**

**1.13 Exercise**

## 1.0 Objectives

By the end of this unit, students should be able to:

- Define the basic concepts of chemical bonding and molecular structure.
- Describe the Valence Bond Theory (VBT) and its role in explaining molecular bonding.
- Understand resonance, hyperconjugation and its effect on molecular stability.
- Illustrate the concept of hybridization and its impact on molecular geometry.
- Represent molecules using orbital pictures to understand bonding patterns.
- Analyze different terms associate with electronic displacements in Molecules

## 1.1 Introduction

Understanding chemical bonding, molecular structure, and electronic effects is essential for explaining the behavior of chemical compounds. Bonding theories describe how atoms form molecules and how molecular structure influences their physical and chemical properties. This unit explores fundamental concepts such as Valence Bond Theory (VBT), hybridization, resonance, and hyperconjugation, which help explain molecular stability and reactivity.

This unit examines electronic displacements, including inductive, mesomeric, electromeric, and steric effects, which impact molecular interactions and chemical behavior. By mastering these principles, students will gain a solid foundation in predicting molecular properties and reaction mechanisms, enhancing their understanding of structural chemistry.

## 1.2 Bonding, Structure and Properties

Bonding refers to the force that holds atoms together in a substance, while structure describes the arrangement of these atoms. The combination of bonding and structure determines the physical and chemical properties of a substance.

**There are two main types of structures:**

**Giant structures:** These extend indefinitely, forming a continuous network of atoms or

ions.

**Molecular structures:** These consist of discrete groups of atoms held together by intermolecular forces.

The properties of a substance are influenced by three key factors:

i) The Type of Basic Particles Present

A substance can be composed of atoms, ions, or molecules. The type of particle determines various properties, such as conductivity and solubility.

- Ionic compounds (e.g., sodium chloride) conduct electricity when molten or dissolved in water due to the presence of free-moving ions.
- Polar molecules or ionic substances tend to dissolve in water, whereas non-polar molecules do not.

ii) The Nature of Bonding Between Particles

The strength of bonding impacts a substance's melting/boiling point, hardness, and other properties. The main types of bonding include ionic, covalent, metallic, and intermolecular forces.

- Strong covalent bonds in giant structures (e.g., silica, SiO?) make the material hard and difficult to melt.
- Weak intermolecular forces in molecular structures (e.g., carbon dioxide, CO?) lead to lower melting/boiling points, as the molecules are easily separated.

iii) The Arrangement of Particles in the Structure

The spatial arrangement of atoms, ions, or molecules influences a substance's properties. E.g.

- Polymers consist of 1-dimensional chains of repeating units.
- Clays have a 2-dimensional sheet-like structure that allows flexibility.
- 3-dimensional networks provide high strength and stability.
- Graphite has layers of 2D sheets, which can slide over one another, making it soft and useful as a lubricant or pencil lead.

- Diamond, in contrast, has a giant 3D covalent structure, making it the hardest natural substance.

Understanding these principles is essential for predicting the behavior of different materials and their practical applications.

## 1.3 Valence bond theory

Valence Bond Theory (VBT) was first introduced by Heitler and London in 1927 and later expanded by Pauling and Slater in 1931. This theory explains how atoms form covalent bonds by overlapping their atomic orbitals, leading to the formation of stable molecules.

### 1.3.1 Basic Concepts of VBT:

VBT is based on the following three concepts:

i) Pairing of Electrons: A covalent bond forms when two unpaired electrons from different atoms come together.

ii) Neutralization of Opposite Spins: The electrons in a bond must have opposite spins to maintain stability.

iii) Orbital Overlapping: When atomic orbitals of two atoms overlap, a common electron density is created, which results in a chemical bond.

### 1.3.2 Postulates of Valence Bond Theory:

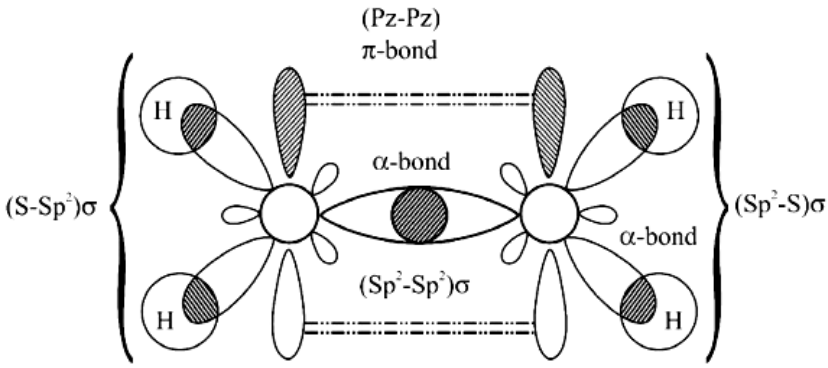
i) The overlapping of two half-filled valence orbitals of two different atoms results in the formation of the covalent bond.

ii) In case the atomic orbitals possess more than one unpaired electron, more than one bond can be formed.

iii) A covalent bond is directional. Such a bond is also parallel to the region of overlapping atomic orbitals.

iv) Based on the pattern of overlapping, there are two types of covalent bonds: sigma bond ($\sigma$) and a pi bond ($\pi$).

The covalent bond formed by sidewise overlapping of atomic orbitals is known as pi bond ($\sigma$) whereas the bond formed by head-on (or axial) overlapping of atomic orbitals along the inter nucleus axis is known as a sigma bond ($\sigma$). The sigma bond, pi bond and P-P overlap is shown below.




Valence Bond Theory explains how covalent bonds form through orbital overlap and electron pairing. It also highlights the directional nature of bonds and the difference between sigma and pi bonds. This understanding is essential in predicting molecular shapes, stability, and chemical reactivity.

**Key Differences Between Sigma and Pi Bonds:**

| Sigma ( σ ) Bond | Pi ( π ) Bond |
|---|---|
| Head-on (axial) overlap | Sidewise (parallel) overlap |
| Stronger due to greater overlap | Weaker due to less overlap |
| Free rotation around the bond | Restricted rotation |
| Single bond in methane ($CH_4$) | Double bond in ethene ($C_2H_4$) |

### 1.3.3 Limitations of VBT:

While Valence Bond Theory (VBT) effectively explains covalent bond formation through orbital overlap, it has several limitations:

1. **Fails to Explain Molecular Shapes Completely:** VBT does not fully explain the geometry and shapes of molecules. Example: It does not predict why methane ($CH_4$) is tetrahedral or why water ($H_2O$) has a bent shape.
2. **Does Not Explain Bond Strength V4ariations:** The theory does not clarify why some bonds are stronger or weaker than others, even when they involve the same elements.
3. **Cannot Explain Delocalization of Electrons:** VBT assumes that electrons are

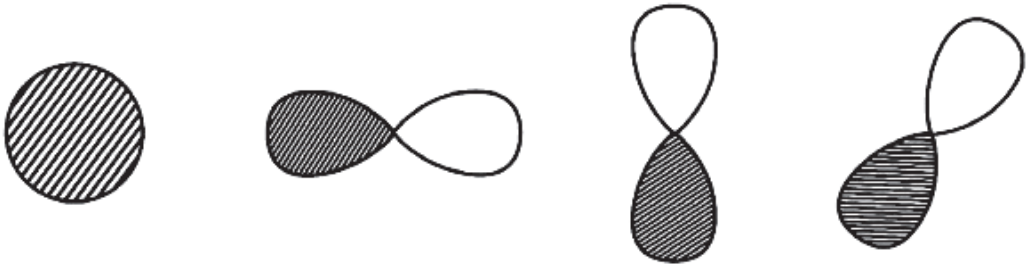
localized between two bonded atoms, but in reality, electrons can be delocalized across multiple atoms, as seen in benzene ($C_6H_6$). Resonance (the concept of multiple structures contributing to a molecule's stability) is not well explained by VBT.

4. It fails to explain the magnetic and spectroscopic properties of molecules. E.g. VBT cannot explain why oxygen ($O_2$) is paramagnetic (attracted to a magnetic field), even though experimental evidence shows that oxygen has unpaired electrons.
5. **Ignores Electron Energies:** VBT does not discuss the energies of electrons in molecules, which are crucial for understanding bond formation and stability.
6. **Limited Explanation of Multiple Bonds:** VBT does not provide a clear distinction between single, double, and triple bonds in terms of bond strength and electron distribution.

## 1.4 Concept of hybridization

Hybridization is the process of mixing two or more atomic orbitals of the same atom to form new orbitals, called hybrid orbitals, which have equivalent energy and shape. This concept was introduced by Linus Pauling to explain molecular shapes that could not be understood using Valence Bond Theory alone.

The individual orbitals (pure orbitals) look something like this.




However, through the process of hybridization, these orbitals combine to form new hybrid orbitals with different shapes and properties, which influence molecular bonding and structure.

**Key Features of Hybridization:**

**Mixing of Atomic Orbitals:** Hybridization occurs when atomic orbitals of similar energy levels (such as s, p, and d orbitals) combine to form new hybrid orbitals.

**Formation of Identical Hybrid Orbitals:** The hybrid orbitals have the same energy and shape but differ in orientation.

**Directional Property:** The hybrid orbitals are arranged in a way that minimizes electron repulsion, determining the geometry of molecules.

**Explains Molecular Shapes:** Hybridization helps explain the bond angles and shapes of molecules, which VBT alone cannot predict.

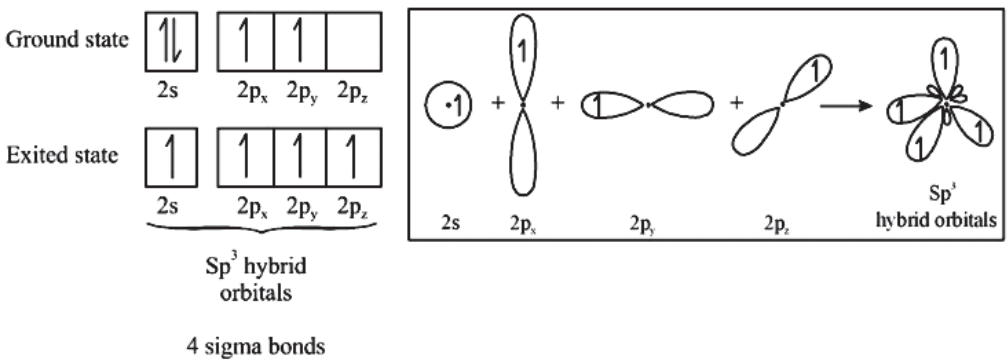
The process of mixing of pure orbitals to give a set of new equivalent orbitals is termed as hybridization.

## 1.5. Types of Hybridisation:

Since carbon does not have any electrons in the d-orbital in either its ground or excited state, only three main types of hybridization occur in organic molecules: $sp^3$, $sp^2$, and sp hybridization. The type of hybridization is determined by the number of sigma ( $\sigma$ ) bonds and lone pairs surrounding the central atom.

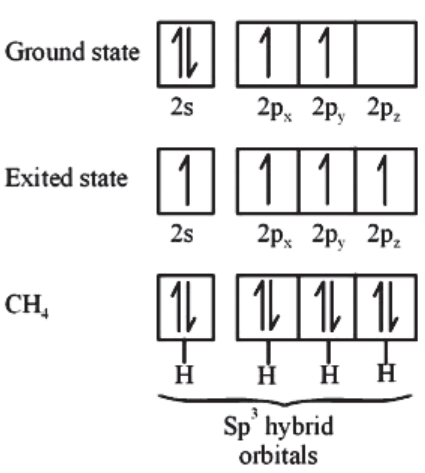
### 1.5.1 $sp^3$ Hybridisation

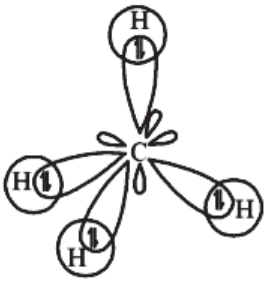
In sp3 hybridization, one 2s and three 2p orbitals of excited carbon intermix together and form 4 hybrid orbitals which are oriented in tetrahedral geometry in space around the carbon atom. Each $sp^3$ hybrid orbital is occupied by one electron.

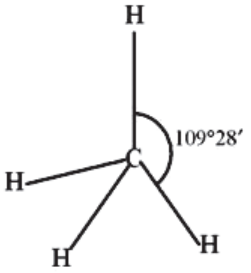


Each of these $sp^3$ orbitals can form $\sigma$-bond with other atom. Thus carbon is forming four single bonds with other atoms in tetrahedral geometry. The bond angles are usually equal to or nearer to 109°28'.

e.g. methone molecule. $CH_4$.



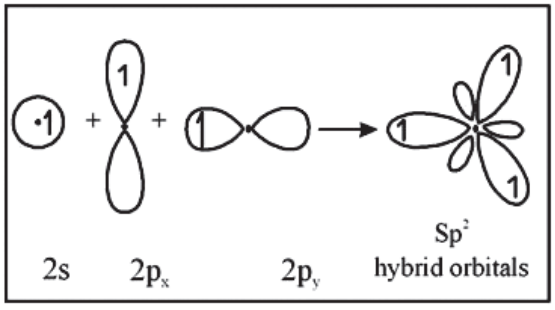



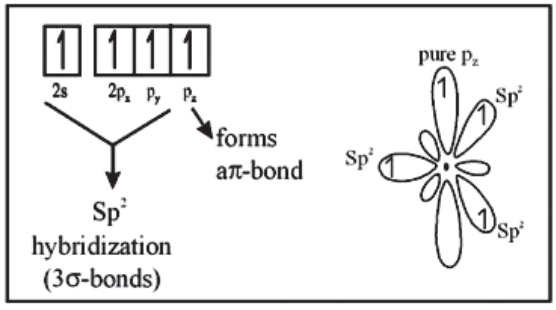




### 1.5.2 $sp^2$ Hybridisation

In $sp^2$ hybridization, there is intermixing of one 2s and two of the 2p orbitals of carbon in the excited state to form three hybrid orbitals. These are oriented in trigonal planar geometry.

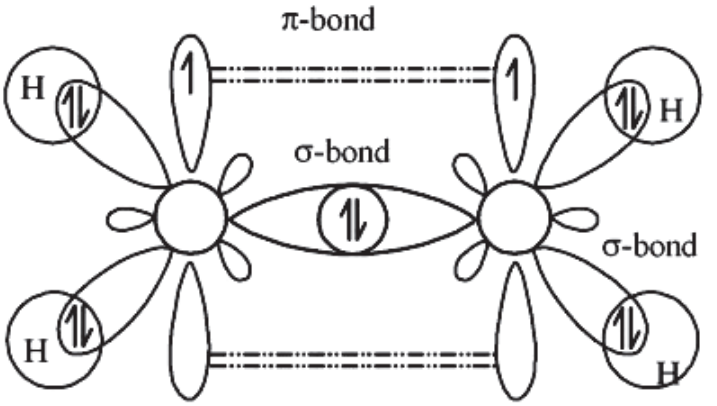
Each $sp^2$ hybrid orbital is occupied by one electron. The remaining pure 2p orbital with one electron lies at right angle to the plane of hybrid orbitals.

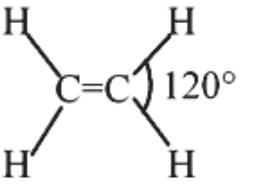



The $sp^2$ hybrid orbital form 3 $\sigma$-bonds and the bond angles are about 120°. The remaining pure 'p' orbital will form a $\pi$-bond. Thus carbon forms total four bonds i.e., three $\sigma$-bonds and one $\pi$-bond.

e.g. ethylene molecule, $C_2H_4$,

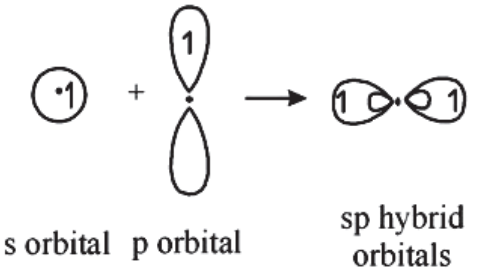


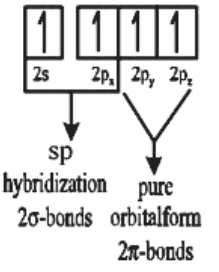



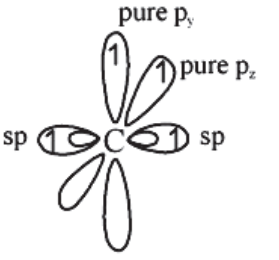

**planar geometry**

### 1.5.3 sp Hybridisation

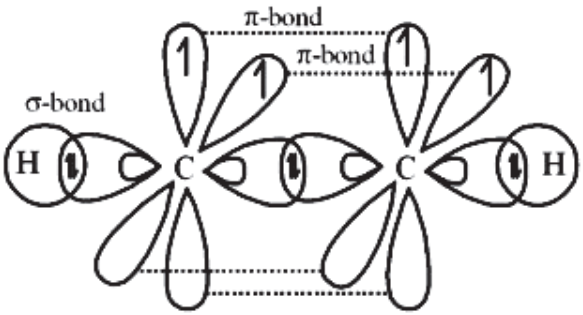
In sphybridization, one 2s and one 2p orbitals of excited carbon intermix to form two sp-hybrid orbitals in linear geometry.

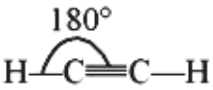



The two sp hybrid orbitals form 2 $\sigma$-bonds in linear geometry. Thus the bond angle will be about 180°. The remaining pure two 'p' orbitals will form two $\pi$-bonds. Thus carbon again forms total four bonds i.e., two $\sigma$-bonds and two $\pi$-bonds.



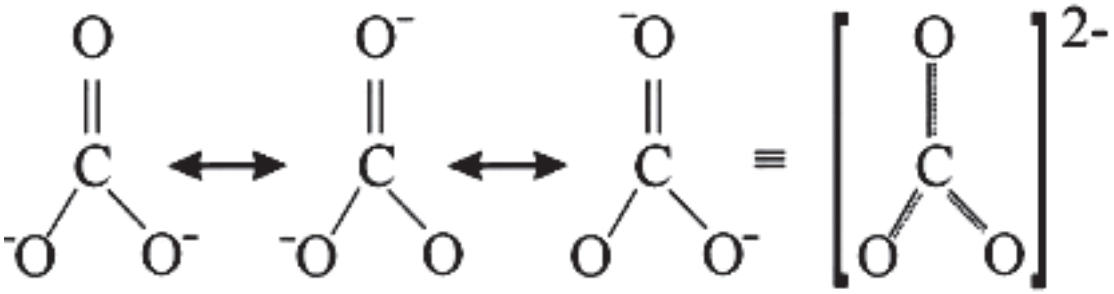




**Linear geometry**

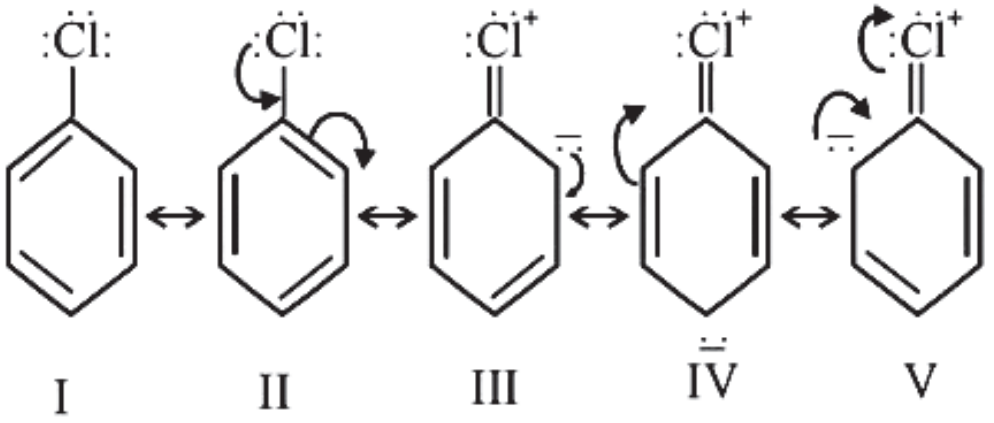
## 1.6 Resonance

When a molecule cannot be completely represented by a single structure but its chemical and physical properties can be described by two or more different structure, then the true structure is said to be resonance hybrid and phenomenon is called resonance.

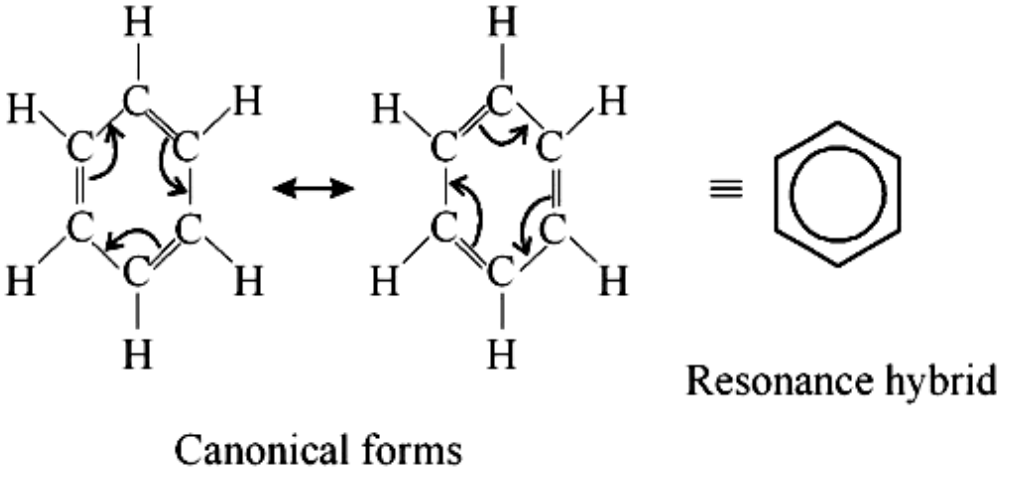
All contributing structures are known as canonical forms or resonance structures. The resonance of carbonate ion is shown below.




Similarly, the resonance of chlorobenzene is represented by five resonating structures.




The overall combination of all canonical forms is known as resonance hybrid. This form is more stable than all canonical forms and shows all the characteristics of the molecule. For example, the response hybrid of benzene is as follow.




## 1.7 Hyperconjugation (no bond resonance or Baker-Nathan Effect)

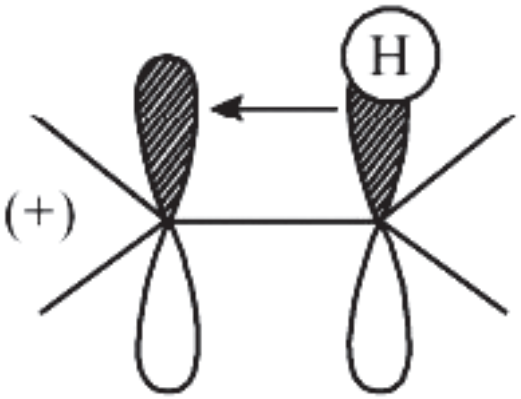
*The delocalization of σ-electrons or lone pair of electrons into adjacent π-orbital or p-orbital is called hyperconjugation.*

- It occurs due to overlapping of $\sigma$-bonding orbital or the orbital containing a lone pair with adjacent $\pi$-orbital or p-orbital.
- It is also known as "no bond resonance" or "Baker-Nathan effect".

**Conditions for hyperconjugation:** There must be a $\alpha$-CH group or a lone pair on atom adjacent to $sp^2$ hybrid carbon or other atoms like nitrogen, oxygen etc.

E.g., Alkenes, alkyl carbocations, alkyl free radicals, nitro compounds with ?- hydrogen

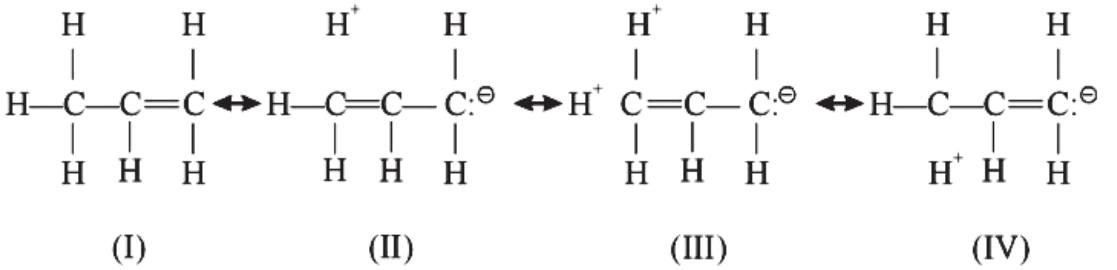
**Illustration of Hyperconjugation:** A '$\sigma$' bond can stabilize an adjacent or neighbouring carbocation by donating electrons to the vacant p orbital. The positive charge is delocalized or spread out. This stabilizing effect is kwon as hyper conjugation. It operates through C-h and C-C bonds.




–Alkyl groups can allow electron release through a mechanism different from induction.

The electrons of C-H '$\sigma$' bond spends some time at the vacant 'P' orbital of Carbocation.

e.g. In propene, the $\sigma$-electrons of C-H bond of methyl group can be delocalized into the $\pi$-orbital of doubly bonded carbon as represented below.



(I) (II) (III) (IV)

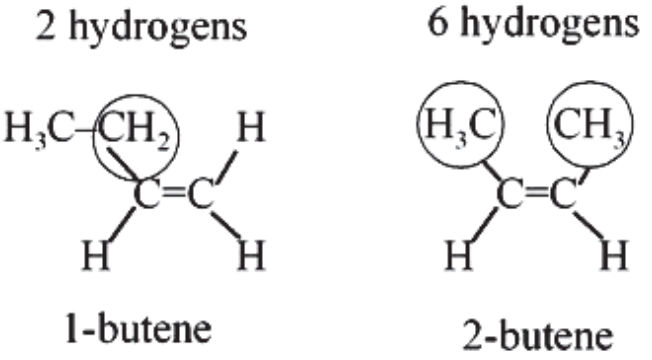
In the contributing structures: (II), (III) & (IV) of propene, there is **NO** bond between an $\alpha$-carbon and one of the hydrogen atom. Hence the hyperconjugation is also known as "**no bond resonance**".

This type of hyperconjugation is also referred to as sacrificial hyperconjugation since one bond is missing.

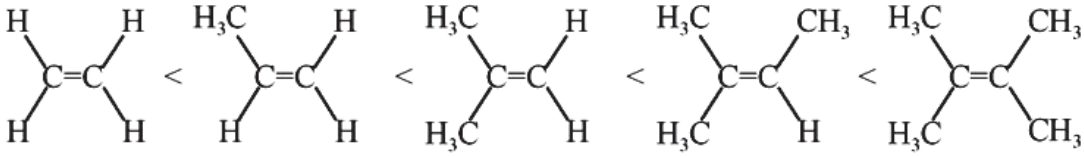
**Application of Hyperconjugation:**

i. **Stability of alkenes:** A general rule is that, the stability of alkenes increases with increase in the number of alkyl groups (containing hydrogens) on the double bond. It is due to increase in the number of contributing no bond resonance structures.

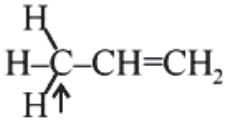
For example, 2-butene is more stable than 1-butene.



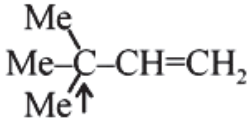

The increasing order of stability of alkenes with increases in the number of methyl groups on the double bond is depicted below.



It is also important to note that the effect of hyperconjugation is stronger than the inductive effect.



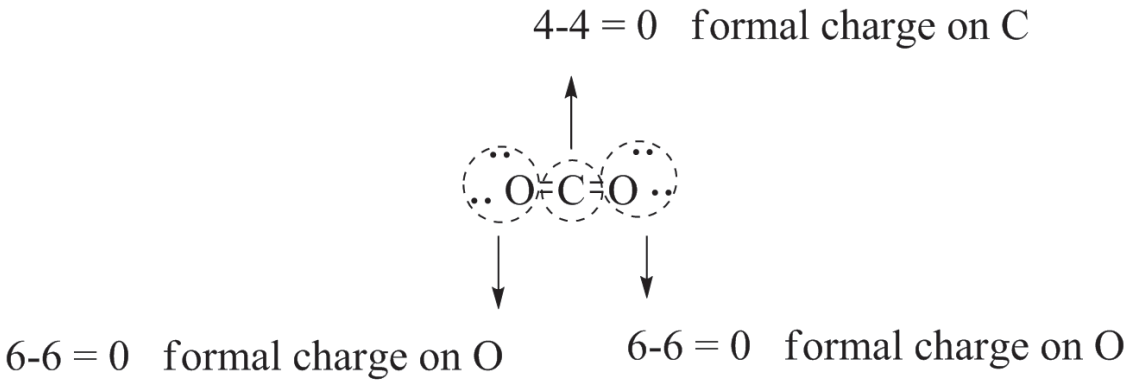
Total hyper conjugative structure = 3
More stable



No such hyper conjugative structure Less stable

## 1.8 Formal charges (FC)

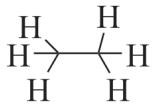
In chemistry, a formal charge (FC) is the charge assigned to an atom in a molecule, assuming that electrons in all chemical bonds are shared equally between atoms, regardless of relative electronegativity.



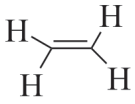
- Formal charge = [No. of valence electrons] - [electrons in lone pairs + 1/2 the number of bonding electrons]
- Formal Charge = [No. of valence electrons on atom] - [non-bonded electrons + number of bonds].

## 1.9 Double bond equivalent (DBE)

DBE=double bond equivalent. It is also called degree of unsaturation. From the structure of the chemicals, each pi bond or ring will generate one DBE.



Ethane
DBE = 0



Ethylene
DBE = 1

Cyclohexane
DBE = 1
(for ring system)

Benzene
DBE = 3+1 = 4

Simpler method for calculating the DBE of a molecule is

$$DBE = C - \frac{H}{2} + \frac{N}{2} + 1$$

Here, C means the number of carbon. H means the number of hydrogen and halogen. N means the number of the nitrogen.

Example:

Ethane ($C_2H_6$) : DBE = C-(H/2)+(N/2)+1= 2-(6/2)+(0/2)+1 = 0

Ethylene ($C_2H_4$) : DBE = C-(H/2)+(N/2)+1= 2-(4/2)+(0/2)+1 = 1

Cyclohexane ($C_6H_{12}$) : DBE = C-(H/2)+(N/2)+1= 6?(12/2)+(0/2)+1 = 1

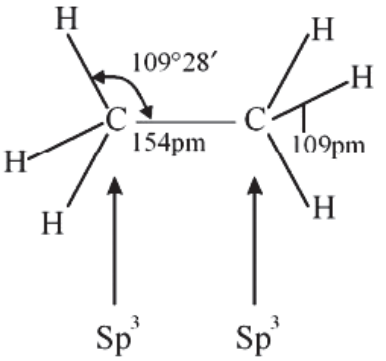
Benzene ($C_6H_6$) : DBE = C-(H/2)+(N/2)+1 = 6-(6/2)+(0/2)+1 = 4

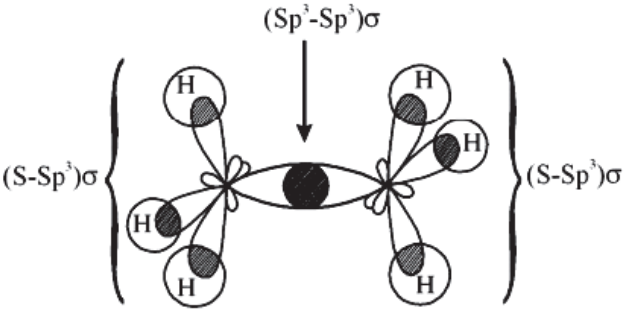
## 1.10 Orbital pictures

A molecular orbital diagram, or molecular orbital picture, is a qualitative descriptive tool

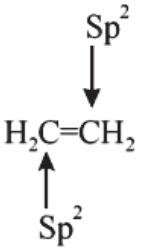
explaining chemical bonding in molecules in terms of molecular orbital theory in general and the linear combination of atomic orbitals method in particular

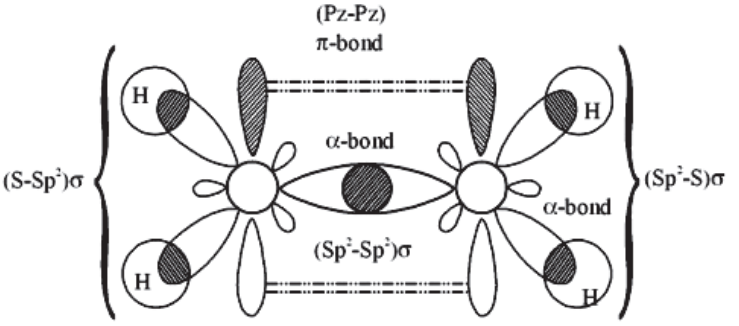
**i) Ethane,** $CH_3$-$CH_3$ **orbital picture**



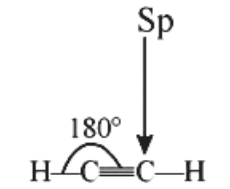




**ii) Ethylene,** $CH_2$=$CH_2$ **orbital picture**



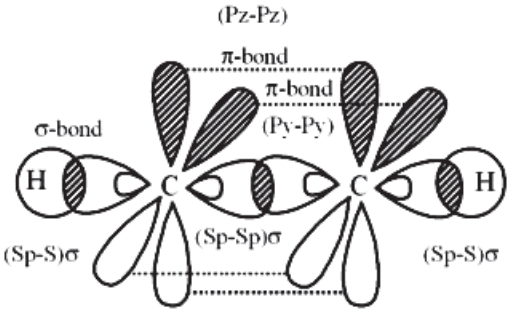



### iii) Acetylene

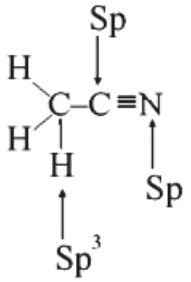



Linear structure of acetylene molecule

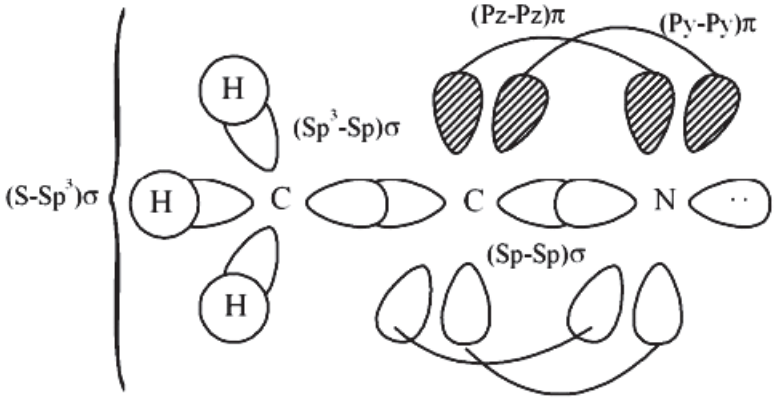
**orbital picture**



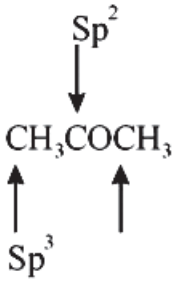

### iv) Acetonitrile, $CH_3CN$

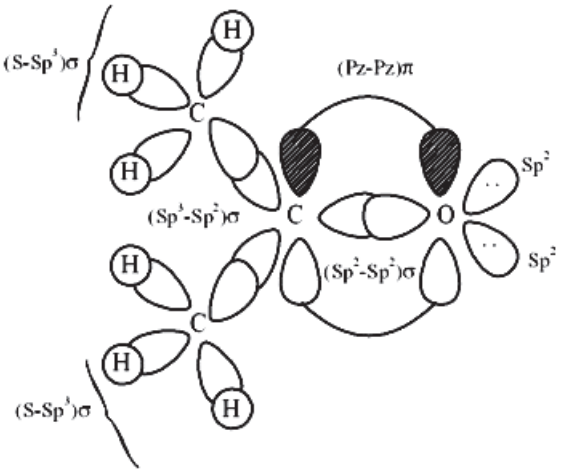



**orbital picture**

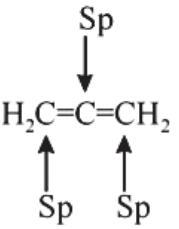


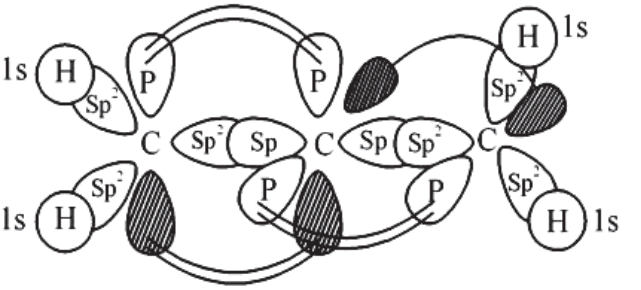
**v) Acetone, $CH_3COCH_3$** **orbital picture**



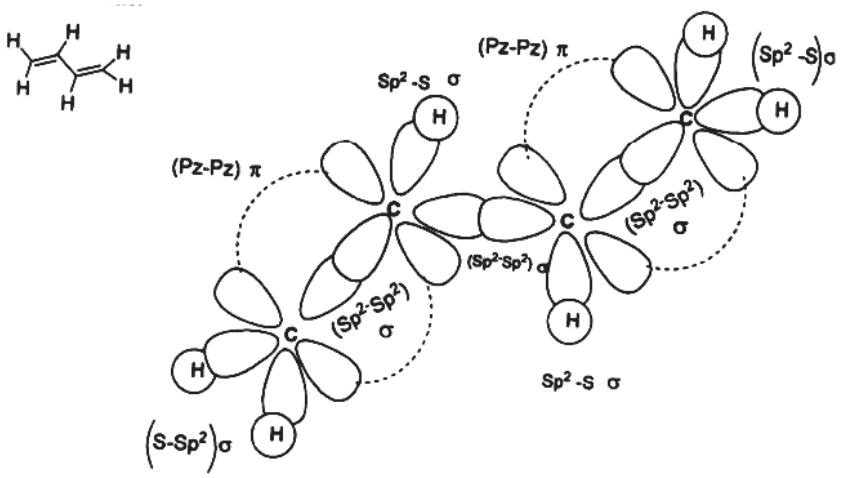




**vi) Allene, $CH_2=C=CH_2$** **orbital picture**



**vii) *s*-trans-1,3-butadiene** **orbital picture**




## 1.11 Electronic displacements

Electronic displacement refers to the movement or shifting of electrons within a molecule due to the influence of electronegative atoms, conjugation, or external factors like electric fields. These displacements play a crucial role in determining reactivity, stability, and molecular properties.

A reaction may occur or may not occur that depends upon the electron density at the site of reaction in the substrates. The factors which influence the electron density are

a) Inductive effect

b) Mesomeric effect or resonance

c) Bond polarisation and polarizability

d) Electromeric effect

e) Steric effect

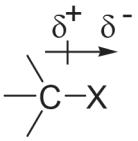
f) Steric inhibition of resonance

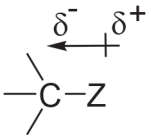
### 1.11.1 Inductive effect:

An inductive effect is an electronic effect due to the polarisation of ? bonds within a

molecule or ion. This is typically due to an electronegatvity difference between the atoms at either end of the bond.

It involves "σ" electrons. In a covalent bond between two different atoms, the electrons are not equally shared. The electrons are attracted towards the more electronegative atom. This effect is shown by drawing an arrow above the line (or on the line) representing the covalent bond.




Electron density is greater near "X" than "C" Electron density is greater near "C" than "Z" Negative inductive effect (-I) Positive inductive effect (+I)

**-I groups:** F, Br, Cl, $NO_2$, OH, OR (R = alkyl or aryl), SH, SR, $NH_2$, $NR_2$, CN, COOH, CHO, COR etc

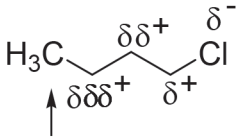
More electronegative group exhibits stronger -I effect.

**+I groups:** Alkyl, aryl, metals (Li, Mg etc)

More electropositive atom or group exhibits stronger +I effect.

**Notes: C-H** bond assumed has zero 'I' effect. Inductive effect rapidly diminishes as the chain length of atoms increases.

e.g.




Experiences negligible –I effect

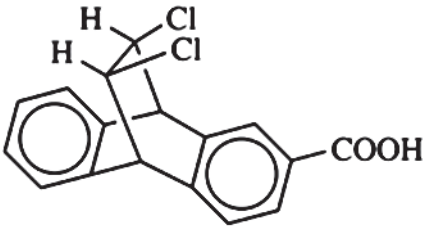
Experiences negligible -I effect

The overall polarity of a molecule by the individual bond polarities are measured by the dipole moment (μ). The higher the dipole moment results the more polar compound.

**Field effects:** It refers to an analogous unequal distribution of electrons operating through space (or through solvent).

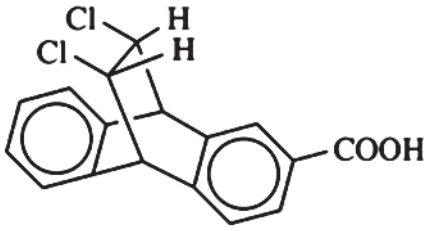
In most cases, inductive and field effects operate together and difficult to separate them. The following system is designed to show only the field effects.

The field effect depends on the geometry of the molecule but the inductive effect depends only on the nature of chemical bonds.




**1**

pKa 6.07 (less acidic)




**2**

pKa 5.67(more acidic)

### 1.11.2 Mesomeric effect (Resonance effect)

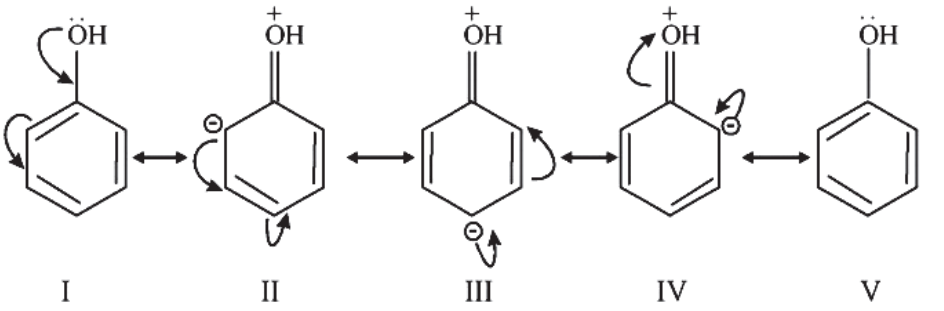
The mesomeric effect (or resonance effect) is the movement of π electrons toward or away from a substituent group.

It is only the electrons not the nuclei that move in the resonance form. Curly arrows are used to represent the movement of 'π' or non bonding electrons to give the different resonating structures and double headed arrow is used to show their relationship.

**+R or +M effect:**

If the π electrons move away from the group and towards the rest of the molecule, the effect is called a +M effect.

e.g. -OH group in benzene ring

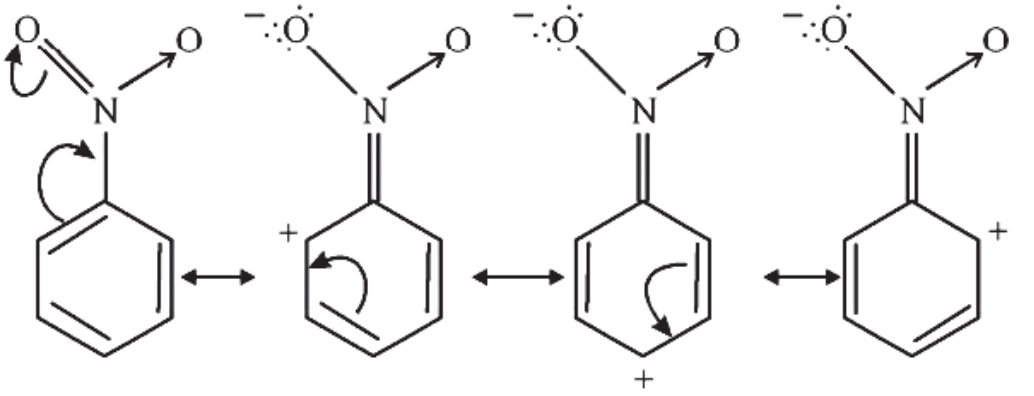



Other +M substituents are -OR, -$NH_2$-OCOR, -$NR_2$, and -NHCOR.

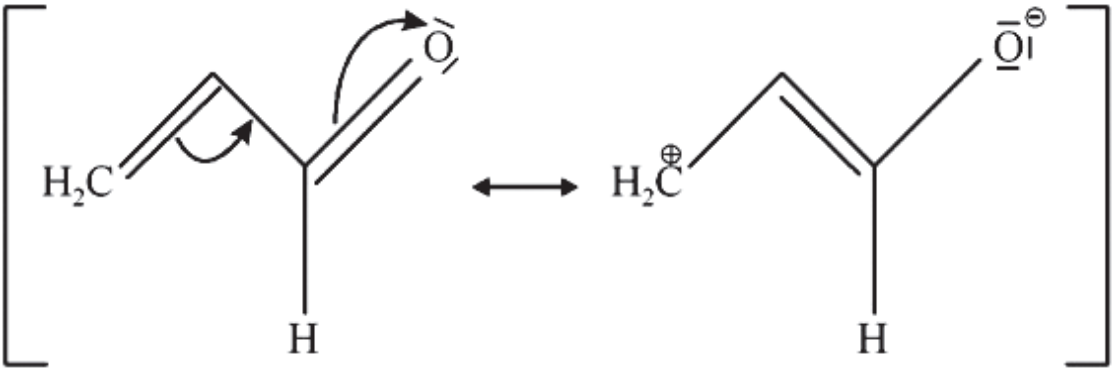
**-R or -M effect:**

If the $\pi$ electrons move away from the rest of the molecule and towards the group, the effect is called a +M effect

e.g. -$NO_2$ group in benzene ring




Carbonyl group attached to $\alpha,\beta$ - unsaturated double bond



Other - M substituents are are –COR, and CN

**Note:** -I is always greater than +R effect only for halogens. In other cases R effect always greater than I effect.

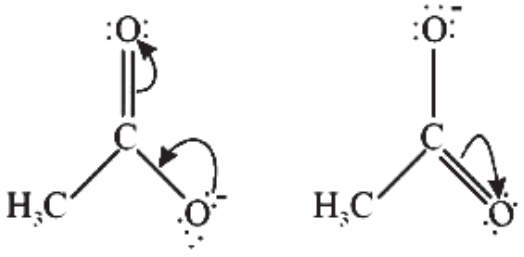
**Rules of Resonance:**

i) All the atoms in the resonating structure must have in the same location in space.

ii) No structure with pentavalent of 'C' and divalent 'H' atom.

iii) All the structure must have same number of paired electrons

iv) Resonance stabilization to be greater when there are at least two equivalent structure of lowest energy (identical canonical form).

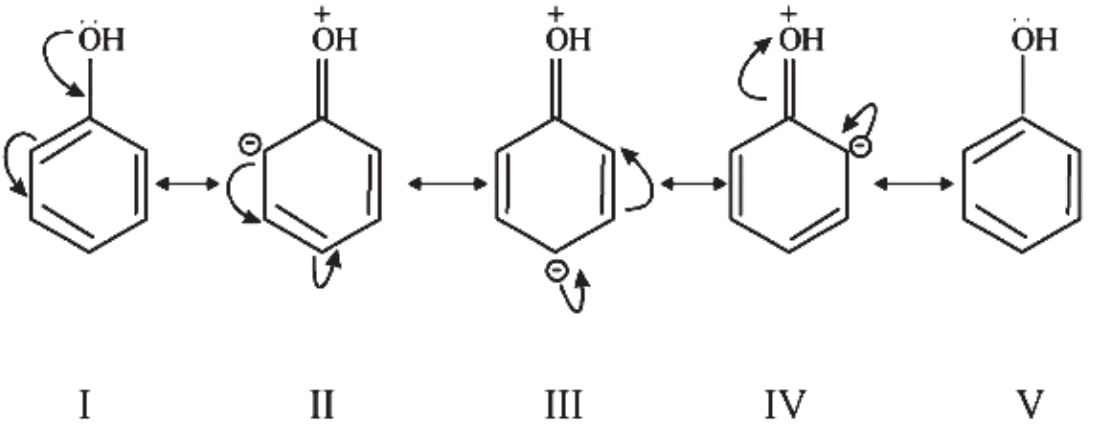


I II

Identical canonical form (I and II)

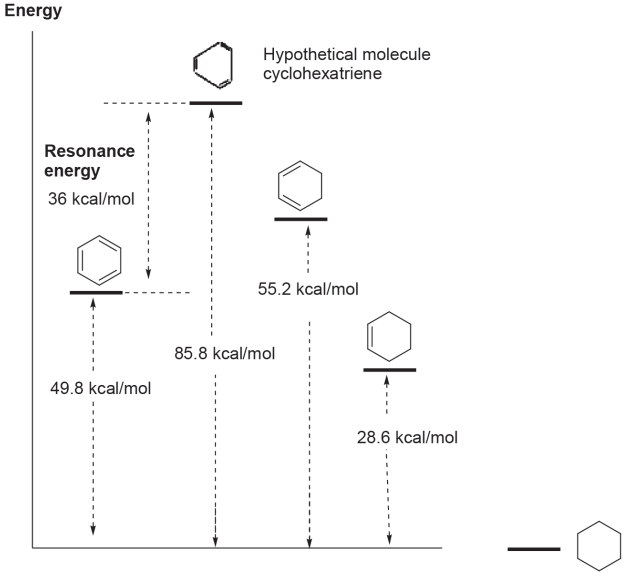
v) Resonance stabilization increases with increasing number of resonating structures.

vi) Resonance structure involves charge separation (e.g. II, III or IV) are less stable than non polar structure (I and V).




vii) Planarity is required for maximum overlapping in a conjugated system.

**Resonance energy:** The *resonance energy* of a compound is a measure of the *extra stability* of the conjugated system compared to the corresponding number of isolated double bonds. This can be calculated from experimental measurements.



The above diagram shows the experimental heats of hydrogenation, $\Delta H_h$, for three molecules, benzene, 1,3-cyclohexadiene and cyclohexene. These are related in that under appropriate conditions that can all be reduced to the same product, cyclohexane.

The $\Delta H_h$ for "cyclohexatriene", a hypothetical molecule in which the double bonds are assumed to be isolated from each other, is calculated to be 3 times the value for cyclohexene. This value reflects the energy we could expect to be released from 3 isolated C=C.

By comparing this value with the experimental value for benzene, we can conclude that benzene is 152 kJ or 36 kcal / mol more stable than the hypothetical system. This is the resonance energy for benzene.

**** More the resonance energy, greater is the stabilization. It is calculated from heat of hydrogenation data.**

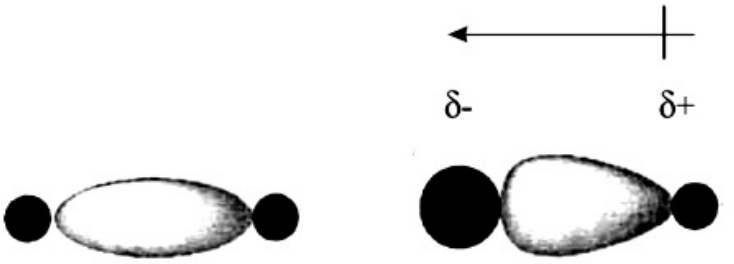
### 1.11.3 Bond polarisation and polarizability

When two identical atoms are connected by a covalent bond, and each atom has the same atoms or groups attached (such as $H_3C\text{-}CH_3$ in ethane), those atoms have identical electronegativities.

This type of covalent bond is non-polarized, and the black dots represent the atoms of the covalent bond. e.g. H-H

If a bond is formed between two atoms that have different electronegativities, the electron density is not equally distributed between the nuclei but is distorted towards the more electronegative atom.

Such a bond is said to be **polarized**; a polarized covalent bond. e.g. H-Cl




Non-polarized bond (H-H) Polarized bond(H-Cl)

**Polarizability** is a measure of how easily an electron cloud is distorted by an external electric field. Typically the electron cloud will belong to an atom or molecule or ion. The electric field could be caused, for example, by an electrode or a nearby cation or anion.

If an electron cloud is easy to distort, we say that the species it belongs to is polarizable.

Polarizability, which is represented by the Greek letter alpha, ?, is experimentally measured as the ratio of **induced dipole moment** p to the electric field E that induces it:

$$\sigma = p/E$$

The units of $\alpha$ are $Cm^2 V^{-1}$.

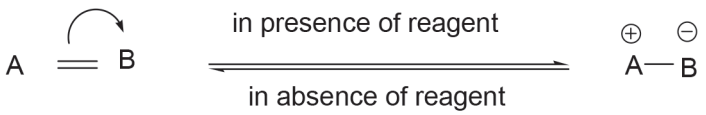
**Example:** Large, negatively charged ions, such as $I^-$ and $Br^-$, are highly polarizable. Small ions with high positive charge, such as $Mg^{2+}$ and $Al^{3+}$ have low polarizability, but they have a high ability to polarize polarizable species, such as $I^-$ and $Br^-$.

**Note:**

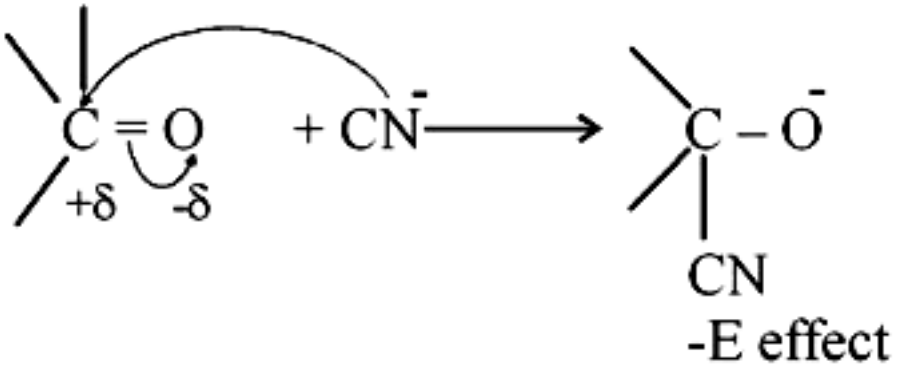
- Bond polarity is a fixed property of the molecule that doesn't depend on the external field. But, polarisability refers to the degree to which the electron clouds in a molecule or atom can be influenced by an external electric field.
- Xenon (Xe) atoms are fairly polarizable compared to helium atoms (He) as their electron cloud is more spread out and less tightly bound. Water is very polar but a lot less polarizable than hexane which is non-polar.
- The overall polarity of a molecule by the individual bond polarities are measured by the dipole moment (μ). The higher the dipole moment results the more polar compound.

### 1.11.4 Electromeric effect

Electromeric effect (denoted as E) may be defined as the complete transfer of shared pair of $\pi$ electrons of multiple bonds to one of the atoms in presence of an attacking reagent.

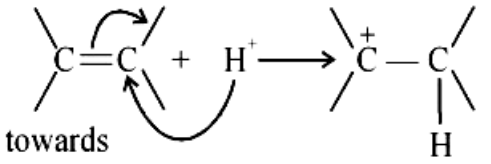



This is a temporary effect because the molecule gains its original electronic nature upon removal of the reagent and takes place between two atoms joined by a multiple bond (double or triple bond).



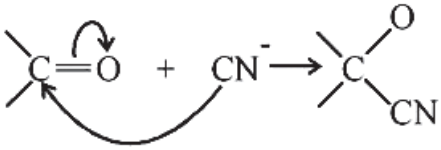

The electromeric shift of electrons takes place only at the moment of reaction. Like I effect it is also classified as +E and -E.

Positive electromeric effect (+E)




Transfer of electrons takes place the attacking reagent

Negative electromeric effect (–E):

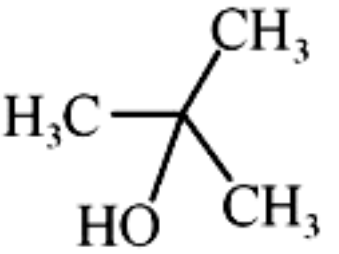



Transfer of electrons takes place away from the attacking reagent

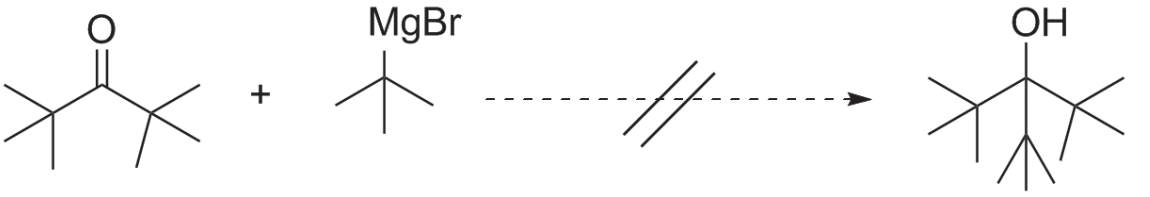
### 1.11.5 Steric Effect:

In general, the steric effect arises from the fact that the atoms composing molecules occupy some degree of space, and when atoms come too close together there is a rise in the energy of the molecule due to the atoms being forced to occupy the same physical space. This increase in energy as atoms are crowded together is called steric repulsion or *steric hindrance*.

- Dramatic effect on the observed or preferred shape of a molecule and its chemical reactivity.
- The three bulky methyl groups in tert-butanol make this molecule so sterically crowded. Both the central carbon atom and the –OH group are called as 'sterically shielded.'



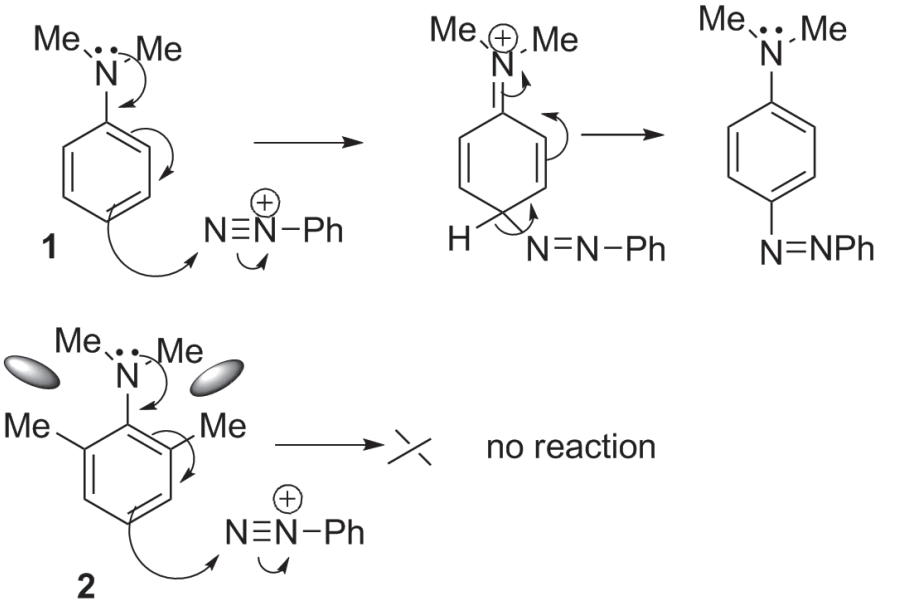

- An example would be a reaction called a Grignard addition, which occurs between a ketone and a magnesium-bromide reagent (called the Grignard reagent).




The Grignard reagent does not work due to steric effects

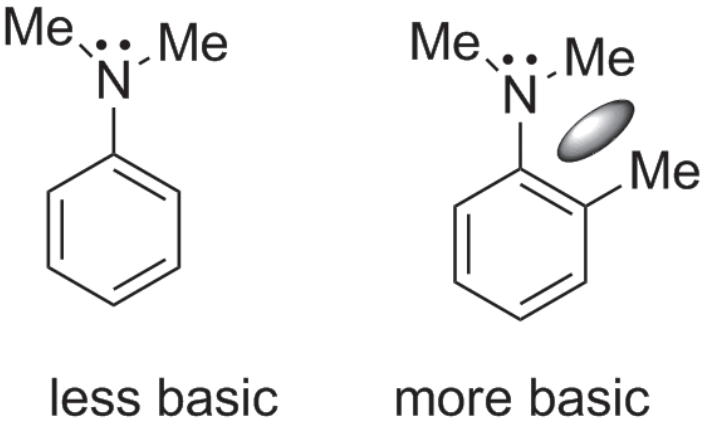
### 1.11.6 Steric inhibition of resonance

The effective delocalization of electrons via $\pi$ orbitals can only take place when the 'P' or $\pi$ orbitals involved in the delocalization becomes parallel or nearly so. If this is prevented the effective overlapping can't take place and delocalization becomes prevented. This effect is known as steric effect or steric inhibition of resonance.




N,N-dimethyl aniline (1) successfully coupled with $PhN_2^+$ although its 2, 6-Dimethyl derivative (2) does not couple. This can be explained in terms of steric inhibition of resonance. The two ortho-methyl groups in 2 are interfering sterically with two *N*-methyl groups and thus they prevents them lying in the same plane. So, effective overlapping between lone pair of electrons of 'N' and $\pi$ system is inhibited and transfer of electronic charge does not take place.

Basicity of some amines is increased by steric inhibition of resonance which decreases the tendency of the lone pair of N to be delocalized in the benzene ring




## 1.12 Summary

- Bonding refers to the forces holding atoms together, while structure describes their arrangement. These determine a substance's physical and chemical properties.
- Substances can have giant structures (continuous networks of atoms/ions) or molecular structures (discrete groups held by intermolecular forces).
- The type of particles, nature of bonding, and arrangement of particles influence conductivity, solubility, melting points, and strength.
- Valence Bond Theory (VBT) explains covalent bonding through orbital overlap and electron pairing, leading to stable molecules.
- Mainly two types of Covalent Bonds, Sigma ( $\sigma$ ) bonds result from head-on overlap (stronger), while Pi ( $\pi$ ) bonds arise from sidewise overlap (weaker).
- Limitations of VBT is that it Cannot fully explain molecular shapes, electron delocalization (resonance), or bond strength variations in molecules.
- Hybridization is the mixing of atomic orbitals to form new hybrid orbitals that explain molecular geometry and bonding.
- Types of Hybridization:

  $sp^3$ (tetrahedral, 109.5°) - seen in methane ($CH_2$).

$sp^2$ (trigonal planar, 120°) - seen in ethene ($C_2H_4$).

sp (linear, 180°) - seen in ethyne ($C_2H_2$).

- The actual structure of some molecules (e.g., benzene) is a hybrid of multiple resonance structures, increasing stability.
- Hyperconjugation is the delocalization of ?-electrons stabilizes carbocations and affects alkene stability.
- Formal Charge (FC) is a way to assign charge to atoms in molecules based on electron distribution.
- Double Bond Equivalent (DBE) indicates degree of unsaturation in a molecule, calculated based on the number of C, H, and N atoms.
- Molecular Orbital Theory (MOT) explains bonding in terms of molecular orbitals rather than atomic orbitals.
- Electronic Displacement Effects includes inductive effect, mesomeric (resonance) effect, electromeric effect, and steric effects, influencing reactivity and stability.
- Inductive Effect is the polarization of $\sigma$-bonds due to electronegativity differences, affecting molecular polarity.

## 1.13 Exercise

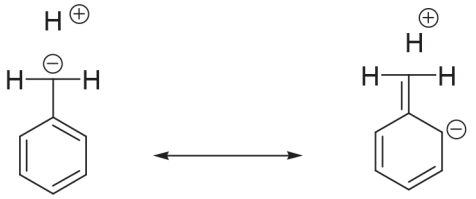
1. Based on the overlapping of orbitals, how many types of covalent bonds are formed and what are they?

**Answer:** Based on the overlapping of orbitals, two types of covalent bonds are formed. These are known as sigma ($\sigma$) and pi ($\pi$) bonds.

- Sigma bonds are formed by the end-to-end overlap of atomic orbitals along the inter-nuclear axis known as a head-on or axial overlap. End-on overlapping is of three types, they are s-s overlapping, s-p overlapping and p-p overlapping.
- A pi bond is formed when atomic orbitals overlap in a specific way that their axes remain parallel to each other and perpendicular to the internuclear axis.

2. Explain the reactivity order towards electrophilic substitution reaction of the following compounds.


**Answer:** Toluene is maximum reactive due to maximum hyperconjugation which develop maximum negative charge on the benzene ring and accelerates attack on benzene nucleus.




For t-butyl benzene there is no ?-C-H bond w.r.t. carbocation. Hence, there is no hyperconjugation and becomes less stable.

3. Calculate formal charge of the following species

i) $BH_4$ ii) $:CH_3$ iii) $CH_3$

**Answer:**

i) The number of valence electrons for boron (B) is 3; the number of non-bonded electrons is zero and the number of bonds around boron is 4.

So formal charge = 3 - (0 + 4) = 3 - 4 = -1

The formal charge of B in $BH_4$ is negative 1.

ii) The number of valence electrons for carbon is 4; the number of non-bonded electrons is two (it has a lone pair) and the number of bonds around carbon is 3.

So formal charge = 4 - (2 +3) = 4 - 5 = -1

The formal charge of C in $:CH_3$ is negative 1.

iii) The number of valence electrons for carbon is 4; the number of non-bonded electrons is zero and the number of bonds around carbon is 3.

So formal charge = 4 - (0 +3) = 4 - 3 = +1

The formal charge of C in $CH_3$ is +1.

4. Calculate their DBE.

1) $C_8H_{10}$ 2) $C^6H_{12}O_6$ 3) $C_3H_4C^{l2}$ 4) $C_8H_7N$ 5) $C_{13}H_{10}$ 6) $C_4H_9NO$

Answer: 1) DBE = C-(H/2)+(N/2)+1 = 8-(10/2)+(0/2)+1 = 4

2)DBE = C-(H/2)+(N/2)+1 = 6-(12/2)+(0/2)+1 = 1

3)DBE = C-(H/2)+(N/2)+1 = 3-(6/2)+(0/2)+1 = 1

4)DBE = C-(H/2)+(N/2)+1 = 8-(7/2)+(1/2)+1 = 6

5)DBE = C-(H/2)+(N/2)+1 = 13-(10/2)+(0/2)+1 = 9

6)DBE = C-(H/2)+(N/2)+1 = 4-(9/2)+(1/2)+1 = 1

5. Calculate the resonance energy of $C_6H_6$ from the given data.

Heat of hydrogenation of cyclohexene is -28.6 Kcal/mole and 1,3-cyclohexadiene is -55.6 kcal/mole. Experimental value of heat of hydrogenation of $C_6H_6$ is -49.8 Kcal/mole.

**Answer:** Therefore, heat of hydrogenation of $C_6H_6$ should be

$-28.6 \times 3 = -85.8$ Kcal/mole

But experimental value is -49.8 Kcal/mole

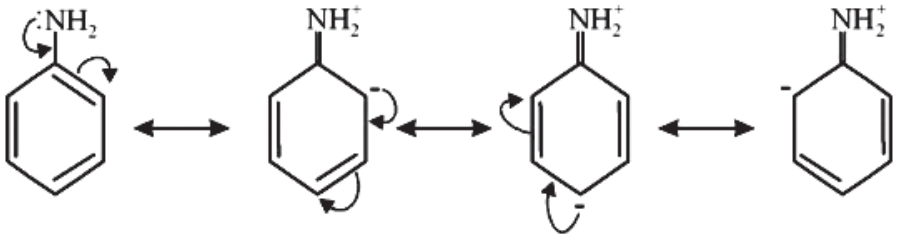
Thus, R.E of $C_6H_6$ = [-85.8- (-49.8)] Kcal/mole

= -36 Kcal/mole (negative value indicates the stabilization energy)

6. Draw the possible resonating structures of aniline.

See 1.2.4

**Hint:**



# Unit 2 ❐ Molecular Orbital Theory

## Structure



## 2.0 Objectives

By the end of the unit learners will be able to

- Explain the basic principles and importance of Molecular Orbital Theory in chemical bonding.
- Describe the formation of bonding and antibonding molecular orbitals.
- Construct molecular orbital diagrams and determine bond order.
- Predict the magnetic properties and stability of molecules using MO theory.
- Compare Molecular Orbital Theory with Valence Bond Theory.

## 2.1 Introduction

Molecular orbital (MO) theory is a method for describing the electronic structure of molecules. Molecular Orbital Theory is primarily used to explain the bonding in molecules that cannot be explained by Valence Bond Theory (VBT). These are molecules that generally involve some form of resonance. Resonance implies that a bond is neither single nor double but some hybrid of the two. Valence bond theory only describes the bonding of single or

double or triple bonds. It does not provide an explanation for resonance bonding. Molecular orbital theory does describe resonance.

## 2.2 The Rules of Molecular Orbital Theory

**First principle:** The number of molecular orbitals produced is always equal to the number of atomic orbitals brought by the atoms that have combined.

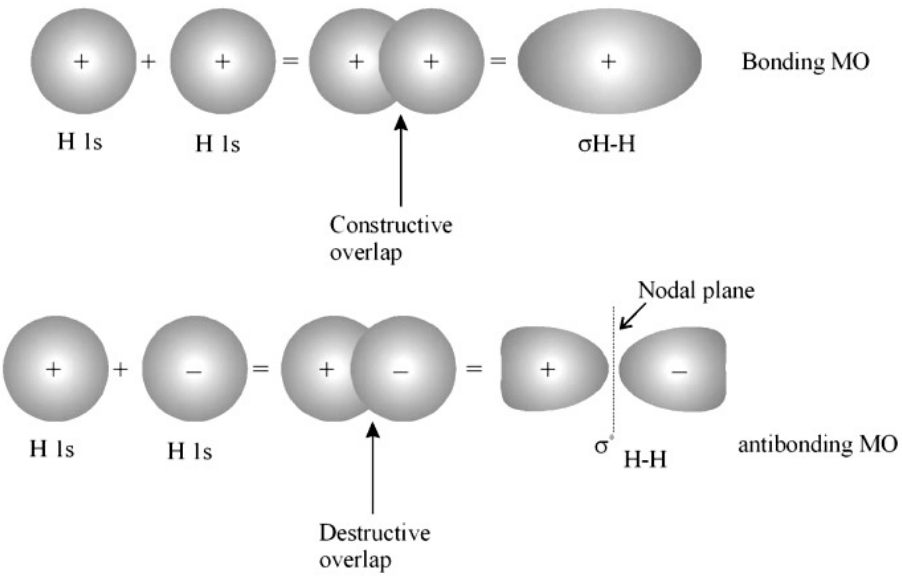
**Second principle:** Bonding molecular orbitals are lower in energy that the parent orbitals, and the antibonding orbitals are higher in energy.

**Third principle:** Electrons of the molecule are assigned to orbitals from lowest to successively higher energy.

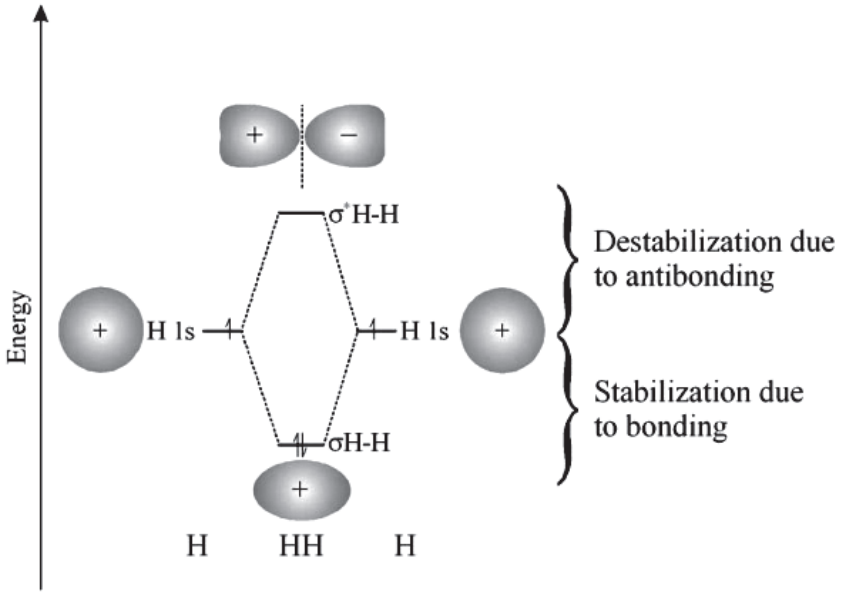
**Fourth principle:** Atomic orbitals combine to form molecular orbitals most effectively when the atomic orbitals are of similar energy.

**Illustration of MO Theory with example:**

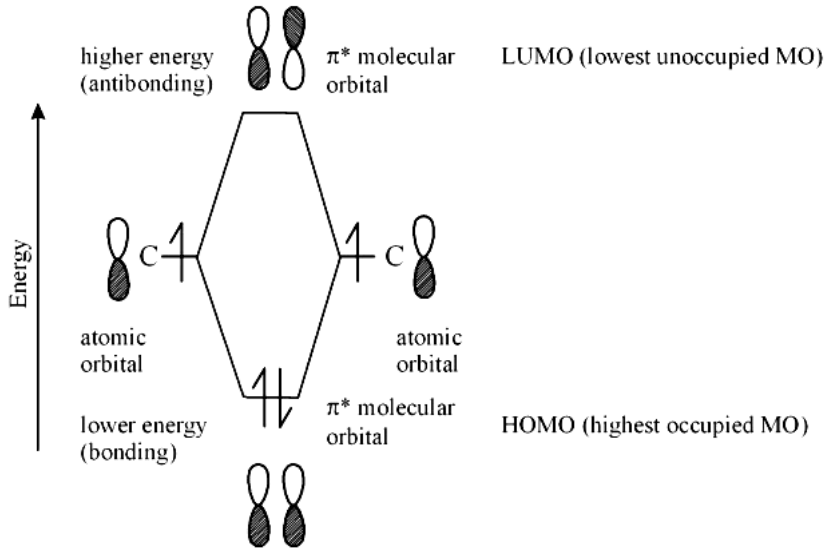
Let us take an example of Hydrogen (H2) molecule (principle 1)



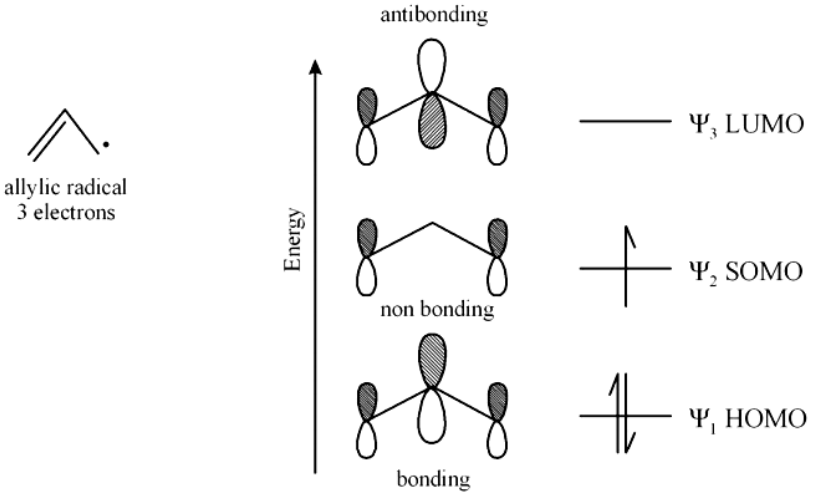
- $H_2$ molecule (principle 2 & 3)




- Energy diagram for two $\pi$ MO in a typical $\pi$-bond: e.g $CH_2 = CH_2$ molecule

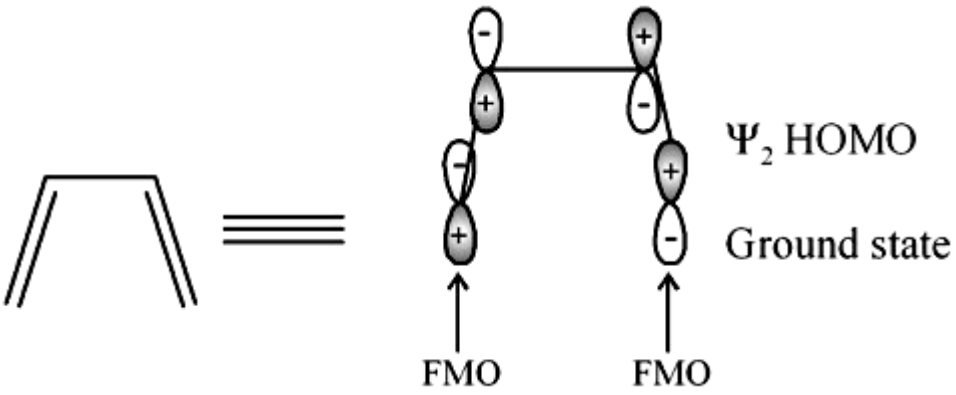


- Energy diagram for allylic radical (bonding, nonbonding and antibonding ? MOs):




## 2.3 Frontier Orbital Theory (FMO)

A powerful practical model for describing chemical reactivity is the frontier molecular orbital(FMO) theory, developed by Kenichi Fukui in 1950's. The important aspect of the frontier electron theory is the focus on the highest occupied and lowest unoccupied molecular orbitals (HOMO and LUMO). This will be discussed later in pericyclic reaction.



## 2.4 Sketch and energy levels of π MOs:

### i) Acylic p orbital system:

**Ethylene system** ( $CH_2$=$CH_2$):

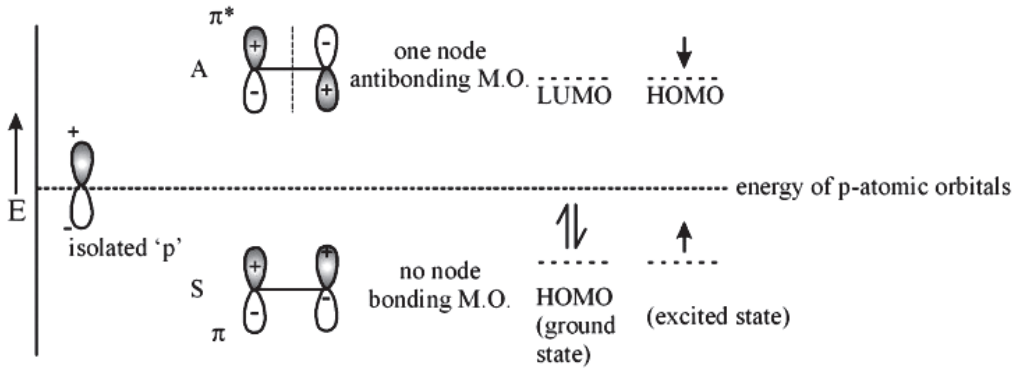



**Fig-1:** Energy levels of π MOs of C=C system

The ground state condition is thermal condition and excited sate condition is photochemical condition. There is no LUMO in excited state condition of ethylene system. (A) & (S) refers to anti-symmetric and symmetric respectively.

**1,3–butadiene** ($CH_2$ = CH – CH = $CH_2$) :

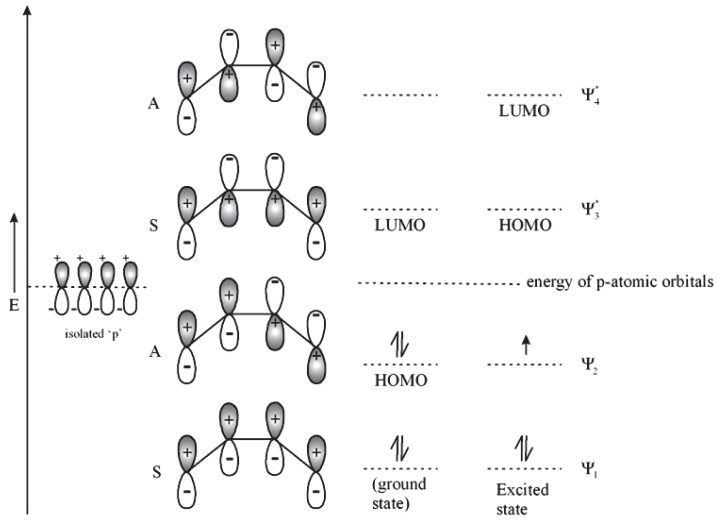
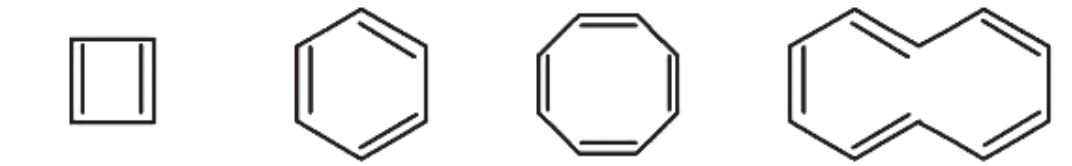



**Fig. 2:** Energy levels of π MOs of conjugated diene system

**ii) Cyclic p orbital system:**

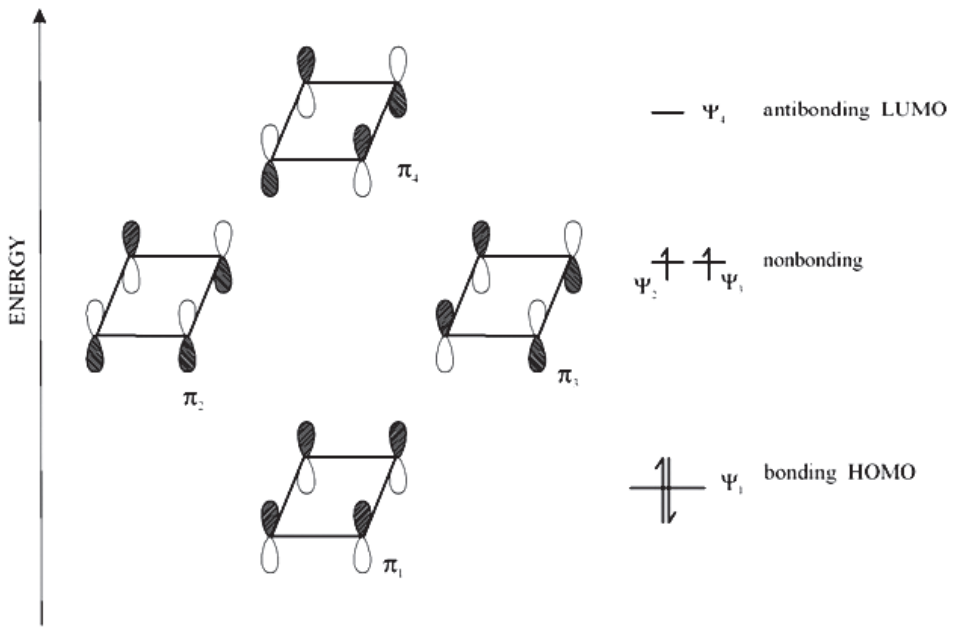
**a. Neutral system**

Annulenes are hydrocarbons with alternating single and double bonds. Benzene is six - membered annulene, so it can be named as [6] annulene.

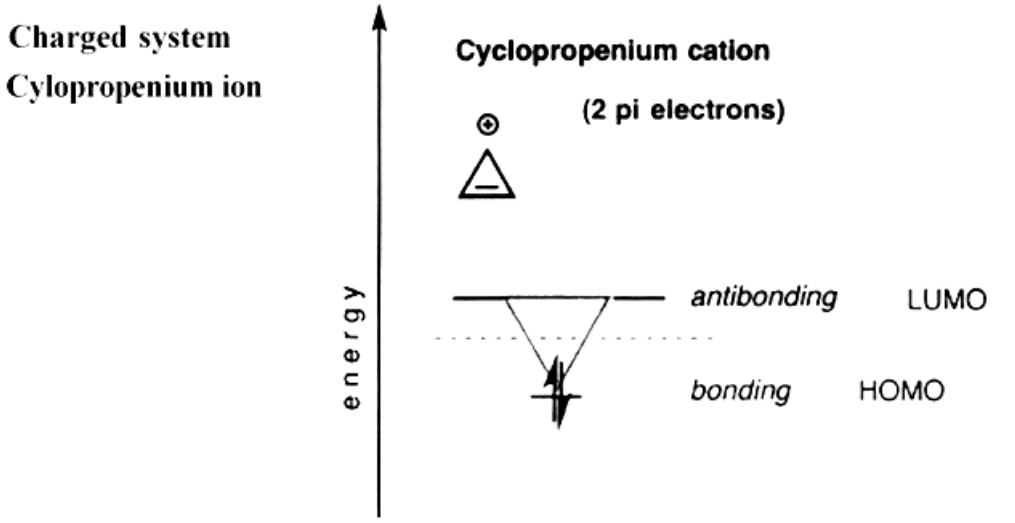


cyclobutadiene [4] annulene | benzene [6] annulene | cyclooctatetraene [8] annulene | cycldecapentaene [10] annulene

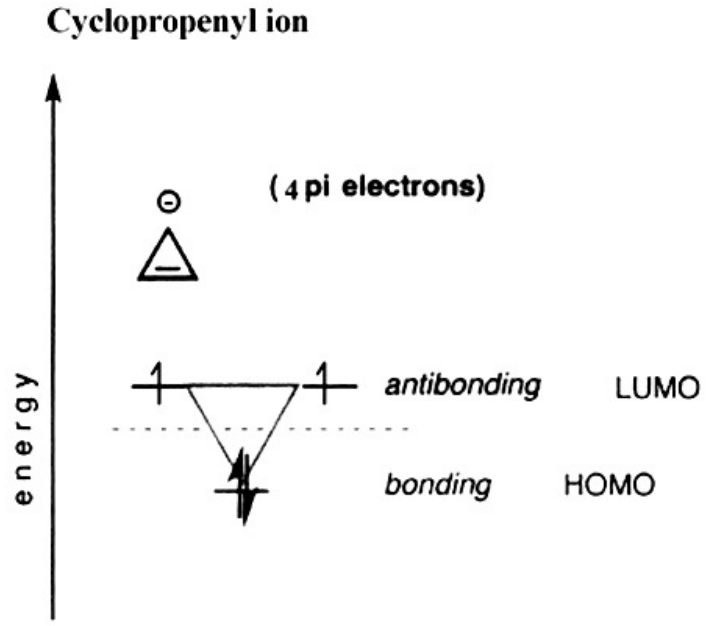
π-M.O.s of [4]annulene:




Energy levels of π MOs of [4] annulene

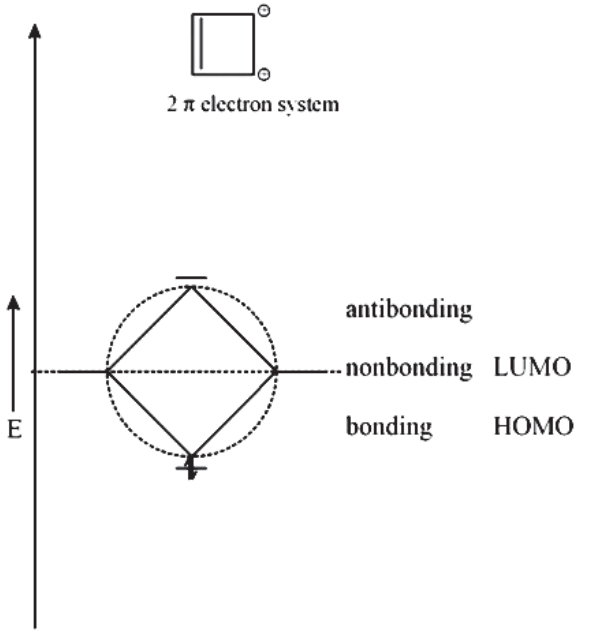



Energy levels of π MOs of charged 3-membered ring system



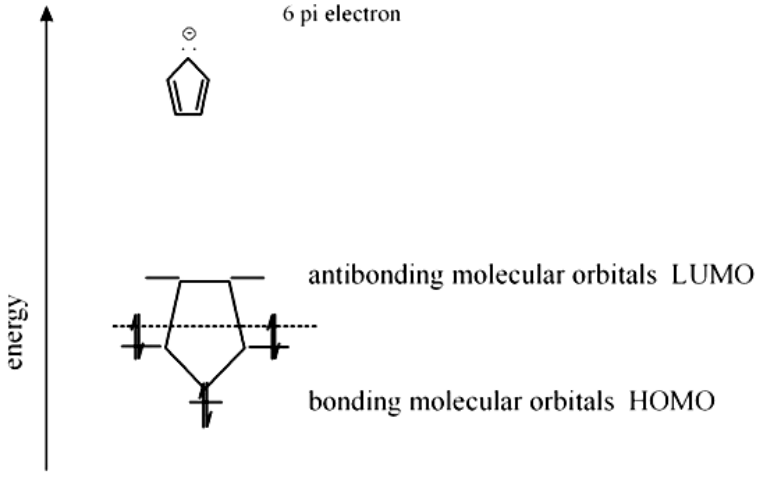

Energy levels of π MOs of charged 3-membered ring system

**Cyclobutenyl dication**




Energy levels of π MOs of charged 4-membered ring system

**Cyclopentadienyl anion**




Energy levels of π MOs of charged 5-membered ring system (anion)

## 2.5 Frost Circles or diagram

We've spent a lot of time in above "building up" and drawing out the molecular orbitals for various conjugated dienes. Now, we'll learn an extremely useful shortcut method that will help us draw the energy levels of cyclic pi-systems very quickly.

This shortcut method is called "Frost Circles", or, sometimes, the "Polygon method".

In 1953, Frost published an article describing this method for drawing out the energy levels in cyclic systems, with a simplified version as follows.

*"A circle… is inscribed with a polygon with one vertex pointing down; the vertices represent energy levels with the appropriate energies".*

Vertices below the halfway mark of the circle are considered bonding orbitals, and vertices above the halfway mark are considered antibonding orbitals. If vertices are exactly in the middle (as they are for 4- and 8- membered rings) they represent non-bonding orbitals.

This idea is presented in the diagram below for 3, 4, 5, 6, 7, and 8-membered rings (Fig-14):

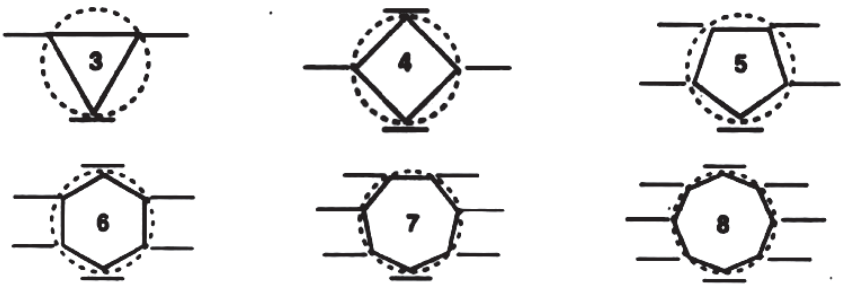
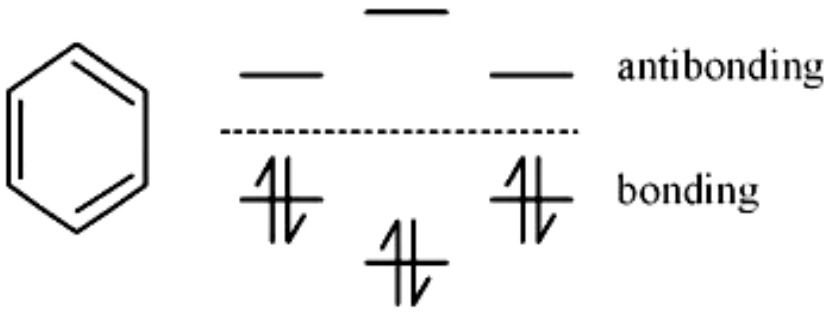


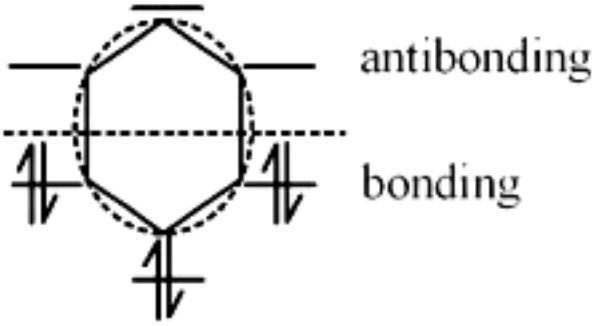

Fig 14.

**Frost circle:** "A circle is inscribed with a polygon with one vertex pointing down; the vertices represent energy levels with the appropriate energies"

**First:** Recall that we saw the energy levels of the molecular orbitals of benzene in Fig: 7.




**Useful observation:** these energy levels can be superimposed on a hexagon with the vertex pointing down. Like this. From Frost diagram:



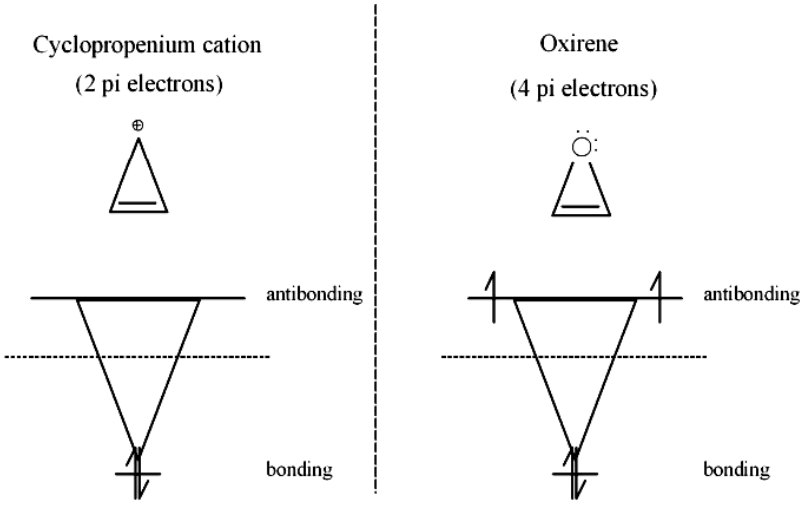

To draw the molecular orbitals of a cyclic pi system, all we have to do is draw the appropriate polygon, vertex-down, and then fill it up with electrons. Frost diagram of various ring systems are given below.

**3-Membered Rings**

There are two important configurations of energy levels for 3-membered cyclic pi systems, depending on the number of pi electrons.

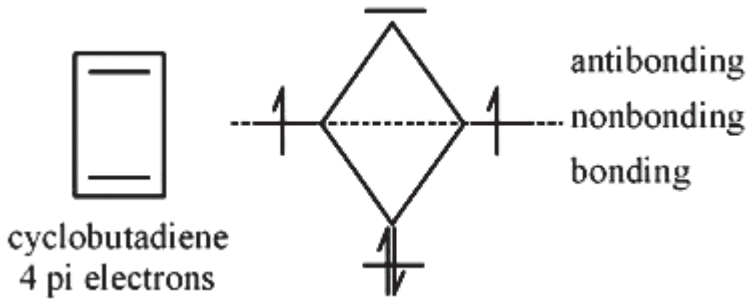
One example is the cyclopropenium cation, which is 2 pi electrons system.

On the other hand, oxirene has 4 pi electrons.




## 4-Membered Rings

**Cyclobutadiene:** The two highest energy levels are each singly occupied (non-bonding) which helps to explain why cyclobutadiene is so spectacularly unstable.

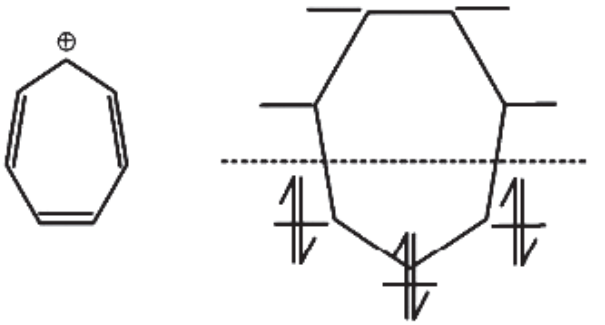



## 7-Membered Rings

Cyclic 7-membered pi systems with 6 pi electrons are predicted to be aromatic.

For a ring entirely comprised of carbon atoms, this corresponds to the **cycloheptatrienyl cation** (sometimes known as the "tropylium ion").

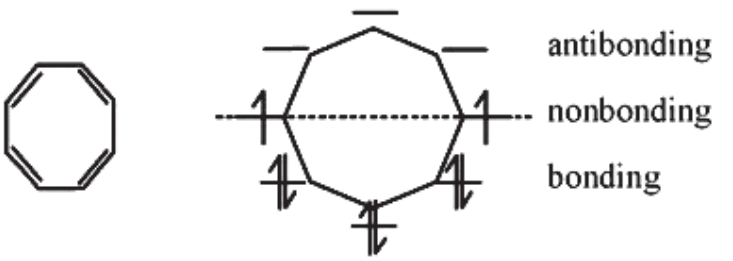
**Cycloheptatrienyl cation (6 pi electrons)**



8-Membered Rings

With 8 pi electrons, cyclooctatetraene is predicted to be antiaromatic, and its molecular orbitals are predicted to look like this:

**Cyclooctatetraene (8 pi electrons)**




## 2.6 Huckel's Rule (4n+2 rule)

In 1931, Erich Hückel postulated that monocyclic, (single ring) planar, delocalized ? electron system having (4*n* + 2) $\pi$ electrons where n equalled any whole number (n = 0, 1, 2, 3,…etc) should be aromatic

For example, the benzene molecule, which has 3 $\pi$ bonds or 6 $\pi$ electrons, is **aromatic.**

- Number of $\pi$ electrons = $4n + 2$
- $6 = 4n + 2$
- n = 1

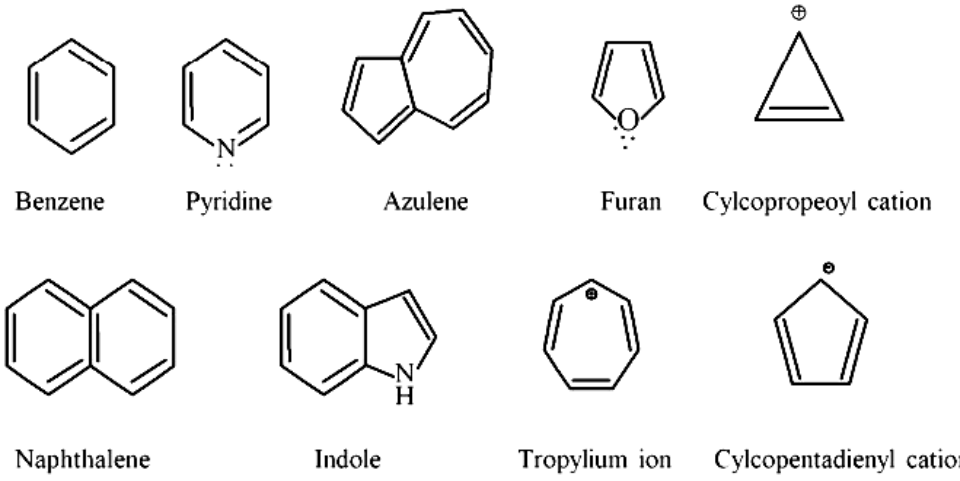
Benzene

However, 1, 3, 5, 7 cyclooctatetraene, which has 4 $\pi$ bonds or 8 $\pi$ electrons, is not only nonaromatic but is actually considered **antiaromatic** because it is even less stable than the open chain hexatriene.

- Number of $\pi$ electrons = 4 n + 2
- $8 = 4n + 2$
- $n = 1.5$

Cyclooctatetraene

Some aromatic molecules are shown below:




Benzene Pyridine Azulene Furan Cylcopropeoyl cation

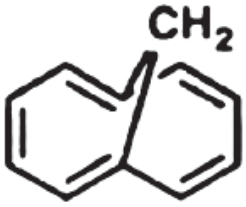
Naphthalene Indole Tropylium ion Cylcopentadienyl cation

**Exception of Huckel's Rule:** The important condition for aromaticity is that the molecule must be flat (planar).One example in this category is the molecule known as [10]-annulene. In the trans, cis, trans, cis, cis isomer, the molecule is cyclic, conjugated, and has 10 pi electrons, but the two marked hydrogens bump into one another when attempting to adopt a flat conformation. The molecule is prevented from adopting planarity due to this punitive Van Der Waals strain , and is therefore not aromatic.

Interestingly, if the hydrogens are removed and replaced with a bridging CH2 group, the strain is relieved and the pi bonds can adopt a planar conformation and becomes aromatic in character.


[10]annulene

not aromatic




aromatic

- Although cyclic, conjugated, 10 pi electrons, it is not flat due to intra H-H repulsions.
- Replacing the intra H-H with bonds to a bridging carbon allows all C=C to be in the same plane

**Antiaromatic compounds**

Cyclic, planar and conjugated molecule having 4n? electrons (n = 1, 2, 3,…etc) should be antiaromatic. Unlike aromatic compounds, antiaromatic compounds are highly unstable and highly reactive.

**Example-1:**

- 4 $\pi$ electrons
- Conjugated
- Planar

Cyclobutadiene

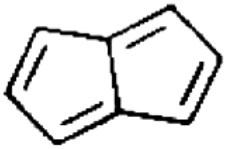
**Example-2:**

The cyclopentadienyl cation is incredibly unstable and difficult to make.

**Example-3:**

The molecule below is called "Pentalene". It has been synthesized, but is only stable below -100 °C. Above this temperature it combines with another molecule of itself.

- 8 $\pi$ electrons
- Conjugated
- Planar



**Pentalene**

Antiaromatic

**Nonaromatic compounds**

The $4n\pi$ electrons (n = 1, 2, 3,…etc) system where continuous overlapping of ring of p orbitals are inhibited, termed as non aromatic compound.

Cyclooctatetraene is anti-aromatic only if it is flat. However, the relatively "floppy" structure of cyclooctatetraene allows for some flexibility. The bonds can rotate away from flatness such that the molecule adopts a "tub-like" shape; thereby avoiding the instability arises from "antiaromaticity".

Antiaromatic

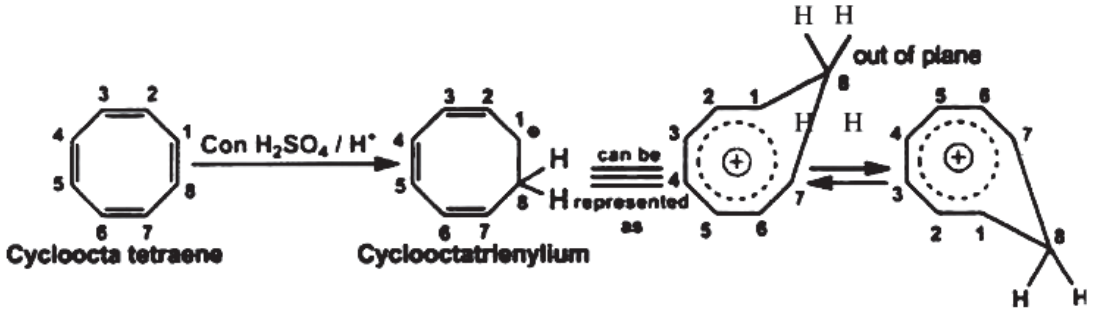
**Tub-shaped, non-aromatic**

Nonaromatic

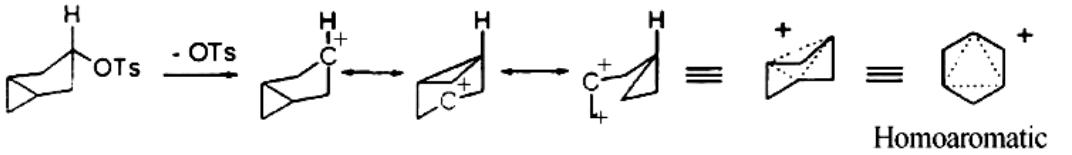
**Homoaromatic compounds**

A homoaromatic compound is defined as a compound that contains one or more sp3 hybridized carbon atom in a conjugated cycle.

**Example1:** Pronounced homoaromaticity is not normally associated with neutral molecules, but mainly with species bearing an electrical charge, e.g., the "homotropylium" cation, C8H9+,




**Example 2:** 3-bicyclo[3.1.0]hexyl cation




## 2.7 Elementary idea about α and β

The Hückel method or Hückel molecular orbital theory, proposed by Erich Hückel in 1930, is a very simple linear combination of atomic orbitals molecular orbitals method for the determination of energies of molecular orbitals of π electrons in π-delocalized molecules, such as ethylene, benzene, butadiene etc.

- This method expresses the molecular orbital energies in terms of two parameters, called α, the energy of an electron in a 2p orbital, and β, the interaction energy between two 2p orbitals (the extent to which an electron is stabilized by allowing it to delocalize between two orbitals).
- The usual sign convention is to let both α and β be negative numbers.

**Measurement of delocalization energies in terms of β for buta-1, 3-diene, cyclobutadiene, hexa-1, 3, 5-triene and benzene.**

The delocalization energy is the extra stabilization that comes from letting the electrons spread over the whole molecule.

**Buta-1, 3-diene:**

Non-delocalized 1,3-butadiene (with a 'wall' between the double bonds):

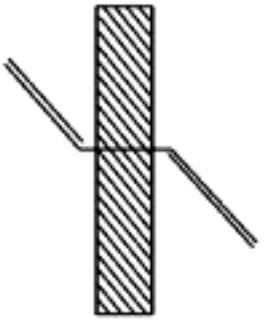


Fig. 1

To find the delocalization energy, first calculate the total p-electron energy of (real) butadiene:

**Calculation:** total 'p' electron energy of 1,3 butadiene (Fig:2)

$= 2(\alpha + 1.62\beta) + 2(\alpha + 0.62\beta)$

$= 4\alpha + 4.4\beta$

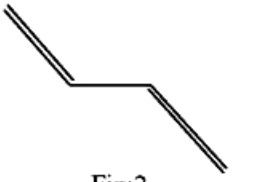


Fig:2

Then calculate the energy of the same number of p electrons in isolated (non-delocalized, Fig: 1) bonds.

p electron energy of an equivalent number of isolated double bonds

= 2(p electron energy of ethene)

$= 2(2\alpha + 2\beta)$

$= 4\alpha + 4\beta$

**Therefore the delocalization energy of butadiene**

$= (4\alpha + 4.48\beta) - (4\alpha + 4\beta)$

$= 0.48\beta$

**Hexa-1,3,5-triene:**

**Calculation:** total 'p' electron energy of benzene (Fig:3)

$= 2(\alpha+2\beta) + 2(\alpha+\beta) + 2(\alpha+\beta)$

$= 6\alpha + 8\beta$

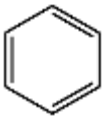


Fig: 3

p electron energy of an equivalent number of isolated double bonds in isolated (non-delocalized, Fig: 4) bonds.

$= 2(\alpha+1.8019\beta) + 2(\alpha+1.2470\beta) + 2(\alpha+0.4450\beta)$

$= 6\alpha + 6.99\beta$

Fig: 4

**Therefore the delocalization energy of hexa-1,3,5-triene**

$= (6\alpha + 8\beta) - (6\alpha + 6.99\beta)$

$= 1.01\beta$

## 2.8 Summary

- Molecular Orbital Theory (MOT) explains chemical bonding beyond Valence Bond Theory, particularly in molecules with resonance.
- In MOT, atomic orbitals combine to form molecular orbitals, which are classified as bonding or antibonding.
- The number of molecular orbitals formed equals the number of atomic orbitals combined.
- Bonding orbitals have lower energy, while antibonding orbitals have higher energy than the parent atomic orbitals.

- Molecular orbitals are filled according to the Aufbau principle, Pauli exclusion principle, and Hund's rule.
- The bond order of a molecule can be determined using molecular orbital diagrams, influencing bond strength and stability.
- Magnetic properties (paramagnetic or diamagnetic) of molecules can be predicted using molecular orbital theory.
- The Frontier Molecular Orbital (FMO) theory focuses on the HOMO (Highest Occupied Molecular Orbital) and LUMO (Lowest Unoccupied Molecular Orbital) to explain chemical reactivity.
- Huckel's Rule (4n+2 rule) determines the aromaticity of cyclic, conjugated $\pi$-electron systems.
- Frost Circles provide a quick method for determining the energy levels of cyclic $\pi$-systems.
- Anti-aromatic compounds contain 4n ?-electrons and are highly unstable.
- Non-aromatic compounds lack continuous conjugation and do not follow aromaticity rules.
- Homoaromatic compounds have interrupted conjugation but still retain aromatic character.
- The Hückel Molecular Orbital (HMO) method helps calculate $\pi$-electron energies and delocalization effects in conjugated systems.
- Delocalization energy stabilizes conjugated molecules, enhancing their chemical stability and reactivity.

## 2.9 Exercise

**1. What is the qualitative idea about molecular orbitals?**

**Answer:** Molecular orbitals (MOs) are formed by the linear combination of atomic orbitals (LCAO). They describe the distribution of electrons in a molecule. Depending on the phase relationship of atomic orbitals, bonding and antibonding molecular orbitals are formed.

**2. What are bonding and antibonding molecular orbitals ?**

**Answer:** Bonding Molecular Orbitals (BMO, $\sigma$, $\pi$): Formed by the constructive interference of atomic orbitals, leading to electron density between nuclei, which stabilizes the molecule.

Antibonding Molecular Orbitals (ABMO, $\sigma$, $\pi$):** Formed by the destructive interference of atomic orbitals, creating a node between nuclei, leading to destabilization.

**3. Define $\sigma$, $\sigma$, $\pi$, and $\pi$ molecular orbitals.**

Answer: $\sigma$ (Sigma) MO: Formed by head-on overlap of atomic orbitals, having electron density along the internuclear axis.

$\sigma$ (Sigma Antibonding) MO : * Formed by destructive interference in a head-on overlap, leading to a node.

$\pi$ (Pi) MO : Formed by the lateral overlap of p orbitals, electron density is above and below the plane of nuclei.

$\pi$ (Pi Antibonding) MO : * Formed by the destructive overlap of p orbitals, containing a nodal plane between nuclei.

**4. What are Frontier Molecular Orbitals (FMO)?**

Answer: Frontier molecular orbitals include the Highest Occupied Molecular Orbital (HOMO) and the Lowest Unoccupied Molecular Orbital (LUMO). These orbitals determine the chemical reactivity of molecules.

**5. Define HOMO, LUMO, and SOMO.**

**Answer:** HOMO (Highest Occupied Molecular Orbital): The highest-energy molecular orbital that contains electrons.

LUMO (Lowest Unoccupied Molecular Orbital): The lowest-energy molecular orbital that does not contain electrons but can accept them.

SOMO (Singly Occupied Molecular Orbital): Present in radicals, it is the molecular orbital with a single electron.

**6. How does the FMO concept help in interpreting chemical reactivity?**

**Answer:** The interaction between the HOMO of one molecule and the LUMO of another governs chemical reactions. A smaller HOMO-LUMO gap indicates higher reactivity.

**7. Sketch and describe the ? molecular orbitals of an acyclic p orbital system, butadiene.**

**Answer:** See text.

Hint: In an acyclic conjugated system (e.g., butadiene), $\pi$ MOs form by the interaction of adjacent p orbitals. The lowest energy $\pi$ MO has no nodes, and the number of nodes increases with energy.

**8. What is a Frost diagram?**

**Answer:** A Frost diagram represents the relative energy levels of molecular orbitals in cyclic conjugated systems. The vertices of a polygon inscribed in a circle represent the energy levels of $\pi$ MOs.

**9. What are $\alpha$ and $\beta$ in Hückel molecular orbital theory?**

**Answer:** $\alpha$ (Coulomb Integral): Represents the energy of an electron in an isolated p orbital.

$\beta$ (Resonance Integral): Measures the interaction between adjacent p orbitals and determines delocalization energy.

**10. How is delocalization energy measured in terms of $\beta$?**

**Answer:** Delocalization energy is the stabilization due to conjugation and is expressed in terms of $\beta$. For example: Buta-1,3-diene: $2\beta$

Cyclobutadiene: $0\beta$ (no stabilization)

Hexa-1,3,5-triene: $4\beta$

Benzene: $6\beta$

**11. State Hückel's rule for aromaticity.**

**Answer:** A cyclic, planar, conjugated system with $(4n + 2)$ $\pi$-electrons (where n = 0, 1, 2…) is aromatic.

**12. Give an example of aromatic, antiaromatic, and non-aromatic molecules.**

**Answer:** Aromatic: Benzene (6 $\pi$-electrons, follows Hückel's rule).

Antiaromatic: Cyclobutadiene (4 $\pi$-electrons, highly unstable).

Non-aromatic: Cyclooctatetraene (non-planar, does not allow ?-electron delocalization).

**13. What is homoaromaticity? Give Example.**

**Answer:** Homoaromaticity occurs when a compound retains aromaticity despite an interruption in conjugation, e.g., cyclopropyl cation.

**Multiple-Choice Questions (MCQs)**

**Q1. What is the primary condition for the formation of a molecular orbital (MO)?**

a) The atomic orbitals must have the same principal quantum number

b) The atomic orbitals must have comparable energy and proper symmetry

c) The atomic orbitals must be of different atoms

d) The atomic orbitals must be in different phases

Answer: b) The atomic orbitals must have comparable energy and proper symmetry

**Q2. Which of the following molecular orbitals corresponds to an antibonding interaction?**

a) $\sigma$

b) $\pi$

c) $\sigma^*$

d) n

Answer: c) $\sigma^*$

**Q3. In a bonding molecular orbital, the electron density is concentrated**

a) Between the nuclei

b) Outside the nuclei

c) At the nucleus of one atom only

d) In the antibonding region

Answer: a) Between the nuclei

**Q4. What does the HOMO (Highest Occupied Molecular Orbital) represent in a molecule?**

a) The lowest energy occupied molecular orbital

b) The highest energy unoccupied molecular orbital

c) The highest energy occupied molecular orbital

d) The bonding molecular orbital

Answer: c) The highest energy occupied molecular orbital

**Q5. Which molecular orbital is responsible for accepting electrons in a chemical reaction?**

a) HOMO

b) LUMO

c) SOMO

d) $\pi^*$

Answer: b) LUMO

**Q6. A molecule with an unpaired electron in its molecular orbital diagram will have:**

a) A HOMO only

b) A LUMO only

c) A SOMO (Singly Occupied Molecular Orbital)

d) No molecular orbitals

Answer: c) A SOMO (Singly Occupied Molecular Orbital)

**Q7. According to Hückel's rule, which of the following is NOT aromatic?**

a) Benzene

b) Cyclobutadiene

c) Pyrrole

d) Naphthalene

Answer: b) Cyclobutadiene

**Q8. The Frost diagram for a cyclic conjugated system is constructed by placing energy levels:**

a) On the circumference of a circle with one vertex at the bottom

b) Randomly inside a circle

c) In a straight line

d) At an angle of 60°

Answer: a) On the circumference of a circle with one vertex at the bottom

**Q9. The energy gap between the HOMO and LUMO in a conjugated system:**

a) Increases with increasing delocalization

b) Decreases with increasing delocalization

c) Remains constant

d) Depends only on the presence of lone pairs

Answer: b) Decreases with increasing delocalization

**Q10. Which of the following compounds has the highest delocalization energy in terms of $\beta$?**

a) Buta-1,3-diene

b) Cyclobutadiene

c) Hexa-1,3,5-triene

d) Benzene

Answer: d) Benzene

**Q11. According to Hückel's rule, how many $\pi$-electrons must a planar, fully conjugated monocyclic system have to be aromatic?**

a) 2n + 1

b) 2n

c) 4n + 2

d) 4n

Answer: c) 4n + 2

**Q12. Which of the following is considered antiaromatic?**

a) Benzene

b) Cyclooctatetraene

c) Cyclobutadiene

d) Anthracene

Answer: c) Cyclobutadiene

**Q13. Which of the following is an example of a non-aromatic molecule?**

a) Benzene

b) Cyclobutadiene

c) Cycloheptatrienyl cation

d) Cycloheptatriene

Answer: d) Cycloheptatriene

**Q14. Homoaromaticity refers to a system where:**

a) Conjugation is continuous without interruption

b) Conjugation is interrupted but still leads to aromatic stability

c) There is no conjugation

d) Only heteroatoms participate in $\pi$-electron delocalization

Answer: b) Conjugation is interrupted but still leads to aromatic stability

**Q15. In the Frost diagram, the energy levels of $\pi$ molecular orbitals in a cyclic system are determined by:**

a) Schrödinger's equation only

b) The number of $\pi$-electrons

c) The symmetry of the molecule

d) The number of atomic orbitals involved

Answer: d) The number of atomic orbitals involved

# Unit 3 ❐ Physical properties of bond

## Structure



## 3.0 Objectives

After studying this topic, students should be able to:

- Explain how hybridization affects bond dissociation energy (BDE) and bond energy.
- Relate bond distances and bond angles to the hybridization of atoms in molecules.
- Describe Baeyer's strain theory and its implications for bond angles in cyclic compounds.
- Explain how intermolecular forces influence melting points, boiling points, and solubility of common organic compounds.
- Determine the polarity of molecules based on their structure and electronegativity differences.
- Predict and compare dipole moments of various organic molecules.
- Explain the relative stabilities of isomeric hydrocarbons using heat of hydrogenation,

heat of combustion, and heat of formation.

## 3.1 Introduction

The properties of chemical bonds play a crucial role in determining the structure, stability, and reactivity of molecules. Hybridization significantly influences bond characteristics such as bond dissociation energy (BDE), bond energy, bond length, and bond angles. The concept of bond angle strain, explained by Baeyer's strain theory, helps in understanding the stability of ring systems.

Intermolecular forces, both covalent and non-covalent, dictate the melting points, boiling points, and solubility of organic compounds. Molecular polarity and dipole moments further impact solubility and intermolecular interactions. Additionally, the relative stabilities of isomeric hydrocarbons can be analyzed using thermodynamic parameters such as heat of hydrogenation, heat of combustion, and heat of formation. Understanding these fundamental principles is essential for predicting chemical behavior and physical properties in organic chemistry. This unit aims to explore how these fundamental concepts shape the behavior of organic molecules, providing a deeper understanding of their structural and energetic properties.

## 3.2 Influence of hybridization on bond properties

- Hybridization greatly affects bond strength, bond length and electronegativity. Greater the *s* – character, closer the orbitals are to the nucleus and hence forms stronger and shorter bonds.
- Bond length and bond strength are inversely related to each other, i.e., greater the bond length, weaker is the bond strength.
- *s*– character in different hybridization states are: $sp^3$ (25%), $sp^2$ (33%), sp (50%).
- Bond strength: alkynes (sp) > alkenes ($sp^2$) > alkanes ($sp^3$).
- Bond length: alkanes ($sp^3$) > alkenes ($sp^2$) > alkynes (sp).

**Example 1: Bond length**

Since the sp hybrid orbital contains more *s*-character (50%), it is closer to its nucleus; therefore, it forms shorter bonds. Because of the same reason $sp^2$ hybrid orbital forms

shorter bonds than $sp^3$ hybrid orbitals.

The single, double and triple bond lengths in carbon follow the order:

$$\text{-C–C} > \text{-C=C-} > \text{-C–C-}$$

**Example 2: Bond enthalpy or bond strength**

The amount of energy required to break one mole of bonds of a particular type between two atoms in a gaseous state is known as bond enthalpy. The stronger the bond, the more energy is required to break it. Because of this reason bond enthalpy is also called bond strength.

The unit of bond enthalpy is KJ $mol^{-1}$.

$$H_2 \rightarrow H(g) + H(g); \qquad \Delta H = 435.8 \text{ KJ mol}^{-1}$$

The strength of the bond increases as the length of the bond decreases. As a result, bond enthalpy decreases from sp to $sp^3$ i.e., : $sp > sp^2 > sp^3$. In terms of C–C bond, bond enthalpy/ bond strength follows the order:

$C \equiv C$ (strongest) > C=C > C-C (weak)

**Example 3: Electronegativity**

The tendency of an atom to attract bonding electrons towards itself is called its electronegativity. The greater the s-character of the hybrid orbitals, the greater is the electronegativity because an *s*- orbital holds electrons more tightly to the nucleus. In terms of electronegativity: $sp > sp^2 > sp^3$

**Bond dissociation energy**

The amount of energy required to break a bond in a molecule is defined as bond dissociation energy or bond strength. It depends upon the type of bond ( $\sigma > \pi$ ) as well as the environment of the bond. It is determined by quantitative measurements of heat of chemical reactions (calorimetry) and by spectroscopic methods.

| Bond | (Kcal/mole) |
|---|---|
| C–H | 99 |
| C–C | 83 |
| C=C | 146 |
| C≡C | 201 |

**Bond energy:**

Average of all the bond dissociation energy is known as bond energy. In $CH_4$ bond dissociation energy and bond energy is same but in $CH_3Cl$ bond dissociation energy differs from bond energy. For homo atomic molecule both energy is in same value.

**Bond length/bond distances:**

The distance between the centers of two atoms bonded covalently is called bond length. It is measured by X-ray crystallography and microwave spectroscopy.

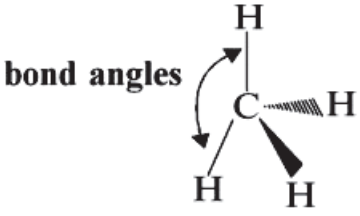
Some common bond lengths are given below.

| | **(Å)** | | **(Å)** |
|---|---|---|---|
| C-H | 1.09 | C=O | 1.20 |
| C-C | 1.54 | C≡C | 0.96 |
| C=C | 1.34 | | |

**Bond angles:**

Bond angle is simply the angle between two bonds or two bonded electron pairs in a compound.

For example in $CH_4$($sp^3$ hybridization) the bond angle is 109 degrees.



**Molecular shapes and bond angles:**

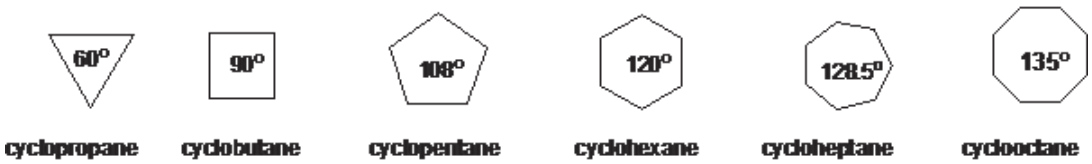
| Number of regions of high electron density around central atom | Arrangement of regions of high electron densityin space | Predicted bond angles | Example | Geometry of molecule |
|---|---|---|---|---|
| 4 | tetrahedral | 109.5° | $CH_4$, methane | tetrahedral |
| | | | $NH_3$, ammonia | pyramidal |
| | | | $H_2O$, water | bent |
| 3 | trigonal planar | 120° | $H_2CO_3$ formaldehyde | trigonal planar |
| | | | $C_2H_4$, ethylene | planar |
| | | | $SO_2$, sulfur dioxide | bent |
| 2 | linear | 180° | $CO_2$, carbon dioxide | linear |
| | | | $C_2H_2$, acetylene | linear |

## 3.3 Concept of bond angle strain and Baeyer's strain theory

Cycloalkanes are very important in components of food, pharmaceutical drugs, and much more. Recall that in alkanes, carbon adopts the sp3 tetrahedral geometry in which the angles between bonds are 109.5°. For some cycloalkanes to form, the angle between bonds must deviate from this ideal angle, an effect known as angle strain. Any deviation from the normal tetrahedral bond angle is known as angle strain.

Additionally, some hydrogen atoms may come into closer proximity with each other than is desirable (become eclipsed), an effect called torsional strain. These destabilizing effects, angle strain and torsional strain are known together as ring strain.

The smaller Cycloalkanes such as cyclopropane (internal bond angle is 60°) and cyclobutane (internal bond angle is 90°) have particularly high ring strains because of their bond angles deviate substantially from 109.5°. Thus cyclopropane and cyclobutane are least stable Cycloalkanes and have greater tendency to undergo ring opening reactions.




**Bayer's strain theory:**

In 1885 *Adolf Baeyer* proposed a theory to explain the relative stability of the first few cycloalkanes. Baeyer postulated that any deviation of bond angles from the normal tetrahedral value would impose a condition of internal strain on the ring.

*Baeyer proposed "any deviation of bond angle from ideal bond angle value (109.5o) will produce a strain in molecule. Higher the deviation lesser the instability"*

**Main assumptions:**

i) According to Baeyer, the bond angle in cyclopentane is 108 ? that is very close to normal tetrahedral angle (109.5 ?), so it is almost free from ring strain and becomes most stable.

ii) Ring systems smaller or larger than cyclopentane are unstable due to higher ring strain.

Thus according to Bayer, the relative order of stability for some common cycloalkanes is

Cyclopentane > Cyclohexane > Cyclobutane > Cyclopropane

But, the actual observed order of stability for these cycloalkanes is asunder.

Cyclohexane > Cyclopentane > Cyclobutane > Cyclopropane.

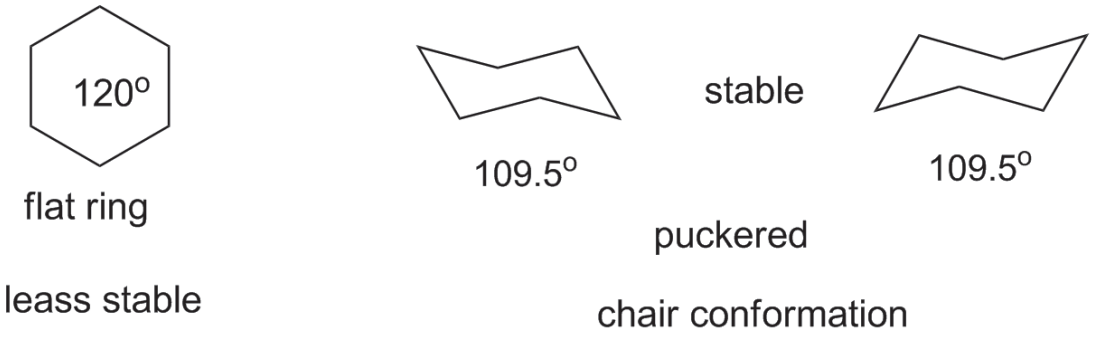
Thus, Bayer made some false assumptions.

i) All ring systems are planar.

ii) The large ring systems involve negative strain hence do not exists

iii) Difficulties in the synthesis of large ring system indicate large rings are too much unstable.

However, it is found later that the bond angle of cyclohexane is almost equal to normal tetrahedral bond angle as the ring is puckered. Puckering of cyclohexane increases its stability.




In conclusion, Baeyer proposed that ring systems smaller or larger than cyclopentane or cyclohexane are unstable due to higher ring strain. Therefore, he assumed that cyclopropane and cyclobutane easily undergo ring opening reaction whereas larger ring systems are difficult to synthesize.

## 3.4 Covalent & non-covalent intermolecular forces

The different intermolecular forces are as follows in strength from weakest to greatest.

1. London Dispersion Forces
2. Dipole-Dipole
3. Hydrogen Bonding
4. Ionic bonding

Dispersion forces act upon all molecules. When heat is added to the system, the heat acts almost like a disruption in which it breaks those bonds.

If there were dipole-dipole intermolecular forces acting in the system, the molecules are more tightly attracted to each other. This is due to the unequal distribution of two bonded atoms. This unequal distribution is caused by one of the atoms being more electronegative than the other. This can also be observed through induction.

Hydrogen bonding creates an intense attraction between the molecules which would make the bonds harder to break. Although they are not technically a type of bond, rather it explains the strong attraction of an electronegative atom towards a proton. These involve oxygen, nitrogen, or fluorine. This is considerably stronger than the previous.

Ionic Bonding is the bonding between a metal and a non-metal. It is much stronger than covalent bonding, therefore trumps the other IM forces.

**Melting point:**

As a solid is heated, its particles vibrate more rapidly as the solid absorbs kinetic energy. Eventually, the organization of the particles within the solid structure begins to break down and the solid starts to melt.

The melting point is the temperature at which a solid changes into a liquid. At its melting point, the disruptive vibrations of the particles of the solid overcome the attractive forces operating within the solid.

The melting point of a solid is dependent on the strength of those attractive forces. Sodium chloride (NaCl) is an ionic compound that consists of a multitude of strong ionic bonds. Sodium chloride melts at 801°C.

In ice individual water molecules are held together by hydrogen bonds. Though hydrogen bonds are the strongest of the intermolecular forces, the strength of hydrogen bonds is much less than that of ionic bonds. So, the melting point of ice is 0 °C.

In conclusion, the melting point is the temperature at which a solid changes into a liquid. Intermolecular forces have a strong influence on melting point.

Boiling point: The boiling point of a substance is the temperature at which it can change its state from a liquid to a gas throughout the bulk of the liquid. At the boiling point, the vapour pressure is equal to the liquid pressure.

A liquid may change to a gas at temperatures below the boiling point through the process of evaporation. Any change of state from a liquid to a gas at boiling point is considered vaporization.

The stronger an intermolecular force, the higher the boiling point of the substance will be. This is because stronger intermolecular bonds require more energy to break. As this energy is supplied in the form of heat when boiling, substances with stronger bonds will have a higher boiling point. The order of strength of intermolecular forces is shown below.

London dispersion < dipole-dipole < hydrogen bonding< ionic bond.

So a substance that contains Hydrogen bonding will have a far greater boiling point than one which contains London dispersion force.

The boiling point of neopentane is only 9.5 °C, significantly lower than those of isopentane (27.7 °C) and normal pentane (36.0 °C). Therefore, neopentane is a gas at room temperature and atmospheric pressure, while the other two isomers are liquids. This can be explained as below.

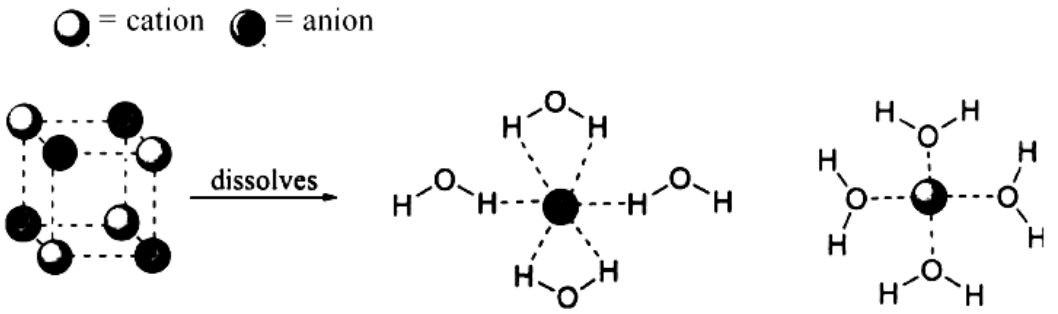
If the numbers of carbons are the same then the boiling point of different isomer depends on the surface area of the molecule. As Van der Waals attractive force is proportional to surface area, straight chain molecule such as normal pentane will have the strongest attractive force among themselves compare to isopentane and neopentane. Strong attractive force will tightly hold the individual molecules and thus need more heat to breakdown this association. So, normal pentane has higher boiling point. On the other hand, the branched alkane such as neopentane is spherical which results least surface area. Consequently, in neopentane the individual molecules are associated with weakest Van der Waals forces. Thus, lower heat or energy is required to break down their association and exhibits lower boiling point.

## 3.5 Effect of Intermolecular Forces on Solubilities

The different types of intermolecular forces (IMFs) exhibited by different compounds can be used to predict whether two different compounds can be mixed to form a homogeneous solution (soluble or miscible).

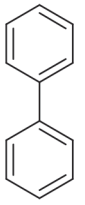
It is common to remember the rule regarding solubility is that 'like dissolves like'. Let's revisit this old rule, and put our knowledge of covalent and noncovalent bonding to work.

If table salt (NaCl) is added to water, the ionic compound dissolves readily in water. Why? Because water, as a very polar molecule, is able to form many ion-dipole interactions with both the sodium cation and the chloride anion, the energy from which is more than enough to make up for energy required to break up the ion-ion interactions in the salt crystal and some water-water hydrogen bonds.




To the end, in place of sodium chloride crystals, we have individual sodium cations and chloride anions surrounded by water molecules - the salt is now in solution (i.e. solvation). Charged species as a rule dissolve readily in water: in other words, they are very hydrophilic(water-loving).

Now, we'll try a compound called biphenyl, which, like sodium chloride, is a colorless crystalline substance.

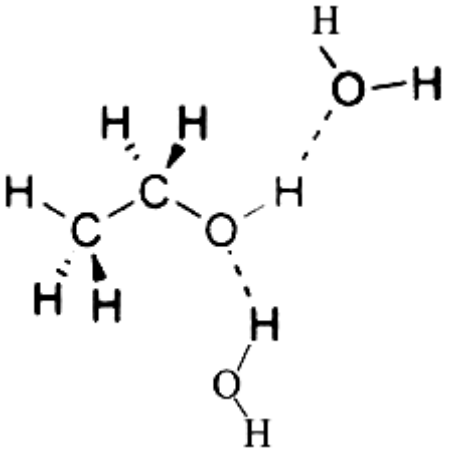


biphenyl, an organic molecule

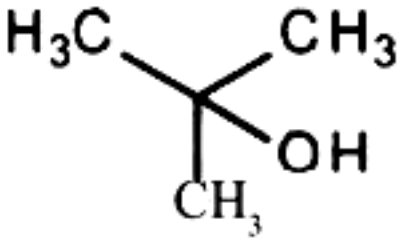
Biphenyl does not dissolve at all in water. Why is this? Because it is a very non-polar organic molecule, with only carbon-carbon and carbon-hydrogen bonds. It is able to bond to itself very well through nonpolar (London dispersion) interactions, but it is not able to form significant attractive interactions with the very polar solvent molecules such as water. Thus, the energetic cost of breaking up the biphenyl-to-biphenyl interactions in the solid is high, and very little is gained in terms of new biphenyl-water interactions. Water is a terrible solvent for nonpolar hydrocarbon molecules: they are very hydrophobic ('water-fearing').

However, alcohols like methanol, ethanol, and propanol - dissolve easily in water. This is because the water is able to form hydrogen bonds with the hydroxyl group in these molecules, and the combined energy of formation of these water-alcohol hydrogen bonds

is more than enough to make up for the energy that is lost when the alcohol-alcohol hydrogen bonds are broken up.



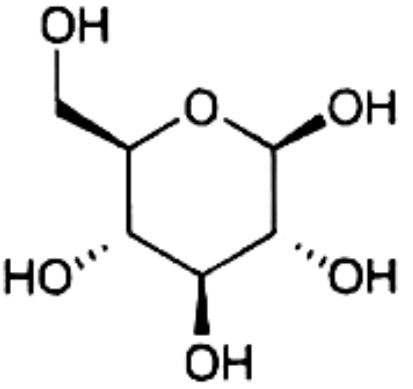

But, *tert*- butanol is immiscible in water. The longer-chain alcohols - pentanol, hexanol, heptanol, and octanol - are increasingly non-soluble. What is happening here? Clearly, the same favorable water-alcohol hydrogen bonds are still possible with these larger alcohols. The difference is that the larger alcohols have larger nonpolar, hydrophobic regions (long carbon chain) in addition to their hydrophilic hydroxyl group. At about four or five carbons, the hydrophobic effect begins to overcome the hydrophilic effect, and water solubility is lost.




*tert*-butanol, water immiscible

Now, try to dissolve glucose in the water - even though it has six carbons just like hexanol, it also has five hydrogen-bonding, hydrophilic hydroxyl groups in addition to sixth oxygen

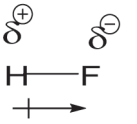
that is capable of being a hydrogen bond acceptor. Thus, glucose is quite soluble in water.




Glucose, water soluble

## 3.6 Polarity of molecules and dipole moments

Introduction: Polarity refers to the physical properties of compounds such as boiling point, melting points and their solubilities. The polarity of bonds is caused due to the interaction of the bonds between molecules and atoms with different electronegativities. Polarity in Chemistry is nothing but the concept of the separation of an electric charge leading a molecule to have a positive and negative end. Consider the below example:




In an H-F bond, the fluorine atom is more electronegative than that of the Hydrogen atom. The electrons eventually spend more time at the Fluorine atom. Thus, polarity can be defined as "a state or a condition of an atom or a molecule having positive and also negative charges."

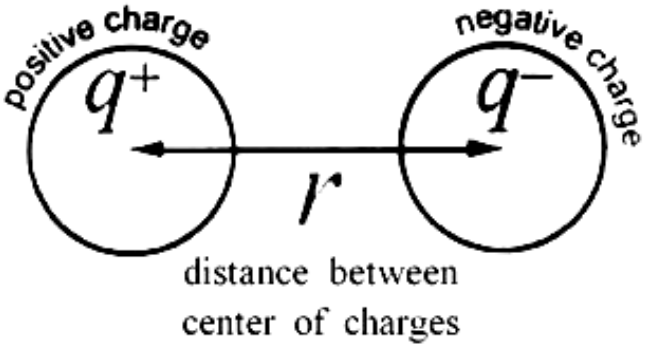
Factors on which the Polarity of Bonds Depends;

i) Relative electronegativity of participating atoms

ii) The spatial arrangement of various bonds in the atom

## 3.7 Dipole Moment

A dipole moment is a quantity that describes two opposite charges separated by a distance. It is a quantity that we can measure for a molecule in the lab and thereby determine the size of the partial charges on the molecule (if we know the bond length). By definition the dipole moment, $\mu$, is the product of the magnitude of the separated charge and the distance of the separation:




$$\underset{\text{dipole moment}}{\mu} = \underset{\text{separated charge}}{q} \cdot \underset{\text{distance between}}{r}$$

**Definition:** The dipole moment of a molecule is the vectorial sum of the individual bond moments present in the molecule.

**Bond moment:** Every bond carries with an electrical moment called the bond moment arising out of the difference in electronegativities.

**Polar bond:** A polar bond is a covalent bond which trying to become ionic.

Bond polarity is measured by the term of dipole moment. It is not possible to measure the dipole moment of an individual bond in a molecule. It is measured by the summation of all individual bond moments.

Dipole moment is abbreviated by 'μ' and unit is debye (D).

Dipole moment, $\mu = (q \times r)$ D Where, q = magnitude of separated charge, r = distance

between two charges

1D = $10^{-8} \times 10^{-10}$ e.s.u. cm.= $10^{-18}$ e.s.u. cm. (Peter Debye won Noble prize in 1936)

Again,

$$\mu r = \sqrt{\mu_1^2 + \mu_2^2 + 2\mu_1^2 \mu_2^2 \cos\theta}$$

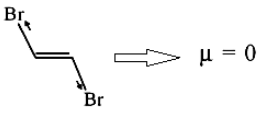
$\mu 1$ = moment of one bond; $\mu 2$ = moment of another bond; $\theta$ = angle between two vectors

Non polar bond:

H–H, Br–Br and N–N ⇨ $\mu = 0$

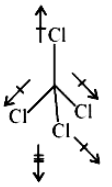
| H–F | H–Cl | H–I |
|---|---|---|
| $\mu = 1.75$ | $\mu = 1.03$ | $\mu = 0.38$ |

$CCl_4$, ⇨ $\mu = 0$

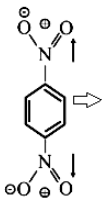



⇨ $\mu = 0$

*trans*-1,2-dibromoethylene




Each C-Br moments acts in opposite direction and in same magnitude. Therefore, they cancelled each other giving the dipole moment to zero.

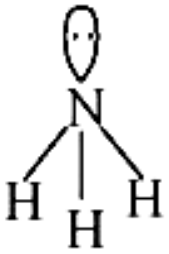


⇨ $\mu = 0$

similarly methane, ethane has no dipole moment but propane has 0.085 D

**$\sigma$ -Moment and $\pi$ -moment:** Electronegativity differences between the adjacent atoms joint by $\sigma$ -bond develops $\pi$-moment. A dipole moment is thus generated is known as $\sigma$-moment or inductive moment. The dipole moment generated by the delocalization of $\pi$-electrons is called as $\pi$-moment or resonance moment.

In $NF_3$, the vectorial sum of three N-F bond moments and N-l.p. moment acts in opposite direction. So, they cancel partially to each other. But, in $NH_3$ both the vectorial sum of three N-H bond moments and N-l.p. moment acts in same direction.


Hence, $NF_3$ has dipole moment 1.47 D but $NH_3$ exhibits μ 0.23 D.

Again, glycine is an α-amino acid which exist as a zwitter ion. So charge separation is greater here and dipole moment value is also high.

$$NH_2 = CH_2 - COOH \leftrightarrow \overset{\oplus}{N}H_2 - CH_2 - CHO\overset{-}{O} \quad \text{As } \mu = e \times d$$

here, e is high so μ is also high

Zwitter ion

This type of charge separation is not possible in propanoic acid. Here, dipole generates only by the electronegativity difference between alkyl group (+I effect) and COOH group (-I effect). So, value dipole moment is lower in propanoic acid.

$$\mapsto$$

$$CH_3 - CH_2 - COOH$$

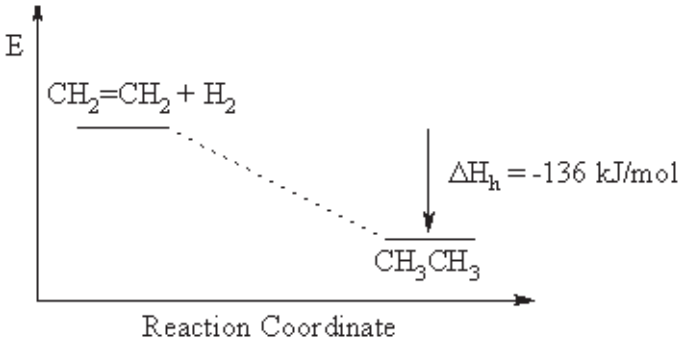
propanoic acid

**Note:** Most important when determining if a molecule has a dipole moment are two factors. One it must have polar covalent bonds. Two, it must have a shape in which all the dipoles don't cancel

## 3.8 Heat of hydrogenation, heat of combustion and heat of formation

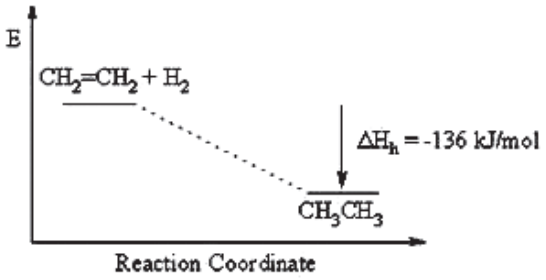
**Heat of hydrogenation** ($\Delta H_h$) can be defined as the amount of heat released upon the addition of $H_2$ to one mole of a compound (e.g. an alkene or alkyne) to generate the corresponding alkane.

- This will usually be an **exothermic** process, as shown in the example below for ethene to ethane.



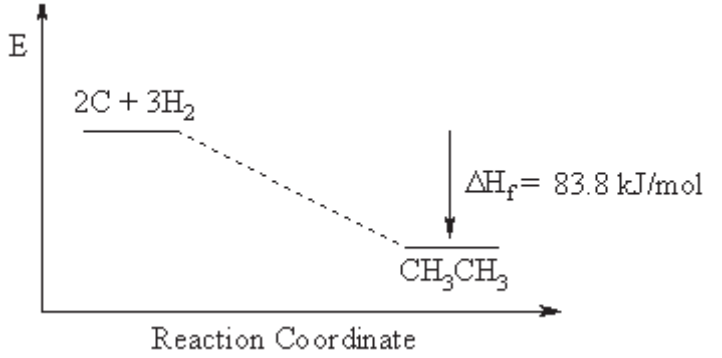

**Heat of combustion** ($\Delta H_C$) can be defined as the heat released when one mole of a compound undergoes complete combustion in $O_2$ to produce $CO_2$ and $H_2O$.

- This will usually be an exothermic process, as shown in the example below.



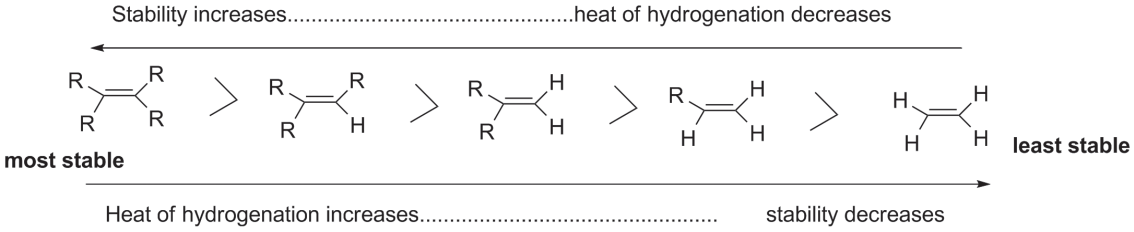

Heat of formation ($\Delta H_f$) can be defined as the heat released if one mole of a compound were formed from its component elements in their standard state.

- These diagrams can be either **endothermic** or **exothermic** processes.

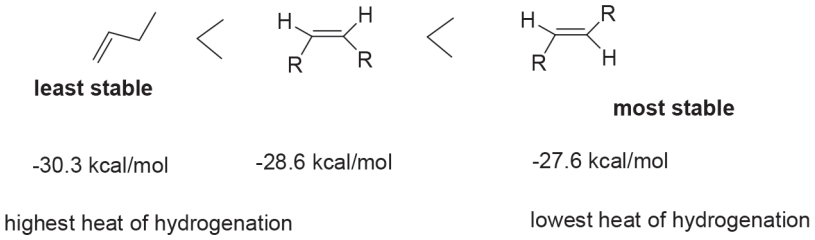


## 3.9 Relative stabilities of isomeric hydrocarbons

The stability of alkene can be determined by measuring the heat of hydrogenation. Since the double bond is breaking in this reaction, the energy released in hydrogenation is proportional to the energy in the double bond of the molecule. This is a useful tool because heats of hydrogenation can be measured very accurately. Stability is simply a measure of energy. Lower energy molecules are more stable than higher energy molecules. More substituted alkenes are more stable than less substituted ones due to hyperconjugation. They have a lower heat of hydrogenation. The following illustrates stability of alkenes with various substituents:




In disubstituted alkenes, trans isomers are more stable than cis isomers due to steric hindrance. Also, internal alkenes are more stable than terminal ones. See the following isomers of butene:




Heats of combustion can also be used to measure the relative stability of isomeric hydrocarbons. They tell us not only which isomer is more stable than another, but by how much. Consider a group of $C_8H_{18}$ alkanes: The relative heat of combustion and their stabilities are shown below.

| Name | Formula | Value of heat of combustion |
|---|---|---|
| Octane | $CH_3(CH_2)_6CH_3$ | 1307.5 kcal/mol (least stable) |
| 2-Methyl heptane | $(CH_3)_2CHCH_2CH_2CH_2CH_2CH_3$ | 1306.3 kcal/mol |
| 2,2-Dimethylhexane | $(CH_3)_3CCH_2CH_2CH_2CH_3$ | 1304.6 kcal/mol |
| 2,2,3,3-tetramethylbutane | $(CH_3)\backslash CC(CH_3)_3$ | 1303.0 kcal/mol (most stable) |

stability increases

Potential energy is comparable with enthalpy; it is the energy a molecule has exclusive of its kinetic energy. A molecule with more potential energy is less stable than an isomer with less potential energy. Since these $C_8H_{18}$ isomers all undergo combustion to the same final state according to the equation

$$C_8H_{18} + 25/2\ O_2 = 8CO_2 + 9H_2O$$

The differences in their heats of combustion translate directly to differences in their potential energies. When comparing isomers, the one with the lowest potential energy (in this case, the lowest heat of combustion) is the most stable. Among the $C_8H_{18}$ alkanes, the most highly branched isomer, 2, 2, 3, 3-tetramethylbutane, is the most stable, and the unbranched isomer octane is the least stable. It is generally true for alkanes that a more branched isomer is more stable than a less branched one.

## 3.10 Summary

- The percentage of s-character in hybrid orbitals affects bond strength, length, and electronegativity ($sp > sp^2 > sp^3$).
- Bonds with greater s-character are shorter and stronger (C?C > C=C > C-C).
- Energy required to break bonds follows the trend $sp > sp^2 > sp^3$, with triple bonds being the strongest.
- Hybrid orbitals with higher s-character are more electronegative ($sp > sp^2 > sp^3$).
- Bond angles depend on hybridization (e.g., CH? - 109.5°, CO? - 180°).
- Baeyer's Strain Theory says that ring strain arises when bond angles deviate from the tetrahedral angle, affecting stability.
- Cyclohexane is most stable due to puckering, whereas cyclopropane and cyclobutane

have high strain.

- Strength order - London dispersion < dipole-dipole < hydrogen bonding < ionic bonding.
- Melting and Boiling Points depend on intermolecular forces; ionic compounds have higher melting points than covalent ones.
- More branched alkanes have lower boiling points due to reduced surface area.
- "Like dissolves like" - polar substances dissolve in polar solvents (e.g., NaCl in water), while nonpolar compounds do not.
- Alcohols dissolve in water due to hydrogen bonding, but longer-chain alcohols become insoluble.
- Polarity and Dipole Moments is determined by electronegativity differences and molecular geometry.
- Product of charge separation and bond length, measured in debye (D). NH? has a higher dipole moment than NF? due to vector addition of bond dipoles.

## 3.11 Exercise

1. The electronegativity of C,H,O,N and S are 2.5, 2.1, 3.5, 3.0 and 2.5 respectively. Which of the following bond is most polar?

A) O - H B) S - H C) N - H D) C - H

Answer: If the difference in the electronegativity between two or more atoms is more, the bond between them is more polar. For the given atoms, we can see that:

- O - H = 3.5 - 2.1 = 1.4
- S - H = 3.5 - 2.5 = 1
- N - H = 3.0 - 2.1 = 0.9
- C - H = 2.5 - 2.1 = 0.4 .

Therefore, the O-H bond is the most polar among the given bonds.

2. Compare the dipole moment between $NF_3$ and $NH_3$.

Answer: 1.3.9.5

3. Dipole moment of glycine is greater than that of propanoic acid. Explain.

Answer: See 13.9.5

4. Arrange the following molecules in order of increasing of dipole moment with reason.

i) $CH_3Cl$, $CH_2Cl_2$, $CHCl_3$ ii) $CH_3CH_2Cl$, $CH_2 = CHCl$, $CH \equiv C\text{-}Cl$

Answer: i) See 1.2.8.3

ii) In ethyl chloride dipole moment arises due to electronegativity difference between ethyl group and Cl atom (only $\sigma$ moment). There is no opposition moment so it possesses high dipole moment.

$$\overset{\mapsto}{CH_3} - \overset{\mapsto}{CH_2} - Cl$$

But in vinyl chloride both the $\sigma$ moment and $\pi$-moment acts in opposite direction. So they cancel partially.

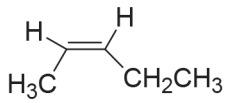
Net dipole moment $(\mu) = \mu\sigma - \overset{\leftarrow \quad \rightarrow}{H_2C=CH-Cl}\ \mu\pi$

**Due to more electronegative nature of alkyne triple bond, the value of $\mu$ $\pi$ is greater for**

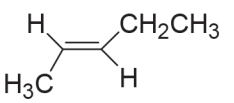
$CH \equiv C\text{-}Cl$. **So, it possesses lower dipole moment than vinyl chloride.**

5. Which is the more stable alkene in each pair?

i)

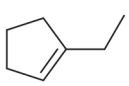



A

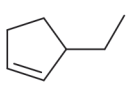



B

ii)



A



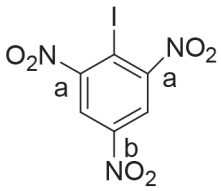
B

Answer: See 1.3.12.3

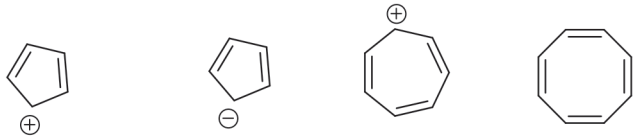
Hint: i) B ii) A

**Additional Questions**

1. Which C-N bond (a or b) has a higher bond length and why?




2. Predict which of the following compounds is aromatic, antiaromatic or nonaromatic and why?



3. Draw all the $\pi$ MOs of allyl cation, allyl anion and allyl radical. Arrange them in order of increasing energy levels. Identify HOMO and LUMO in each case.
4. Arrange the following compounds in order of their boiling point and explain.

n-pentane, iso-pentane and neo-pentane.

5. Why ethanol is water soluble but tert-butanol is immiscible in water?
6. How do you differentiate *cis*-2-butene and *trans*-2-butene by considering their physical properties?
7. Arrange the following compounds in order of their stability and explain.

2-Methyl heptane, 2,2-Dimethylhexane and n-octane.

8. State and explain Bayer's strain theory.
9. What are the Bayer's false assumptions regarding relative the stability of cycloalkanes?
10. How will you separate *ortho-nitrophenol* and *para*-nitrophenol?

Answer: See text (Hint: Different boiling points due to hydrogen bonding effects. Separation can be done by distillation technique).

11. Arrange n-butane, n-hexane and n-octane according to their boiling points and explain.

**Multiple-Choice Questions (MCQs)**

**1. Which of the following hybridization states corresponds to the shortest bond length?**

A) sp

B) $sp^2$

C) $sp^3$

D) None of these

Answer: A) sp

**2. The bond dissociation energy (BDE) generally follows which trend with respect to hybridization?**

A) $sp^3 > sp^2 > sp$

B) $sp^2 > sp^3 > sp$

C) $sp > sp^2 > sp^3$

D) No specific trend

Answer: C) $sp > sp^2 > sp^3$

**3. Which of the following statements about bond angles is correct?**

A) $sp^3$ hybridized atoms have bond angles of approximately 120°

B) $sp^2$ hybridized atoms have bond angles of approximately 180°

C) sp hybridized atoms have bond angles of approximately 180°

D) Bond angles are not influenced by hybridization

Answer: C) sp hybridized atoms have bond angles of approximately 180°

**4. Baeyer's strain theory states that:**

A) Cyclic compounds are always more stable than their acyclic counterparts

B) Smaller ring systems (like cyclopropane) have higher strain due to bond angle deviation from the ideal 109.5°

C) Cyclohexane has the highest angle strain

D) Bond strain decreases with decreasing ring size

**Answer:** B) Smaller ring systems (like cyclopropane) have higher strain due to bond angle deviation from the ideal 109.5°

**5. Which of the following cyclic compounds is expected to have the highest ring strain?**

A) Cyclopropane

B) Cyclobutane

C) Cyclopentane

D) Cyclohexane

Answer: A) Cyclopropane

**6. Which of the following intermolecular forces has the strongest influence on boiling point?**

A) London dispersion forces

B) Dipole-dipole interactions

C) Hydrogen bonding

D) Van der Waals forces

Answer: C) Hydrogen bonding

**7. Why do alcohols have higher boiling points compared to alkanes of similar molecular mass?**

A) Alcohols have stronger London dispersion forces

B) Alcohols form hydrogen bonds

C) Alkanes have stronger dipole-dipole interactions

D) Alcohols have a lower molecular mass

Answer: B) Alcohols form hydrogen bonds

**8. Which of the following compounds is most soluble in water?**

A) Hexane

B) Ethanol

C) Benzene

D) Ether

Answer: B) Ethanol

**9. Which of the following molecules has zero dipole moment?**

A) $H_2O$

B) $CO_2$

C) $NH_3$

D) $CHCl_3$

Answer: B) CO?

**10. The dipole moment of $NH_3$ is higher than that of $NF_3$ because:**

A) $NH_3$ has stronger hydrogen bonding

B) $NF_3$ has a symmetrical structure

C) The lone pair-bond dipole interactions in $NH_3$ reinforce each other

D) The electronegativity of N is higher than F

Answer: C) The lone pair-bond dipole interactions in $NH_3$ reinforce each other

**11. The isomer of butane with lower heat of combustion is:**

A) n-Butane

B) Isobutane

C) Both have equal heat of combustion

D) None of these

Answer: B) Isobutane

**12. Which factor contributes most to the relative stability of isomeric hydrocarbons?**

A) Bond polarity

B) Molecular weight

C) Heat of combustion

D) Number of hydrogen atoms

Answer: C) Heat of combustion

**13. Among the following alkenes, which has the highest heat of hydrogenation?**

A) Ethene

B) 1-Butene

C) 2-Butene

D) 2-Methylpropene

Answer: A) Ethene

# Unit 4 ❐ Mechanistic classification of reaction

## Structure



## 4.0 Objectives

After going through this unit, learners will be able to-

- Understand the Mechanistic Classification of Organic Reactions
- Define and distinguish addition, elimination, and substitution reactions.

- Differentiate between homolytic (radical) and heterolytic (ionic) bond fission.
- Explain the curly arrow notation to represent electron movement in reaction mechanisms.
- Define electrophiles and nucleophiles with elementary concepts.
- Explain free energy, equilibrium, enthalpy, and entropy in the context of organic reactions.
- Calculate Enthalpy Change Using Bond Dissociation Energy (BDE)

## 4.1 Introduction

The *mechanism* of a chemical reaction is the sequence of events that take place as reactant molecules are converted into products. The study of kinetics includes very complex and sophisticated reactions that cannot be analyzed without a proposed mechanism, a series of steps that a reaction takes before reaching the final products.

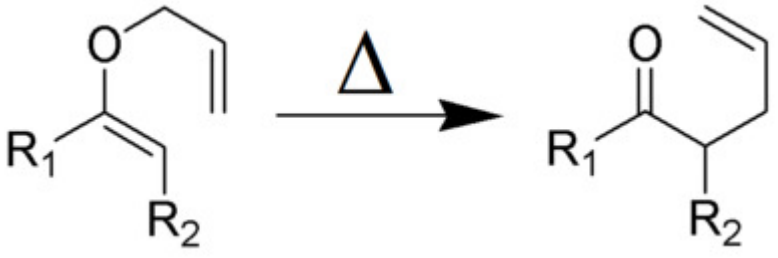
Collectively, an overall reaction and a reaction mechanism consist of multiple elementary processes. These elementary steps are the basic building blocks of a complex reaction, and cannot be broken down any further.

A reaction mechanism is only a guess at how a reaction proceeds.

- **Chemical reaction,** a process in which one or more substances, the reactants, are converted to one or more different substances, the products.

  $CO + NO_2^{\cdot} \rightarrow CO_2 + NO$

- **Organic reactions** are chemical reactions involving organic compounds.



- **Reaction mechanism:** A mechanism is only a hypothesis which can explain a particular reaction. It is the step by step sequence of elementary reactions by which overall chemical change occurs.
- Which bonds are broken, which are formed, in what sequence/order, how many steps are involved and relative rates of each such steps are the details one can obtain through the study of reaction mechanism.

## 4.2 Mechanistic classification

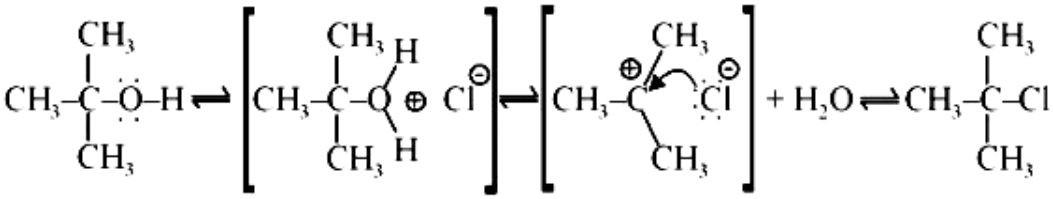
Mechanistic classification categorizes chemical reactions based on the way bonds are broken and formed at the molecular level. It provides insights into the reaction pathway, the nature of intermediates, and the role of reagents. The three main types of reactions based on mechanism are:

**a) Ionic reaction:** Reactions which involve charged species and the bonding together of electrophiles and nucleophiles are ionic or polar reactions.

Ionic reactions normally take place in liquid solutions, where solvent molecules assist the formation of charged intermediates.

**Example:** Treatment of *tert*-butanol with HCl produces *tert*-butyl chloride as shown below. This type of reaction is known as Substitution reaction.

**Mechanistic pathway:**



**b) Radical reaction:** A **free-radical reaction** is any chemical reaction involving free radicals. This reaction type is abundant in organic reactions.

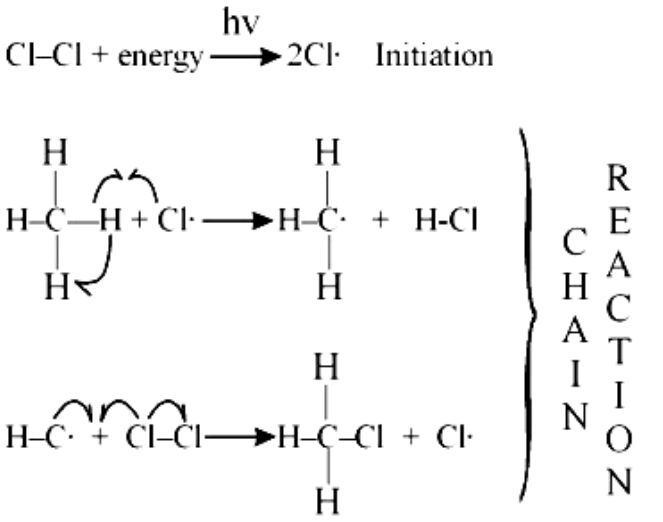
Many radical reactions are chain reactions with a chain initiation step, a chain

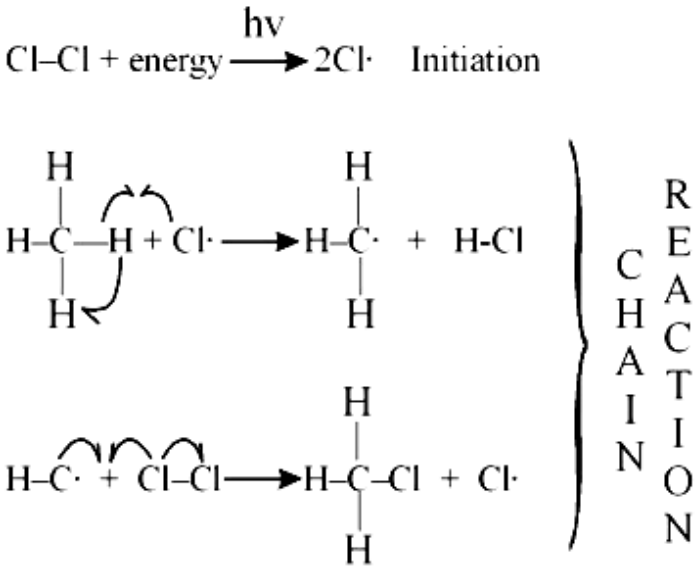
propagation step and a chain termination step.

**Example:** Chlorination of methane in presence of light energy.

$$CH_4 + Cl_2 + \text{energy} \rightarrow CH_3Cl + CH_2Cl_2 + CHCl_3 + CCl_4 + HCl$$

**Mechanism**:



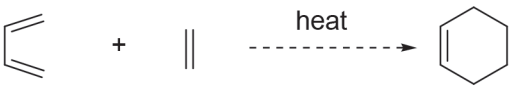



**c) Pericyclic reaction:** Pericyclic is the name for the family of concerted **reactions** involving no charged intermediates with a single cyclic transition state.

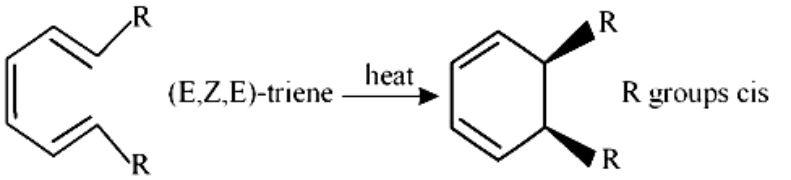
The word **'pericyclic'** comes from how the electrons flow round the outside of the ring.

**Example:** Cycloadditions, sigmatropic rearrangements and electrocyclic **reactions** are the three main types.

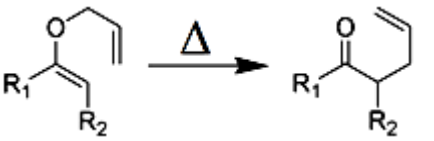
a) Diels-Alder reaction:




b) Electrocyclic reaction:




c) [3,3]-sigmatropic rearrangement:




## 4.3 Type of reaction

Chemical reactions can be classified based on how atoms or groups rearrange within molecules. The three fundamental types of reactions are:

i) Addition reactions

ii) Elimination reactions

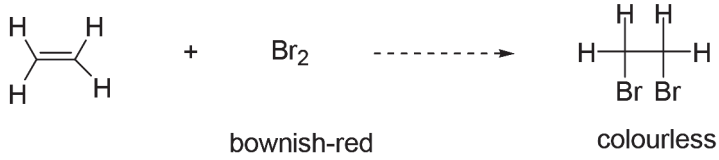
iii) Substitution reactions

### 4.3.1 Addition reactions:

Addition reaction, any of a class of chemical reactions in which an atom or group of atoms is added to a molecule.

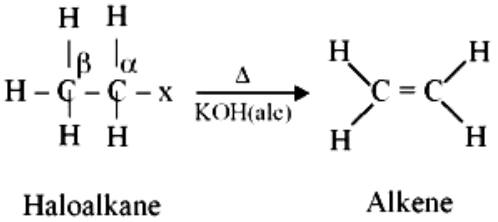
Two or more molecules combine to form a larger one (product).

**Example:** When bromine is added to ethylene the red colour of bromine disappears.




### 4.3.2 Elimination reaction:

Any of a class of organic chemical reactions in which a pair of atoms or groups of atoms are removed from a molecule, usually through the action of acids, bases, or metals and, in some cases, by heating to a high temperature.




### 4.3.3 Substitution reaction:

*Substitution reaction* (also known as single displacement **reaction** or single **substitution reaction**) is a chemical reaction during which one functional group in a chemical compound is replaced by another functional group.

**Example:** Aqueous NaOH mediated hydrolysis of iodomethane produces methanol via substitution reaction.

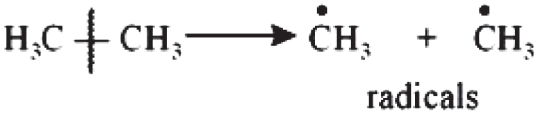
$$CH_3I + NaOH \rightarrow CH_3OH + CH_3I$$

## 4.4 Nature of bond cleavage

Chemical reactions involve making and breaking covalent bonds. When a bond is broken, the electrons have to go somewhere

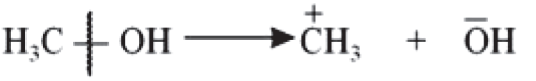
There are two ways:

**i) Homolytic cleavage:** A covalent **bond** breaks in such a way that each of the bonded atoms gets one of the shared electrons.




- Resulting species are called free radicals.
- Radicals are important intermediates in organic chemistry.

**ii) Heterolytic cleavage:** A covalent bond breaks in such a way that one of the bonded atoms gets both of the shared electrons.



Resulting species are called cations and anions.

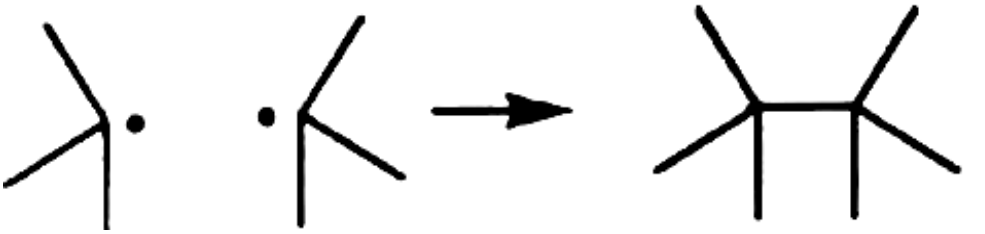
## 4.5 Nature of bond formation

Bond formation occurs when atoms combine to create a stable molecular structure. It involves sharing or transferring electrons and can be categorized into two types:

**i) Homogenic bond formation:** Homogenic bond formation combines two fragments, each contributing one electron to the bond pair.

This type of bond formation does not involve ions but radicals.

**Example:** Addition of two tert-butyl radicals

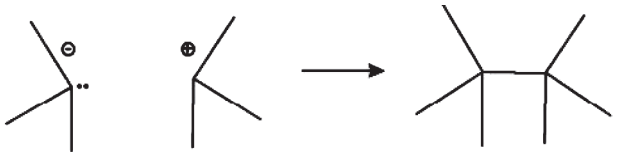


**ii) Heterogenic bond formation:** Heterogenic bond formation combines two fragments with both electrons of the bond pair contributed by one fragments. That is,

1. One fragment supplies two electrons.
2. One fragment supplies no electrons.

3. This type of bond formation generally involves ions.

**Example:** Reaction between cations and anions



## 4.6 Type of reagents

The term **"reagent"** denotes a chemical ingredient (a compound or mixture, typically of inorganic or small organic molecules) introduced to cause the desired transformation of an organic substance. Examples include the Collins **reagent**, Fenton's **reagent**, and Grignard **reagents etc**.

### 4.6.1 Reagent classification

Basically two types-

iv) Electrophiles

v) Nucleophiles

**Electrophile:** A molecule or ion that accepts a pair of electrons to make a new covalent bond is called an electrophile. "E" or "E+" are common abbreviations for generic electrophiles.

**Example:**

$H_3O^+$ $CH_3Br$ $NO_2^+$ and $CH_3MgBr$

**Nucleophile:** A molecule or ion that donates a pair of electrons to form a new covalent bond is called a nucleophile. "Nu" or Nu - are common abbreviations for generic nucleophiles.

**Example:**

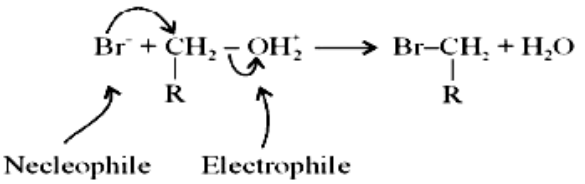
$NH_3$ $HO^-$ $H_2O$

### 4.6.2 Curly arrow rules in representation of mechanistic steps

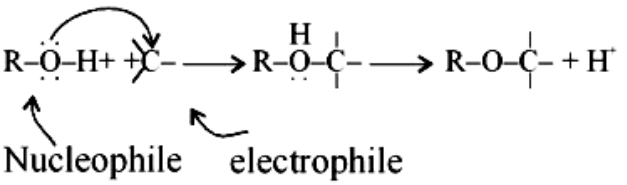
- Electrons always flow from nucleophile to electrophile


**Example 1:** Using the curved arrows shown below, label each reactant as a nucleophile or electrophile.

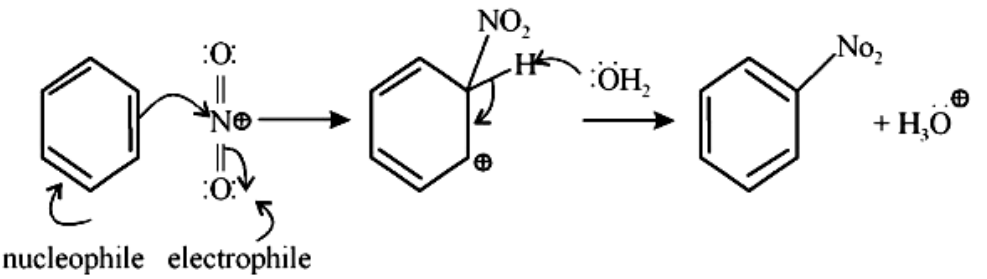
i)




ii)




iv)




**Reactive intermediates:** carbocations (carbenium and carbonium ions), carbanions, carbon radicals, carbenes: generation and stability, structure using orbital picture and electrophilic/ nucleophilic behavior of reactive intermediates (elementary idea).

## 4.7 Reaction thermodynamics

Reaction thermodynamics is the study of energy changes that occur during a chemical reaction. It focuses on the relationship between enthalpy $(\Delta H)$, entropy $(\Delta S)$, and free energy $(\Delta G)$ to determine whether a reaction is spontaneous, non-spontaneous, or at equilibrium. Relationship between $\Delta G, \Delta H$ and $\Delta S$ using the Gibbs free energy equation:

$$\Delta G = \Delta H - T\Delta S$$

**Thus, key aspects include:**

- Free energy $(\Delta G)$ : Determines spontaneity of a reaction.
- Enthalpy $(\Delta H)$ : Measures heat absorbed or released.
- Entropy $(\Delta S)$ : Represents disorder or randomness in a system.
- Bond Dissociation Energy (BDE): Helps calculate enthalpy changes.
- Equilibrium: Achieved when $\Delta G = 0$, meaning no net energy change.

## 4.8 Free energy and equilibrium

The balance between reactants and products in a reaction will be determined by the free energy difference between the two sides of the reaction. The greater the free energy difference, the more the reaction will favor one side or the other. The smaller the free energy difference, the closer the mixture will get to equal parts reactants and products.

When the balance lies in equilibrium, reaction is described by the equilibrium constant. The equilibrium constant is just the ratio of concentration of products to that of reactants, once the reaction has settled to equilibrium. That's the point at which the forward and reverse reactions are balanced, so that the ratio of concentration of products to reactants is unchanging.

- A reaction has reached equilibrium when the reaction has stopped progressing, so that the amount of reactants that have turned into products remains constant, and the amount of reactants left over stays constant.
- The equilibrium constant is the ratio of products to reactants when the reaction has

reached equilibrium.

A large number (like a thousand) of the equilibrium constant means that there are much more products than reactants at equilibrium. On the other hand, a very small fraction (like one millionth) indicates that the reaction does not proceed very far, producing only a tiny amount of products at equilibrium.

- Every reaction has an equilibrium constant
- A very large equilibrium constant (in the millions or billions) means the reaction goes "to completion", with all reactants essentially converted into products
- A tiny equilibrium (very close to zero) constant means the reaction hardly moves forward at all.

The equilibrium constant is related to the standard free energy change of the reaction by the expression:

$$\text{Ink} = -\Delta G^0 / RT \text{.....(1)}$$

The sign of $\Delta G^0$ tells us whether products or reactants are favoured at equilibrium. If $\Delta G^0$ is negative for a reaction, the products will be favoured at equilibrium. If $\Delta G^0$ is positive, the reactants will be favoured at equilibrium. If $\Delta G^0$ is zero, the equilibrium constant for the reaction will be 1.

## 4.9 Enthalpy and entropy factor

A small change in $\Delta G^0$ makes a big difference in K. The relation between $\Delta G^0$ (change in standard Gibbs free energy), $\Delta H^0$ (standard enthalpy change of reaction) and $\Delta S^0$ (standard entropy change of reaction) is given below-

The change in enthalpy $(\Delta H^0)$ in a chemical reaction is the amount of heat change. Since breaking of bonds requires energy and making of bonds liberates energy, the enthalpy change indicates whether the products have more stable bonds than the starting materials or not. T is the temperature in Kelvin at which the reaction is carried out. $\Delta S^0$ represents the entropy difference between the reactants and products. If $\Delta S^0$ is positive then the reaction is favourable towards products. The entropy factor is a measure of degree of

disorder of system. The positive value of $\Delta S^0$ indicates that the products have more freedom i.e., more disorderness than reactants.

If weaker bonds are broken and stronger bonds are formed, heat is evolved and the reaction is exothermic. In an exothermic reaction, the enthalpy term makes a favorable negative contribution to $\Delta G$. If stronger bonds are broken and weaker bonds are formed, then heat is consumed and the reaction is endothermic.

- Standard free energy change $(G^0)$ : It is the difference in free energy between the reactants and products (all are in their standard states).
- Standard enthalpy change $(\Delta H^0)$ : The Standard enthalpy change of a reaction is the difference in bond energies as well as resonance, strain, and salvation energies between the reactants and products (all are in their standard states).
- Standard entropy change $(\Delta S^0)$ : The standard entropy change is a measure of the energy released or consumed due to increase or decrease in disorder or randomness of the system on going from starting materials to final products.

## 4.10 Calculation of enthalpy change via BDE

- Bond energies (bond enthalpies) can be used to estimate the heat of a reaction (enthalpy change of a reaction, $\Delta H^0$).

$\Delta H^0_{(reaction)}$ = sum of the bond energies of bonds being broken - sum of the bond energies of the bonds being formed.

$$\Delta H^0_{(reaction)} = \sum H_{(reactant\ bonds\ broken)} - \sum H_{(product\ bonds\ formed)}$$

- Steps for calculating heat of reaction (enthalpy change of reaction), $\Delta H^0$ from bond energies of reactants and products:

    1. Write the balanced chemical equation, with all reactants and products in the gaseous state.

       If a reactant or product is NOT in the gaseous state, you will need to use Hess's Law to include the relevant energy (enthalpy) for the change of state.

2. Write the general equation for the heat of reaction (enthalpy of reaction):

$$\Delta H^0_{(\text{reaction})} = \sum H_{(\text{reactant bonds broken})} - \sum H_{(\text{product bonds formed})}$$

3. Substitute bond energy values into the equation and solve for $\Delta H^0_{(\text{reaction})}$

For the general chemical reaction in which reactants form products:

| | | | |
|---|---|---|---|
| **chemical reaction** | reacants | $\rightarrow$ | products |
| **bonds are** | broken | $\rightarrow$ | made |
| **energy is** | absorbed | $\rightarrow$ | released |

A chemical reaction will be endothermic if the energy absorbed to break bonds in the reactant molecules is greater than the energy released when bonds are formed in the product molecules.

$$H_{\text{break bonds}} > H_{\text{make bonds}} \; ; \; \Delta H_{\text{reaction}} \text{ is positive}$$

A chemical reaction will be exothermic if the energy absorbed to break bonds in the reactant molecules is less than the energy released when bonds are formed in the product molecules.

$$H_{\text{break bonds}} < H_{\text{make bonds}} \; ; \; \Delta H_{\text{reaction}} \text{ is negative}$$

That is, if we add together the bond energies of all the bonds that need to be broken in the reactant molecules, and, add together all the bond energies of all the bonds we need to make in order to produce product molecules, then we can subtract one from the other to arrive at an estimate of the enthalpy change for the overall chemical reaction:

$\Delta H^0_{(\text{reaction})}$ = sum of the bond energies of bonds being broken - sum of the bond energies of the bonds being formed.

$$\Delta H^0_{(\text{reaction})} = \sum H_{(\text{reactant bonds broken})} - \sum H_{(\text{product bonds formed})}$$

**Example 1.** For example, we could use the bond energies to calculate the heat of reaction (enthalpy change for the reaction), $\Delta H^0$, for the reaction:

$$CH_{4(g)} + 4Cl_{2(g)} \rightarrow CCl_{4(g)} + 4HCl_{(g)}$$

The bonds that need to be broken in the reactant molecules are:

- C-H bonds (there are 4 of these in a $CH_4$ molecule so we need to break 4 lots of C-H bonds)
- Cl-Cl bonds (there is 1 of these in each $Cl_2$ molecule, BUT, we need 4 lots of $Cl_2$ molecules to balance the equation, so, 4 lots of Cl-Cl bonds need to be broken)

The bonds that need to be made when the products are formed are:

- C-Cl bonds (there are 4 lots of C-Cl bonds in each CCl4 molecule so we need to make 4 lots of C-Cl bonds)
- H-Cl bonds (there is only 1 H-Cl in each HCl molecule, but we need 4 lots of HCl molecules so we will need to make 4 lots of H-Cl bonds)

We will need to use published values of bond energies (bond enthalpies) to calculate the value of the heat of reaction (enthalpy change for the reaction).

Our solution to the problem is shown below:

1. Write the balanced chemical equation, with all reactants and products in the gaseous state.

$$CH_{4(g)} + 4Cl_{2(g)} \rightarrow CCl_{4(g)} + 4HCl_{(g)}$$

2. Write the general equation for the heat of reaction (enthalpy change for the reaction):

$$\Delta H^0_{(reaction)} = \sum H_{(reactant\ bonds\ broken)} - \sum H_{(product\ bonds\ formed)}$$

3. Substitute bond energy values into the equation and solve for $\Delta H^0_{(reaction)}$

$$CH_{4(g)} + 4Cl_{2(g)} \rightarrow CCl_{4(g)} + 4HCl_{(g)}$$

| Energy absorbed to break bonds | | Energy released to form bonds | |
|---|---|---|---|
| bond type | bond energy | bond type | bond energy |
| 4 × C-H | 4 × 413 = 1652 | 4 × C - Cl | 4 × 339 = 1356 |
| 4 × Cl - Cl | 4 × 243 = 972 | 4 × H - Cl | 4 × 432 = 1728 |
| $\sum H$ (reactant bonds broken) = 2624 | | $\sum H$ (product bonds formed) = 3084 | |

4. $\Delta H^0_{(reaction)} = 2624 - 3084 = -460\ kJ\ mol^{-1}$

5. Note that the reaction is exothermic, $\Delta H$ is negative $(\Delta H = -460\,kJ\,mol^{-1})$

**Example 2:**

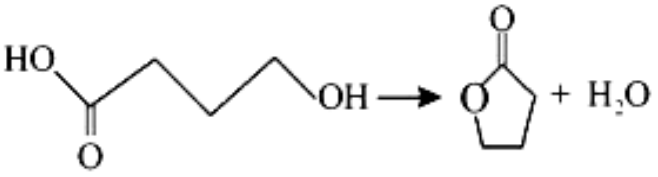
$$CH_3–CH = CH–CH_3 + H_2 \rightarrow CH_3–CH_2–CH_2–CH_3$$

| Bonds formed | (Kcal/mole) | Bonds broken | (Kcal/mole) |
|---|---|---|---|
| 2C-H | 196.4 | H-H | 103.2 |
| C-C | 80.5 | C=C | 145 |
| Total energy released = 276.9 | | Total energy consumed = 248.2 | |

$$\Delta H^0_{(reaction)} = \sum H_{(reactant\ bonds\ broken)} - \sum H_{(product\ bonds\ formed)}$$
$$= -276.9 + 248.2$$
$$= -28.7\ Kcal/mole$$

## 4.11 Intermolecular and intramolecular reactions

Intra-molecular esterification (i.e., lactone formation) is more favourable than intermolecular. Similarly intra-molecular hemiacetal formation is more favourable than intermolecular. These facts can be explained on the basis of entropy factor.




$$CH_3COOH + MeOH \rightarrow CH_3–OOCH_3 + H_2O$$

In each case, the bonds formed (C-O & O-H) corresponds to those broken. So is likely to be very small. This would not be true if there is significant strain in the lactone. In the esterification the changes in both translational entropy and rotational entropy are negligible since there is no change in the number of particles and the change in internal freedom $(\Delta S_{vib})$ is also likely to be negligible. Hence both $\Delta H$ and $\Delta S$ are not far from zero. So that $\Delta G$ nearly equal to zero and K=1. For lactonisation the number of particles is increased and hence there is an increase in translational entropy and rotational entropy but there is

corresponding loss in internal freedom. But overall change in entropy is positive. Consequently $\Delta G$ is negative and lactonisation is essentially complete.

For smaller ring, however the enthalpy change is less favourable because of strain in the ring and for larger rings the entropy term becomes increasingly less favourable as the size of ring is increased.

## 4.12 Summary

- Reaction Mechanism describes the step-by-step sequence of elementary reactions that lead to the overall chemical transformation.
- Ionic Reactions involve charged intermediates, facilitated by solvents. Radical Reactions involve free radicals and proceed via initiation, propagation, and termination steps. Pericyclic Reactions occur through a cyclic transition state without charged intermediates.
- Electrophiles are Electron-deficient species that accept electrons but Nucleophiles are Electron-rich species that donate electrons.
- Curly Arrow Representation: Used to depict electron flow in reaction mechanisms from nucleophiles to electrophiles.
- Reaction Thermodynamics determines reaction feasibility based on enthalpy $(\Delta H)$, entropy $(\Delta S)$, and Gibbs free energy $(\Delta G)$. $\Delta G = \Delta H - T\Delta S$
- Exothermic reactions release energy $(-\Delta H)$. Endothermic reactions absorb energy $(+\Delta H)$. Positive $\Delta S$ favors disorder and reaction spontaneity.
- Bond Dissociation Energy (BDE) and Enthalpy Change $(\Delta H) = \sum$(BDE of bonds broken) - $\sum$(BDE of bonds formed).
- Reactions are exothermic if the bonds formed are stronger than those broken.
- Intramolecular Reactions (e.g., lactonization) are entropically favored. Intermolecular Reactions require higher activation energy and are often less favorable.

## 4.13 Exercise

1. What is a reaction mechanism, and why is it important in the study of kinetics?
2. Differentiate between ionic and radical reactions with examples.
3. What are the three main types of pericyclic reactions?
4. Explain the mechanism of methane chlorination in the presence of light.
5. Define addition, elimination, and substitution reactions with suitable examples.
6. How does a substitution reaction differ from an elimination reaction?
7. Explain the difference between homolytic and heterolytic bond cleavage.
8. What type of species are produced in homolytic cleavage?
9. How do electrophiles and nucleophiles differ in terms of electron transfer?
10. Why do electrons always flow from nucleophiles to electrophiles?
11. How do thermodynamic factors like enthalpy, entropy, and Gibbs free energy determine the feasibility of a chemical reaction?
12. What does a negative $\Delta G$ indicate about a reaction?
13. How is Gibbs free energy $(\Delta G)$ related to enthalpy $(\Delta H)$ and entropy $(\Delta S)$?
14. How does the equilibrium constant relate to the standard free energy change?
15. Why is a reaction exothermic when stronger bonds are formed?
16. What is the significance of the entropy factor in determining reaction feasibility?
17. What happens when the energy required to break bonds is greater than the energy released during bond formation?
18. Why is the reaction $CH_4 + 4Cl_2 \rightarrow CCl_4 + 4HCl$ exothermic?
19. Why is intramolecular esterification more favorable than intermolecular?
20. What is the difference between intermolecular and intramolecular reactions, and how does entropy influence their favorability?

**Multiple-Choice Questions (MCQs)**

**1. Which of the following reactions involve charged species and bond formation between electrophiles and nucleophiles?**

A) Radical reactions

B) Pericyclic reactions

C) Ionic reactions

D) Photochemical reactions

Answer: C) Ionic reactions

**2. Which of the following is an example of a radical reaction?**

A) Hydrolysis of alkyl halides

B) Chlorination of methane in the presence of light

C) Diels-Alder reaction

D) SN1 reaction

Answer: B) Chlorination of methane in the presence of light

**3. Which reaction type involves a cyclic transition state without the formation of ionic intermediates?**

A) Ionic reaction

B) Radical reaction

C) Pericyclic reaction

D) Nucleophilic substitution

Answer: C) Pericyclic reaction

**4. What type of reaction is represented by the addition of HBr to ethene?**

A) Addition reaction

B) Elimination reaction

C) Substitution reaction

D) Rearrangement reaction

Answer: A) Addition reaction

**5. Which of the following is an example of an elimination reaction?**

A) Formation of ethene from ethanol in the presence of acid

B) Addition of bromine to an alkene

C) Substitution of Br in CH3Br with OH?

D) Formation of tert-butyl carbocation

Answer: A) Formation of ethene from ethanol in the presence of acid

**6. In homolytic cleavage, the bond breaks in such a way that:**

A) One atom retains both electrons

B) Each atom gets one electron

C) A cation and an anion are formed

D) One atom donates electrons to another

Answer: B) Each atom gets one electron

**7. Which of the following statements about electrophiles is correct?**

A) Electrophiles donate electrons

B) Electrophiles have a positive charge or partial positive charge

C) Electrophiles are electron-rich species

D) Electrophiles are repelled by nucleophiles

Answer: B) Electrophiles have a positive charge or partial positive charge

**8. The movement of electron pairs in reaction mechanisms is represented using:**

A) Straight arrows

B) Curly arrows

C) Wavy arrows

D) Dotted arrows

Answer: B) Curly arrows

**9. Which thermodynamic quantity determines whether a reaction is spontaneous?**

A) Enthalpy ($\Delta H$)

B) Entropy ($\Delta S$)

C) Gibbs free energy ($\Delta G$)

D) Bond dissociation energy (BDE)

Answer: C) Gibbs free energy ($\Delta G$)

**10. If the equilibrium constant (K) of a reaction is very large, the reaction:**

A) Proceeds to completion

B) Hardly moves forward

C) Is at equilibrium with equal amounts of reactants and products

D) Requires external energy input

Answer: A) Proceeds to completion

**11. The equation $\Delta G = \Delta H - T\Delta S$ represents the relationship between:**

A) Enthalpy and entropy only

B) Free energy, enthalpy, and entropy

C) Free energy and equilibrium constant

D) Bond energy and reaction mechanism

Answer: B) Free energy, enthalpy, and entropy

**12. In an exothermic reaction, which of the following is true?**

A) Heat is absorbed

B) Heat is released

C) The reaction cannot occur spontaneously

D) The reactants have lower bond energy than the products

Answer: B) Heat is released

**13. The bond dissociation energy (BDE) is used to calculate:**

A) The entropy change of a reaction

B) The enthalpy change of a reaction

C) The spontaneity of a reaction

D) The equilibrium constant

Answer: B) The enthalpy change of a reaction

**14. In an intramolecular reaction, the reacting groups are present:**

A) In two different molecules

B) In the same molecule

C) In different phases

D) Only in ionic form

Answer: B) In the same molecule

# Unit 5 ❐ Reactive intermediates

## Structure



## 5.0 Objectives

After studying this topic, learners will be able to:

- Understand the concept of reactive intermediates and their role in organic reaction mechanisms.
- Identify different types of reactive intermediates including carbocations, carbanions, carbon radicals, and carbenes.
- Differentiate between carbenium and carbonium ions based on their structure and stability.
- Explain the generation and stability factors of reactive intermediates.
- Analyze the structure of reactive intermediates using orbital diagrams.
- Describe the electrophilic and nucleophilic behavior of these intermediates in chemical reactions.
- Predict the reactivity and stability of reactive intermediates based on electronic and steric effects.

## 5.1 Introduction

Reactive intermediates are short-lived, highly reactive species that play a crucial role in organic reaction mechanisms. These intermediates form during the transformation of reactants into products and influence the reaction pathway, rate, and selectivity. The main types of reactive intermediates include carbocations (carbenium and carbonium ions), carbanions, carbon radicals, and carbenes.

Each of these species has unique structural characteristics, stability factors, and reactivity patterns. Carbocations are electron-deficient species acting as electrophiles, while carbanions are electron-rich species functioning as nucleophiles. Radicals contain unpaired electrons and undergo chain reactions, while carbenes exhibit both electrophilic and nucleophilic behavior. Understanding the generation, stability, and orbital structures of these intermediates is essential for predicting reaction mechanisms and designing synthetic pathways in organic chemistry.

## 5.2 Reactive intermediates

A reactive intermediate or an intermediate is a short-lived, high-energy, highly reactive molecule.

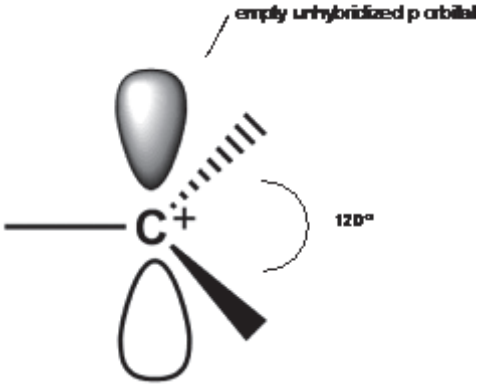
- When generated in a chemical reaction, it will quickly convert into a more stable molecule.
- Their importance lies in the assignment of reaction mechanisms on the pathway from the starting substrate to stable products.
- These reactive intermediates are not isolated, but are detected by spectroscopic methods or trapped chemically or their presence is confirmed by indirect evidence.

**Examples:** Carbocations (carbenium and carbonium ions), carbanions, carbon radicals, and carbenes:

## 5.3 Carbocations

Carbocations are the key intermediates in several reactions and particularly in nucleophilic substitution reactions.

Structure of Carbocations: Generally, in the carbocations the positively charged carbon atom is bonded to three other atoms and has no nonbonding electrons. It is $sp^2$ hybridized with a planar structure and bond angles of about 120°. There is a vacant unhybridized p orbital which in the case of $CH_3^+$ lies perpendicular to the plane of C–H bonds.

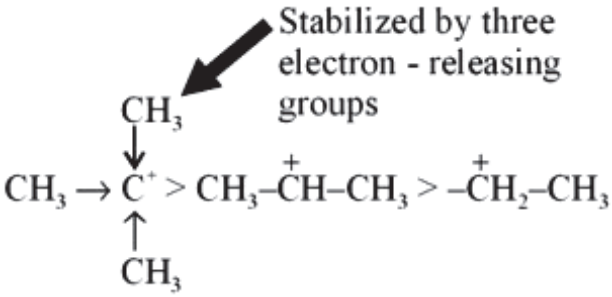



**Stability of Carbocations:**

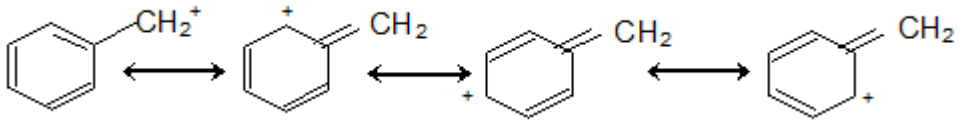
Stability of carbocations 3° > 2° > 1° > $CH_3^+$

Thus one finds that addition of HX to three typical olefins decreases in the order $(CH_3)2C{=}CH_2 > CH_3\text{-}CH = CH_2 > CH_2 = CH_2$.

This is due to the relative stabilities of the carbocations formed in the rate determining step which in turn follows from the fact that the stability is increased by the electron releasing methyl group (+I), three such groups being more effective than two, and two more effective than one.



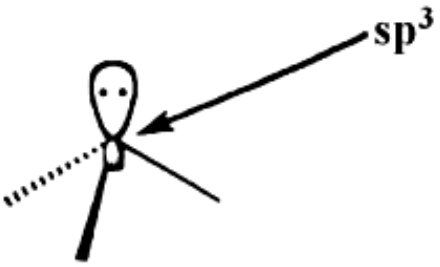

- **Electron release:** Disperses charge, stabilizes carbocation.
- Benzyl cation is highly stabilized by the following type of resonance.



## 5.4 Carbanions

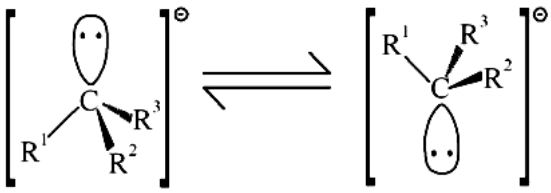
Negatively charged trivalent carbon atom.

**Structure of Carbanions:** A carbanion possesses an unshared pair of electron and thus represents a base. The best likely description is that the central carbon atom is $sp^3$ hybridized with the unshared pair occupying one apex of the tetrahedron.




Pyramidal

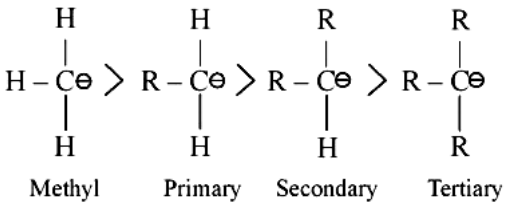
- Carbanions would thus have pyramidal structures similar to those of amines.
- It is believed that carbanions undergo a rapid interconversion between two pyramidal forms.



**Pyramidal inversion**

**Stability of Carbanions:**

$3°, 2° < 1° < CH_3^-$

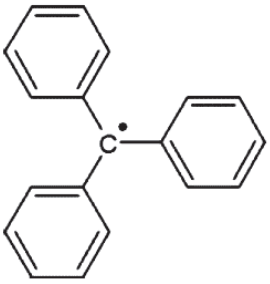



**Properties of Carbanions:** Carbanions are nucleophilic and basic and in this behavior these are similar to amines, since the carbanion has a negative charge on its carbon, to

make it a powerful base and a stronger nucleophile than an amine. Consequently a carbanion is enough basic to remove a proton from ammonia

## 5.5 Carbon radicals

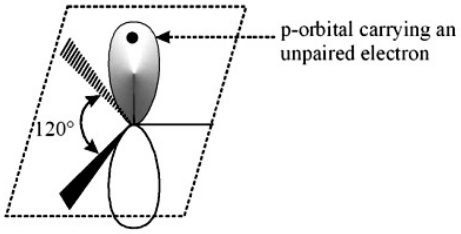
In this module an overview of carbon radicals are given. Some preliminary examples of their structure, properties, generation and reactions are provided.

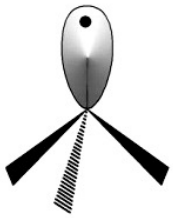


The first organic free radical identified was triphenylmethyl radical formed by abstraction of chlorine by silver metal. This species was discovered by Moses Gomberg in 1900 at the University of Michigan USA.

- A radical is a reactive intermediate with a single unpaired electron, having very short lifetime. It is represented by atom with one dot
- Carbon radical is a neutral carbon species with three single bonds and one unpaired electron.

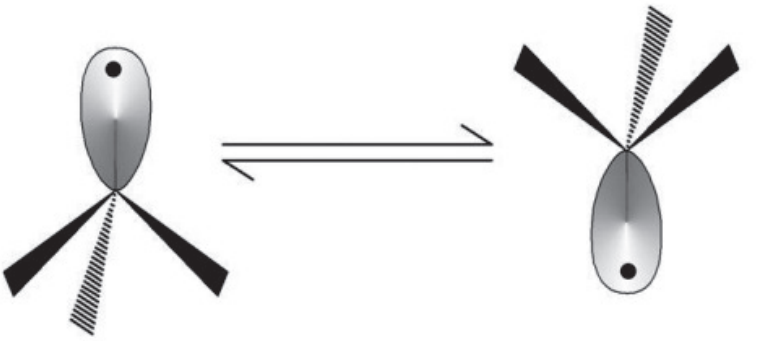
**Structure:** A carbon radical is $sp^2$ hybridized with an unpaired single electron occupying an unhybridized p-orbital, having trigonal pyramidal or planar geometry possessing an angle of $120^o$



$sp_z$ Hybridised carbon having rigid pyrimidal geometry

- Like carbanions, carbon radicals undergo a rapid interconversion between two pyramidal forms.



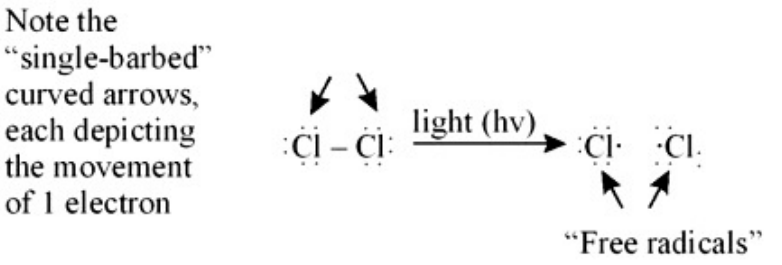
Flexible pyramidal geometry

- In most of the cases the pyramidal geometry is observed, especially when heteroatom's are $\pi$ electron donating substituent or electronegative groups like **flourine** or **oxygen** are present. However, some of the lower group of **alkyl class likes methyl** posses **planer geometry**, t-butyl show pyramidal geometry with a slight characteristic of planer geometry.

**Generation:** Homolytic cleavage of a covalent bond produces radicals. In this process each of the atoms of a covalent bond gets one of the bonding electrons.

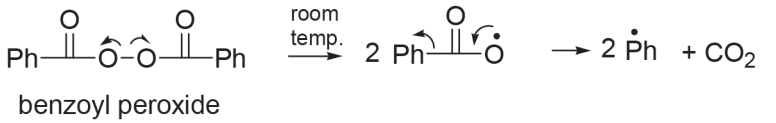
$$A - B \qquad A^{\bullet} + B^{\bullet}$$

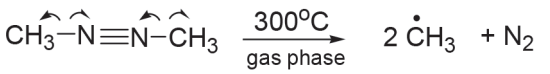
**Example:** formation of chlorine radicals in presence of light.



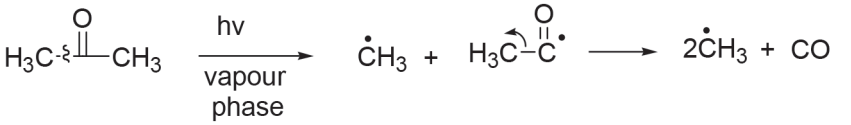
Free radicals may be generated by the following way.

i) **Thermolysis:** Thermal decomposition of weak covalent bonds gives free radicals.

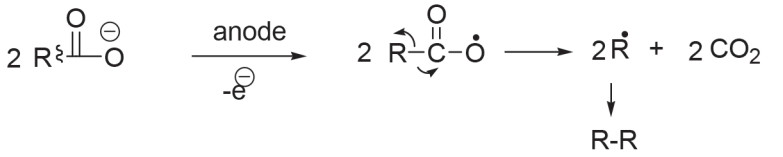


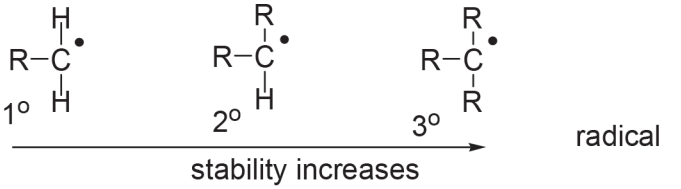

ii) **Photolysis:** Photochemical dissociation (visible or UV light) of covalent bonds may generate free radicals.



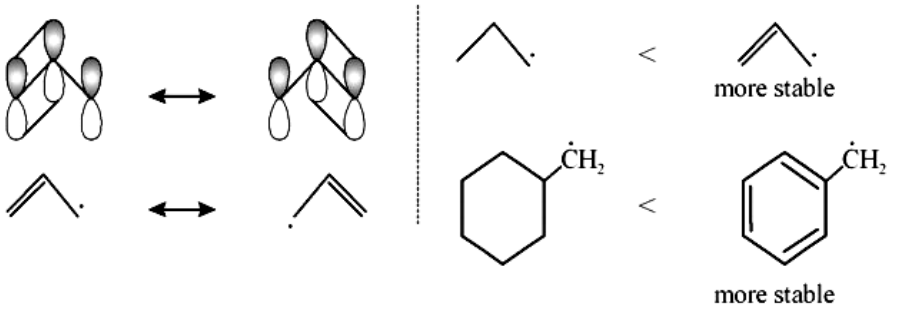

iii) **Redox reaction:** Single electron transfer reactions (SET) are very much useful to produce free radicals. One such reaction is the Kolbe electrolysis of the salts of carboxylic acids.



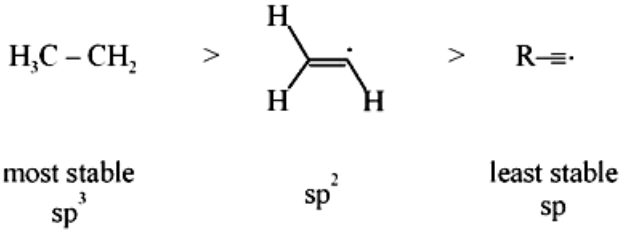

**Stability:** Like carbonium ions, a tertiary free radical is more stable than a secondary which in turn is more stable than a primary.



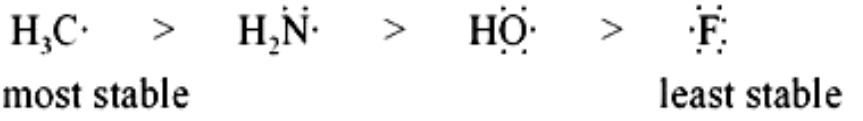
- Free radicals are stabilized by resonance.




- Free radicals decrease in stability as the % of s-character in the orbital increases [i.e. as the half-empty orbital becomes closer to the nucleus]. For that reason, free radical stability decreases as the atom goes from $sp^3$ –> $sp^2$ –> sp




- Across a row of the periodic table, free radicals decrease in stability as the electronegativity increases.




## 5.6 Carbenes

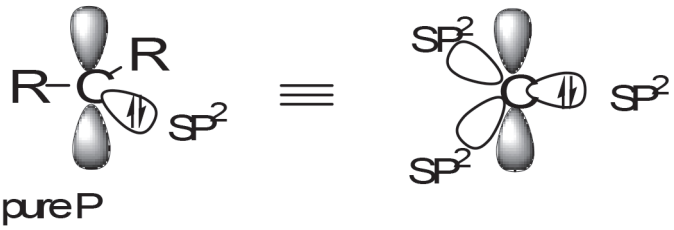
Carbenes are neutral divalent species containing a carbon atom with only six valence electrons. Carbenes are usually formed from precursors by the loss of small, stable molecules.

The simplest member of the class is methylene, a non isolable species of molecular formula $H_2C$: besides the most common carbene is $CCl_2$:

**Classifications:** The structure, stability and reactivity of carbenes are very dependent on the electron configuration of the carbenic atom. The major division that is used to classify carbenes is whether the two non-bonding electrons are paired **(singlet)** or unpaired **(triplet).**

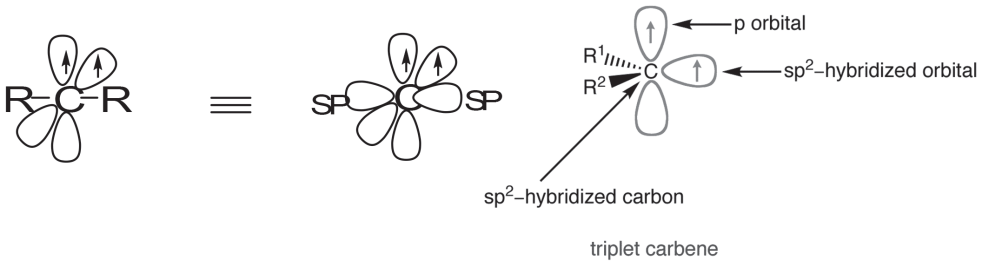
Singlet carbene: In singlet state a carbon atom is approximately $Sp^2$ hybridized. Two of three $Sp^2$ hybrid orbitals are used in forming two covalent bonds where as the third orbital contains the unshared pair of electrons. The bond angle would be expected to be less than normal 120 $^0$C due to L.P. - L.P.> L.P.-B.P.> B.P.-B.P. repulsions.

(Singlet state: carbocation-like in nature, trigonal planar geometry, electrophilic character).

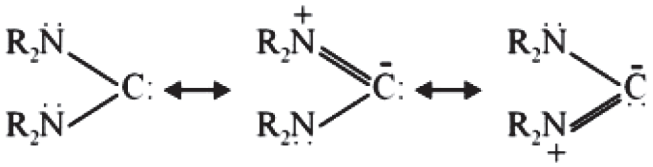



**Triplet carbene:** In triplet state a carbon atom is Sp hybridized and it is linear. These two hybrid orbitals are involved in bond formation with two groups and the remaining two electrons are placed one each of the two unhybrid orbitals). $Sp^2$ triplet carbene are also possible.

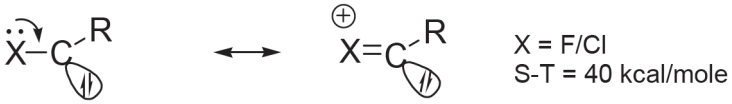
(Triplet state: diradical-like in nature, linear geometry)




**Stability:** Carbenes in which the carbon of carbene is attached to two atoms, each bearing a lone pair of electron are more stable due to resonance.



- **Triplet Carbenes are more stable than singlet Carbene.**
- In general dialkyl carbenes ($R_2C$:) are ground state triplet. Lone pair donors can stabilize the singlet state more than triplet state by '$\pi$' -donation into the vacant 'P' orbital.

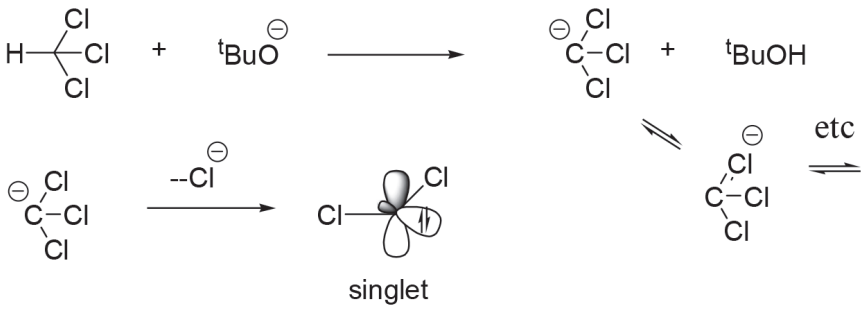



- For $H_2C$: or $Li_2C$:, triplet state is more stable than singlet state and the energy difference is 10-20 kcal/mole.
- Because of these properties, the parent carbene :$CH_2$ (or dialkyl carbene) has a triplet ground state.

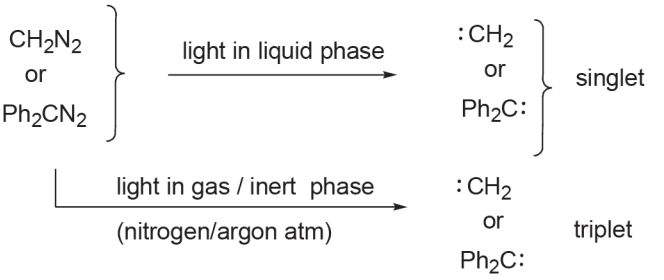
**Properties:** A singlet carbene may act as a Lewis bases and can donate it,s non-bonded electron pair. Again, by accepting two electrons in the vacant 'p' orbital it can acts as a Lewis acid. Triplet carbene acts as diradical.

**Formation reactions of carbenes:**

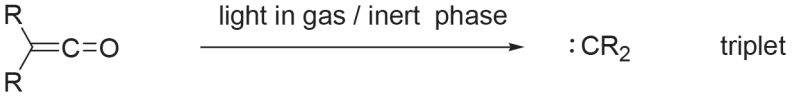
a) Reaction between $CHCl_3$ and strong base e.g. $^{-}OH$ or $^{t}BuO^{-}$



b) Photolysis or thermolysis of diazocompounds

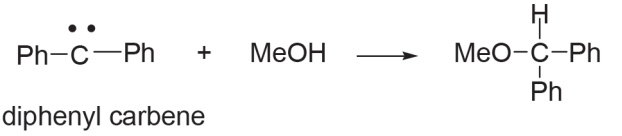



c) photolysis of ketenes:

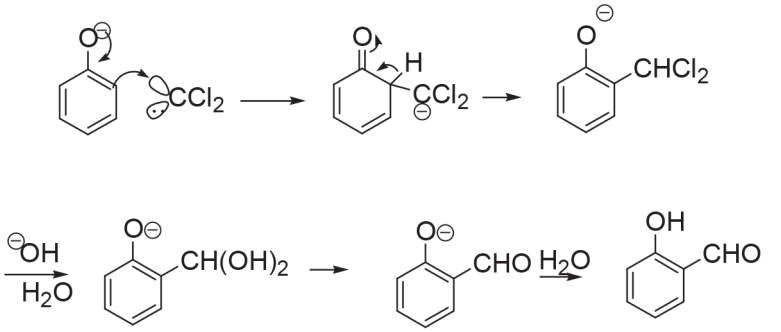



**Reactions of carbene:**

i) Acts as electrophile




In Reimer Tiemann Reaction:

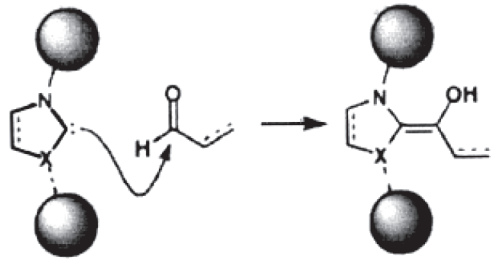


ii) Acts as nucleophile

N-Heterocyclic carbene acts as nucleophile.


(Ad = alkyl or aryl group

**Example:**




nucleophile

## 5.7 Summary

- Reactive Intermediates are Short-lived, high-energy species crucial in organic reaction mechanisms.
- Reactive intermediates include carbocations, carbanions, carbon radicals, and carbenes.
- Carbocations are positively charged carbon species, $sp^2$ hybridized, stabilized by inductive and resonance effects.
- Carbanions are negatively charged carbon species, $sp^3$ hybridized, nucleophilic and highly basic.
- Carbon Radicals are neutral species with an unpaired electron, $sp^2$ hybridized, stabilized by resonance and hyperconjugation.

- Carbenes are neutral divalent carbon species, classified into singlet and triplet states.
- Reactive intermediates are formed through homolysis, heterolysis, photolysis, redox reactions, or base-induced elimination.
- Stability Factors of reactive Intermediates depend on resonance, inductive effects, steric hindrance, and hybridization.
- Carbocations act as electrophiles, carbanions as nucleophiles, radicals undergo chain reactions, and carbenes exhibit dual reactivity.

## 5.8 Exercise

1. What are carbocations, and in which reactions do they play a key role?
2. Describe the structure of a carbocation and explain its hybridization.
3. Why are tertiary carbocations more stable than primary and secondary carbocations?
4. How does resonance stabilize benzyl carbocations?
5. What is a carbanion, and how does its structure differ from a carbocation?
6. Explain the hybridization and geometry of carbanions.
7. Why are carbanions considered strong nucleophiles and bases?
8. Define a carbon radical and describe its electronic structure.
9. Explain why tertiary radicals are more stable than primary radicals.
10. What are carbenes, and how are they classified?
11. Differentiate between singlet and triplet carbenes in terms of structure and stability.
12. What are some common methods for generating carbenes?
13. Explain the role of carbenes in the Reimer-Tiemann reaction.
14. How can a singlet carbene act as both a nucleophile and an electrophile?
15. Predict the stability order of the following carbocations: $CH_3^+$, $(CH_3)3C^+$, $C_6H_5CH_2^+$, and $CH_3CH_2^+$.
16. Which intermediate is most likely to form in a nucleophilic substitution reaction: a carbocation or a carbanion? Why?

**Multiple-Choice Questions (MCQs)**

**1. What is a reactive intermediate?**

A) A stable organic molecule

B) A short-lived, high-energy species formed during a reaction

C) A product of a completed reaction

D) A molecule that does not participate in reactions

Answer: B) A short-lived, high-energy species formed during a reaction

**2. Which of the following is NOT a type of reactive intermediate?**

A) Carbocation

B) Carbanion

C) Carbyne

D) Carbene

Answer: C) Carbyne

**3. What is the hybridization of a typical carbocation?**

A) $sp^3$

B) $sp^2$

C) sp

D) $dsp^2$

Answer: B) $sp^2$

**4. Which of the following factors increases the stability of a carbocation?**

A) Presence of electron-withdrawing groups

B) Presence of electron-donating groups

C) Decreasing alkyl substitution

D) High electronegativity of carbon

Answer: B) Presence of electron-donating groups

**5. Which of the following carbocations is the most stable?**

A) Methyl carbocation ($CH_3^+$)

B) Primary carbocation ($CH_3CH_2^+$)

C) Secondary carbocation ($CH_3CH^+CH_3$)

D) Tertiary carbocation ($(CH_3)3C^+$)

Answer: D) Tertiary carbocation ($(CH_3)3C^+$)

**6. What is the geometry of a carbanion?**

A) Linear

B) Planar

C) Pyramidal

D) Tetrahedral

Answer: C) Pyramidal

**7. Carbanions are best described as:**

A) Electrophilic species

B) Nucleophilic species

C) Neutral species

D) Unstable radicals

Answer: B) Nucleophilic species

**8. Which statement is true about carbon radicals?**

A) They have a full octet of electrons

B) They contain an unpaired electron

C) They are highly stable

D) They do not participate in chain reactions

Answer: B) They contain an unpaired electron

**9. The hybridization of a carbon radical is usually:**

A) $sp^3$

B) $sp^2$

C) sp

D) $dsp^3$

Answer: B) $sp^2$

**10. What is the order of stability of carbon radicals?**

A) Methyl > Primary > Secondary > Tertiary

B) Tertiary > Secondary > Primary > Methyl

C) Primary > Tertiary > Methyl > Secondary

D) Methyl > Secondary > Primary > Tertiary

Answer: B) Tertiary > Secondary > Primary > Methyl

**11. Which method is NOT a common way to generate carbon radicals?**

A) Homolytic cleavage

B) Photolysis

C) Redox reactions

D) Electrophilic addition

Answer: D) Electrophilic addition

**12. What is the ground state of methylene (:CH2)?**

A) Singlet

B) Triplet

C) Both singlet and triplet

D) None of the above

Answer: B) Triplet

**13. Which of the following carbenes is more stable?**

A) Singlet carbene

B) Triplet carbene

C) Both are equally stable

D) None of the above

Answer: B) Triplet carbene

**14. How can carbenes be generated?**

A) Reaction of $CHCl_3$ with a strong base

B) Photolysis of diazocompounds

C) Photolysis of ketenes

D) All of the above

Answer: D) All of the above

**15. Which reaction involves the generation of a carbene?**

A) Kolbe electrolysis

B) Reimer-Tiemann reaction

C) Aldol condensation

D) Diels-Alder reaction

Answer: B) Reimer-Tiemann reaction

# Unit 6 ❐ Concept of organic acids and bases

## Structure

## 6.0 Objectives

After studying this unit, learners will be able to:

- Understand the effect of molecular structure on acidity and basicity.
- Analyze how different substituents influence the acidic and basic properties of organic and inorganic compounds.
- Examine the role of solvents in modulating acidity and basicity in different chemical environments.
- Explain the concept of a proton sponge and its significance in acid-base chemistry.
- Define and compare gas-phase acidity and basicity with solution-phase properties.
- Understand the Hard and Soft Acids and Bases (HSAB) principle and its theoretical framework.
- Correlate acidity and basicity with reactivity in organic synthesis and catalysis.

## 6.1 Introduction

Acidity and basicity are crucial in chemistry, influencing reaction mechanisms and molecular stability. Their strength depends on molecular structure, substituents, and solvent effects. The HSAB principle helps explain reaction selectivity by classifying acids and bases based on polarizability and charge density. Additionally, distinguishing nucleophilicity from basicity is essential for understanding reactivity. This unit explores these key topics, providing a comprehensive understanding of how structure, environment, and fundamental chemical principles dictate acidity, basicity, and reactivity in organic chemistry.

## 6.2 Acid and Base

An **Arrhenius acid** is any species that increases the concentration of $H^+$ in aqueous solution. In aqueous solution, $H^+$ ions immediately react with water molecules to form **hydronium ions**, $H_3O^+$. For example, let's consider the dissociation reaction for hydrochloric acid, HCl, in water;

$$HCl\ (aq) \rightarrow H^+\ (aq) + Cl^-\ (aq)$$

When we make an aqueous solution of hydrochloric acid, then it dissociates into $H^+$ ions and $Cl^-$ ions. Since this result in an increase in the concentration of $H^+$ ions in solution, hydrochloric acid is an Arrhenius acid.

An Arrhenius base is defined as any species that increases the concentration of hydroxide ions, $OH^-$, in aqueous solution. An example of an Arrhenius base is the highly soluble sodium hydroxide, NaOH. Sodium hydroxide dissociates in water as follows:

$$NaOH(aq) \rightarrow Na^+(aq) + OH^-(aq)$$

In water, sodium hydroxide fully dissociates to form $OH^-$ and $Na^+$ ions, resulting in an increase in the concentration of hydroxide ions. Therefore, NaOH is an Arrhenius base.

Lewis' theory specifically stated that an acid is a species that accepts an electron pair while a base donates an electron pair.

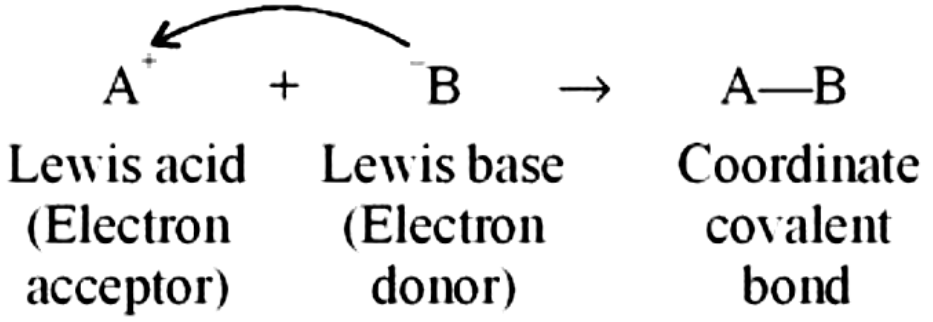



Figure 11: A Lewis Base (B) donates its electrons to a Lewis Acid (A) resulting in a coordinate covalently bonded compound, also known as an adduct.

The reaction of a Lewis acid and a Lewis base will produce a coordinate covalent bond, as shown in Figure 11 above. A coordinate covalent bond is just a type of covalent bond in which one reactant gives it electron pair to another reactant. In this case the lewis base donates its electrons to the lewis acid. When they do react this way the resulting product is called an addition compound, or more commonly an adduct.

- **Lewis Acid:** a species that accepts an electron pair (i.e., an electrophile) and will have vacant orbitals
- **Lewis Base:** a species that donates an electron pair (i.e., a nucleophile) and will have lone-pair electrons

When Lewis acid bonds with a base, the acid uses its lowest unoccupied molecular orbital or LUMO.

- Various species can act as Lewis acids. All cations are Lewis acids since they are able to accept electrons. (e.g., $Cu^{2+}$, $Fe^{2+}$, $Fe^{3+}$)
- An atom, ion, or molecule with an incomplete octet of electrons can act as a Lewis acid (e.g., $BF_3$, $AlF_3$).
- Molecules where the central atom can have more than 8 valence shell electrons can be electron acceptors, and thus are classified as Lewis acids (e.g., $SiBr_4$, $SiF_4$).
- Molecules that have multiple bonds between two atoms of different electronegativities (e.g., $CO_2$, $SO_2$) behave as Lewis acids.

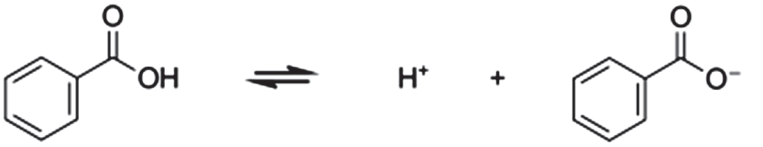
Lewis Bases donate an electron pair. Lewis Bases utilize the highest occupied molecular orbital or HOMO. An atom, ion, or molecule with a lone-pair of electrons can thus be a Lewis base. Each of the followings can ‘‘give up’’ their electrons to an acid, e.g., $OH^-$, $CN^-$, $CH_3COO^-$, $H_2O$:, :$NH_3$, $CH_3$-$NH_2$ etc.

Each acid has its own dissociation constant (Ka). The larger the dissociation constant, the more will be the strength of acid. Dissociation constant may otherwise be written as PKa = ?logKa. Stronger acids have smaller PKa values.

There are two types of acids in general:

1. **Neutral acids:** Neutral acids are such molecules which have no overall charge, e.g., HCl, HBr, $CH_3COOH$, PhCOOH (benzoic acid), etc.

These acids release anionic conjugate bases, negatively charged conjugate bases, such as $Cl^-$, $Br^-$, $CH_3COO^-$, $PhCOO^-$ (benzoate anion) etc.

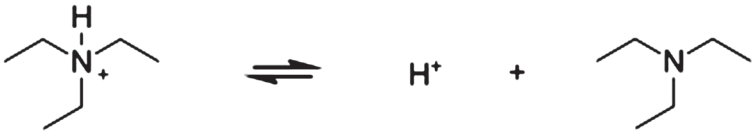



benzoic acid
**(neutral acid)**

benzoate anion
**(anionic conjugate base)**

2. **Cationic acids:** These are positively charged species. Usually the acids in this class are protonated nitrogens or oxygens, such as $NH_4^+$ (ammonium ion), $Et_3NH^+$ (triethylammonium ion), $C_5H_5NH^+$ (pyridinium ion), $H_3O^+$ (hydronium ion), and protonated carbonyls ($R_2C{=}OH^+$) and alcohols ($R{-}OH_2^+$).

These acids release neutral conjugate bases, conjugate bases with no overall charge, such as $NH_3$ (ammonia), $Et_3N$ (triethylamine), $C_5H_5N$ (pyridine), $H_2O$ (water), and neutral carbonyls ($R_2C{=}O$) and alcohols (R–OH).




protonated triethylamine
**(cationic acid)**

triethylamine
**(neutral conjugate base)**

We have to remember that a strong acid is an acid that releases weak (stable) conjugate base, whilst a weak acid is an acid that releases strong (unstable) conjugate base. Therefore, to predict the acidity of neutral acids, we have to examine the stability of their conjugate bases.

Cationic acids release neutral conjugate bases. Neutral conjugate bases are generally stable. Cationic acids however, may or may not be stable. If the cationic acids are unstable, they give away their proton easily, hence they are strong acids. If the cationic acids are stable, they don't give away their proton easily, hence they are weak acids. Therefore, to predict the acidity of cationic acids, we have to examine their own stability.

Therefore, the question that we need to address is; what are the factors that can make the charged species more stable? Now we will look at the various factors that influence the acidity of organic compounds.

## 6.3 Factors that influence the acidity

Factors that affect the strength of acidity of molecules are given below-

**1. Hybridisation:** The sp hybridisation has 50% s character, which stabilises the negative charge of a species. We get stronger acids as we go from **$sp^3$** to **$sp^2$** to **sp** hybridizations.

**2. Electronegativity:** As we go across the periodic table, the electronegativity effect

outweighs the bond strength effect. We get stronger acids as we go from left to right due to the increase of electronegativity.

**3. Bond strength:** As we go down the periodic table, the effect of bond strength become more significant compared to electronegativity. We get stronger acids due to the decrease in bond strength.

**4. Inductive effect:** Electronegative atoms are electron-withdrawing groups. They pull electron density towards themselves, making the conjugate base of an acid more stable, and therefore making the acid stronger.

**5. Resonance:** Resonance stabilises charged species. The more they're stabilised by resonance, the more acidic they become.

**6. Aromaticity:** Aromatic conjugate bases are stable and make for stronger acids. Anti aromatic conjugate bases are unstable and make for weaker acids.

**7. Solvation:** Conjugated bases that can be well solvated by the solvent molecules give stronger acids.

Let us understand above factors with examples.

### 6.3.1. Hybridisation

In organic chemistry, there are three types of hybridisation: sp3 (for single bonds), sp2 (for double bonds), and sp (for triple bonds).

Let's compare the acidity between ethane (an alkane), ethylene (an alkene), and acetylene (an alkyne).

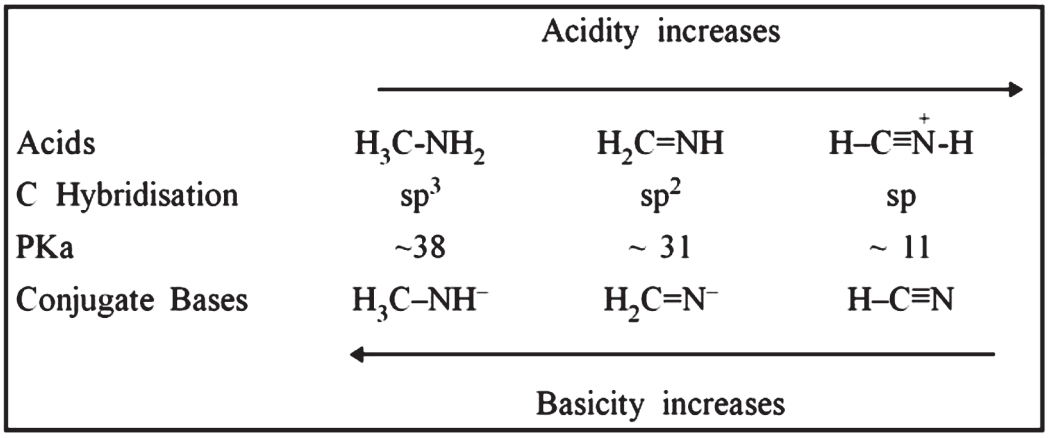
| | Acidity increases → | | |
|---|---|---|---|
| Acids | $H_3C–CH_3$ | $H_2C=CH_2$ | $H–C\equiv C–H$ |
| C Hybridisation | $sp^3$ | $sp^2$ | sp |
| pKa | ~50 | ~43 | ~25 |
| Conjugate Bases | $H_3C–CH_2^-$ | $H_2C=CH^-$ | $H–C\equiv C^-$ |
| | stability increases → | | |

An alkene is about 107 times more acidic than an alkane, and an alkyne is about 1015 times more acidic than alkane. Alkyne (sp hybridisation) have more s character than alkene ($sp^2$) and alkane ($sp^3$). Why does having more s character means more acidic? Recall from your general chemistry or physical chemistry lectures that the s orbital is spherical around the centre of the atom (nucleus). On the other hand, each of the p orbitals (px, py, and pz) has two lobes with a node near the nucleus. A node is a part of the orbital that has no electron density.

This means that the s orbital can feel the positive charge of the nucleus better than the p orbitals (because of the presence of nodes in the p orbitals). A negative charge in the s orbital is able to feel the positive charge from the nucleus. The positive charge from the nucleus stabilises negative charge (opposites attract).

Therefore, a negative charge can be stabilised better by the s orbital rather than by the **p** orbital. This is why more **s** character means more negative charge stabilization. The three examples above are neutral acids that release anionic conjugate base. The negative charge of the conjugate base is stabilised better as the **s** character increases. This makes **$sp^2$** hybridisation better at stabilising negative charge than **$sp^3$** hybridisation (alkene is more acidic than alkane). This also makes ***sp*** hybridisation (alkyne) the most acidic amongst the three.

This is also evident in the nitrogen analogues:




The above three examples in the nitrogen analogues are (from left to right) amine, imine, and protonated nitrile. Amine and imine are neutral acids but protonated nitrile is a cationic

acid. Therefore, the explanation mentioned above can easily be applied to amine and imine, but what about protonated nitrile? The nitrile is **sp** hybridised, and that more **s** character means more negative charge stabilisation. The protonated nitrile has a positive charge and therefore gets destabilised by the s character. Therefore, the cationic acid is destabilized and releases its proton easily and becomes a strong acid.

### 6.3.2. Electronegativity and Bond Strength:

It is known to us the followings;

- Electronegativity increases from left to right
- Electronegativity decreases from top to bottom
- Atomic radius (size) decreases from left to right causing bond strength to increase
- Atomic radius (size) increases from top to bottom causing bond strength to decrease

Now, have a look at the trends in acidity within the periodic table:

Acidity increases & Basicity of conjugate base decreases as electronegativity increases →

| | **C** | **N** | **O** | **F** |
|---|---|---|---|---|
| Acids → | $CH_4$ | $NH_3$ | $H_2O$ | HF |
| $pK_a$ → | 50 | 38 | 15.7 | 3.2 |
| conjugate bases → | $CH_3^-$ | $NH_2^-$ | $OH^-$ | $F^-$ |
| | **Si** | **P** | **S** | **Cl** |
| | $SiH_4$ | $PH_3$ | $H_2S$ | HCl |
| | 35 | 27 | 7 | –7 |
| | $SiH_3^-$ | $PH_2^-$ | $SH^-$ | $Cl^-$ |
| | **Ge** | **As** | **Se** | **Br** |
| | $GeH_4$ | $AsH_3$ | $H_2Se$ | HBr |
| | 25 | 22 | 4 | –9 |
| | $GeH_3^-$ | $AsH_2^-$ | $SeH^-$ | $Br^-$ |
| | | | **Te** | **I** |
| | | | $H_2Te$ | HI |
| | | | 3 | –10 |
| | | | $TeH^{3-}$ | $I^-$ |

Acidity increases & Basicity of conjugate base decreases as bond strength decreases due to the increase in radius (size) ↓

Some of you may ask yourself this: 'acidity increases as electronegativity increases when we go across (left to right) the periodic table, but acidity also increases as electronegativity decreases when we go down (top to bottom) the periodic table. Why??

Others may also ask this: 'acidity increases as size increases when we go down (top to bottom) the periodic table, but acidity also increases as size decreases when we go across (left to right) the periodic table. Why??'

You may also ask the other way around for each case, but regardless how you ask your question, this seemingly contradictory trend can actually be explained easily:

- Across the periodic table, acidity is influenced by electronegativity
- Down the periodic table, acidity is influenced by bond strength

**6.3.2.1. Across the Periodic Table, Acidity is influenced by Electronegativity**

'As we go across the periodic table, acidity increases as electronegativity increases'

The increase in electronegativity means the species is able to stabilise negative charge better. Compare the following acids from the first row:

| | Acidity increases → | | | |
|---|---|---|---|---|
| Acids | $CH_4$ | $NH_3$ | $H_2O$ | HF |
| $PK_a$ | 50 | 38 | 15.7 | 3.2 |
| Conjugate Bases | $CH_3^-$ | $NH_2^-$ | $OH^-$ | $F^-$ |
| | ← Basicity increases | | | |

The acids are neutral, so they release anionic conjugate bases. The negatively charged species gets more and more stabilised as its electronegativity increases. Therefore, conjugate base gets more and more stabilised by the increased electronegativity. The stability order of conjugate bases is as follows:

$$CH_3^- < NH_2^- < OH^- < F^-$$

The bond strength does not significantly affect the acidity when you go across the periodic table, because the elements in the same row have similar energy level and overlap of

orbitals between H and the element itself. Therefore the acidity order is $CH_4 < NH_3 < H_2O < HF$.

### 6.3.2.2. Down the Periodic Table, Acidity is Influenced by Bond Strength

'As we go down the periodic table, acidity increases as bond strength decreases'

As you go down the periodic table, the atomic radius (size) becomes larger. This means that the orbital overlap between the element and H gets more and more ineffective. In turn, this causes the acid to release its proton more easily. Compare the following acids from the halogen group:

Acidity increases →

| Acids | HF | HCl | HBr | HI |
|---|---|---|---|---|
| PKa | 3.2 | –7 | –9 | –10 |
| Conjugate Bases | $F^-$ | $Cl^-$ | $Br^-$ | $I^-$ |

← Basicity increases

The increase in size and the decrease in bond strength affect the acidity more than the increase in electronegativity as we go down the periodic table. Therefore HI becomes the strongest acid amongst the other acids in its group.

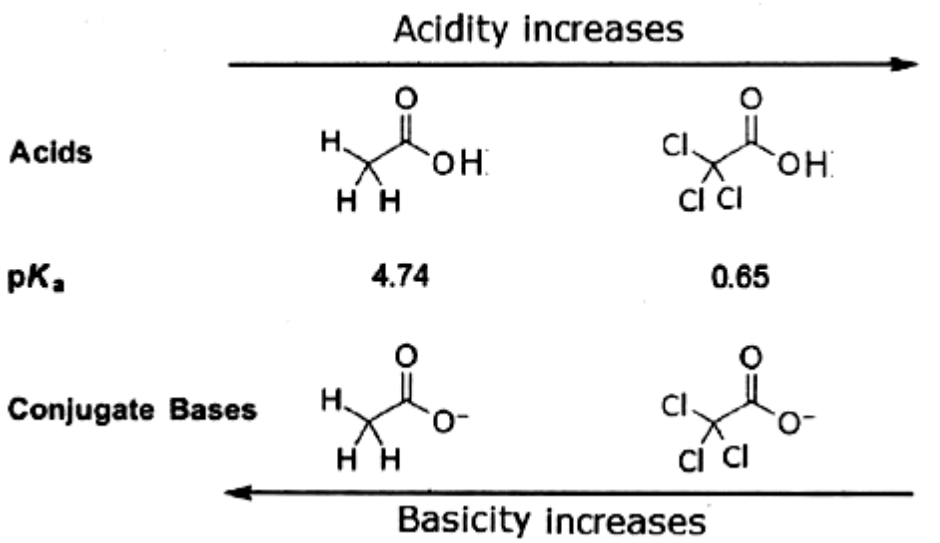
### 6.3.3 Inductive effect

In the section above, it has been shown how electronegativity affects the acidity of the $H^+$ directly bonded to the electronegative atom. Here, we shall see that an electronegative functional group can also affect the acidity of $H^+$ that is several bonds away from itself. We shall also see a non-electronegative functional group that affects the acidity of the aforementioned $H^+$. Both of these groups affect the acidity of the $H^+$ through the $\sigma$ bonds. This effect is known as the inductive effect.

Substituted carboxylic acids are well known examples for this effect. A carboxylic acid is a neutral acid; in solution, it dissociates to give proton and carboxylate anion as its conjugate base. If the carboxylate anion can be stabilised, the carboxylic acid gets stronger. carboxylic acids are used as examples in this section.

### 6.3.3.1. Electron-withdrawing Inductive Effect

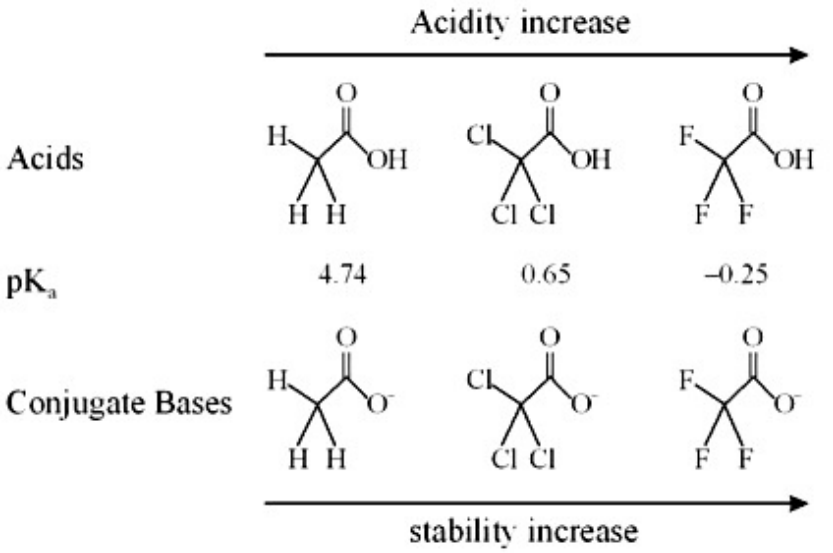
Electronegative atoms or groups affect the acidity of $H^+$ by inductively pulling the electron density towards itself through the ? bonds, therefore weaking the O–H bond in COOH and making the $H^+$ easier to be released. They also stabilise negatively charged species, therefore the conjugate base is stabilised, making the carboxylic acid a stronger acid. This type of group is known as the electron-withdrawing group (EWG). The 'electron-pulling through the $\sigma$ bonds' phenomenon is known as the electron-withdrawing inductive effect, also known as the '-I effect'. Have a look at the acetic acid derivatives below.



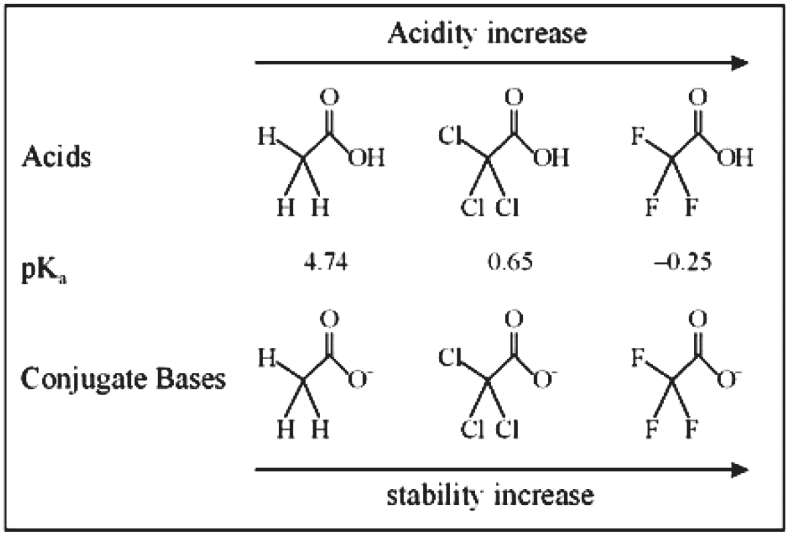

The electronegativity of the chlorine atom pulls electron density away from the acidic H towards itself, making chloroacetic acid about 4 orders of magnitude (104 times) more acidic than normal acetic acid! This shows the inductive effect that chlorine has.

**More electron withdrawing atoms/groups means more acidity.**

As the number of chlorine atom increases, the inductive effect becomes stronger. Hence, trichloroacetic acid is a stronger acid than dichloroacetic acid, which in turn is a stronger acid than (mono)chloroacetic acid. All of them are more acidic compared to unsubstituted acetic acid.

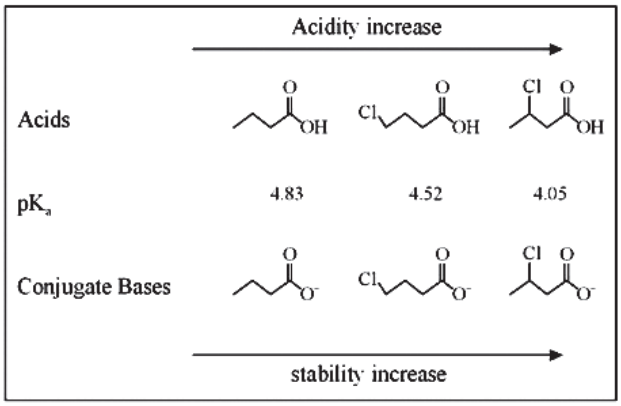



**The addition of more electronegative EWGs** means more stability of conjugate base and more acidity of the corresponding acid. The acidity of trichloroacetic acid (TCA) and trifluoroacetic acid (TFA) is compared below:




Since fluorine is more electronegative than chlorine, therefore its inductive effect is greater than that of chlorine, causing the pKa of TFA to be smaller than TCA. This means that TFA is more acidic than TCA. **Closer EWG means more acidity.**

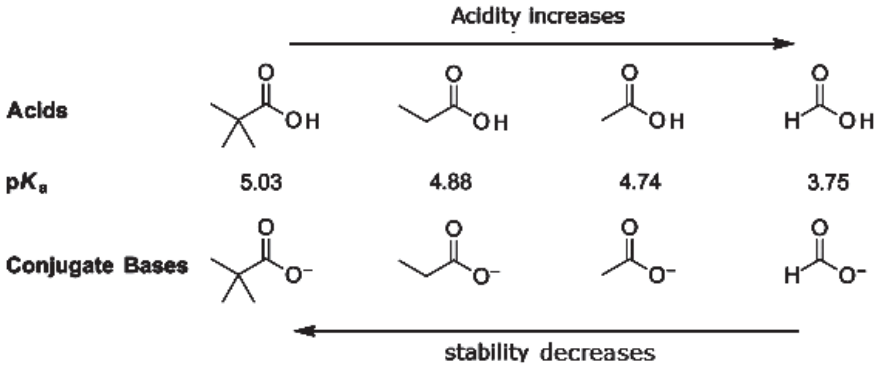
The closer the EWG is to the COOH, the stronger the electron withdrawing power and also the stronger inductive effect is, and the more acidity.



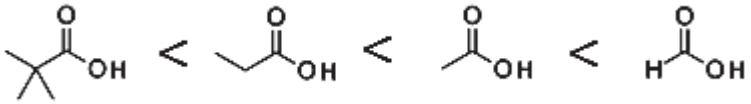

The chlorine atom in 2-chlorobutanoic acid is closer to the carboxylic group than that in 3-chlorobutanoic acid. Therefore, the stability of the corresponding conjugate bases increases from left to right resulting the mentioned order of acidity.

### 6.3.3.2. Electron-donating Inductive Effect

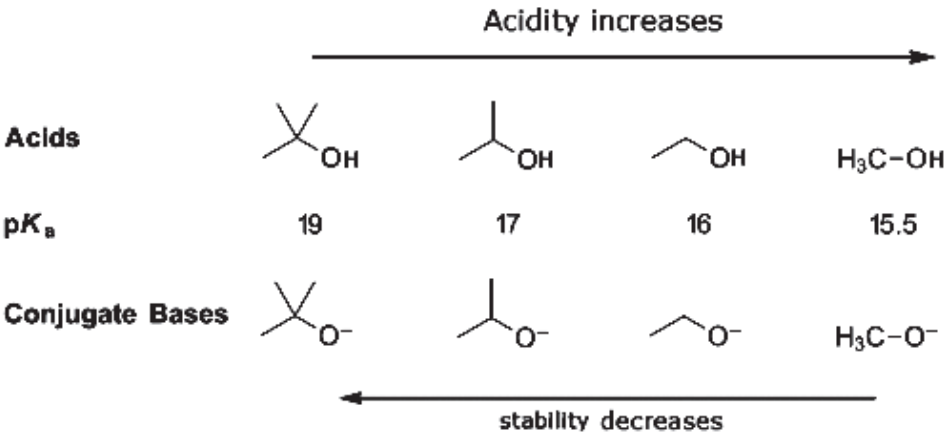
Alkyl functional group affects the acidity of $H^+$ by inductively pushing the electron density away from it through the $\sigma$ bonds, therefore strengthening the O-H bond in COOH and making the $H^+$ more difficult to be released. They destabilise negatively charged species, therefore the conjugate base is destabilised, making the carboxylic acid a weaker acid. This type of group is known as the electron-donating group (EDG). The 'electron-pushing through the $\sigma$ bonds' phenomenon is known as the electron-donating inductive effect, sometimes written as '+I effect'. Have a look at the acetic acid derivatives below.



The methyl groups push electron density away from themselves towards the carboxylate group. It destabilises the anionic conjugate bases. With increasing the number of methyl groups (EDG) the electron density is increased more and the decrease in stability of conjugate base is more making the following acidity order...



Similar effect is also observed in alcohols:




Larger number of methyl groups (EDGs) increases the electron density on -O- and therefore making the alcohol less acidic. This causes the t-butanol to have to largest pKa value in the series above.

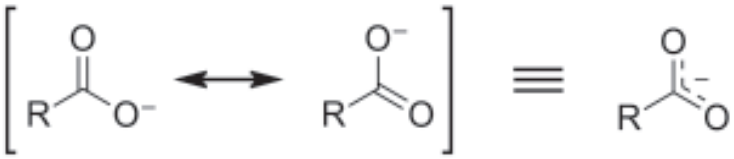
### 6.3.4. Resonance (Delocalisation)

Resonance can greatly stabilise charged species through the delocalisation of charge. Since the acidity of organic compounds is influenced by the stability of conjugate bases (charged species), resonance plays an important role in determining the acidity of various compounds. Similar to the inductive effect, there are functional groups that are electron-withdrawing and electron-donating through resonance. Through resonance, EWGs increases the acidity of a compound and EDGs decreases the acidity.

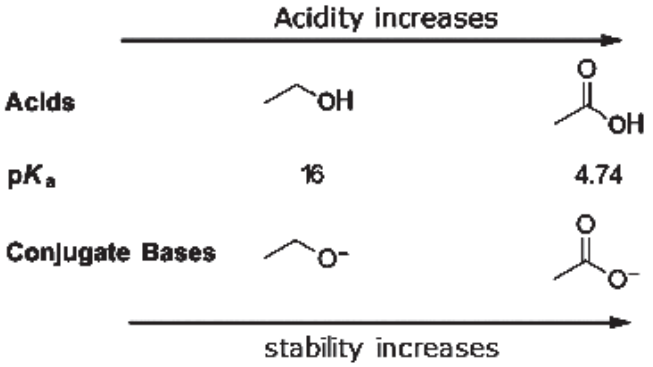
#### 6.3.4.1. Resonance in Carboxylic Acids

This resonance stabilises the carboxylate anion (conjugate base of carboxylic acid), making

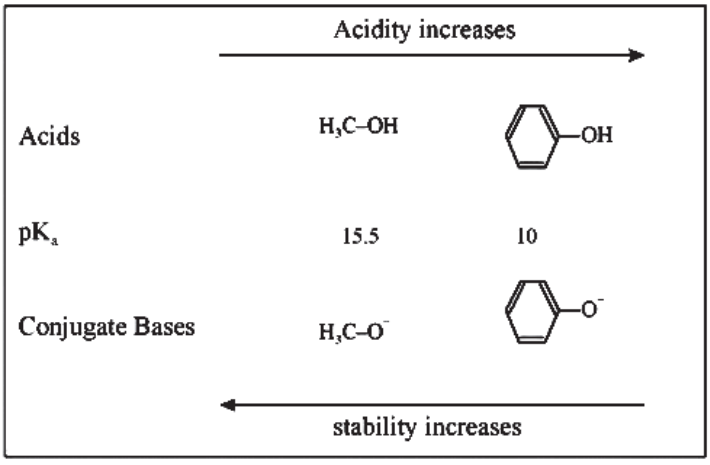
carboxylic acids as acidic. We can compare the pKas of ethanol and acetic acid to see how the resonance increases the acidity of carboxylic acids:



The resonance stabilises the anionic conjugate base so much so that acetic acid is more acidic than ethanol.

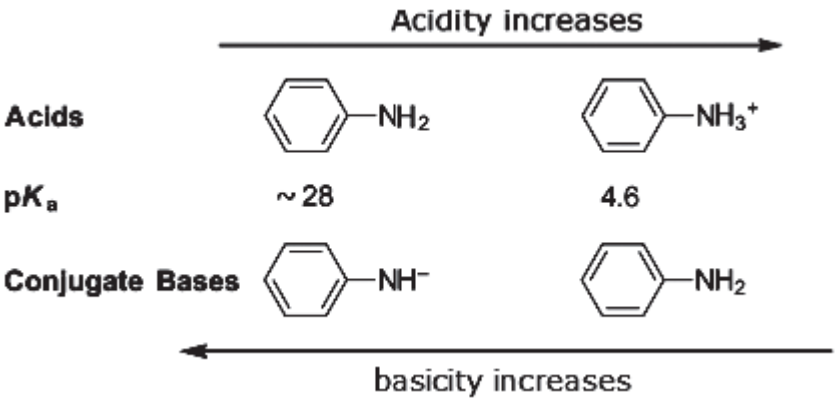



Now acitdity is compared between a non-conjugated alcohol (methanol) and a conjugated alcohol (phenol):



The negative charge in the phenoxide anion (anionic conjugate base of phenol) is stabilised by delocalisation to the aromatic ring, while there is no such stabilisation in conjugate base (methoxide ion) of methanol rather methoxide ion is destabilized by +I effect of methyl group.. This makes the phenol more acidic than methanol

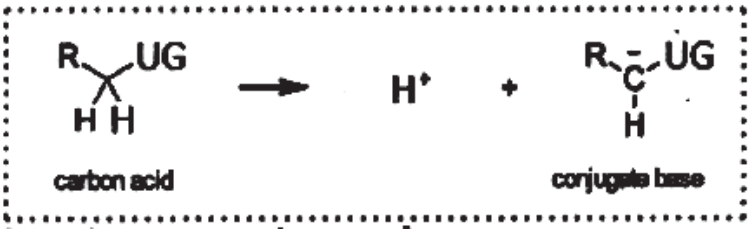
You can observe something interesting when comparing neutral and protonated aniline



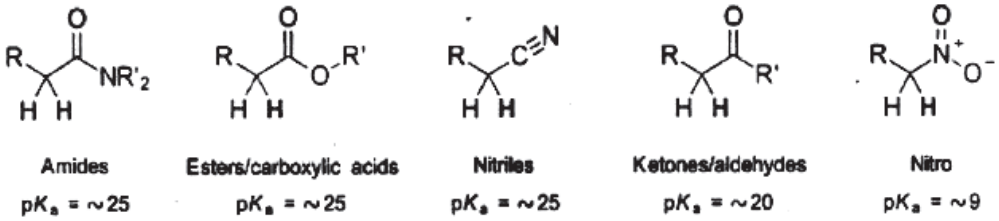

In neutral aniline, the free electron pair of the nitrogen delocalises to the benzene ring, giving stability. Protonation of the aniline nitrogen takes away the conjugation, making the anilinium (which is a cationic acid) unstable. Instability of a cationic acid makes a strong acid. This, in conjunction with the stabilisation of aniline as a conjugate base, makes anilinium a strong acid, as proved by its smaller pKa value of 4.6, compared to aniline's 28.

### 6.3.4.2. Acidity Assisted by Resonance to Neighbouring Unsaturated Groups

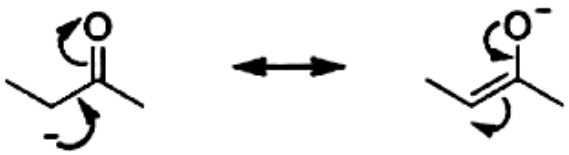
Hydrogens bonded to a carbon adjacent to one or more unsaturated groups are acidic. This carbon is known as the ?-carbon, whilst its hydrogen is known as the ?-hydrogen. Deprotonation of ?-hydrogens results in the formation of carbanion, called the ?-carbanion. Overall, this type of acid is known as carbon acid.



Examples of UG (unsaturated groups)




The reason α-hydrogens are acidic is because their conjugate bases are stabilised through conjugation with the unsaturated groups. For example, in butanone:

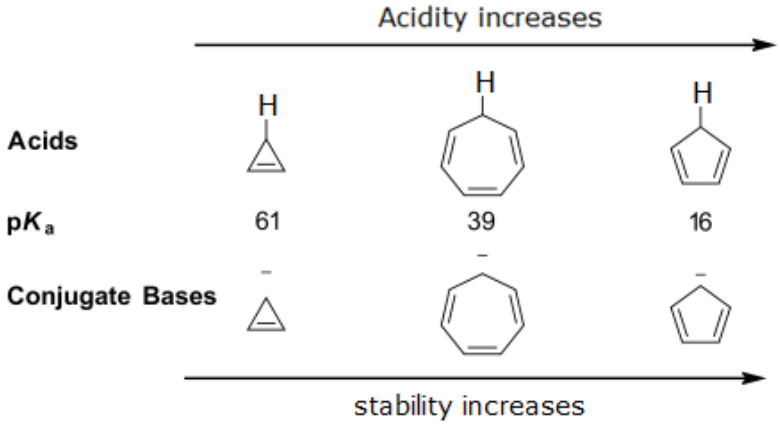


The carboxylic acid family (acids, esters, and amides) give larger pKa, meaning they are less acidic than aldehydes/ketones. The reason for this is because the OR and NR2 groups in the carboxylic acid family is more involved in resonance with the carbonyl group. Because of this, the ?-carbanion has to 'compete' and 'share' the resonance with the carbonyl group. This makes the ?-hydrogen of the carboxylic acid family more acidic than the aldehydes/ ketones.

In aldehydes/ketones, the ?-carbanion has carbonyl group only for itself, making the resonance stabilisation better. This makes their ?-hydrogens more acidic.

### 6.3.5. Aromaticit

We know that there are aromatic and anti aromatic compounds. Aromaticity stabilises compounds and therefore making acids stronger. If a compound releases an aromatic conjugate base, the aromaticity stabilises the conjugate base, which make the compound a stronger acid. If the released conjugate base is anti aromatic, the anti aromaticity destabilises the conjugate base, making the compound a weaker acid.



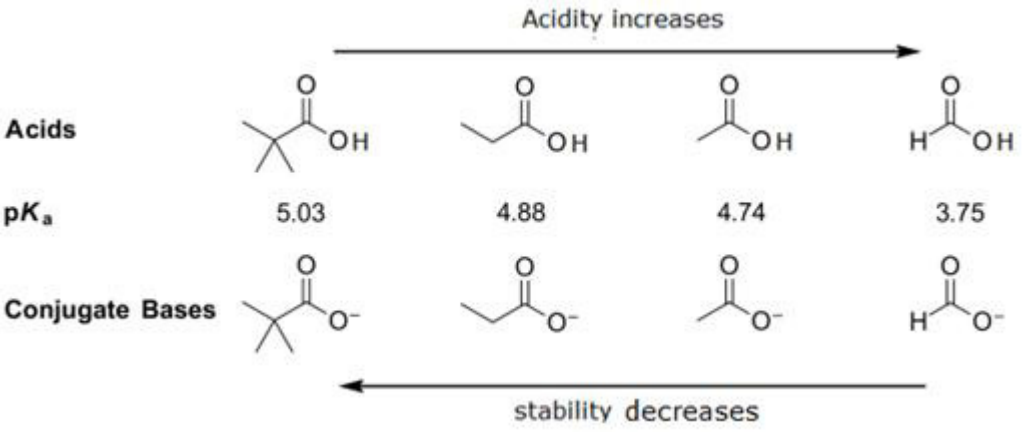

The conjugate base of cyclopropene is anti aromatic and therefore very much unstable. On the other hand, the conjugate base of cycloheptatriene is not planar; making it nonaromatic and therefore unstable than the conjugate base of cyclopentadiene which is aromatic. The acidity order is cyclopropene < cycloheptatrien < cyclopentadiene.

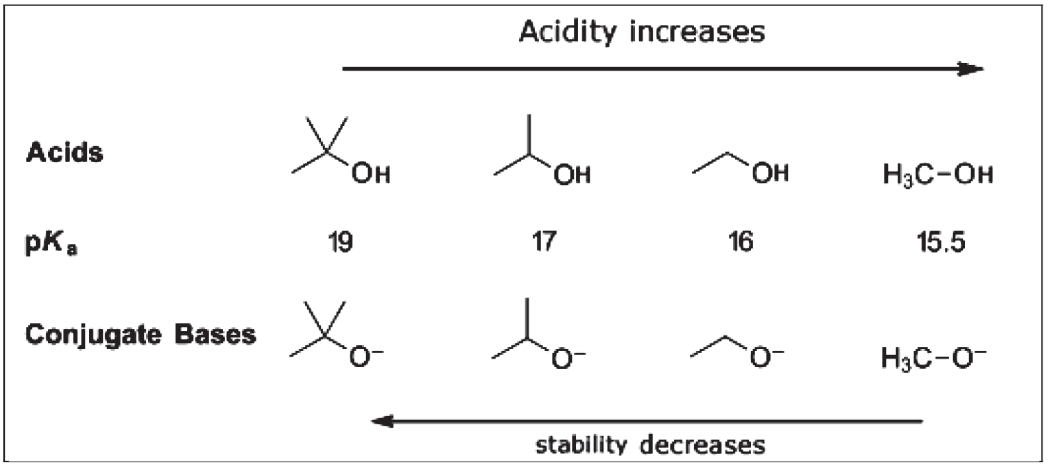
### 6.3.6. Solvation

A species is considered as an acid if it is able to separate its proton from its conjugate base. In order to do that, solvent plays a great role. In the absence of solvent, it is hard to separate a positive charge (proton) from a negative charge (conjugate base). This separation is greatly assisted by solvent; the solvent molecules orient themselves around the solute, separating the oppositely charged species. This process is known as solvation. Basically, it is difficult to achieve separation of proton at room temperature without the help of solvent, so the role of solvent is very crucial. All of the compounds used as examples in the previous sections may become more or less acidic when dissolved in different solvent.

Solvent that can better stabilise the conjugate base of a neutral acid makes it a stronger acid. The ability of the solvent to stabilise the conjugate base depends on many things. One of which is the molecular structure of the acid/conjugate base itself.

Now compare the pKa of several decreasingly-bulky alcohols and carboxylic acids:




The bulkiness of the methyl groups hampers the solvation of the conjugate bases by solvent molecules. This destabilises the conjugate bases, making the compounds increasingly less acidic as bulkiness increases. Therefore, aside from the effect of EDG in those examples, solvent also affects their acidity. The solvent itself is also an important factor. The pKa values, measured in water are different to those measured in DMSO. Here are a few examples:

| Acid Name | Acid Formula | pKa (water) | pKa (DMSO) |
|---|---|---|---|
| Trifluorosulfonic acid | $CF_3SO_3H$ | -14 | 0.3 |
| Hydrobromic acid | HBr | -9 | 0.9 |
| Hydrochloric acid | HCl | -7 | 1.8 |
| Hydrobromic acid | HF | 3.2 | 15 |
| Acetic acid | $CH_3COOH$ | 4.74 | 12.3 |
| Phenol | $C_6H_5OH$ | 10 | 18 |
| Methanol | $CH_3OH$ | 15.5 | 28 |
| Water | $H_2O$ | 15.7 | 32 |
| Ammonia | $NH_3$ | 38 | 41 |

The pKa values in DMSO are larger than the pKa values in water. This means that in DMSO, the acids are less acidic. Some are monumentally larger (e.g. trifluorosulfonic acid is almost 14 orders of magnitude less acidic in DMSO than in water), and some are not (e.g. ammonia is only 3 orders of magnitude less acidic in DMSO than in water). Water is able to form H-bonding with conjugate base and also have more powerful dipolar interaction with conjugate base than DMSO which has less dielectric constant.

Therefore, DMSO as an organic solvent is not as good as water in stabilising the anionic conjugate base and hence, the acids show less acidity in DMSO.

## 6.4 Factors affecting the basicity

The higher is the pKaH, the stronger is the base. But we haven't yet dug into the key concepts that help us evaluate, for example, why pyridine (pKaH = 5.2) is less basic than piperidine (pKaH = 11), or why the nitrogen of a nitrile is much less basic than the nitrogen of an amine.

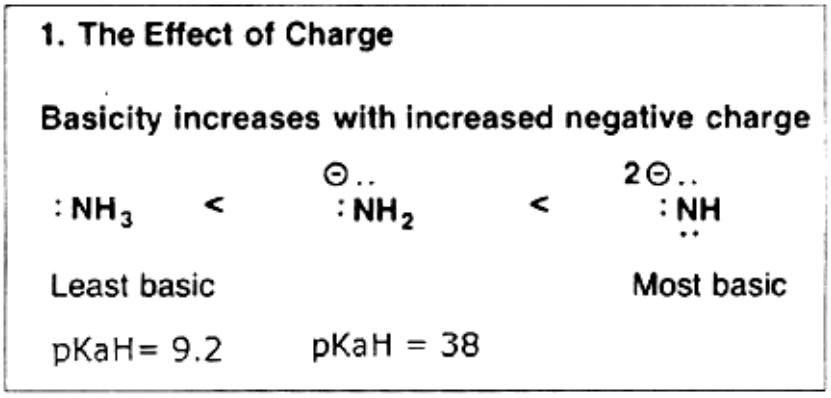
Since acidity and basicity are opposite sides of the same coin, the key factors which affect acidity also affect the basicity. So evaluating basicity involves taking those same concepts but working in the opposite direction. Generally speaking, the more unstable an electron pair is, the more basic it is. So using the same principles we outlined above, one

could increase basicity by removing inductive effects, removing delocalization through resonance, or bringing the charge farther away from the nucleus.

Let's examine the key factors in turn and apply them to obtain some key trends for the basicity of amines.

### 6.4.1 Increases Negative Charge on Nitrogen:

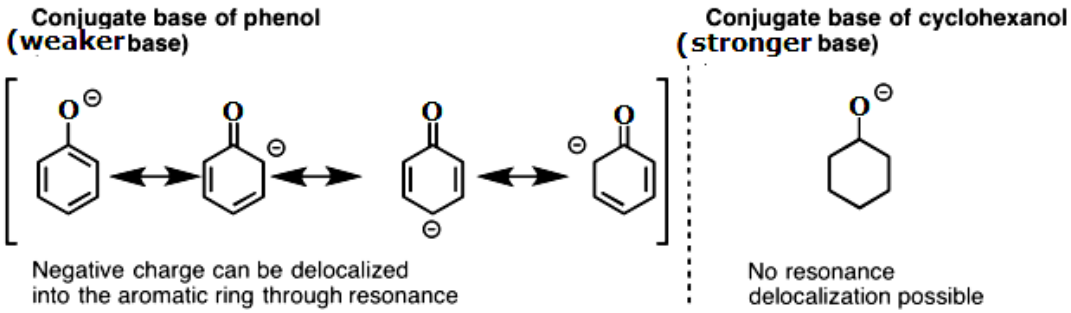
This is possibly the simplest factor to evaluate. If "basicity" can roughly be translated as "electron-pair instability", and instability increases with charge density, then basicity should increase with increased negative charge. Now, compare ammonia, ($NH_3$) with its conjugate base, the amide anion $NH_2^-$. The amide anion ($pK_aH$ of 38) is stronger base than $NH^3$ ($pK_aH$ of 9.2). It can be used to deprotonate terminal alkynes (pKa = 25), for example, whereas ammonia will not.




Continuing this trend, the conjugate base of the amide ion, the amide dianion $NH^{(2-)}$ should be an even stronger base, but it seems to be prohibitively difficult to make.

### 6.4.2 Resonance:

Delocalization of lone pair into a larger pi system through resonance give low density of electron resulting the lower basicity. For example, conjugate base of cyclohaxanol is more basic than phenoxide because the conjugate base of phenol (phenoxide) can be stabilized through resonance whereas the conjugate base of cyclohexanol cannot.

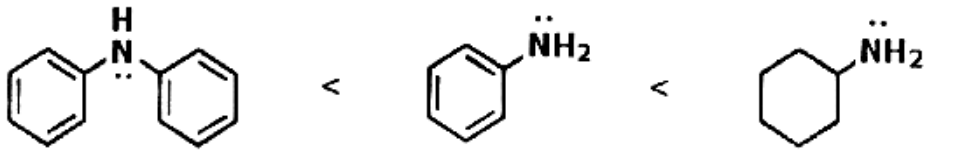



By analogy, we should also expect that aniline is a weaker base than cyclohexylamine. That is indeed the case! The the pKaH of aniline is 4.6, and pKaH of cyclohexylamine is 11.2. (The higher is the pKaH, the stronger is the base). The basicity is decreased even further when a second phenyl ring is attached to the nitrogen (pKaH = 0.78).

**2. Resonance-Stabilized Amines Are Less Basic**

Amine lone pairs that are conjugated with pi bonds (i.e. that can participate in resonance) are stabilized relative to non-conjugated amines

Resonance stabilization decreases basicity




Aniline

Cyclohexylamine

**Least basic**

**Most basic**

**pKaH = 0.78**

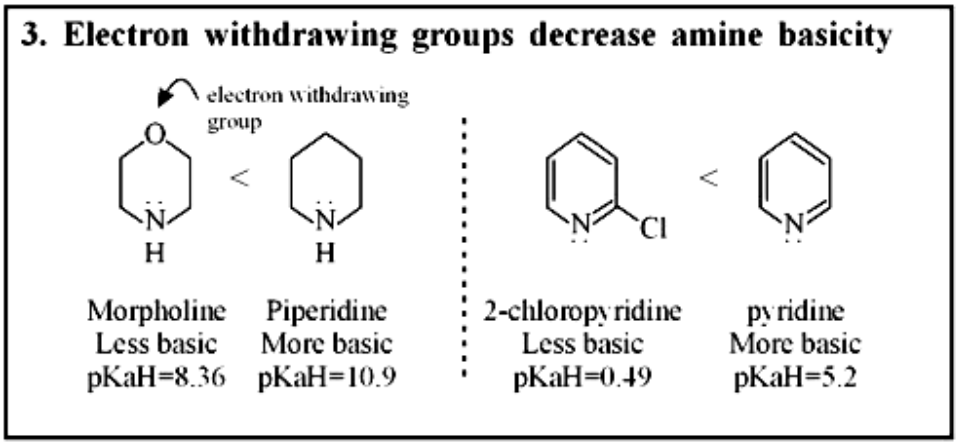
**pKaH = 4.6**

**pKaH 11.2**

### 6.4.3 Inductive effect

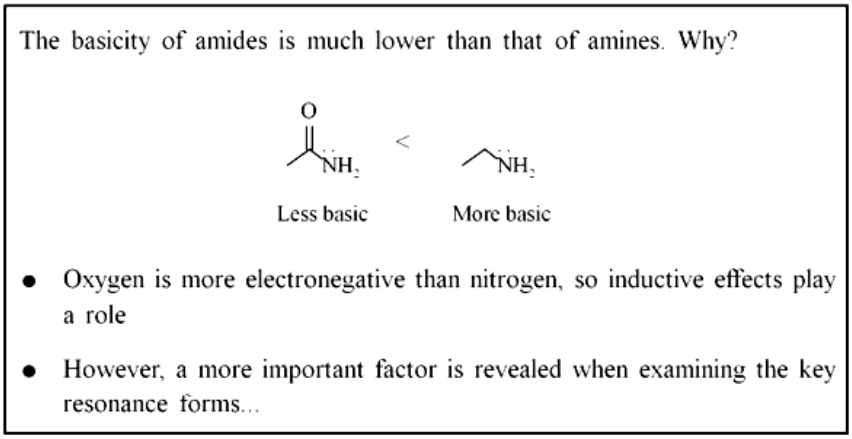
Lower charge density = more stability = lower basicity.

Hence, we'd expect that electron withdrawing groups on amines should likewise decrease their basicity. And they do! Witness morpholine ($pK_aH = 8.36$) compared to piperidine ($pK_aH = 11$), or 2-chloropyridine ($pK_aH = 0.49$) versus pyridine ($pK_aH = 5.2$).




### 6.4.4. Pi-Acceptors and Pi-Donors property

We've seen that resonance tends to decrease basicity (Factor 2) and so do inductive effects (Factor 6.4.3). That said, how do you explain why amides are significantly less basic than amines? Is it resonance? Is it inductive effects? Is it both?

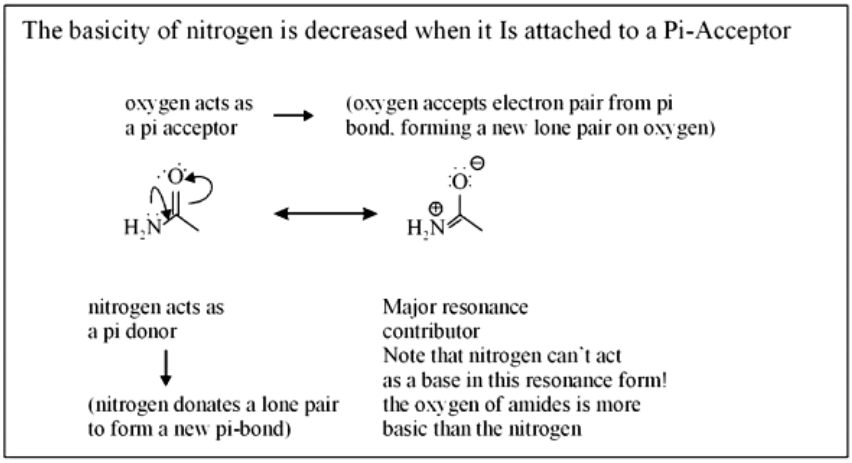



It seems worthwhile to devote a section to how the basicity of nitrogen is affected by its interactions with other functional groups in a pi-system. Specifically, the basicity of nitrogen is decreased when it acts as a pi-donor, and the basicity of nitrogen is increased when it acts as a pi-acceptor.

**Nitrogen is less basic when it is a pi-donor**

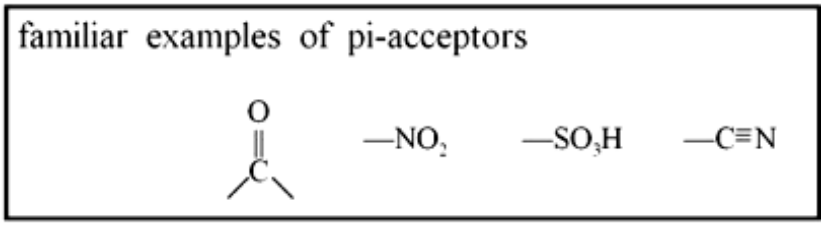
Back to our amide example. Why is it less basic?

The first factor is that electron-withdrawing oxygen is present, which can remove some of the electron density from nitrogen. However, this is outweighed by the fact that there is a significant resonance form where the nitrogen lone pair forms a new pi bond with carbon (we call this, "**pi-donation**") resulting in a pair of electrons moving from the C-O pi bond to the oxygen (we call this acting as a "**pi acceptor**").




Look at that resonance form on the right. The nitrogen doesn't have a lone pair anymore, and therefore it **cannot act as a base.** Therefore, t**he basicity of nitrogen is decreased when attached to a pi-acceptor.**

What are pi-acceptors, again? You might recognize that "**Pi acceptors**" all belong in the category of "**meta- directors**" in benzene nucleus.




[$CF_3$ is an example of a functional group that is a **meta** director but not a pi acceptor, since it has no pi bonds]

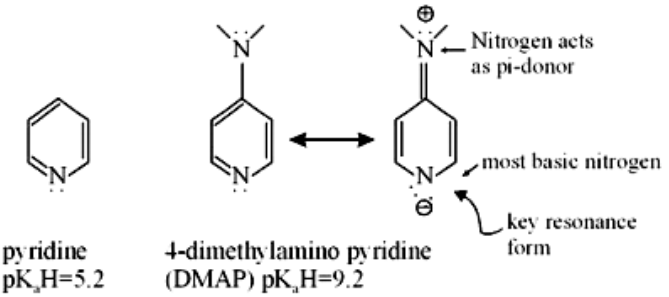
**Nitrogen as a pi-acceptor**

One question may arise that this can work in the opposite direction. Can the basicity of

nitrogen be increased when it is attached to a pi-donor? Absolutely. A great comparison is pyridine (pKaH = 5.2) and 4-dimethylamino pyridine (DMAP). Attachment of the strongly pi-d0nating NMe2 group to the 4-position results in a 104 increase in basicity of the ring nitrogen (pKaH = 9.2). Examining the resonance forms of DMAP is illuminating. In the key resonance form, the nitrogen in the ring bears a negative charge.

**Basicity is Increased By Pi-Donation**

Compare pyridine ($pK_aH = 5.2$) with 4-dimethylaminopyridine ($pK_aH = 9.2$)




pyridine $pK_aH=5.2$

4-dimethylamino pyridine (DMAP) $pK_aH=9.2$

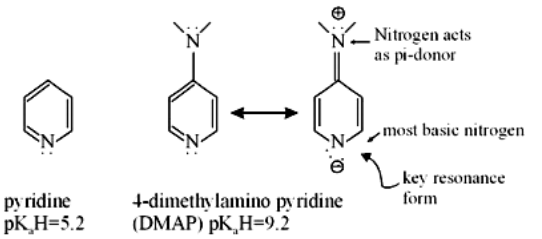
4-methoxypyridine (pKaH=6.5) is also more basic than pyridine, but the effect is less pronounced since $-OCH_3$ is a weaker pi donor than $N(CH_3)_2$

The ring nitrogen of DMAP is the most basic nitrogen, not the NMe2! The NMe2 is made less basic by being a pi-donor (see above) but the pyridine nitrogen is made more basic because it is the pi-acceptor here.

Another example of how basicity of nitrogen can be increased by attachment to pi-donors is found in guanidines. In guanidine there are two pi-donating NH2 groups which can donate electron density to the (pi-accepting) C=NH.

**Basicity is Increased By Pi-Donation**

Compare pyridine ($pK_aH$ = 5.2) with 4-dimethylaminopyridine ($pK_aH$ = 9.2)




pyridine $pK_aH$=5.2

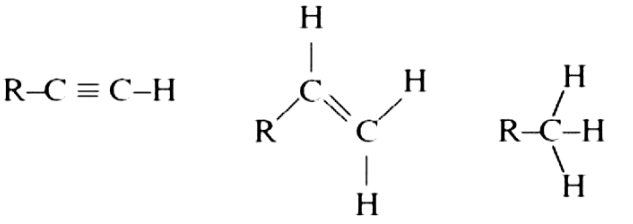
4-dimethylamino pyridine (DMAP) $pK_aH$=9.2

4-methoxypyridine (pKaH=6.5) is also more basic than pyridine, but the effect is less pronounced since $-OCH_3$ is a weaker pi donor than $N(CH_3)_2$

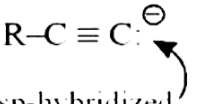
### 6.4.5. Hybridization

One of the more remarkable acidity trends is that alkynes are unusually acidic (pKa = 25) relative to alkenes (pKa's around 43) and alkanes (pKa's >50).

**Review: Alkynes are Unusually Acidic**

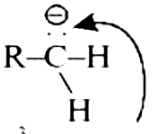



conjugate base




sp-hybridized
(50% s-character,
more closely held to
nucleus, more stable)

conjugate base

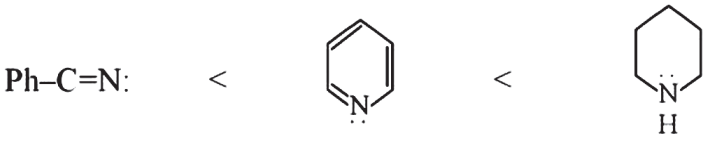



$sp^3$-hybridized
(25% s-character,
less closely held to
nucleus, less stable)

The explanation is that the sp-hybridized orbitals of alkynes bear 50% s-character, and as the 2s orbital is closer to the nucleus than the 2p orbitals, the resulting lone pair of the conjugate base "feels" more of the positive charge from the nucleus than would a lone pair in an sp3 hybridized orbital (25% s-character). It's similar to why a lone pair is more stable on a more electronegative atom like fluorine than on a less electronegative atom like carbon.

Knowing this, how would you predict the relative basicity of nitriles, pyridine, and piperidine?

5. The Effect of Hybridization
Basicity increases with decreasing s-character

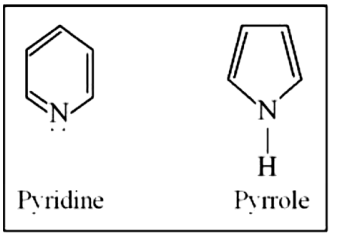



| Hybridization of nitrogen | sp | $sp^2$ | $sp^3$ |
|---|---|---|---|
| pKaH | –10 | 5.2 | 11 |
| | **least basic** | | **most basic** |

By analogy to alkynes, we'd expect the lone pairs in sp-hybridized nitriles to be the most stable and hence the least basic. We'd therefore expect the lone pairs in $sp^3$-hybridized amines to be the least stable and hence the most basic. This is borne out by pKaH values. The pKaH of benzonitrile (pKaH = -10) indicates that nitriles are very weak bases indeed. We can likewise explain the lower basicity of pyridine (pKaH = 5.2) versus piperidine (pKaH = 11) by the orbital hybridization. (Not resonance, by the way! The lone pair in pyridine is in the plane of the ring, and thus not in conjugation with the p-orbitals).

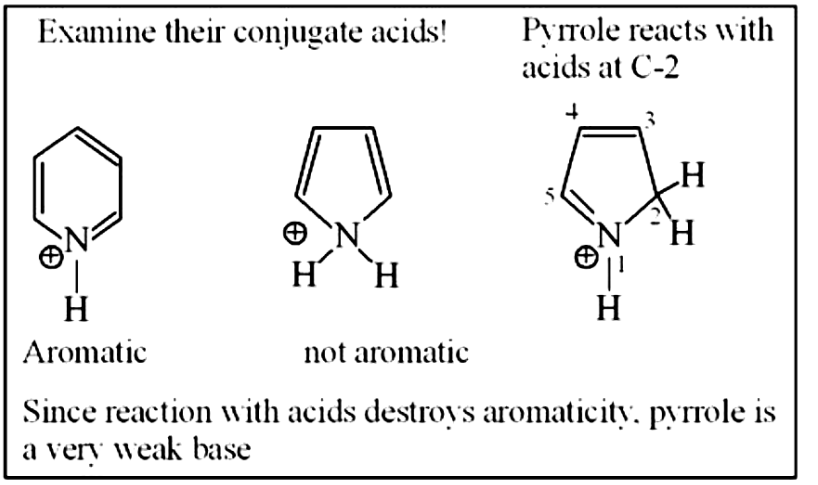
### 6.4.6 Aromaticity

What's more basic between pyridine and pyrrole?



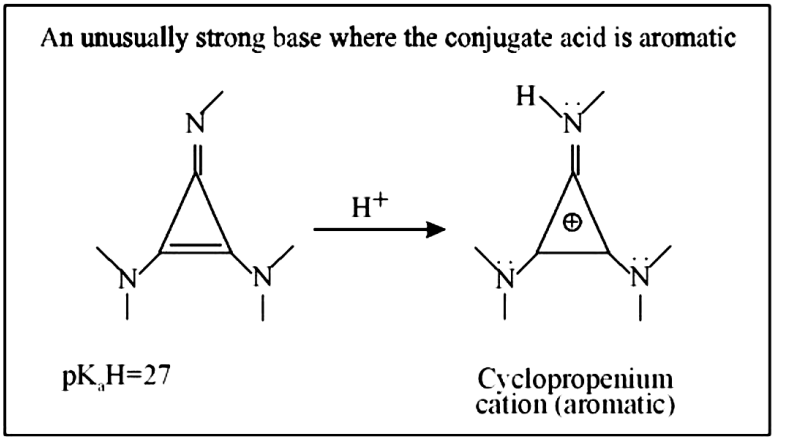
It turns out that the nitrogen in pyrrole is unusually non-basic. In fact, even when subjected to acid, pyrrole reacts at carbon (C-2), and not on the nitrogen. Pyridine [ pKaH = 5.2] is far more basic than pyrrole [pKaH about -3.6 ]

Draw the conjugate acid of pyrrole. Notice anything?




The conjugate acid is not aromatic. Removal of the lone pair on nitrogen through protonation would destroy the conjugation of the lone pair with the other p orbitals of the ring and render the molecule non aromatic.

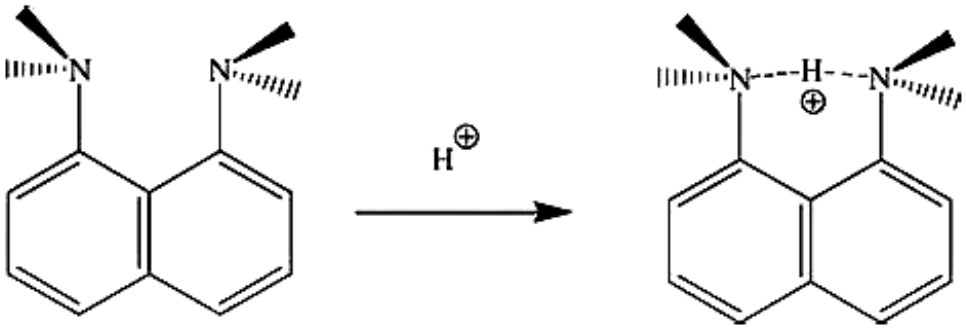
Here is a fun example where nitrogen is unusually basic due to aromaticity. A family of imine "superbases" has been developed by the research group of Tristan Lambert at Columbia.



Note how a significant resonance form of the conjugate acid is a substituted version of the aromatic cyclopropenium cation. This helps to drive the equilibrium towards the conjugate acid. The pKaH here is about 27.

## 6.5 Proton Sponge

1,8-Bis(dimethylamino) naphthalene is an organic compound, classified as a peri-naphthalene, i.e. a 1,8-disubstituted derivative of naphthalene. Owing to its unusual structure, it exhibits exceptional basicity. It is often referred by the trade name Proton Sponge,




This compound is a diamine in which the two dimethylamino groups are attached on the same side (peri position) of a naphthalene ring. This molecule has several very interesting properties; one is its very high basicity; another is its spectroscopic properties. With a pKa of 12.34 for its conjugate acid in aqueous solution, 1,8-bis(dimethylamino)naphthalene is one of the strongest organic bases. The high basicity is attributed to the relief of strain upon protonation and/or the strong interaction between the nitrogen lone pairs. Additionally, although many aromatic amines such as aniline show reduced basicity (due to nitrogen being $sp^2$ hybridized; its lone pair occupying a 2p orbital and interacting and being withdrawn by the aromatic ring), this is not possible in this molecule, as the nitrogens' methyl groups prevent its substituents from adopting a planar geometry, as this would require forcing methyl groups from each nitrogen atom into one another - thus the basicity is not reduced by this factor which is found in other molecules. It is sterically hindered, making it a weak nucleophile. Because of this combination of properties, it has been used in organic synthesis as a highly selective non-nucleophilic base.

Proton sponge also exhibits a very high affinity for boron, and is capable of displacing hydride from borane to form a boronium-borohydride ion pair.

## 6.6 HSAB Principle

HSAB concept is an initialism for "hard and soft (Lewis) acids and bases", also known as the Pearson acid-base concept, HSAB is widely used in chemistry for explaining stability of compounds, reaction mechanisms and pathways. It assigns the terms 'hard' or 'soft', and 'acid' or 'base' to chemical species. 'Hard' applies to species which are small, have high charge states (the charge criterion applies mainly to acids, to a lesser extent to bases), and are weakly polarizable. 'Soft' applies to species which are big, have low charge states and are strongly polarizable. The concept is a way of applying the notion of orbital overlap to specific chemical cases.

According to HSAB concept, hard acids prefer binding to the hard bases to give ionic complexes, whereas the soft acids prefer binding to soft bases to give covalent complexes. It is sometimes referred to as Hard-Soft Interaction Principle (HSIP).

- The large electronegativity differences between hard acids and hard bases give rise to strong ionic interactions.
- The electronegativities of soft acids and soft bases are almost same and hence have less ionic interactions. i.e., the interactions between them are more covalent.
- The interactions between hard acid - soft base or soft acid - hard base are mostly polar covalent and tend to be more reactive or less stable. The polar covalent compounds readily form either more ionic or more covalent compounds if they are allowed to react.

## 6.6.1 Characteristics of hard, soft & borderline acids & bases

| Type of Acid/Base | Characteristics | Examples |
|---|---|---|
| Hard acids | * Atomic centres of small ionic radii (<90 pm).<br>* High positive charge.<br>* Empty orbitals in their valence shells.<br>* Low electronegativity (0.7-1.6) and low electron affinity.<br>* Likely to be strongly solvated.<br>* High energy LUMO. | $H^+$, $Li^+$, $Na^+$, $K^+$, $Be^{2+}$, $Mg^{2+}$, $Ca^{2+}$, $Sr^{2+}$, $Sn^{2+}$<br>$Al^{3+}$, $Ga^{3+}$, $In^{3+}$, $Cr^{3+}$, $Co^{3+}$, $Fe^{3+}$, Ir3+, $La^{3+}$, $Si^{4+}$, $Ti^{4+}$, $Zr^{4+}$, $Th^{4+}$,$U^{4+}$, $VO^{2+}$, $UO_2^{2+}$<br>$BeMe_2$, $BF_3$, $BCl_3$, $B(OR)_3$, $AlMe_3$ |
| Soft acids | * Large radii (>90 pm).<br>* Low or partial positive charge.<br>* Completely filled orbitals in their valence shells.<br>* Intermediate electronegativities (1.9-2.5)<br>* Low energy LUMO's with large magnitude of LUMO coefficients. | $Cu^+$, $Ag^+$, $Au^+$, $Hg^+$ , $Cs^+$ , $Tl^+$ , $Hg^{2+}$, $Pd^{2+}$, $Cd^{2+}$, $Pt^{2+}$<br>Metal atoms in zero oxidation states<br>$BH_3$ |
| Border line acids | * They have moderate charge density and polarizability.<br>* They can react with both hard and soft bases but prefer borderline bases.<br>* Their interactions are neither highly ionic (like hard acids) nor highly covalent (like soft acids). | $Fe^{2+}$, $Co^{2+}$, $Ni^{2+}$, $Cu^{2+}$, $Zn^{2+}$, $Pb^{2+}$, $B(CH_3)_3$, $SO_2$, $NO^+$ |
| Hard bases | * Small radii (around 120pm) & highly solvated .<br>* electronegative atomic centres (3.0-4.0).<br>* Weakly polarizable.<br>* Difficult to be oxidized.<br>* High energy HOMO. | $H_2O$, $OH^-$, $F^-$, $Cl^-$, $CH_3CO^{2-}$, $PO_4^{3-}$, $SO_4^{2-}$, $CO_3^{2-}$, $NO^{3-}$, $ClO_4^-$, ROH, $RO^-$, $R_2O$, $NH_3$, $RNH_2$, $N_2H_4$ |

| | | |
|---|---|---|
| Soft bases | * Large atoms (>170 pm) with intermediate electronegativity (2.5-3.0).<br>* High polarizability<br>* Easily undergo oxidation.<br>* Low energy HOMO's but large magnitude HOMO coefficients. | $S^{2-}$, RSH, $RS^{-}$, $R_2S$, $I^{-}$, $CN^{-}$, $SCN^{-}$, $S^2O3^{-}$, $R_3P$, $R_3As$, $(RO)_3P$, RNC, CO, $C_2H_4$, $C_6H_6$, $R^{-}$, $H^{-}$ |
| Border line bases | * They have moderate electron donor ability.<br>* They can form stable complexes with both hard and soft acids.<br>* Their bonding nature is between ionic and covalent. | Aniline, pyridine, N3-, Br-, NO2-, $SO_3^{2-}$, $N_2$ |

### 6.6.2 Application of HSAB in organic chemistry:

Site preference:

1) RCOX is a hard acid and reacts with the nitrogen end of SCN- ion to form an acyl isothiocyanate.

$$CH_3COX + SCN^- \xrightarrow{-X^-} CH_3(O)NCS$$

2) Whereas the softer methyl group bonds to the Sulfur atom and forms methyl thiocyanate.

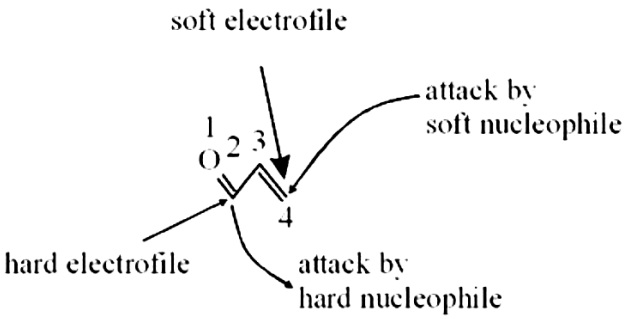
$$CH_3COX + SCN^- \xrightarrow{-X^-} CH_3(O)NCS$$

**Nucleophilic addition of $\alpha,\beta$-unsaturated carbonyl compounds:**

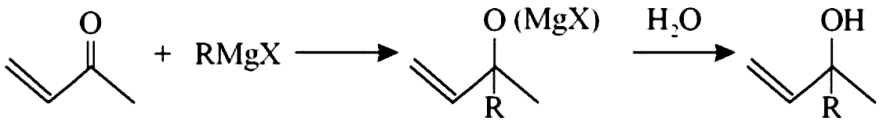
The $\alpha,\beta$-unsaturated carbonyl compounds have two type of carbon electrophilic centers.

1) Carbonyl carbon - Hard electrophilic center.

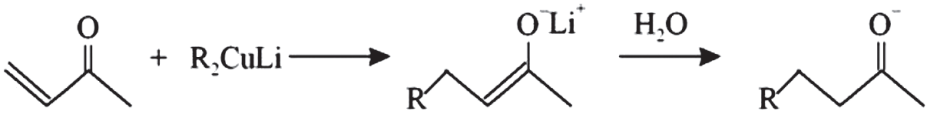
2) -carbon - Soft electrophilic center.



Therefore, the hard nucleophiles like Grignard reagents attack the carbonyl carbon (hard electrophile) resulting in 1,2-nucleophilic addition to C=O group.




Whereas, the soft nucleophiles like Lithium organocuprates, thiols etc., attack the ?-carbon (soft nucleophile) resulting in 1,4-conjugate addition.




## 6.7 Nucleophilicity Vs Basicity

First of all, remember that basicity is a subset of nucleophilicity. All nucleophiles are Lewis bases; they donate a lone pair of electrons. A "base" (or, "Bronsted base") is just the name we give to a nucleophile when it's forming a bond to a proton (H+). To summarize, when we're talking about basicity and nucleophilicity, we're talking about these two types of events.

- **Basicity:** Involves the nucleophile attacking hydrogen.
- **Nucleophilicity:** nucleophile attacks any atom other than hydrogen. Because we're talking about organic chemistry here, for our purposes, this is going to mean "carbon" most of the time.

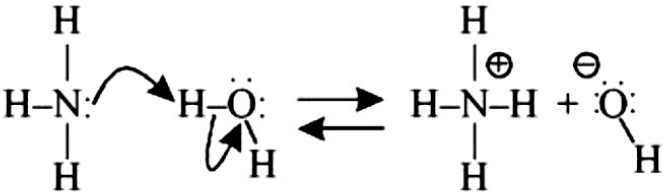
So how do reactions of nucleophiles at hydrogen differ from reactions of nucleophiles at carbon? Well, they're more easily reversible, for one thing. We can measure acidity (and, by extension, basicity) through the measure known as pKa, which is a reflection of the position of the equilibrium between an acid and its conjugate base.

Let's put it up in a graphic:

**What's a base?**

- A base donates a pair of electrons to a proton

**Example:**



pKa = 15 pKa = 10

weaker base stronger base

**How do we measure basicity?**

- Because most species can participate in reversible acid-base reactions, we can measure basicity by the position of an equilibrium.
- In other words, we're measuring relative stability of the species involved. "Stability" is a thermodynamic property. Acid-base reactions reflect relative stabilities.

Because we can measure the equilibrium constants for reversible acid-base reactions, we can get a fairly good idea of the relative strengths of acids and bases. There are some complications; solvent effects can play a role in stabilities, for instance but overall, the pKa table is our friend. It's a great "reactivity ladder" to hang our hats on. The more unstable a lone pair of electrons is, the more basic it will be (and vice versa).

And then there's nucleophilicity. How is nucleophilicity different from basicity? Well, since it's not limited to simply forming a bond to hydrogen anymore, this leads to some extra complications. Let's just talk about the measurement problem first.

Many reactions of nucleophiles are not reversible. A bond forms, a bond breaks, and that's the end of the reaction. The problem with this from a measurement standpoint is that we often can't determine an equilibrium constant for a reaction. And if we can't do that, then we can't develop a reactivity scale based on equilibria. If we can't measure equilibria, then what do we do? Well, we use the next best measurement available: to measure reaction rates.

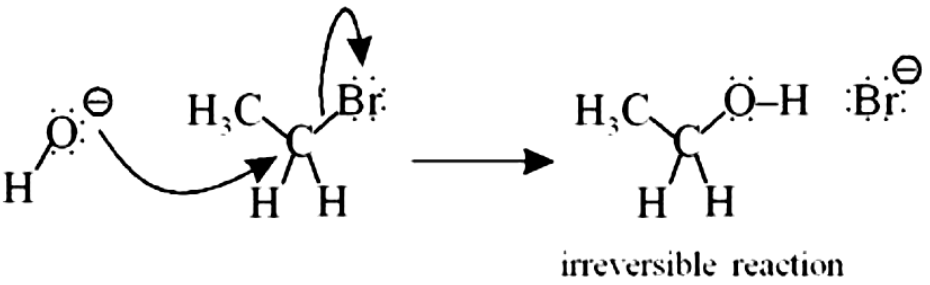
There's one important thing to remember with reaction rates. They don't always reflect overall stability. There are a few more variables at play here.

**Factor #1:** Steric hindrance. Reactions where nucleophiles attack carbon-based electrophiles are significantly more sensitive to steric effects, because empty orbitals on carbon are not as accessible. Steric hindrance is like a fat goalie.

**Factor #2:** Solvents. The medium (solvent) in which a reaction takes place can greatly affect the rate of a reaction. Specifically, the solvent can greatly attenuate (reduce) the nucleophilicity of some Lewis bases through hydrogen bonding.

**What's a nucleophile?**

- A nucleophile donates a pair of electrons to an atom other than hydrogen (for the purposes of organic chemistry, this usually implies carbon ) Example




irreversible reaction

**How do we measure nucleophilicity?**

- Reactions of nucleophiles with carbon are most often irreversible and are not in equilibrium.
- Therefore we have to measure nucleophilitity by the rate of the reaction. Rates do not always reflect relative stabilities!
- Nucleophilicity roughly parallels basicity, but two additional factors can come into play

**i) Steric hindrance:** Reactions where carbon is an electrophile are often more difficult than reactions where a proton is the electrophile, because the orbitals involved are not as accessible This is called "steric hindrance", and it can affect the how fast a nucleophile will react with an electrophile (and by definition, its nucleophilicity)

**ii) Solvation:** The medium (solvent ) in which a reaction takes place can greatly affect the rate of a reaction. Specifically, the solvent can greatly affect the nucleophilicity of a Lewis base through hydrogen- bonding interactions

## 6.8 Summary

- Arrhenius Acid: Increases $H^+$ concentration in aqueous solution (e.g., $HCl \rightarrow H^+ + Cl^-$). Arrhenius Base: Increases $OH^-$ concentration in aqueous solution (e.g., $NaOH \rightarrow N^{a+} + OH^-$).
- Lewis Acid accepts an electron pair (electrophile) and has vacant orbitals. Examples: Cations ($Cu^{2+}$, $Fe^{2+}$, $Fe^{3+}$), electron-deficient molecules ($BF_3$, $AlF_3$), and molecules with multiple bonds ($CO_2$, $SO_2$).
- Lewis Base donates an electron pair (nucleophile) and has lone-pair electrons. Examples: $OH^-$, $CN^-$, $CH_3COO^-$, $H_2O$, $NH_3$.
- Stronger acids produce weak, stable conjugate bases. Weaker acids produce strong, unstable conjugate bases.
- Electron-Withdrawing Groups (EWG) increase acidity by stabilizing conjugate bases (e.g., Cl in chloroacetic acid). Electron-Donating Groups (EDG) decrease acidity by destabilizing conjugate bases (e.g., alkyl groups in carboxylic acids and alcohols).
- sp-hybridized nitrogens (e.g., nitriles) are the least basic, while $sp^3$-hybridized nitrogens (e.g., amines) are the most basic. Benzonitrile (pKaH = -10) is much less basic than piperidine (pKaH = 11).
- Protonation disrupting aromaticity lowers basicity. Pyrrole (pKaH $\approx$ -3.6) is less basic than pyridine (pKaH = 5.2) since its lone pair is involved in aromaticity.
- HSAB Principle states that Hard acids prefer binding to hard bases (ionic bonds), while soft acids bind to soft bases (covalent bonds). Example: Hard nucleophiles (Grignard reagents) attack carbonyl carbons, while soft nucleophiles (thiols) prefer -$\beta$ carbons.
- Basicity is a thermodynamic property (equilibrium-based), while nucleophilicity is kinetic (rate-based). Steric hindrance and solvents strongly affect nucleophilicity but not necessarily basicity.

## 6.9 Exercise

1. Which is more acidic between methanol and methane?

2. Arrange the following compounds according to their acid strength
3. $CH_3$-$CH_2$-COOH, $CH_2$=CH-COOH, CH≡C-COOH
4. Arrange the following compounds according to their acidity

   $CH_3$-$CH_2$-$CH_2$-COOH, $CH_3$-$CH_2$-CH(Cl)-COOH, $CH_3$-CH(Cl)-$CH_2$-COOH, $CH_2$(Cl)-$CH_2$-$CH_2$-COOH
5. Which is more acidic between p-chloro phenol and p-fluoro phenol?
6. 2, 6-dihydroxy benzoic acid is a much stronger acid than 2-hydroxy benzoic acid. Explain.
7. Why is N,N-dimethyl aniline a weak base than N,N,2,6-tetramethyl aniline?
8. What is the difference between an Arrhenius acid and a Lewis acid?
9. Why is HF a weaker acid than HI despite fluorine being more electronegative?
10. Why is trichloroacetic acid more acidic than chloroacetic acid?
11. Why is phenol more acidic than methanol?
12. How does bond strength influence acidity trends down a group in the periodic table?
13. Why is an alkyne (sp-hybridized) more acidic than an alkene ($sp^2$-hybridized) or an alkane ($sp^3$-hybridized)?
14. Why is pyridine (pKaH = 5.2) less basic than piperidine (pKaH = 11)?
15. Why is the nitrogen in a nitrile much less basic than the nitrogen in an amine?
16. Why is the amide anion ($NH_2^-$) a stronger base than ammonia ($NH_3$)?
17. Why is phenoxide less basic than the conjugate base of cyclohexanol?
18. Why is aniline (pKaH = 4.6) a weaker base than cyclohexylamine (pKaH = 11.2)?
19. Why is morpholine (pKaH = 8.36) less basic than piperidine (pKaH = 11)?
20. Why is 2-chloropyridine (pKaH = 0.49) less basic than pyridine (pKaH = 5.2)?
21. Why are amides significantly less basic than amines?
22. Why is pyridine (pKaH = 5.2) more basic than pyrrole (pKaH = -3.6)?
23. How does the NMe? group in DMAP increase the basicity of pyridine?

24. Why are nitriles less basic than amines?
25. Why is pyrrole unusually non-basic?
26. What is a proton sponge?
27. Why is 1,8-bis(dimethylamino)naphthalene an exceptionally strong base?
28. What does the HSAB principle state about acid-base interactions?
29. How does HSAB explain site preference in reactions of RCOX with SCN??
30. What is the difference between nucleophilicity and basicity?

**Multiple-Choice Questions (MCQs)**

**1. Which of the following is an example of an Arrhenius base?**

a) HCl

b) NaOH

c) NH??

d) CH?COOH

Answer: b) NaOH

**2. According to Lewis' theory, a Lewis acid is a substance that:**

a) Donates an electron pair

b) Accepts an electron pair

c) Increases the concentration of OH?

d) Decreases the concentration of H?

Answer: b) Accepts an electron pair

**3. Which of the following is a Lewis base?**

a) $Cu^{2+}$

b) $BF_3$

c) $OH^-$

d) $AlF_3$

Answer: c) $OH^-$

**4. What is the relationship between the strength of an acid and its pKa value?**

a) Stronger acids have higher pKa values

b) Stronger acids have lower pKa values

c) The strength of an acid is independent of pKa

d) Acids with higher Ka have higher pKa

Answer: b) Stronger acids have lower pKa values

**5. Which of the following is a neutral acid?**

a) HCl

b) $NH_4^+$

c) $H_3O^+$

d) $Et_3NH^+$

Answer: a) HCl

6. **As we move down the periodic table, acidity increases due to:**

a) Increasing bond strength

b) Decreasing bond strength

c) Decreasing atomic radius

d) Increasing electronegativity

Answer: b) Decreasing bond strength

**7. Which hybridization leads to the highest acidity in organic compounds?**

a) $sp^3$

b) $sp^2$

c) sp

d) None of the above

Answer: c) sp

**8. What is the effect of an electron-withdrawing group (-I effect) on acidity?**

a) Decreases acidity

b) Increases acidity

c) Has no effect on acidity

d) Makes the base weaker

Answer: b) Increases acidity

**9. Which of the following is NOT a Lewis acid?**

a) $Fe^{3+}$

b) $AlF_3$

c) $NH_3$

d) $CO_2$

Answer: c) $NH_3$

**10. Which of the following is the strongest acid?**

a) HF

b) HCl

c) HBr

d) HI

Answer: d) HI

**11. Why is piperidine more basic than pyridine?**

A) Piperidine has an sp-hybridized nitrogen.

B) Pyridine undergoes stronger inductive effects.

C) The nitrogen lone pair in pyridine is delocalized in the aromatic ring.

D) Piperidine has a resonance structure that stabilizes its lone pair.

Answer: C) The nitrogen lone pair in pyridine is delocalized in the aromatic ring.

**12. Which of the following is expected to be the weakest base?**

A) Piperidine (pKaH = 11)

B) Pyridine (pKaH = 5.2)

C) Benzonitrile (pKaH = -10)

D) Cyclohexylamine (pKaH = 11.2)

Answer: C) Benzonitrile (pKaH = -10)

**13. What effect do electron-withdrawing groups have on amine basicity?**

A) They increase basicity.

B) They decrease basicity.

C) They have no effect on basicity.

D) They increase resonance stabilization.

Answer: B) They decrease basicity.

**14. Why is pyrrole much less basic than pyridine?**

A) Pyrrole's nitrogen is $sp^3$ hybridized.

B) Protonation of pyrrole nitrogen disrupts aromaticity.

C) Pyrrole undergoes strong inductive effects.

D) Pyrrole has a higher pKaH than pyridine.

Answer: B) Protonation of pyrrole nitrogen disrupts aromaticity.

# Unit 7 ❐ Tautomerism

## Structure



## 7.0 Objectives

By the end of this unit, students should be able to:

- Understand Fundamental Concepts of Tautomerism
- Explain the significance of tautomerism in organic chemistry.
- Describe the nature of equilibrium in simple carbonyl compounds.
- Evaluate Factors Influencing Keto-Enol Tautomerism
- Discuss solvent effects, temperature, and steric hindrance on tautomeric composition.
- Analyze given organic structures to determine likely tautomeric forms.
- Understand the impact of tautomerism on the stability and properties of compounds.

## 7.1 Introduction

Tautomerism is a fundamental concept in organic chemistry that describes the dynamic equilibrium between two or more isomeric forms of a molecule, typically involving the shift of a hydrogen atom and a rearrangement of bonding electrons. This phenomenon

plays a crucial role in determining the stability, reactivity, and physical properties of organic compounds.

This unit explores different types of tautomerism, including prototropy, valence tautomerism, and ring-chain tautomerism, and examines the equilibrium composition in various systems such as simple carbonyl compounds, 1,2- and 1,3-dicarbonyl systems, and phenols. Special emphasis is placed on keto-enol tautomerism, one of the most significant forms of tautomerism, which influences a wide range of chemical and biochemical processes.

## 7.2 Tautomerism

The phenomenon in which two structural isomers undergo rapid interconversion and exist in dynamic equilibrium in the liquid state or in solution under normal laboratory condition is known as tautomerism.

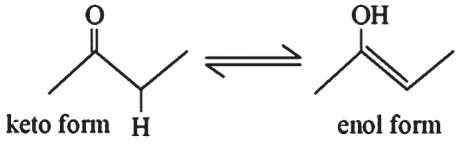
The two forms are known as tautomers. The tautomers differ from each other in electron distribution and in position of relatively mobile atom or group.

The tautomerism is classified into cationotropy and anionotropy depending upon whether atom or group of atoms shifts as cation or anion.

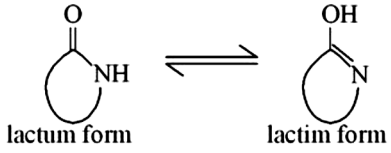
## 7.3 Prototropy

The cationotropy in which the migrating cation is proton is known as prototropy. Some examples of prptotropy are given below:

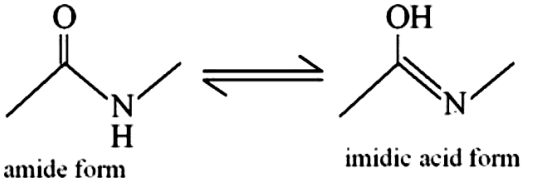
i) Keto-enol tautomerism:




ii) Lactum-lactim tautomerism:

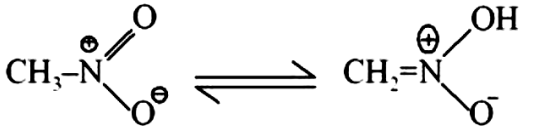


iii) Amide-imidic acid tautomerism:



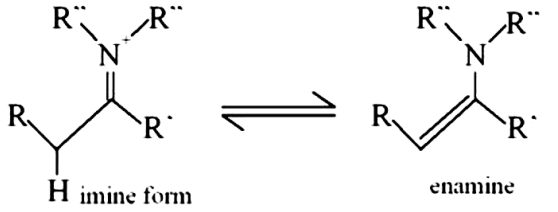

amide form imidic acid form

iv) Nitro-acenitro tautomerism:



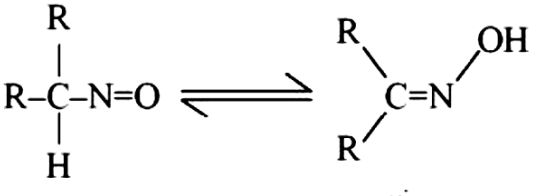

Nitro form Acinitro form

v) Imine-enamine tautomerism:




imine form enamine

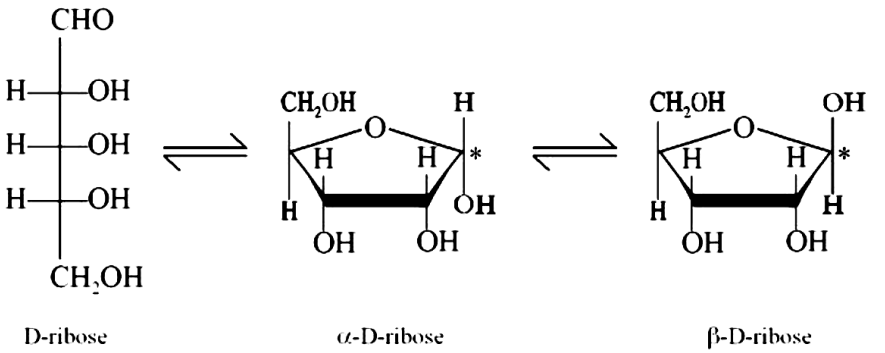
vi) Nitroso-oximino tautomerism:




nitroso oxime

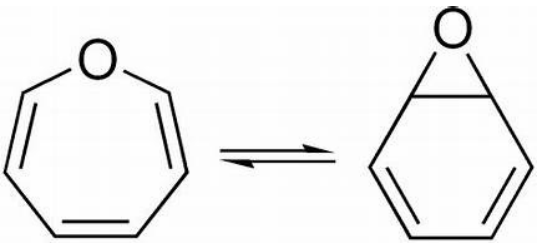
## 7.4 Ring chain tautomerism

The type of tautomerism where ane tautomer is cyclic and the other is acyclic, is known as ring chain tautumerism.




## 7.5 Valence tautomerism

Tautomerism involving change in interatomic distances through the formation of new bonds by redistribution of valence electrons within a molecule without migration of any atom from the rest in any intermediate step is termed as valence tautomerism.




## 7.6 Factors affecting the keto-enol tautomerism

The several factors that are affecting stability of keto-enol tautomerism are detailed below-

**i) Conjugation:** Out of the 2 possible tautomers, say keto-enol tautomers, the one with greater $\pi - \pi$ or any other possible conjugated system would prevail i.e keto-enol equilibrium shifts more towards more conjugated tautomer.

**ii) Hydrogen bonding:** For example in 1,3 -dicarbonyls, $CH_3$-CO-$CH_3$-CO-$CH_3$, the enol form of $CH_2$=C(OH)-CH=CO-$CH_3$ is more stable as the Hydroxyl group involves in Intermolecular Hydrogen bonding, which stabilizes enol form in water solvent.

**iii) Nature of solvent:** The enol percentage is dependent on the type of solvent. For example in 2,4-pentane dione, enol form has lesser enol percentage (4% in water), as lone

electron pairs on oxygen forms H-bonding with enol hydrogen. This causes enol hydrogen and lone pair of electrons on oxygen atom less available to form H-bonding with water molecule. Keto form is more stable due to H-bonding with water molecules. As a consequence, enol percentage of compound in benzene is 95%.

**iv) Temperature:** It has a role on keto-enol equilibrium.

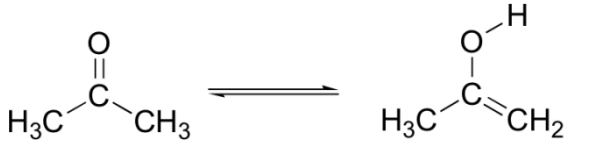
**v) Steric factor** also plays a part.

## 7.7 Composition of equilibrium in different systems

Keto-enol tautomerism is an equilibrium between the keto and enol forms of carbonyl compounds, and its composition depends on factors like molecular structure, solvent, temperature, and substituents. Below is few examples of the keto-enol equilibrium composition in different systems.

### 7.7.1. Simple ketone

Acetone exists exclusively in keto form. This can be explained on the basis of bond energies. The bonding differences between the keto and enol structures are shown below;




**keto** form of acetone **enol** form of acetone

keto: C=O double bond, C-C single bond, C-H bond

enol: C=C double bond, C-O single bond, O-H bond

If we look up the bond energies for these bonds we find

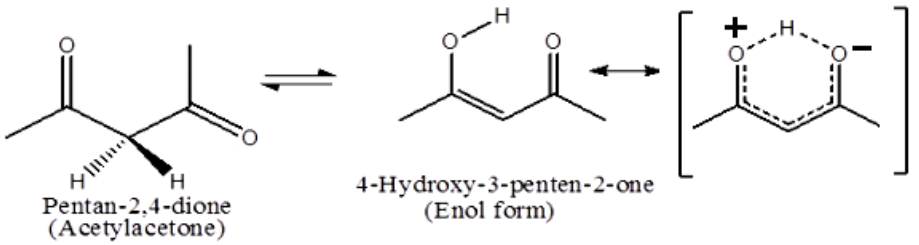
keto: 745 + 347 + 413 = 1505 kJ/mol

enol: 614 + 358 + 467 = 1439 kJ/mol

This rough calculation tells us that, generally, the keto form will predominate. However the energy difference between the two forms is only 66 kJ/mol, a relatively small number; so it is likely that small differences can cause a dramatic shift in the relative concentrations of the two species.

### 7.7.2. 1,3-dicarbonyl system

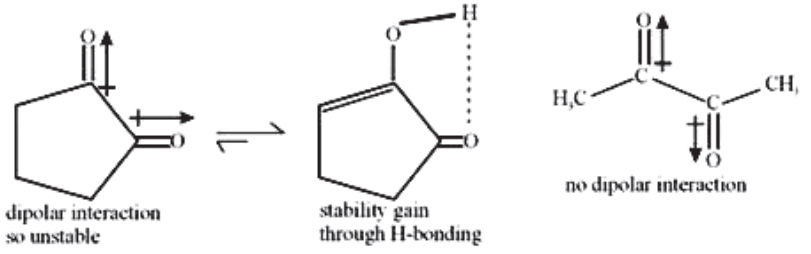
The enol content of acetylacetone in equilibrium is very high (?80%). Acetylacetone (2,4-pentanedione) exists in two isomeric forms, shown below.




The Ketoform is on the left, and the enol form is on the right. These two undergoes interconvertion to each other, but the process is slow enough that an NMR spectrum will show signals from each separate isomer. The 2,4-pentanedione enol form is more stable enol, since the lone pair on the enol oxygen can delocalize across the five atoms to the electronegative carbonyl oxygen. It is also stabilised by an internal hydrogen bond referred to as chelated enol.

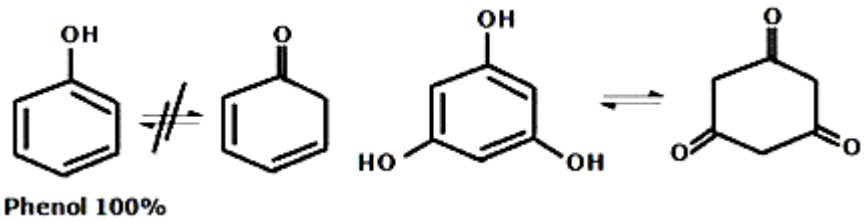
### 7.7.3. 1,2-dicarbonyl system

1,2 cyclopentadione exist exclusively in enol form, whereas biacetyl exist almost exclusively in keto form. In biacetyl the C=O group rotates around the single bond to avoid dipolar repulsion and gain stability. Therefore instead of forming an intramolecular H-bonded enol, the biacetyl take anti conformation and remain almost exclusively in keto form.



### 7.7.4. Phenol system

For phenol there is no evidence for the existence of the keto form. The resonance stabilization of the aromatic ring in phenol is very high and so phenol is highly stable than its keto form. Whereas, phloroglucinol shows ketonic activity. With increase in number of phenolic -OH groups the difference in stability between the enol and keto form tends to decrease because the resonance energy becomes progressively less able to overcome the energy difference.




Phenol 100%

## 7.8 Summary

- Tautomerism is a dynamic equilibrium between structural isomers that interconvert by shifting a hydrogen atom and rearranging bonding electrons.
- The major types of Tautomerism include prototropy, valence tautomerism, and ring-chain tautomerism.
- Prototropy is a type of tautomerism where a proton (H?) migrates between two isomers, seen in keto-enol tautomerism, lactam-lactim tautomerism, and nitro-aci-nitro tautomerism.
- Valence Tautomerism involves redistribution of valence electrons, leading to new bond formations without atom migration.
- Keto-Enol Tautomerism is a specific type of prototropy where a keto form (C=O) and an enol form (C=C-OH) exist in equilibrium.
- Greater ?-? conjugation stabilizes the enol form. Intramolecular H-bonding (e.g., in 1,3-dicarbonyls) stabilizes the enol form. Protic solvents stabilize the keto form, while nonpolar solvents favor the enol form. Higher temperatures can shift equilibrium toward the enol form.

- Acetone predominantly exists in the keto form due to higher bond energy stability.
- Acetylacetone (2,4-pentanedione) exhibits 80% enol content due to resonance and intramolecular hydrogen bonding.
- 1,2-Cyclopentadione exists exclusively in enol form. Biacetyl remains mostly in keto form due to dipolar repulsion avoidance.
- Phenol exists only in the enol form due to strong aromatic ring resonance stabilization. Phloroglucinol, with multiple hydroxyl groups, shows keto-enol equilibrium.

## 7.9 Exercise

1. Write down the principle differences in tautomerism and resonance.
2. Define prototropy and give three examples of tautomeric systems that exhibit prototropy.
3. What is valence tautomerism, and how does it differ from prototropy?
4. Explain why acetylacetone (2,4-pentanedione) has a high enol content.
5. Compare the tautomeric composition of 1,2-dicarbonyl systems like 1,2-cyclopentadione and biacetyl.
6. Why does phenol exist exclusively in its enol form, whereas phloroglucinol shows ketonic activity?
7. Discuss the effect of temperature on keto-enol equilibrium.
8. Why does steric hindrance affect the keto-enol tautomeric balance?
9. The enol content of Ph-CO-$CH_2$-Ph at equilibrium is very small. Explain.
10. The enol content of 4,4,4 trifluoro-2-butanone is larger than that of 2-butanone. Explain
11. 2,3-dimethyl 2-cyclobutenone exists exclusively in the keto form. Explain
12. The enol content of acetyl acetone at equilibrium is very large in n-hexane (92%), medium in acetonitrile (58%), and small in water (15%). Explain.

**Multiple-Choice Questions (MCQs)**

**1. Which of the following is NOT a type of tautomerism?**

a) Prototropy

b) Valence tautomerism

c) Resonance tautomerism

d) Ring-chain tautomerism

Answer: c) Resonance tautomerism

**2. Tautomerism typically involves the migration of which group?**

a) A halogen atom

b) A proton

c) A metal ion

d) A carbonyl group

Answer: b) A proton

**3. Which of the following compounds predominantly exists in the keto form?**

a) Acetone

b) Phenol

c) Acetylacetone

d) Phloroglucinol

Answer: a) Acetone

**4. What is the primary reason keto-enol tautomerism occurs in carbonyl compounds?**

a) The presence of acidic $\alpha$-hydrogen

b) The presence of an aromatic system

c) The presence of a metal catalyst

d) The high boiling point of carbonyl compounds

Answer: a) The presence of acidic $\alpha$-hydrogen

**5. Which factor stabilizes the enol form in keto-enol tautomerism?**

a) High temperature

b) Steric hindrance

c) Intramolecular hydrogen bonding

d) Low pH

Answer: c) Intramolecular hydrogen bonding

**6. In which solvent does the enol percentage of 2,4-pentanedione increase significantly?**

a) Water

b) Benzene

c) Methanol

d) Acetone

Answer: b) Benzene

**7. Which of the following is an example of ring-chain tautomerism?**

a) Acetone

b) Glucose

c) Acetylacetone

d) Phenol

Answer: b) Glucose

**8. Which type of tautomerism involves the redistribution of valence electrons without the migration of atoms?**

a) Prototropy

b) Ring-chain tautomerism

c) Valence tautomerism

d) Keto-enol tautomerism

Answer: c) Valence tautomerism

**9. Which form of phenol is more stable?**

a) Keto form

b) Enol form

c) Both forms are equally stable

d) Stability depends on the solvent

Answer: b) Enol form

**10. Why does phloroglucinol exhibit ketonic activity while phenol does not?**

a) Phloroglucinol has more hydroxyl groups, reducing resonance stabilization

b) Phloroglucinol has stronger hydrogen bonding

c) Phenol is more volatile than phloroglucinol

d) Phenol has a higher melting point

Answer: a) Phloroglucinol has more hydroxyl groups, reducing resonance stabilization

# Unit 8 ❐ Reaction kinetics

## Structure

## 8.0 Objectives

By the end of this unit, students should be able to:

- Define and explain the rate constant and its dependence on temperature and reaction conditions.
- Distinguish between reaction order and molecularity, with examples.
- Construct and analyze free energy diagrams for different reaction pathways.
- Explain the distinction between kinetically controlled and thermodynamically controlled products.
- Define the primary and secondary kinetic isotope effects (kH/kD).
- Explain Hammond's postulate and its implications for transition state structure.

## 8.1 Introduction

Reaction kinetics studies the rates of chemical reactions and the factors affecting them. It helps predict reaction behavior, optimize conditions, and understand mechanisms.

This unit covers rate laws, rate constants, order and molecularity, and energy profiles, including activation energy and transition states. It also explores catalysis, kinetic vs. thermodynamic control, temperature effects, and isotope effects. Understanding these concepts is essential for controlling chemical reactions in scientific and industrial applications.

## 8.2 Rate of reaction

The rate of reaction, or reaction velocity, refers to the change in concentration of a substance per unit time. It is expressed as the decrease in reactant concentration or the increase in product concentration over time. If C represents the reactant concentration at time t, the rate is given by -dC/dt. Similarly, if x represents the product concentration at time t, the rate is dx/dt.

### 8.2.1 Rate equation

Reaction rate depends on the concentration of reactants. A rate equation is the relationship between the concentration of reactants and the observed rate for the general reaction-

$$aA + bB = cC + dD$$

$$\text{Rate } (r) = K\,[A]^a\,[B]^b$$

We can't guess or calculate the rate equation from just the stoichiometry of the reaction. The rate equation depends on the mechanism of the reaction and on the rates of individual step in the mechanism.

### 8.2.2. Units of Reaction Rate

The rate of reaction is typically expressed in concentration change per unit time. The most common unit is:

mol·L-1·s-1(molarity per second)

However, depending on the reaction, it can also be expressed in:

- g/L•s (grams per liter per second)
- atoms or molecules per second

### 8.2.3. Factors Affecting the Rate of Reaction

Several factors influence how fast a reaction occurs:

- **Concentration of Reactants:** A higher reactant concentration generally increases the rate due to more frequent molecular collisions.
- **Temperature:** Higher temperatures provide molecules with more kinetic energy, increasing the frequency and energy of collisions.
- **Catalysts:** Catalysts speed up reactions by lowering activation energy without being consumed in the process.
- **Surface Area (for solid reactants):** Finely divided solids react faster due to a greater surface area available for interaction.
- **Pressure (for gases):** Increasing pressure raises the concentration of gas molecules,

enhancing the reaction rate.

- **Nature of Reactants:** Ionic reactions tend to occur faster than covalent ones due to fewer bond rearrangements.

### 8.2.4. Importance of Reaction Rate

Understanding reaction rates is crucial in various fields:

- Industrial Chemistry: Optimizing reaction conditions for faster production.
- Pharmaceuticals: Controlling drug synthesis and stability.
- Biochemistry: Studying enzyme-catalyzed reactions.
- Environmental Science: Monitoring pollutant degradation.

## 8.3 Order of a reaction

The order of a reaction is the sum of the exponents of the concentration terms in the rate law equation of a chemical reaction. It represents the dependence of the reaction rate on the concentration of reactants.

For a general reaction:

$$aA + bB \rightarrow \text{Products}$$

The rate law is expressed as:

$$\text{Rate} = k[A]^m [B]^n$$

where:

- k is the rate constant.
- m and n are the reaction orders with respect to reactants A and B.
- Overall order of reaction = m + n.

The order of a reaction is determined experimentally and does not always correspond to the stoichiometric coefficients of the balanced chemical equation. It helps in understanding reaction mechanisms and predicting how changes in reactant concentration affect the reaction rate.

**Types of Reaction Orders**

**a) Zero-Order Reaction (Order = 0):** The rate of reaction is independent of the concentration of reactants.

**Rate law:** Rate=k

Example: Decomposition of ammonia on a platinum surface: 2NH3?N2+3H2

**b) First-Order Reaction (Order = 1):** The rate is directly proportional to the concentration of one reactant.

**Rate law:** Rate=k$[A]^1$

Example: Radioactive decay of isotopes

**c) Second-Order Reaction (Order =2):** The rate depends on the square of one reactant's concentration or the product of two reactant concentrations.

**Rate law:** Rate= k$[A]^2$ or Rate=k[A][B]

Example: Reaction between hydrogen and iodine: $H_2+I_2 \rightarrow 2HI$

**d) Third-Order and Higher Reactions (Order $\geq$3):** Rare in nature due to complex molecular interactions.

Rate law: Rate=k$[A]^n$ (where n= 3,4,5,…)

**Example:** $2NO + O_2 \rightarrow 2NO_2$ (third-order reaction).

## 8.4 Molecularity

Molecularity refers to the number of reactant molecules that collide simultaneously to bring about a chemical reaction in an elementary step. It is a theoretical concept applicable only to elementary reactions and is always a whole number (1, 2, or 3).

Both molecularity and order of reaction describe aspects of how a reaction proceeds, but they differ in meaning, determination, and applicability.

**Molecularity vs. Order of Reaction**

| Property | Molecularity | Order of Reaction |
|---|---|---|
| Definition | The number of reactant molecules colliding in an elementary step of a reaction. | The sum of the exponents of the concentration terms in the rate law of the reaction. |
| Applicability | Only for elementary reactions. | Can be applied to both elementary and complex reactions. |
| Determination | Determined by the reaction mechanism (the number of molecules involved in a single step). | Determined experimentally from the rate equation. |
| Possible Values | Always a whole number (1, 2, or 3); values greater than 3 are highly unlikely. | Can be a whole number, fraction, or even zero. |
| Dependence on Experiment | Theoretically predicted from the reaction mechanism. | Determined experimentally through rate measurements. |
| Changes with Conditions? | No, molecularity is a fixed property of an elementary step. | Yes, order of reaction can change with different conditions (e.g., changing solvent, catalyst, or temperature). |
| Example | For the elementary reaction: $2NO+O_2 \rightarrow 2NO_2$, the molecularity is 3 (termolecular). | The rate law for the same reaction is Rate = $k[NO]^2[O_2]$, so the order of reaction is 2 + 1 = 3. |

## 8.5 Rate determining step (r.d.s.)

The rate-determining step (R.D.S.) is the slowest step in a reaction mechanism that limits the overall reaction rate. Since a multi-step reaction proceeds through a series of intermediate steps, the step with the highest activation energy acts as a bottleneck, controlling how fast the reaction progresses.

Key Features of r.d.s..:

1. **Slowest Step:** Among all steps in a reaction mechanism, R.D.S. has the highest energy barrier and takes the longest time to occur.
2. **Controls Overall Rate:** The rate of the entire reaction depends on the R.D.S. rather than the faster steps.

3. **Determines the Rate Law:** The reactants involved in the R.D.S. appear in the experimental rate law.
4. **Not Necessarily the First Step:** The R.D.S. can occur at any stage in the reaction mechanism.
5. **Activation Energy Barrier:** It is the step requiring the most energy to proceed.

Let us understand with an Example of SN1 Reaction i.e. Unimolecular Nucleophilic Substitution

**For the SN1 reaction:**

$$R\text{-}X \rightarrow R^{+} + X^{-} \text{ (slow step, R.D.S.)}$$

$$R^{+} + Nu^{-} \rightarrow R\text{-}Nu \text{ (fast step)}$$

The first step (formation of the carbocation) is the slowest and determines the reaction rate. The rate law depends only on the concentration of R-X, not the nucleophile.

Rate = k[R-X], showing first-order kinetics.

Thus, the rate-determining step is the critical step that dictates how fast a reaction occurs. Understanding it helps in predicting reaction rates, optimizing conditions, and designing catalysts for industrial and laboratory applications.

## 8.6 Transition state

In every step, reactant go to product (or intermediate) through a high energetic activated complex known as transition state, that means a transition state (T. S.) is a structure that that represents an energy maximum on passing from reactant to product. It is not a real molecule; it may have partially formed or broken bonds and may have more atoms or groups around the central atom than the allowed valence bond rules. It can't be isolated because it is an energy maximum. A transition state is often shown by putting it in square brackets with a double dagger superscript.

**Key Characteristics of the Transition State:**

1. **Highest Energy Point:** It is the peak of the energy diagram and corresponds to the maximum potential energy along the reaction path.
2. **Short-Lived:** The transition state exists for an extremely brief moment before forming

the products or reverting to reactants.

3. **Partial Bond Formation & Breaking:** Bonds are simultaneously breaking and forming, creating a hybrid structure that is neither reactant nor product.
4. **Unstable & Cannot Be Isolated:** Unlike reaction intermediates, the transition state cannot be detected or isolated because it exists only for an instant.
5. **Symbolized by a Double Dagger (#):** Represented as TS# in reaction mechanisms

## 8.7 Activation energy

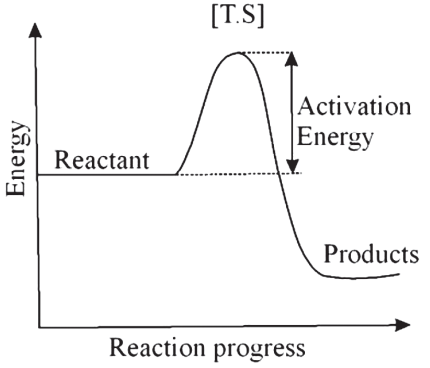
Activation energy (Ea) is the minimum energy required for reactants to successfully transform into products by passing through a high-energy transition state. It acts as an energy barrier that must be overcome for a reaction to proceed.

During a chemical reaction, reactant molecules must collide with sufficient energy to break existing bonds and form new ones. If their energy is below the activation energy, the reaction will not occur. However, if they have energy equal to or greater than Ea , they reach the transition state and convert into products.

The reaction rate is directly influenced by the activation energy of the rate-determining step—the slowest step in a reaction mechanism. A lower activation energy allows more molecules to overcome the barrier, leading to a faster reaction, while a higher activation energy slows the reaction down.

## 8.8 Reaction energy diagram

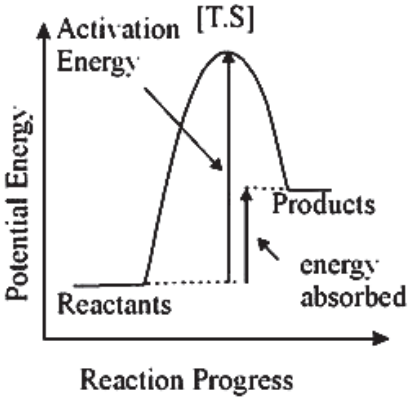
To depict graphically the energy changes during transformation from starting material to product. For exothermic reaction, the energy profile diagram is given below-




In an exothermic reaction the products have less energy than the reactants, so energy is released

Also in an exothermic reaction weaker bonds are broken and stronger bonds are made, so overall energy is released

In case of endothermic reaction-

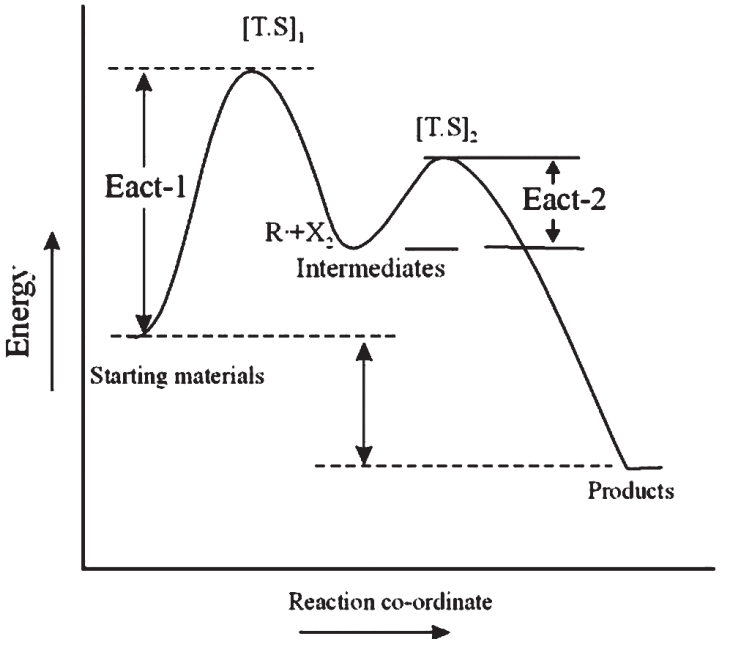



In an endothermic reaction the products have more energy than the reactants, so energy is taken in

Also in an endothermic reaction stronger bonds are broken and weaker bonds are made, so overall energy is taken in

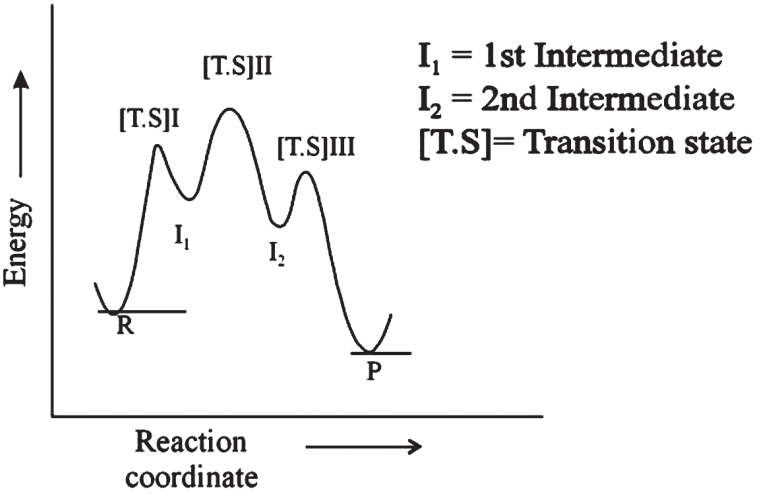
The energy profile diagram considering the following condition is given below ……..

$\Delta H$ = -Ve, [T.S]2 is more stable than [T.S]1

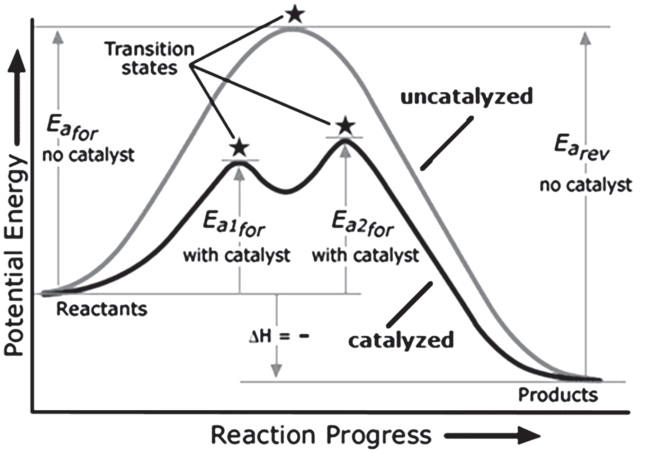



**Problem:** Draw a energy profile diagram of a three step exothermic process in which the 2nd step is rate determining step and 2nd intermediate is more stable than the first intermediate.

**Solution:**




Energy profile diagram of a catalyzed reaction compared to uncatalyzed reaction-….




Ea for = activation energy for forward reaction

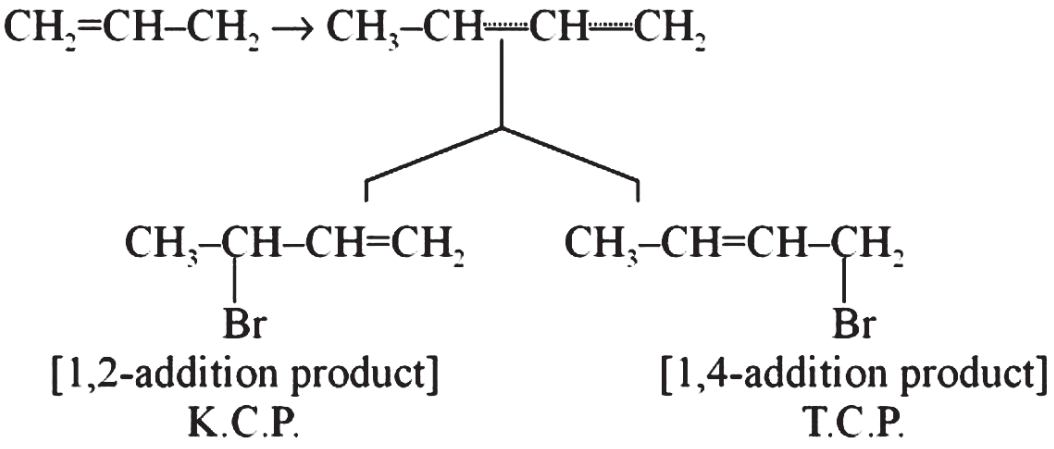
Ea rev = activation energy for reverse reaction

## 8.9 Thermodynamically controlled and kinetically controlled reactions

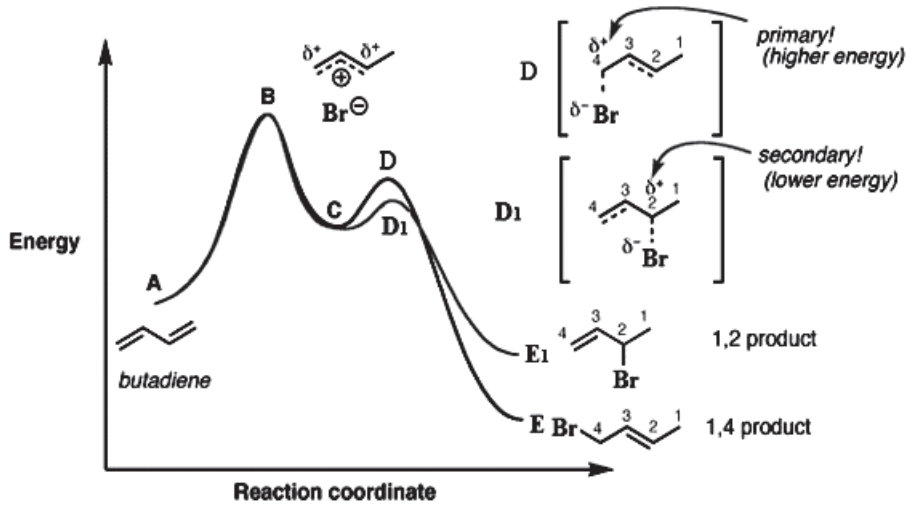
Thermodynamically controlled reactions are those where the products are interconvertible and remain in equilibrium under the reaction condition and the degree of formation of product i.e., concentration of product depends on the relative thermodynamic stability of the product.

Kinetically controlled reactions are those parallel reactions where the products are not interconvertible and the concentration (or degree of formation of product) of different products is controlled by the rate of reaction.

**Example:** The addition of HBr to butadiene gives 1, 2-addition product at lower temperature but at higher temperature 1, 4-addition product is major.




**Energy coordinate for 1 ,2- versus 1,4- additions to butadiene**




The height of transition states $D_1$ and D (and therefore their reaction rate from carbocation C ) is related to the stability of the positive charge in $D_1$ and D.

The lower the energy, the faster reaction . So $E_1$ is formed faster from C here since the energy of transition state $D_1$ is less than D

The energy of $E_1$ and E is related to the greater stability of the 1,4 alkene in this case (disubstituted versus monosubstituted ). E has a more substituted double bond than $E_1$ so it is more stable.

## 8.10 Primary and secondary kinetic isotope effect

A large difference in the rate of a reaction is observed when one of the atoms of a bond that breaks in the r.d.s. is replaced by its isotope. This is called primary kinetic isotope effect.

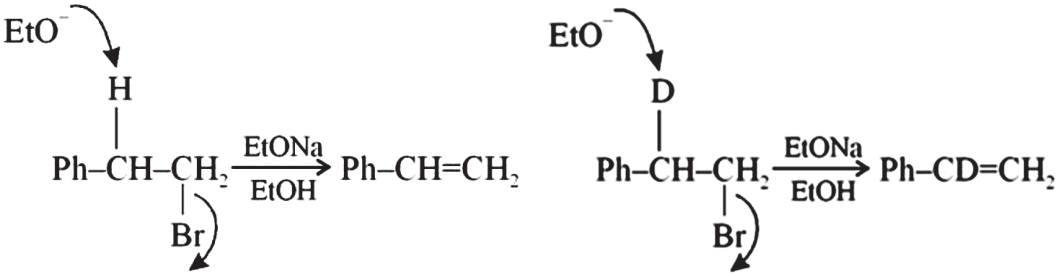
If a C-H bond breaks in r.d.s. of a reaction, substitution of H by D results in decrease in reaction rate and that is because the C-D bond is stronger than C-H bond.

Deuterium isotope effect has also been observed in reaction in which the C-H bond does not break at all. Such effect is known as secondary isotope effect.

### 8.10.1 Example of primary kinetic isotope effect:

In case of E-2 reaction of 2-phenyl-1-bromo ethane with NaOEt/EtOH, KH/KD is 7.1. If

the β -H atoms with respect to Br atom are replaced by 'D' then the rate becomes slow i.e., C-H bond breaking involves r.d.s.



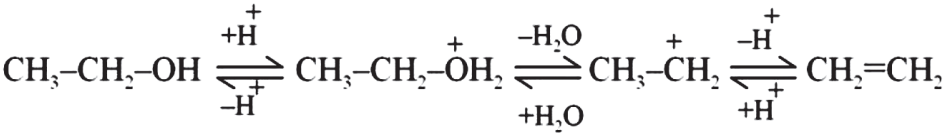

### 8.10.2 Example of secondary kinetic isotope effect:

The solvolysis of t-butylchloride –D9 is found to be slower than that in the corresponding t-butylchloride. The KH/KD is 2.32. The difference in the rate has been attributed to an electronic effect. There is a decrease of hyperconjugative electron release of the deuterated methyl group in the T.S. because of stronger C-D compared to C-H bond. This is secondary kinetic isotope effect.

## 8.12 Principle of microscopic reversibility

The principle of microscopic reversibility state that the same pathway that is travelled in the forward direction of a reaction will be travelled in reverse direction (run under the same condition), since it affords the lowest energy barrier for either process.

It implies that the forward and backward reaction must follow the same mechanism. For instance, in the dehydration of alcohol using acid, an olefin is formed presumably via a carbocation. As consequence of this principle is that the reverse reaction i.e., acid catalysed hydration of olefin to alcohol must involve the same carbocation.



## 8.12 Hammond postulate

The Hammond postulate is a fundamental concept in reaction kinetics that helps predict the structure of a transition state (T.S.) based on the relative free energy of reactants, products, and intermediates. Since the transition state is highly unstable and short-lived, its precise structure is difficult to determine experimentally. However, by understanding the structure of more stable reaction intermediates, we can infer key details about the transition state using Hammond's postulate.

Hammond's postulate states: "For any single reaction step, the geometry of the transition state resembles the species (reactant or product) to which it is closer in free energy."

This principle applies differently to exothermic and endothermic reactions:

**a) Exothermic Reactions:** In an exothermic reaction, the transition state is closer in energy to the reactants than to the products. Therefore, the T.S. structure resembles the reactants more than the products, meaning it retains more characteristics of the starting materials before the reaction completes.

**b) Endothermic Reactions:** In an endothermic reaction, the transition state is closer in energy to the products than to the reactants. Consequently, the T.S. structure resembles the products more than the reactants, indicating that the system has already undergone significant transformation toward product formation.

**Significance of Hammond's Postulate**

**1.Reaction Mechanism Insights:** It helps in understanding whether a reaction proceeds through an early (reactant-like) or late (product-like) transition state.

**2. Predicting Rate Dependence:** Since the activation energy is related to the transition state's energy, reactions with early T.S. tend to be faster than those with late T.S.

**3. Catalysis and Stability:** The principle is widely used to explain the effects of catalysts, substituents, and reaction conditions on reaction rates.

## 8.13 Summary

- The rate constant (k) varies with temperature and reaction conditions, typically following the Arrhenius equation.

- Reaction order is determined experimentally and may be a fraction, while molecularity is a theoretical concept and always a whole number.
- Kinetically controlled products form faster but may be less stable, while thermodynamically controlled products are more stable but take longer to form.
- The replacement of hydrogen with deuterium can slow down a reaction if bond breaking is involved in the rate-determining step.
- Hammond's Postulate states that the transition state structure resembles the reactants in exothermic reactions and the products in endothermic reactions.
- The reaction rate is the change in concentration of reactants/products per unit time and follows a rate equation based on reactant concentrations.
- Factors Affecting Reaction Rate are the Concentration, temperature, catalysts, surface area, pressure (for gases), and nature of reactants all influence reaction speed.
- Order of a Reaction is the sum of exponents in the rate law determines reaction order, which dictates how concentration changes impact rate.
- Molecularity of a Reaction is the number of reactant molecules colliding in an elementary step; differs from reaction order.
- Rate-Determining Step (RDS) is the slowest step in a multi-step mechanism, dictating the overall reaction rate and appearing in the rate law.
- Catalysts lower the activation energy, increasing reaction rates without being consumed in the process.
- The principle of microscopic reversibility state that the forward and backward reaction must follow the same mechanism (run under the same condition)

## 8.14 Exercise

1. Define the rate constant and explain how it depends on temperature and reaction conditions.
2. What is the difference between reaction order and molecularity? Provide examples.
3. Define kinetically controlled and thermodynamically controlled products with examples.

4. What is the primary kinetic isotope effect? How does it differ from the secondary kinetic isotope effect?
5. Explain Hammond's postulate and its significance in understanding transition state structures.
6. Define the rate of reaction and write its mathematical expression in terms of reactant and product concentrations.
7. Why do catalysts speed up a reaction without being consumed?
8. Define the order of a reaction and explain how it is determined experimentally.
9. What is the difference between molecularity and reaction order? Provide an example where the order of reaction does not match molecularity.
10. What is the rate-determining step (R.D.S.), and why is it important in a reaction mechanism?
11. What are the key characteristics of a transition state?
12. How is the transition state different from an intermediate?
13. Draw an energy profile diagram of a three step exothermic reaction in which the 2nd step is rate controlling and the 2nd unstable intermediate is more stable than the first.
14. How does the presence of a catalyst affect the activation energy of a reaction?
15. Differentiate between thermodynamically controlled and kinetically controlled reactions with an example.
16. What do you mean by kinetically and thermodynamically controlled product?
17. Explain the concept of the primary kinetic isotope effect with an example.
18. What is the secondary kinetic isotope effect, and how does it influence reaction rates?
19. What is the principle of microscopic reversibility, and why is it important in reaction mechanisms?
20. Explain Hammond's postulate using an example of an exothermic reaction.

**Multiple-Choice Questions (MCQs)**

**1. What does the rate constant (k) depend on?**

a) Temperature and reaction conditions

b) Only concentration of reactants

c) The stoichiometric coefficients

d) Volume of the reaction vessel

Answer: a) Temperature and reaction conditions

**2. What is the correct expression for the rate of a reaction where A and B react to form products?**

a) Rate = $k[A]^m[B]^n$

b) Rate = k[A + B]

c) Rate = $k[A]^2 + [B]^2$

d) Rate = $[A]^m + [B]^n$

Answer: a) Rate = $k[A]^m[B]^n$

3. What are the units of reaction rate commonly expressed in?

a) $mol \cdot L^{-1} \cdot s^{-1}$

b) g/mL

c) atm/L

d) L/mol

Answer: a) $mol \cdot L^{-1} \cdot s^{-1}$

**4. Which of the following factors does NOT affect the rate of a reaction?**

a) Surface area of solid reactants

b) Presence of a catalyst

c) Color of the reactants

d) Concentration of reactants

Answer: c) Color of the reactants

**5. What is the overall order of a reaction with the rate law: Rate = $k[A]^2[B]$?**

a) 1

b) 2

c) 3

d) 4

Answer: c) 3

**6. Which type of reaction order indicates that the rate is independent of reactant concentration?**

a) Zero-order

b) First-order

c) Second-order

d) Third-order

Answer: a) Zero-order

**7. Which of the following reactions is an example of a first-order reaction?**

a) $2NH_3 \rightarrow N_2 + 3H_2$

b) Radioactive decay of isotopes

c) $2NO + O_2 \rightarrow 2NO_2$

d) $H_2 + I_2 \rightarrow 2HI$

Answer: b) Radioactive decay of isotopes

**8. Molecularity of a reaction can be:**

a) Any real number

b) Any positive integer

c) A fraction

d) A negative integer

Answer: b) Any positive integer

**9. In a reaction mechanism, the rate-determining step is:**

a) The fastest step in the reaction

b) The slowest step with the highest activation energy

c) The step with the lowest activation energy

d) Always the first step

Answer: b) The slowest step with the highest activation energy

**10. The transition state of a reaction is characterized by:**

a) Being a real molecule that can be isolated

b) Partial bond formation and breaking

c) A lower energy than reactants and products

d) A stable intermediate

Answer: b) Partial bond formation and breaking

**11. Activation energy is defined as:**

a) The total energy of reactants

b) The minimum energy required for a reaction to proceed

c) The maximum energy released during a reaction

d) The energy needed to form a catalyst

Answer: b) The minimum energy required for a reaction to proceed

**12. Which of the following reactions is kinetically controlled?**

a) A reaction where the product depends on thermodynamic stability

b) A reaction where the product is determined by the reaction rate

c) A reaction at equilibrium

d) A reaction catalyzed by an enzyme

Answer: b) A reaction where the product is determined by the reaction rate

**13. The primary kinetic isotope effect occurs when:**

a) An isotope substitution affects the rate-determining step

b) An isotope substitution has no effect on reaction rate

c) The reaction forms an equilibrium mixture of isotopes

d) The solvent changes the reaction pathway

Answer: a) An isotope substitution affects the rate-determining step

**14. According to Hammond's postulate, the transition state in an exothermic reaction resembles:**

a) The reactants

b) The products

c) The intermediates

d) The catalyst

Answer: a) The reactants

# Unit 9 ❐ Bonding Geometries & Molecular Representations of Organic Molecules

## Structure



## 9.0 Objectives

By the end of this unit learners will be able to know :

- Explain the hybridization concept leading to the tetrahedral geometry of carbon.
- Define chirality and asymmetric carbon centers.
- Interpret and Differentiate Molecular Representations e.g. Fischer, Sawhorse, Flying-Wedge, and Newman projections.
- Demonstrate the interconversion between Fischer, Sawhorse, Flying-Wedge, and Newman projections.

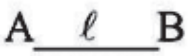
## 9.1 Introduction

Stereochemistry is the branch of chemistry that deals with the three-dimensional structure of molecules. Molecular geometry is defined by parameters such as bond lengths, bond angles, and dihedral angles, which determine the spatial arrangement of atoms in a molecule.

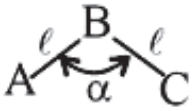
In organic chemistry, carbon serves as the fundamental building block, forming covalent bonds and adopting a tetrahedral geometry when $sp^3$ hybridized. This tetrahedral nature contributes to molecular asymmetry, leading to chirality and stereoisomerism, which significantly influence the physical and chemical properties of organic compounds. Understanding these spatial arrangements is essential for analyzing molecular interactions, reactivity, and stereochemical relationships.

## 9.2 Geometrical parameters

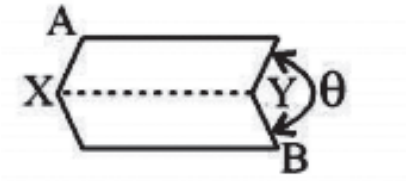
Bond length (l ): The bond length of a diatomic molecule AB can be defined as the equilibrium value of the distance between the centres of the two atomic nuclei connected by one or more covalent bonds as shown.




**Bond Angle (a) :** It is the angle subtended by the centres of three atomic nuclei connected together as in A-B-C.




Dihedral angle ( $\theta$ ) : The angle beween two planes A-X-Y etc. and X-Y-B in a nonlinear molecule A-X-Y-B is known as the dehedral angle ? as shown below.



**Vander Waals radii of atoms or groups:**

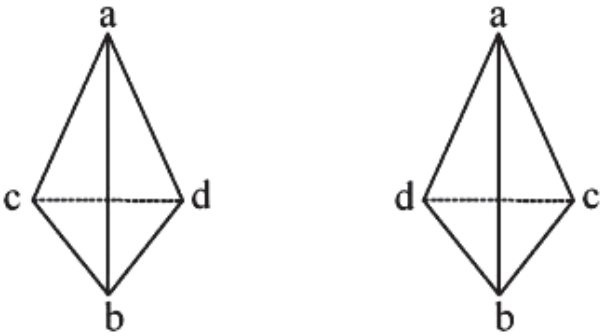
When two nonbonded atoms or groups (ligands) are close to each other there appears an attractive force between the electrons of one atom and the nucleus of the other and repulsive forces between the nuclei and between the electrons of the two atoms. The distance at which the attractive and repulsive forces balance each other is called the van der Waals radii of the two atoms or groups (ligands). The van der Waals radii of some ligands are:

H (120 pm), C (150 pm), CH, (200 pm), N (150 pm), Cl (180 pm), Br (195 pm), I (215 pm).

Other parameters determining geometry of the molecule concerned will be discussed elsewhere.

## 9.3 Tetrahedral nature of carbon and concept of asymmetry

In 1874, van't Hoff and Le Bel working independently of each other, proposed the tetrahedral geometry of carbon compounds. According to them, a tetrahedral carbon with four different atoms or groups called ligands such as Cabcd can be represented by 1 and 1' in both of which carbon atom (not shown in the diagram) is considered to be at the centre and four ligands a, b, c and d are arranged tetrahedrally around the central atom to which they are linked.




1 1′

When the ligands are joined to the central carbon atom by chemical bonds, the tetrahedral structures 1 and 1' appear as three-dimensional perspective formulae 2 and 2' on two-dimensional paper.

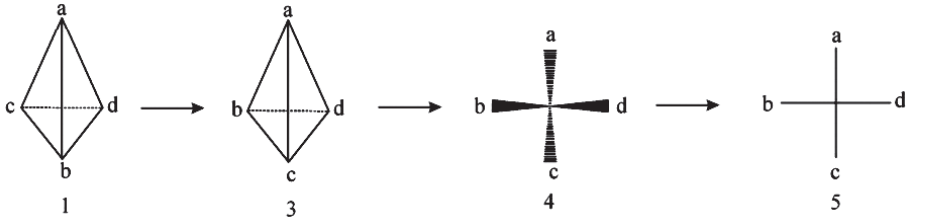

In 2 and 2', bonds with uniform lines lie in the plane of the paper, the thick end of the wedge are in the front and the dotted lines are behind the plane. The structures 2 and 2' are called flying wedge formula. They form non-superimposable mirror images of each other. A Cabcd type of molecule that is not superimposable on its mirror image is called chiral and exists as a pair of enantiomers. A molecule with one chiral centre is called asymmetric molecule.

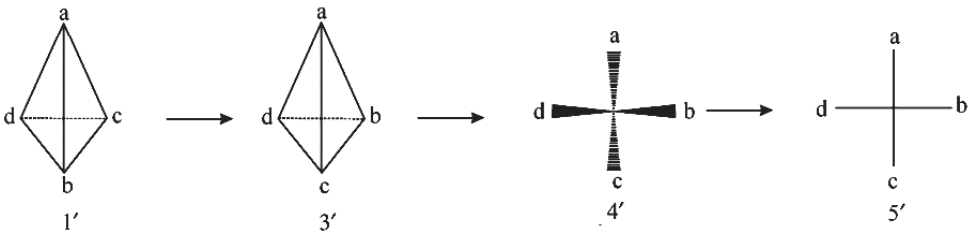
## 9.4 Molecular representation

Since stereochemistry refers to molecules in three dimensions, appropriate modes of representations of three-dimensional molecules on two-dimensional paper is essential. Several two-dimensional projection formulas have been developed to represent molecules having three-dimensional structures. These projection formulas are 1) Fischer 2) Sawhorse 3) Newman and 4) Flying-Wedge.

### 9.4.1 Fischer projection formula :

If the positions of the tetrahedral structures are slightly changed, 1 and 1' assume the geometric figures 3 and 3' in which b and d are horizontally placed.






When the ligands a, b, c and d are joined to the central carbon atom by chemical bonds, 3 and 3' give three-dimensional perspective formula 4 and 4' on two-dimensional paper in which the horizontal ligands b and d are above the plane and towards the observer while the vertical ligands are below the plane and away from the observer. When 4 and 4' are projected on the plane of the paper they are transformed respectively into two dimensional geometric figures 5 and 5'. The structures 5 and 5' are called Fischer projection formulae. There are some limitations of Fischer projection formula.

1 . The projection formula cannot be lifted out of the plane of the paper.

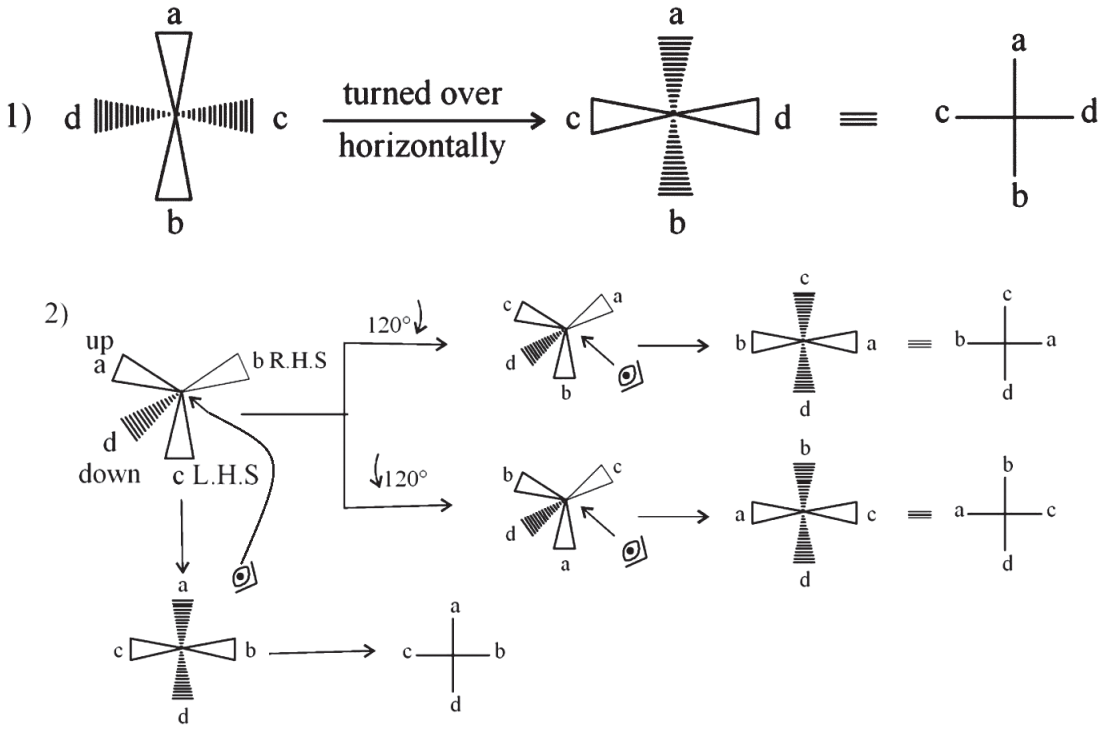
2. The projection formula is not allowed to rotate through 90° or 270° although it is permissible to rotate through 180° or 360°.

3. Single exchange of a pair of ligands results in an enantiomeric structure while double exchange between two pairs leads to an equivalent structure.

**Problem :** How would you convert the following by exchange of ligands?

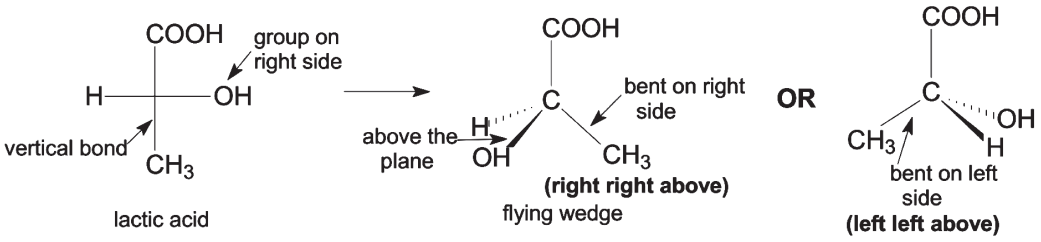
**Solution Hint:** i) double exchange between -H & -CH, and -OH & -CO2H, ii ) double exchange of ligands.

Conversion of Flying Wedge formula having one chiral centre to Fischer projection (F.P) formula.

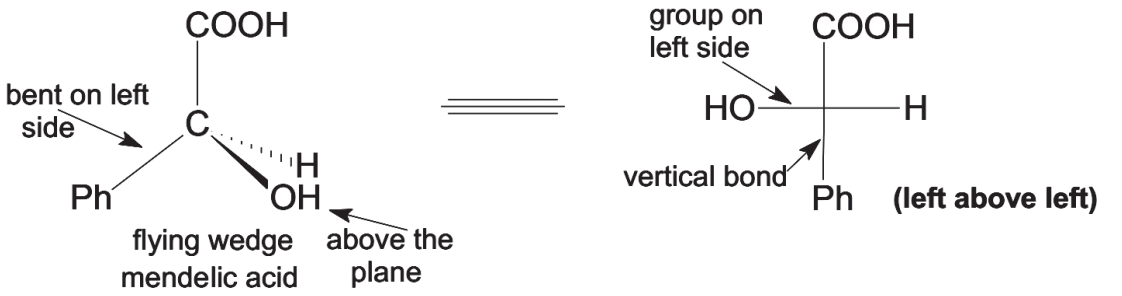



### 9.4.2 Conversion Fischer projection to flying-wadge and vice versa

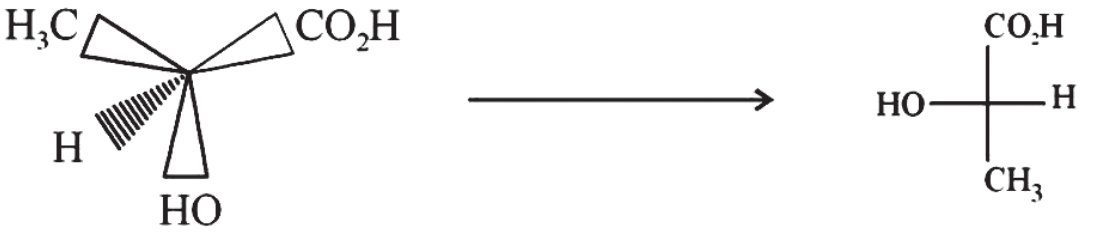
Conversion of Fischer projections to flying-wadge and vice versa may be carried out as follows:



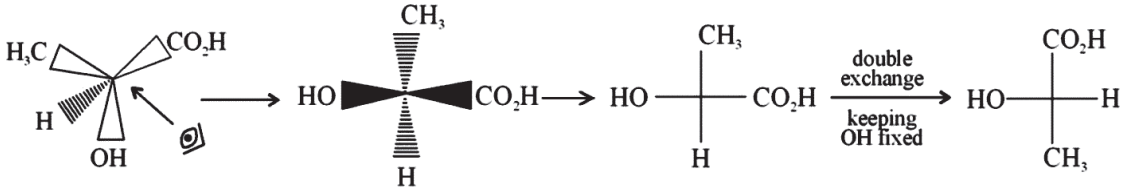
Here vertical bonds in Fischer projection are considered to be in the plane of the paper and horizontal bonds are to be above and below the plane. The reverse method may be followed as given below:



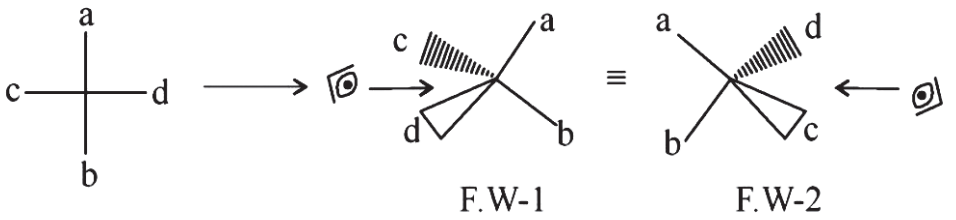

**Problem :** How would you transform the following 3D-perspective formula of lactic acid to F.P.?



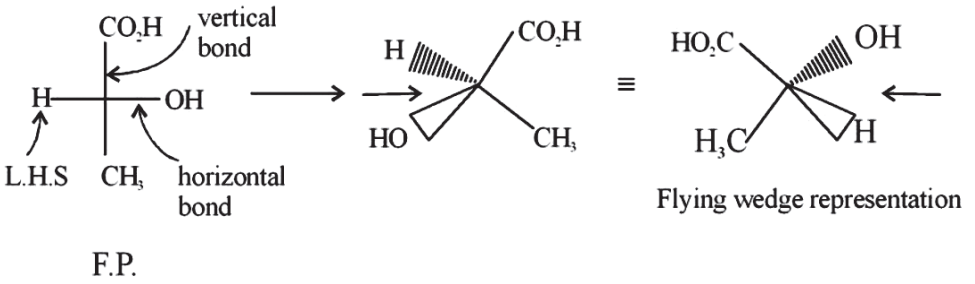

**Solution:**




Interconversion of F.P into F.W (flying wedge):

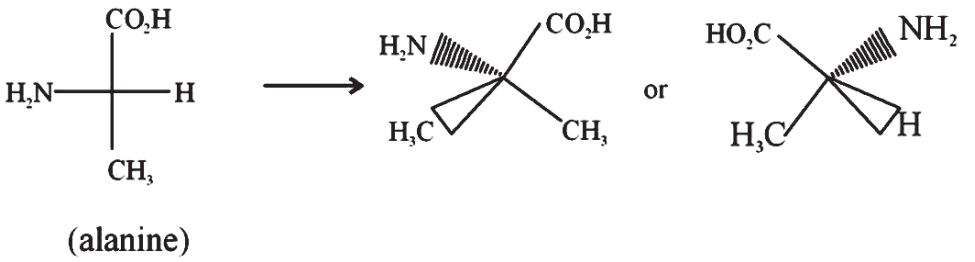



For conversion of F.P to F.W, the vertical bonds a- C- b in F.P are drawn in a plane as bent bonds as in F.W-1 and F.W-2 above. We are now to look at these bonds such that the vertical bonds are away from us so that our left hand will be below the plane and right hand above in F.W-1 and reverse in F.W-2. The bonds above the plane are represented by thick wedge and nearer to the bottom of the vertical bond while the bonds below the plane are represented by dotted lines and closer to the top of the vertical bond as shown in F.W-1 and F.W-2.

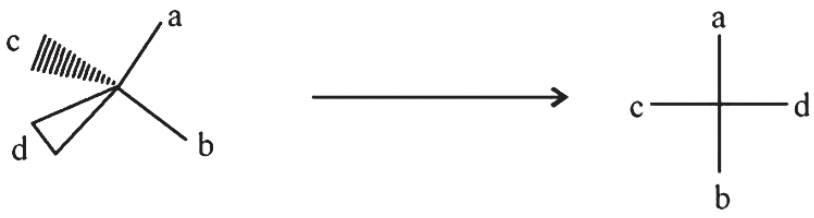



**Problem :** Convert alanine from its F.P. to F.W

**Solution:**

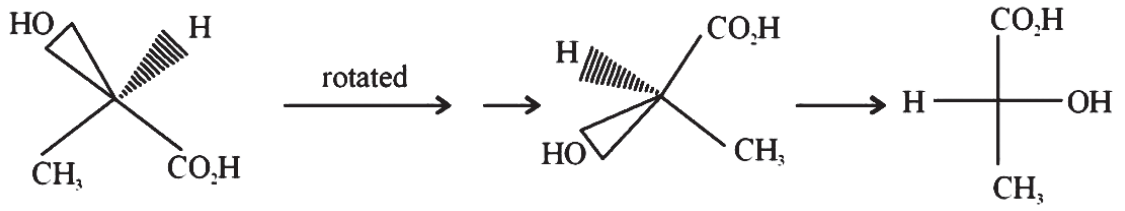



Conversion of F.W to F.P

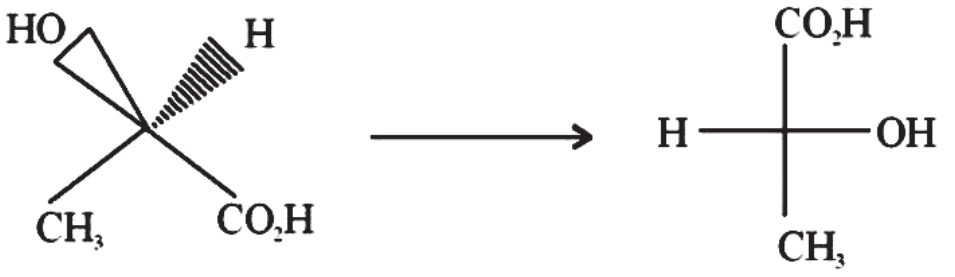



In this case, the F.W is viewed in a manner such that the vertical bonds are away from the observer. The left-handed ligand will then be at the horizontal left and right handed ligand at the horizontal right. The vertical and horizontal bonds are drawn and the ligands are properly placed to get F.P. formula.

**Problem: Convert the following:**



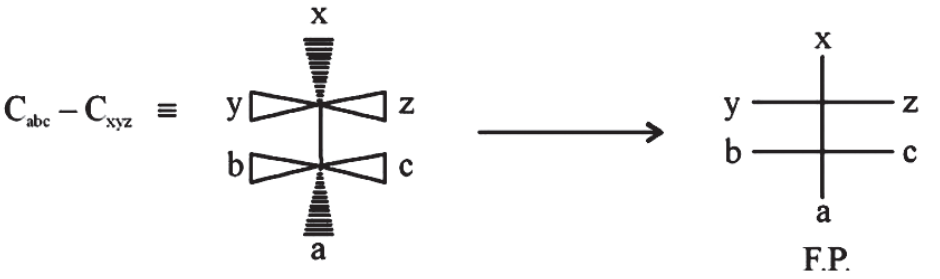

**Solution:**




### 9.4.3 Fischer projection formula for molecules having two chiral centres.

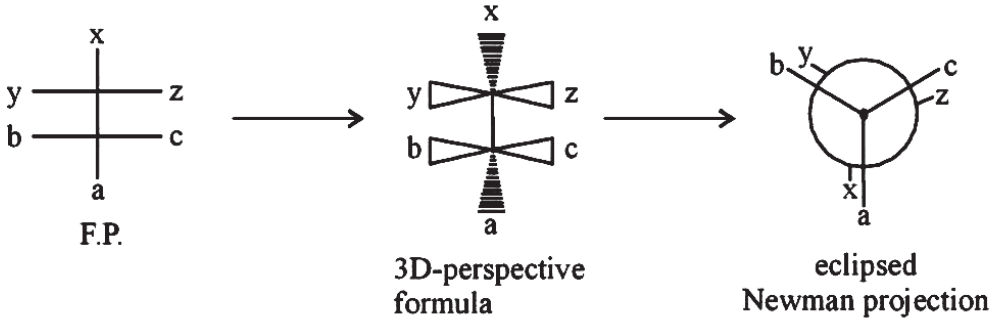
Fischer projection formula with two chiral centres such as Cabc — Cxyx can be represented

in a similar way as molecules with one chiral centre.



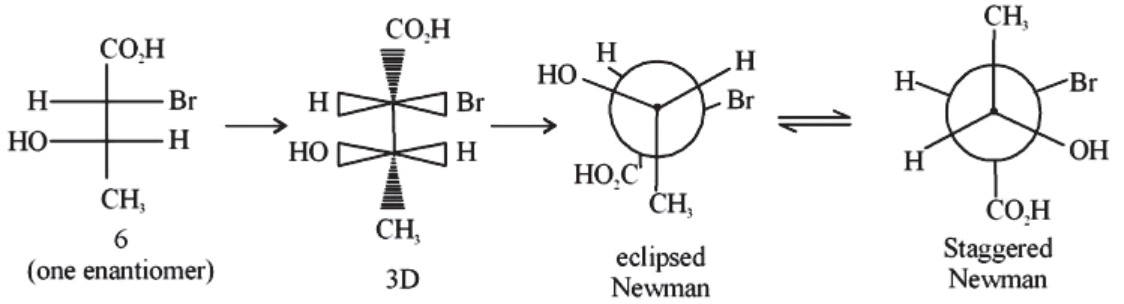

Fischer projection having two chiral centres is an energetically unfavourable formula. It may be extended to an eclipsed Newman projection, sawhorse projection and flying wedge formula.

### 9.4.4 Newman projection formula




In Newman projection, 3D-perspective formula is viewed from front to back along C-C bond. The bonds are projected in a vertical plane and are represented as superposed circles (only one being shown in the diagram). The centre of the circle represents the front carbon atom and the periphery the back atom. In the case above, F.P. is converted into an eclipsed Newman projection through the 3D-perspective formula. When the front or back carbon atom is rotated through 180°, it gives staggered Newman projection.

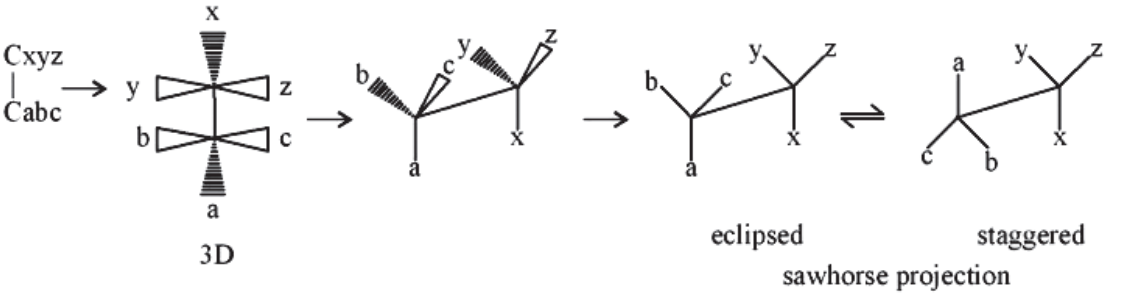
These are illustrated with 2-bromo-3-hydroxybutanoic acid 6



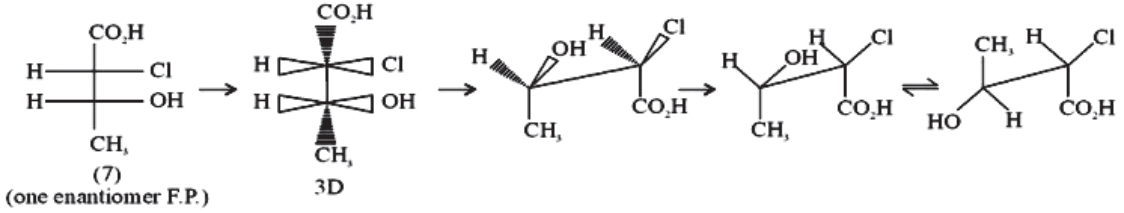

So, we can directly convert a molecule with two chiral centres in F.P. to the corresponding Newman projection.

### 9.4.5 Sawhorse projection formula

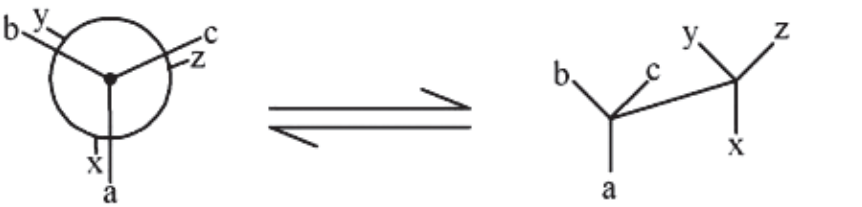
In this case, C-C bonds in 3D-perspective formula is viewed from an angle such that after projection C-C bond will appear as an oblique line called diagonal line. The bonds attached to each chiral centre are then projected into the same vertical plane as usual to give eclipsed or staggered sawhorse projection formula.




2-Chloro-3-hydroxybutanoic acid (7) can be cited as an example:



• Interconversion of Newman to sawhorse formula and vice versa

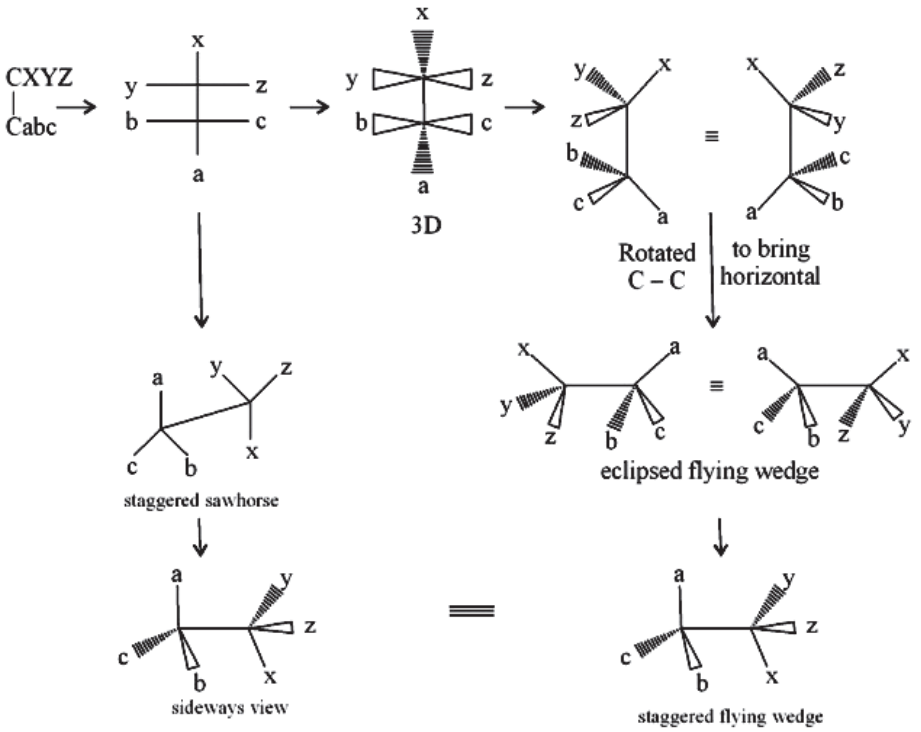



eclipsed Newman projection

eclipsed sawhorse projection

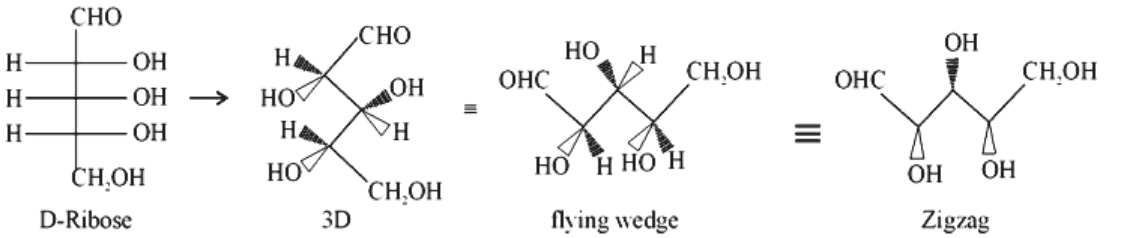
### 9.4.6 Flying wedge formula with two chiral centres

3D-perspective formula with two chiral centres can be represented by flying wedge formula in a similar manner as with one chiral centre. The vertical bonds are considered to be in the plane of the paper and one of the horizontal bonds will be above and another below the plane.



So, sideways view of staggered sawhorse is the same as that of staggered flying wedge. A molecule with two or more chiral centres can be represented by flying wedge and zigzag formula. The zigzag formula is simpler and can be used in place of flying wedge if it has a hydrogen atom at each chiral centre.

This is illustrated by giving an example of D-ribose



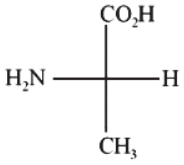

## 9.5 Summary

- Three basic parameters namely bond length, bond angle and dihedral angle which determine the geometry of a molecule have been defined.
- van der Waals radii of atoms or groups have also been defined.
- Tetrahedral nature of carbon and concept of asymmetry are discussed.
- Three-dimensional molecular structures on two-dimensional paper namely Fischer projection, flying wedge representation, Newman projection and sawhorse formula are delineated.

## 9.6 Exercises

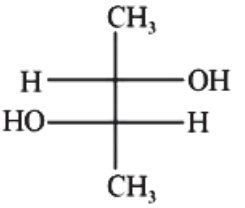
### A. Sample Questions

**1. Interconvert the molecular structures as indicated.**

(a) 

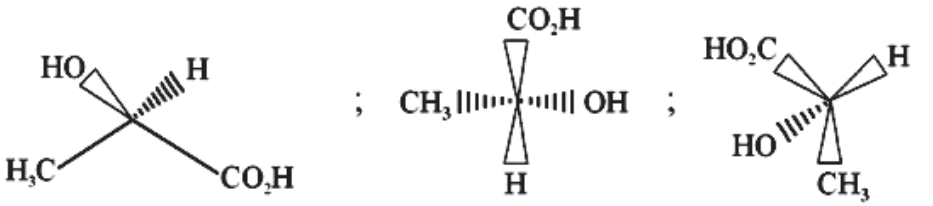
to flying wedge

**2. Determine whether the following structures are equivalent.**

(b) 

to Newman projection

**3. Give the Fischer projection for the following 3D-perspective formulae and state whether they are identical.**




Answer : 1 . (a ) to (c ). See text, 2. Equivalent, 3. See text.

**B. Additional question**

1. What are bond length, bond angle, and dihedral angle? Explain briefly.
2. Explain the tetrahedral nature of carbon and its role in chirality.
3. Differentiate between Fischer projection and flying wedge representation.
4. Explain the concept of enantiomers with respect to chiral molecules.
5. How can a Fischer projection be converted into a flying wedge representation?
6. What is the sawhorse projection formula? How does it differ from the Newman projection?
7. Differentiate between enantiomers and asymmetric molecules.
8. Describe the Fischer projection formula and its limitations.
9. Define chirality and give an example of a chiral molecule.

10. How would you convert the Fischer projection of lactic acid into a flying wedge representation?

**C. Multiple Choice Question (MCQ)**

**1. What is the primary geometry of carbon when it is $sp^3$ hybridized?**

A) Linear

B) Trigonal planar

C) Tetrahedral

D) Octahedral

Answer: C) Tetrahedral

**2. Which molecular representation method uses horizontal and vertical bonds to depict 3D structures?**

A) Newman projection

B) Sawhorse projection

C) Fischer projection

D) Flying-wedge projection

Answer: C) Fischer projection

**3. Which of the following projections is best suited to visualize conformational isomerism?**

A) Fischer projection

B) Newman projection

C) Flying-wedge projection

D) Sawhorse projection

Answer: B) Newman projection

**4. The angle between two planes containing different sets of three atoms in a molecule is called**

A) Bond angle

B) Torsional angle

C) Dihedral angle

D) Van der Waals radius

Answer: C) Dihedral angle

**5. Which of the following molecules is chiral?**

A) $CH_4$

B) $CCl_4$

C) CHBrClF

D) $CO_2$

Answer: C) CHBrClF

**6. Which molecular representation method uses solid and dashed wedges to indicate 3D structures?**

A) Fischer projection

B) Newman projection

C) Flying-wedge projection

D) Sawhorse projection

Answer: C) Flying-wedge projection

**7. Which molecular representation method shows a C–C bond as a diagonal line with attached groups angled accordingly?**

A) Fischer projection

B) Newman projection

C) Flying-wedge projection

D) Sawhorse projection

Answer: D) Sawhorse projection

# Unit 10 ❐ Symmetry Elements and operations

## Structure



## 10.0 Objectives

After studying this unit, students will be able to:

- Differentiate between chiral and achiral molecules.
- Analyze Symmetry Elements and Point Groups
- Distinguish between asymmetric and dissymmetric molecules.
- Understand the concept of epimers and their significance in stereochemistry.
- Explain stereogenicity, chirotopicity, and pseudoasymmetry in molecular structures.

## 10.1 Introduction

Symmetry is an aesthetic design of object found in various fields in nature. It plays an important role in science, spectroscopy, dipole moments, optical activity, crystal as also chemical structure all of which depend on symmetry. It generally refers to the rigid molecular structure and can better be explained in a geometric sense. Stereochemistry which is related to the molecular geometry can be described in terms of symmetry. Symmetry of a molecule can be studied with help of symmetry elements and corresponding symmetry operations.

## 10.2 Symmetry elements

Symmetry elements are geometric entities such as a point, a line or a plane with respect to which symmetry operations can be performed.

**Symmetry operations:** Symmetrical operations are geometrical operations such as rotation about an axis, reflection in a plane etc. which bring the molecule to a position indistinguishable from the original one. There are four types of symmetry elements and corresponding symmetry operations as shown in Table 1 below.

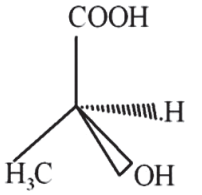
| **Symmetry elements** | **Symmetry Operations** |
|---|---|
| 1. Alternative axis of Symmetry (Cn) | 1 . Rotation about the axis (Cn) |
| 2. Plane of symmetry ( $\sigma$ ) | 2. Reflection in the plane ( $\sigma$ ) |
| 3. Centre of symmetry or inversion centre (i ) | 3. Inversion through the centre (i ) |
| 4. Improper axis of symmetry (Sn ) | 4. Rotation about the axis followed by reflection in a plane perpendicular to the axis (Sn ) |

## 10.3 Proper axis of symmetry (Cn)

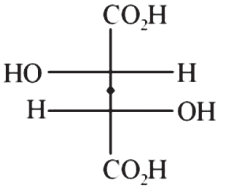
A proper axis of symmetry is an axis within a molecule such that if the molecule is rotated about this axis through an angle of (360°/n), an equivalent structure from the original results. It is denoted by Cn where n is the order of rotation. This operation is called Cn operation. Molecules with different order of proper axis are discussed below:

**C1 axis:** In a true sense, C, axis does not represent a first order proper axis because rotation of any molecule through an angle of 360° about any axis gives rise to the original. $C_1$ axis is therefore, called a trivial axis. This is an identity operation symbolised as I or E. Tetrahedral molecules such as Cabcd where a,b,c and d are achiral ligands have $C_1$ axis.

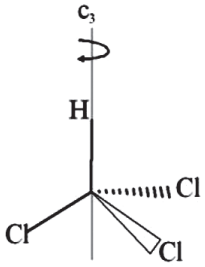
Example: Lactic acid.




**$C_2$ axis:** Rotation of a molecule through 180° about $C_2$ axis produces a structure indistinguishable from the original. Example: Optically active tartaric acid



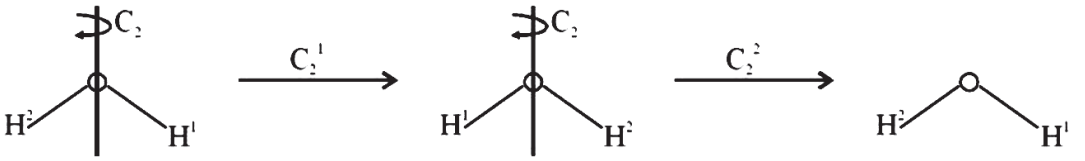

**$C_3$ axis:** Rotation of a molecule by 120° about C3 axis will give rise to an equivalent molecule. Example: Chloroform



Similarly, rotation of a molecule by 90° about C, will give an equivalent structure an so on.

**Identity operation, E**

A proper axis of symmetry of order n, Cn generates n operations such as $C_n^1$, $C_n^2$, $C_n^3$….. $C_n^{n-1}$, $C_n^n$. This nth operation, $C_n^n$ is the identity operation i.e., $C_n^n = E$ i.e, In the case of $H_2O$

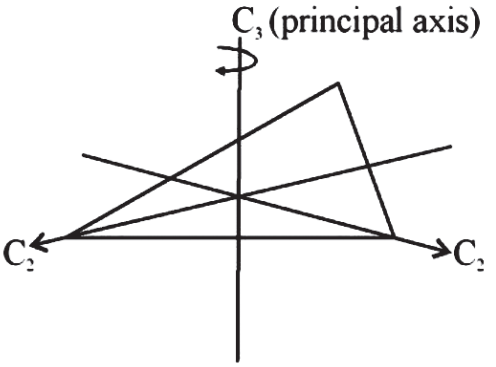



$C_2^2 = E$.

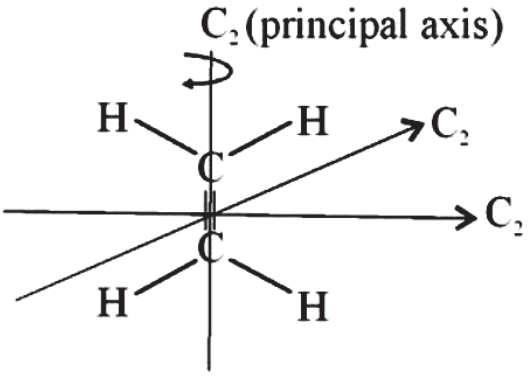
When a molecule possesses only one proper axis of symmetry, the Z axis is considered as the proper axis of rotation and is called the principal axis. Example: $C_2$ axis in water along z axis is the principal axis.

If a molecule has more than one Cn axis of different order the axis having the highest order is placed vertically along the Z axis and is considered as the principal axis.

Example: Cyclopropane



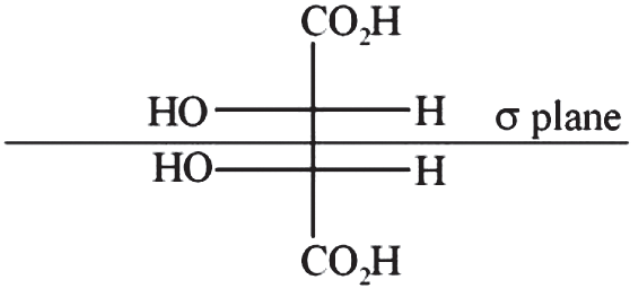

If a molecule possesses several Cn axes of the same order, the axis which passes through the maximum number of atoms is placed along Z axis and is considered as the principal axis. Example: ethylene.




Rotation is a real operation and Cooperation is called the symmetry operation of the first kind.

## 10.4 Plane of symmetry ($\sigma$):

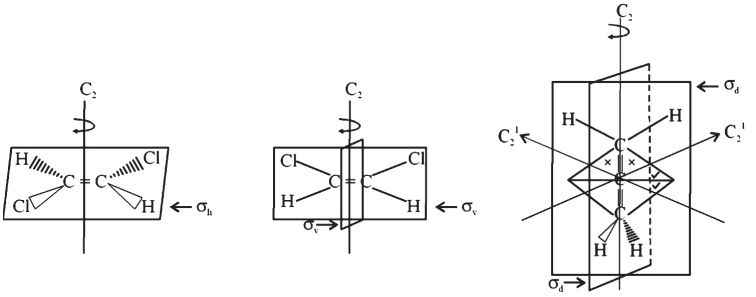
A plane of symmetry is a plane bisecting a molecule into two halves which are mirror images of each other. The reflection of the two halves across the plane produces a structure indistinguishable from the original one. Example: meso-Tartaric acid




Identity operation: Two successive s operations lead to an identity operation. That is, $\sigma \times \sigma = E$.

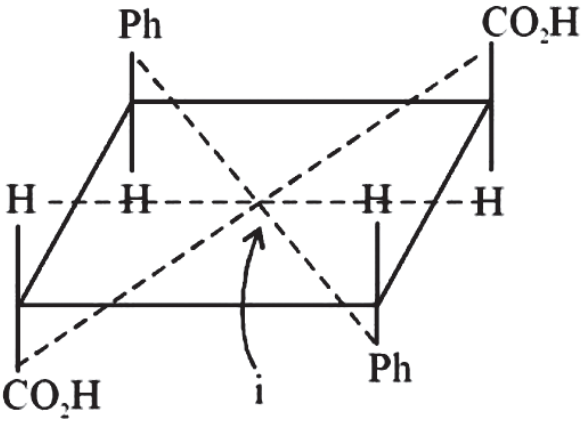
When a molecule contains the principal axis, Cn along with symmetry plane, $\sigma$ it is necessary to replace by $\sigma$u, $\sigma$v or $\sigma$d| as the case may be. When the symmetry plane $\sigma$ is perpendicular to the principal axis, Cn it is called horizontal symmetry plane and is symbolised as $\sigma$h. On the other hand, when the symmetry plane a contains the Cn, it is called vertical symmetry plane and is denoted by $\sigma$v. When a bisects the angle between

two C, axes, it is called diagonal symmetry plane and is designated $\sigma$d.




## 10.5 Centre of symmetry or inversion centre (i)

A centre of symmetry or inversion centre is a point within a molecule such that if a line is drawn from an atom or group to this point and extended an equal distance to the other side it will encounter an equivalent atom or group. The inversion centre as also the inversion operation are denoted by 'i'. Example: $\alpha$-Truxillic acid




In an inversion operation there is mutual exchange of like pairs of ligands within the molecule.

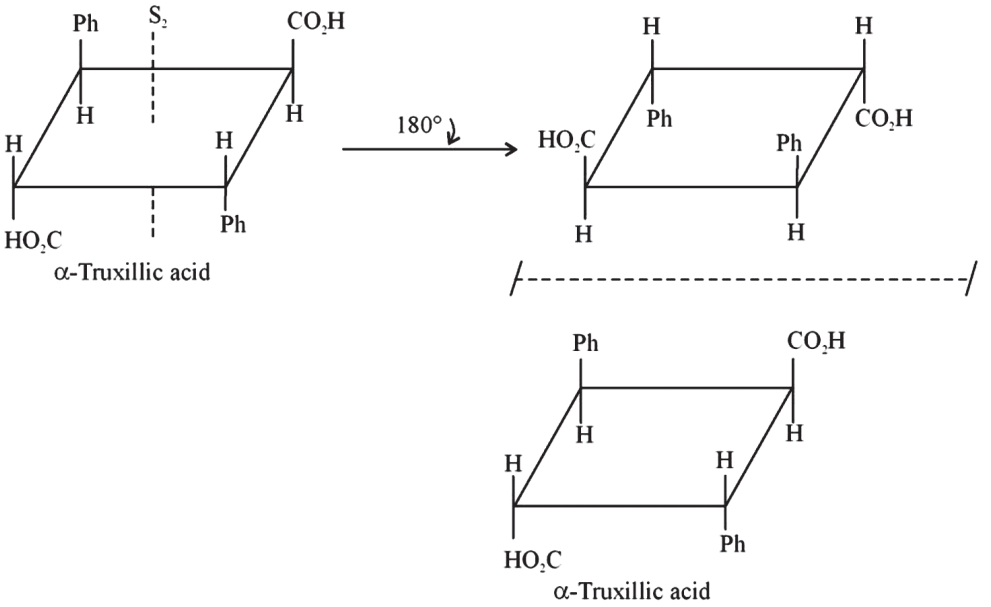
Identity operation: Two successive i operations lead to an identity operation. That is, i × i = E

## 10.6 Improper axis of symmetry (Sn)

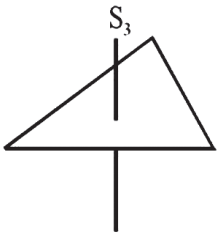
An improper axis of symmetry of order n is an axis such that rotation of the molecule about this axis through (360°/n) followed by reflection in a plane perpendicular to the axis produces a structure indistinguishable from the original one. It is denoted by Sn. The operation due to improper axis is called Sn operation which can be represented as below,

$$S_n = \frac{360°}{n} \times \sigma \text{ or } S_n = \sigma \times \frac{360°}{n} \text{ when n = 2, } S_2 = 180° \times \sigma = \sigma \times 180°.$$

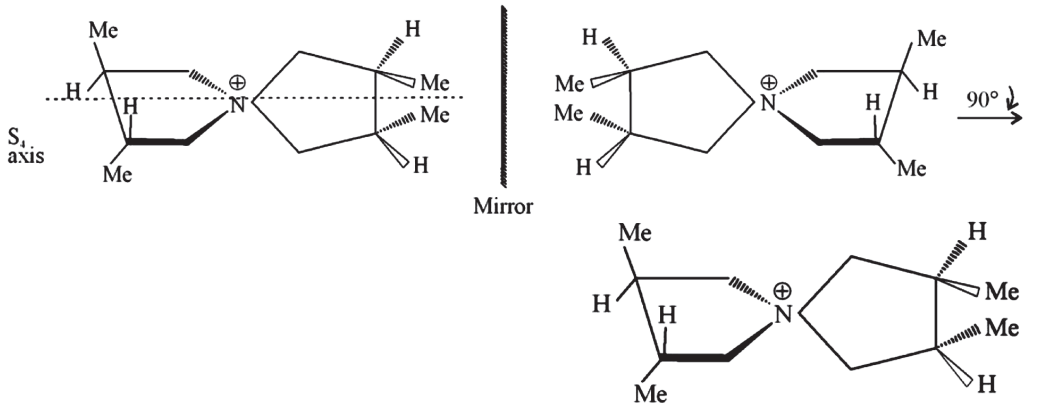
An example of molecule with an $S_2$ axis is α-truxillic acid.



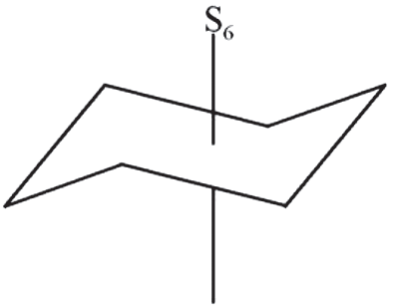

An example of molecule possessing an $S_3$ axis is cyclopropane.



Molecules having an $S_4$ axis. Example : 3AB'A-Tetramethyl-spiro-i 1.r )-dipyrrolidinium ion




A molecule with an $S_6$ axis. Example: Cyclohexane chair




It is to be noted that when a molecule possesses an Sn axis as the only symmetry element the order of n must be even. In that case, the Sn axis coexists with Cn/2 axis. When n is odd, the Sn axis cannot be the only symmetry element and will exist in conjunction with other symmetry elements like Cn axis and $\sigma$ plane.

In the case of even order Sn axis, when n = 4x + 2 (x = 0, 1, 2, 3.. . ), there will be centre of symmetry, i but when n = 4x (x = 0, 1, 2, 3...) there will be no centre of symmetry, i.

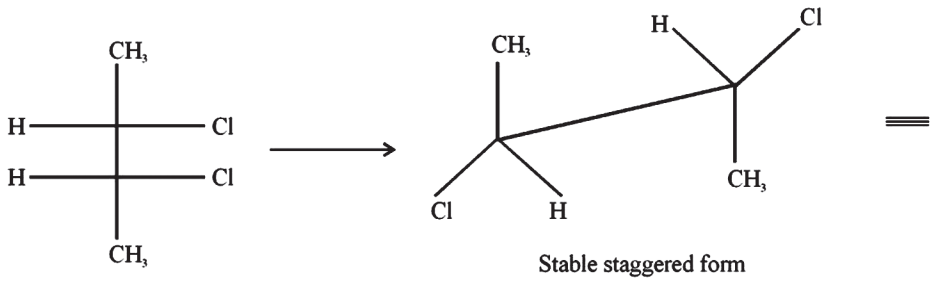
Sn operation is thus the successive Cn operation followed $\sigma$ byoperation across the plane perpendicular to the $C_2$ axis or the reverse

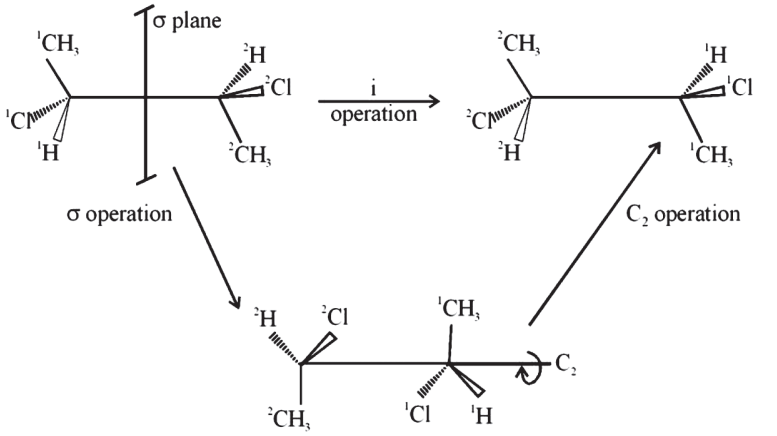
$$Sn = Cn \times \sigma = \sigma \times Cn$$

It can be shown that an $S_2$ operation is equivalent to an i operation and $S_1$ operation is equivalent to operation.

That is (i) $S_2 = C_2 \times \sigma = \sigma \times C_2 = i$ and (ii ) $S_1 = C_1 \times \sigma = \sigma \times C_1$

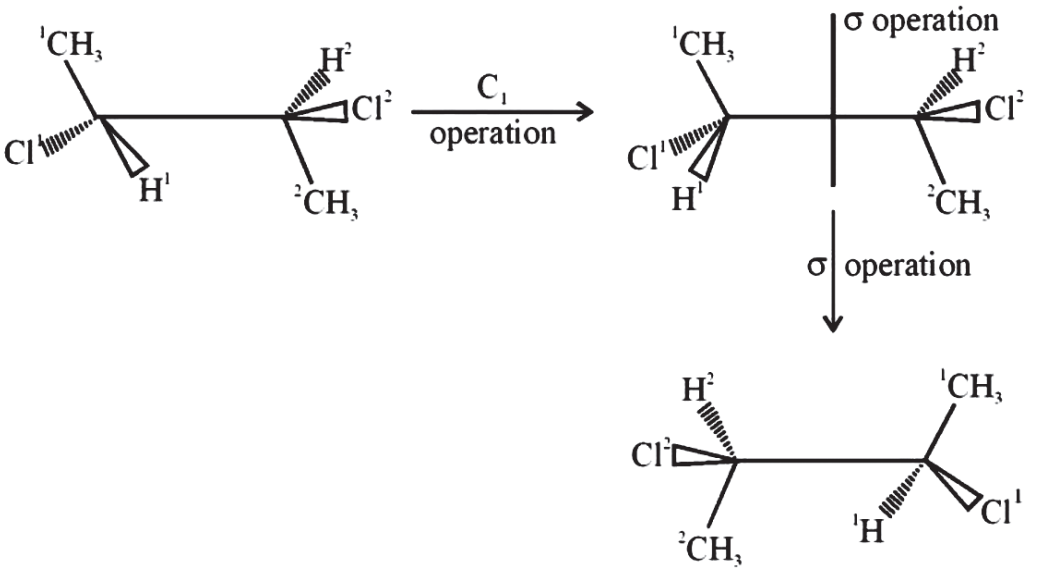
( i ) This is illustrated with an example of meso-2, 3-dichlorobutane



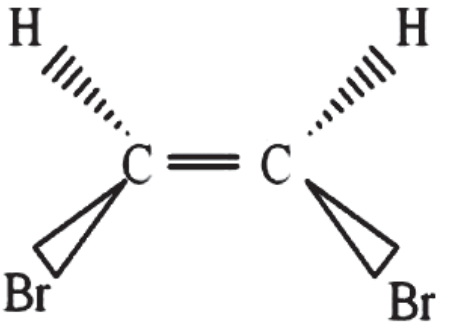

Thus S2 = $\sigma \times C_2 = i$

(ii) S1 = C1 × $\sigma = \sigma \times C_1$, Illustration




## 10.7 Point Groups in Molecular Symmetry

A point group is a classification system used in symmetry analysis of molecules based on their symmetry elements (such as mirror planes, rotational axes, and inversion centers). It helps in understanding molecular properties, spectroscopy, and reactivity. Let us consider trans-l ,2-dibromoethylene as a model compound



It has four symmetry operations E, C2, $\sigma$n and i corresponding to the symmetry elements C2, $\sigma$ and a combination of the two. These four symmetry operations form a group. Since all these symmetry operations intersect at a common point called the centre of gravity of the molecule which is not shifted during these operations and hence this point of symmetry operations is called a point group. Every molecule can be assigned to a point group that depends on the relevant set of symmetry7 operations. A group of molecules with the same set of symmetry operations is called a symmetry point group. The group of symmetry operations E, C2, $\sigma$n and i is called C2h point group. The total number of symmetry operations of a molecule belonging to a point group is called the order of the point group. The total number of indistinguishable arrangements that can be generated by all possible rotations of the molecule is called the symmetry number $\sigma$ of the molecule. We can combine the symmetry elements following some rules.

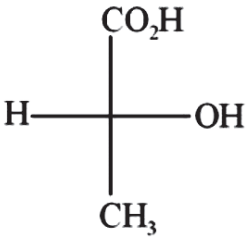
1) The presence of a C2 axis and a plane perpendicular to it implies the existence of an S2 axis (i.e. an inversion centre i).

2) n cannot coexist with d

3) An Sn axis always coaxial with Cn axis.

**10.7.1 Point groups of chiral molecules**

**C1 point group:** A molecule with only C1 axis of symmetry belongs to point group. Example: Lactic acid




The order of this point group is 1

Operators E

Sym. No. $\sigma$ = 1

Molecules to this point group are chiral or asymmetric. They are optically active.

Cn point group: Molecules with only n-fold proper axis of symmetry belong to Cn point group and are chiral.

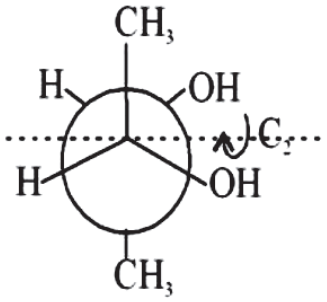
Order of this point group Cn is n.

Operators $C_n^1$, $C_n^2$, $C_n^3$ ….. $C_n^{n-1}$, $C_n^n$ (= E)

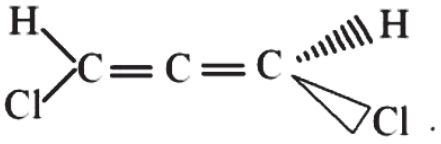
Symmetry number $\sigma$ = n

Molecules belonging to this point group are dissymmetric and optically active.

C2 point group. Examples



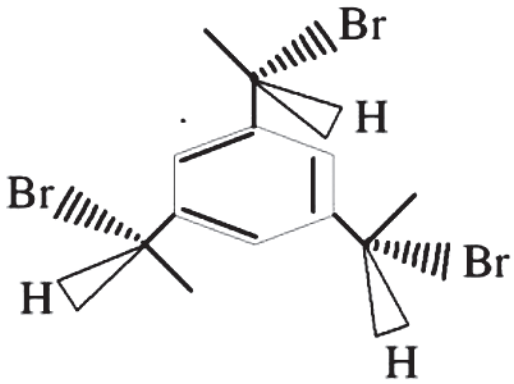

Butane-2,3-diol




1,3-Dichloroallene

The order of C2 is 2, operators E, C2, $\sigma$ = 2.

**C3 point group:** Example.



The order of C3 is 3

Operators $C_1^1$, $C_3^2$

$\sigma = 3$

Dn point group: When a molecule has a Cn axis as the principal axis and nc2 axes lying perpendicular to the Cn axis it belongs to Dn point group.

That is, Dn = Cn + nC2 ($\perp$)

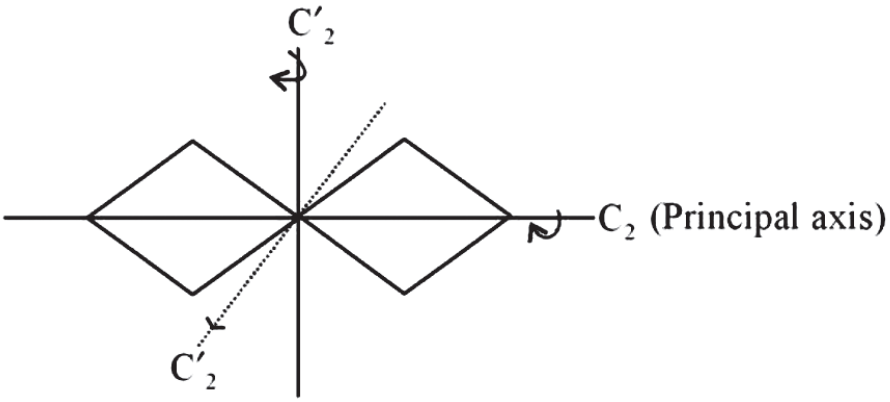
The order of a Dn point group is 2n

Operators E, Operators $C_n^1$, $C_n^2$, $C_n^3$ ….. $C_n^{n-1}$, $nC^2$

$\sigma = 2n$

Molecules belonging to Dn point group are chiral or dissymmetric. These molecules are optically active.

**D2 point group:** Example twist-boat conformation of cyclohexane

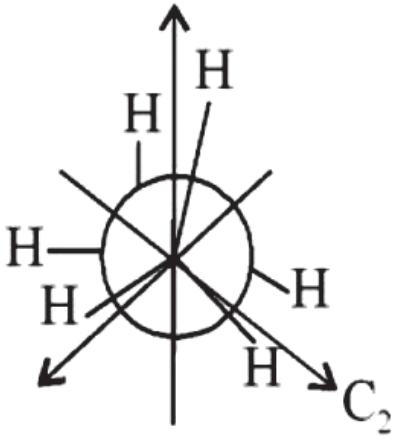



The order of D2 is 4

Operators E, C2, $2C_2^1$

$\sigma = 4$

**D3 point group:** Example, skew form of ethane




C3 axis passes through C-C bond, 3C2 axes passing through the mid-point of C-C bond and bisecting the dihedral angle.

The order of this point group D3 is 6

Operators E, $C_3^1$, $C_3^2$, $3C_2$

Symmetry number $\sigma = 6$

**10.7.2 Point groups of achiral molecules**

Molecules belonging to point groups other than Cl, Cn and Dn generally have o plane, inversion centre, i or Sn axis and are therefore, achiral. These molecules are optically inactive.

**$S_n$ point group :**

A molecule that contains an even order $S_n$ axis but no plane belongs to $S_n$ point group. The $S_n$ axis necessarily coexists with $C_n/2$ axis. An even order $S_n$ axis generates.

$S_n^1$, $S_n^2$, $S_{n3}$ ... ... $S_n^{n-1}$, $S_n^n$ (E)

The order of this point group is n

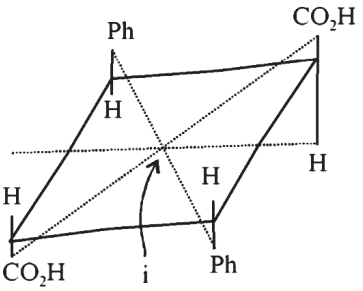
operators E, $S_n^1$, $S_{n2}$ ... $S_n^{n-a}$

Symmetry number, =n/2

But whern n is oddd, $S_n$ axis generates 2n operations. Operators $S_n^1$, $S_n^2$, $S_n^3$ ... ... $S_n^{2n-1}$, $S_n^{2n}$ ($\equiv$ E). In this case, $S_n$ axis cannot exist alone but coexists with $C_n$ and $\delta_n$. The molecule with odd order $S_n$ axis are thus placed under $C_{nh}$ point group.

**S2 point group:** As $S_2$i, so this point group is also called $C_i$ point group.

**$C_i$ point group:** Example, α-Truxillic acid



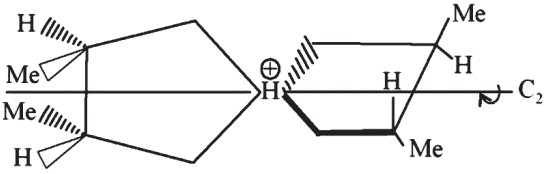

The order of $C_i$ is 2

Operators E, i

$\sigma$ = 1

**$S_4$ point group:**

Example: 3, 4, 3′, 4′-Tetramethyl-spiro-(1,1′)-dipyrrolidinium ion.




The order of $S_4$ is 4

Operators $S_4^1$, $S_4^2$, ($C_2^1$), $S_4^3$, $S_4^4$ (E)

Symmetry number, =2

**$C_{nh}$ point group:**

A molecule that has a $C_n$ axis and $_n$ belongs to $C_{nh}$ point group. These molecules are achiral and iptically inacative.

The order of $C_{nh}$ is $2_n$

Operators $C_n^1$, $C_n^2$, $C_n^3$ ... $C_n^n$ (E), $_n S_n^1$, $S_n^2$ .. $S_n^{n-1}$

Sytmmetry number, = n

**$C_{1h}$ point group:**

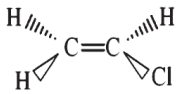
Since $C_{1h} = C_1 \times \sigma_h$

$= E \times \sigma_h$

$= \sigma$ (symmetry plane)

So, $C_{1h}$ is called $C_s$ (s stands for symmetry plane).

Example:



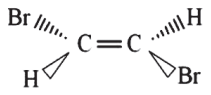

Vinyl chloride

The order of $C_s$ is 2

Operators E, $\sigma$

Symmetry number, $\sigma = 1$

**$C_{2h}$ point group.** Example



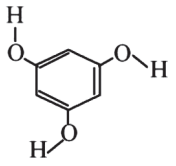

trans-1,2-Dibromoethylene

The order of $C_{2h}$ is 4

Operators E, $C_2$, $\sigma_h$ i

Symmetry number, $\sigma = 2$

**$C_{3h}$ point group:** Example: Phloroglucinol




The order of $C_{3h}$ is 6

Operators E, $C_3^1$, $C_3^2$, $\sigma_h$, $S_3^1$, $S_3^2$

Symmetry number $\sigma = 3$

**$C_{nv}$ point group:**

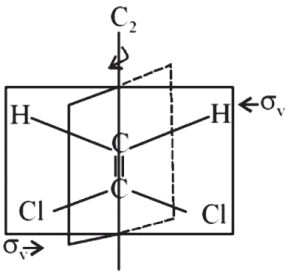
A molecule that has a $C_n$ axis and $n\sigma_v$ planes belongs to $C_{nv}$ point group.

The order of $C_{nv} = 2n$

Operators $C_n^1$, $C_n^2$, $C_n^3$ ... $C_n^{n-1}$, $C_n^n$ ($\equiv$ E), $n\sigma_v$

Symmetry number, $\sigma = n$

**$C_{2v}$ point group:** Example, 1,1-Dichloroethylene




The order of $C_{2v}$ is 4

Operators E, $C_2^1$, $2\sigma_v$

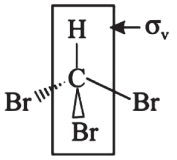
Symmetry number $\sigma = 2$

**$C_{3v}$ point group : Example Bromoform**

The order of C3v is 6

Operators E, $C_3^1$, $C_3^2$, $3\sigma_v$

**Symmetry number $\sigma = 3$**



**$D_{nh}$ point group:** $D_{nh} = D_n + \sigma_h$

$= C_n + nC_2 (\perp) + \sigma_h$

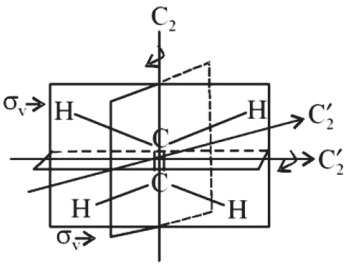
The existence of $\sigma_h$ and $nC_2$ lying in the same plane ensures the presence of $n\sigma_v$. Also, $C_n \times \sigma_h = S_n$

Thus, $D_{nh} = C_n + nc_2 (\perp) + n\sigma_v + \sigma_h + S_n$

The order of $D_{nh}$ is 4n

Symmetry number $\sigma = 2n$

**$D_2h$ point group:** Example. Ethylene

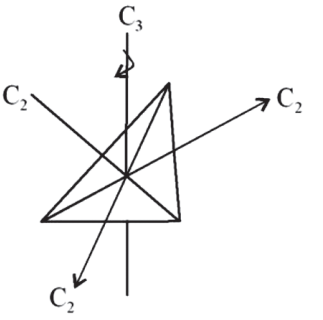



The order of $D_{2h}$ is 8

Operators E, $C_2^1$, $2C_2^1$, $2\sigma_v$, $\sigma_h$, i

Symmetry number, $\sigma = 4$.

**$D_3h$ point group:** Example. Cyclopropane




The order of $D_{3h}$ is 12

Operators E, $C_3^1$, $C_3^2$, $3C_2$, $3_v\sigma$, $\sigma_h$, $S_3^1$, $S_3^2$

Symmetry number = 6

**$D_{nd}$ point group:** $D_{nd} = D_n + n\sigma_d$

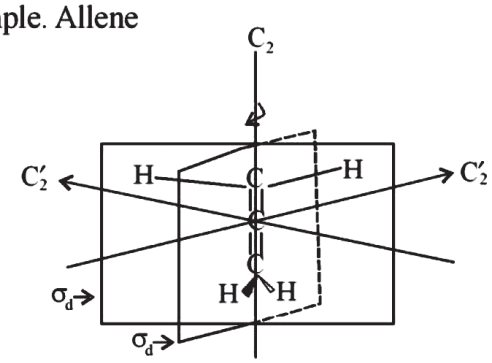
$= C_n + nC_2 (\perp) + n\sigma_d$

The order of $D_{nd}$ is 4n

Operators E, $C_n^1$, $C_n^2$, ...$C_n^{n-1}$, $nC_2$, $n\sigma_d$, $nS_{2n}$

Symmetry number $\sigma = 2n$.

**$D_{2d}$ point group:** Example. Allene

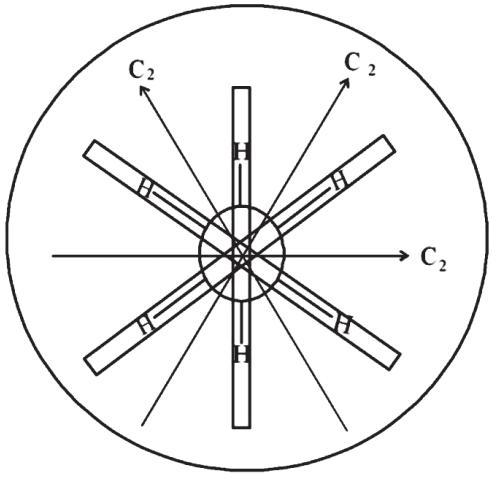



The order of $D_{2d}$ is 8

Operators E, $C_2^1$, $2C_2^1$, $2\sigma_d$, $S_4^1$, $S_4^3$

Symmetry number $\sigma = 4$.

**$D_{3d}$ point group:** Example. Staggered ethane



The molecule has a $C_3$ axis passing through C-C bond, $3C_2$ axes passing through the mid-point of the C-C bond and $3_d$ planes each bisecting two $C_2$ axes.

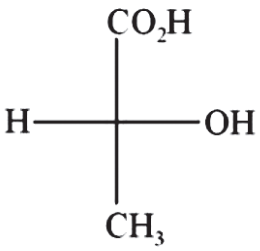
The order of $D_{3d}$ is 12

Operators Em $C_3^1$, $C_3^2$, $3C_3$, $3\sigma_d$, i, $S_6^1$, $C_6^2$

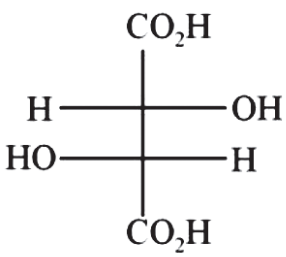
Symmetry number $\sigma$ =6

## 10.8 Symmetry and Chirality

A molecule can form only one mirror image which may or may not be superimposable with the original. A molecule with proper axis of symmetry Cn is not superimposable with its mirror image. But a molecule with Cn, i or Sn axis is superimposable with its mirror image. The property due to which a molecule is non-superimposable with its mirror image is called chirality. Such a molecule is called chiral. A chiral molecule rotates the plane of a plane polarised light and is optically active. Chirality is independent on the chiral centre. It is the symmetry criteria that dictate the chirality. The molecule must be dissymmetric in order to be chiral. Dissymmetry' denotes the absence of improper elements of symmetry' such as plane, i centre and Sn axis. All dissymmetric molecules are thus chiral and optically active. Molecules belonging to C1, Cn and Dn point groups are chiral or dissymmetric. Asymmetry denotes the absence of symmetry elements Cn ( n > 1 ) axis, a plane, i centre or Sn axis in a molecule and such a molecule is asymmetric and optically active. Molecules, in particular, belonging to C1 point group are asymmetric. For example, lactic acid is asymmetric but (+) tartaric acid is dissymmetric.




Lactic acid

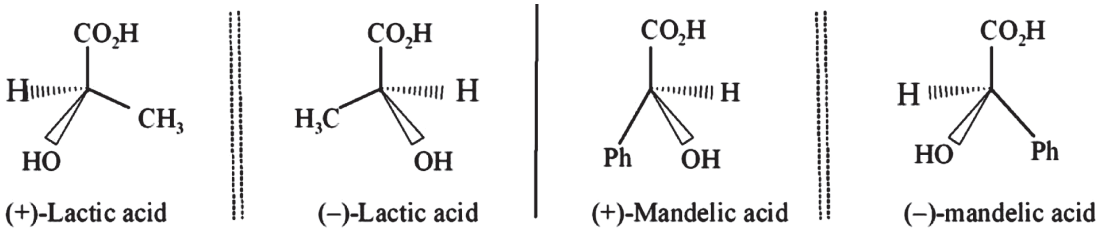



(+)-Tartaric acid

## 10.9 Steresisomers

Stereoisomers are isomeric compounds but differing in the arrangement of their atoms or groups (ligands) in three-dimensional space. The relationship between the isomers is described by isomerism e.g. enantiomerism, diastereomerism etc. Enantiomers are stereoisomers that bear a non-superimposable mirror image relationship to each other. The existence of enantiomers is associated with at least one chiral centre. Thus Cabcd type molecules exist as a pair of enentiomers as shown here.


Specific examples are lactic acid, mandelic acid etc.

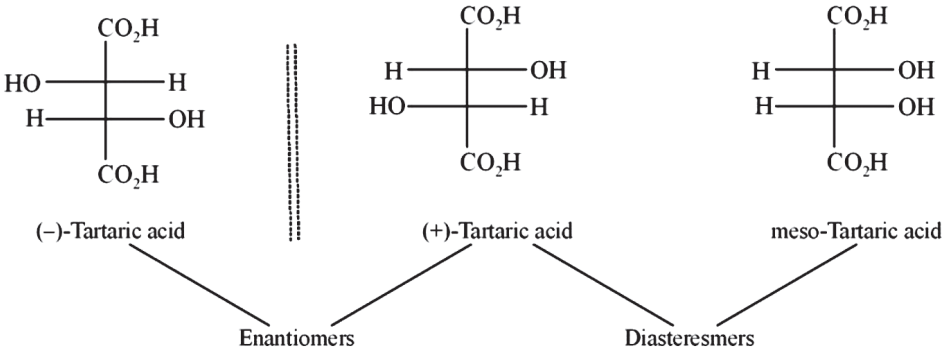



Enantiomers have identical physical and chemical properties. They behave differently towards a plane polarised light. One enantiomer rotates the plane of a plane polarised light in a clockwise direction and is called dextrorotatory while the other rotating in an anticlockwise direction and is called laevorotatory.

Diastereomers are stereoisomers that do not have a mirror image relationship to each other. For the existence of diastereomers corresponding to a given structural formula there

must be at least two chiral centres (or correctly two dissymmetric groupings) in the given structure.

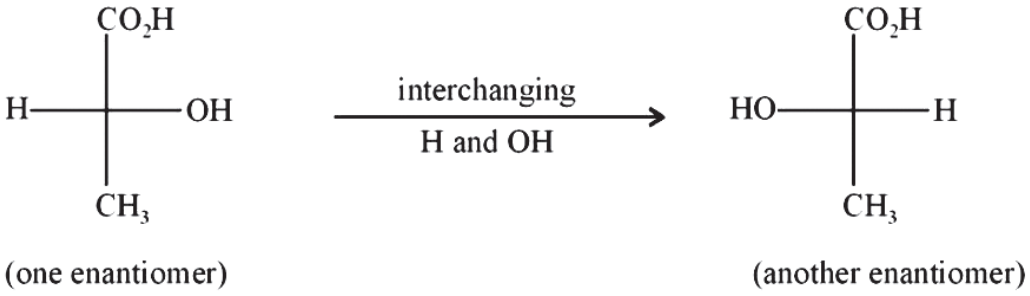
Tartaric acid provides an example.




Each pair of enantiomer is diastereomeric with any other pair. Unlike enentiomers, diastereomers differ in most of their physical and chemical properties. They may be or may not be chiral. Chiral diastereomers are opically active and exist as (± )-pair.

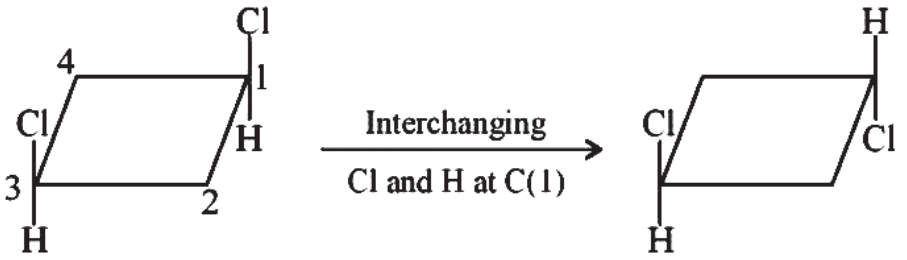
## 10.10 Stereogenecity

According to Mislow, the chiral centre should be called a stereogenic centre. A stereogenic centre is a centre where interchanging the position of two ligands produces a stereoisomer. Let us take the example of lactic acid. In lactic acid, the chiral centre is attached with -H, -OH, -$CH_3$ and -$CO_2H$. If we interchange the position of H and OH we will get a stereoisomer as shown below



The chiral centre is called the stereogenic centre. The phenomena involving interchanging of ligands giving thereby enantiomer or diastereomer is called stereogenecity.

All chiral centres are stereogenic but all stereogenic centres are not chiral. For example, 1,3-dichlorocyclobutane exists as cis and trans-diastereomers as shown below.

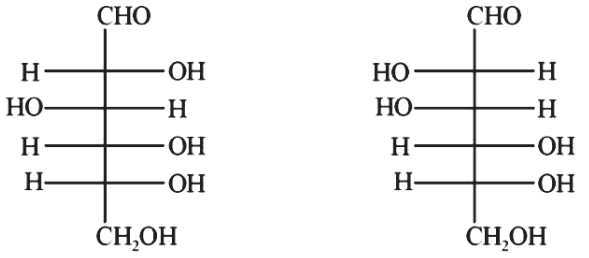



cis isomer trans isomer

The carbon atoms C(1) and C(3) in both the diastereomers are achiral because each is linked to two identical $CH_2$ ligands but stereogenic.

## 10.11 Epimers

Epimers are diastereomers that differ in the arrangement of ligands at one stereogenic centre in a compound containing a multistereogenic centres. For example, D. glucose and D-mannose differ in the arrangement of ligands at C(1) and are epimers to each other.

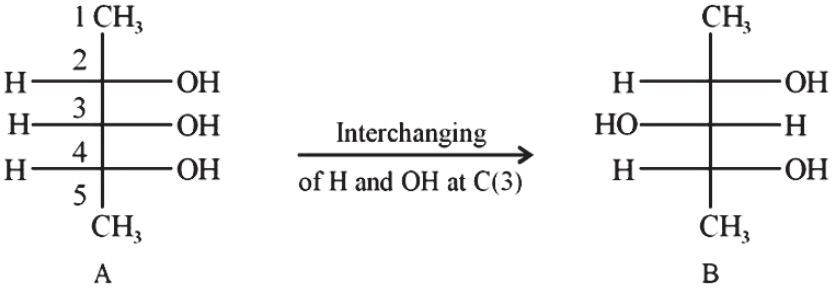



D-Glucose D-Mannose

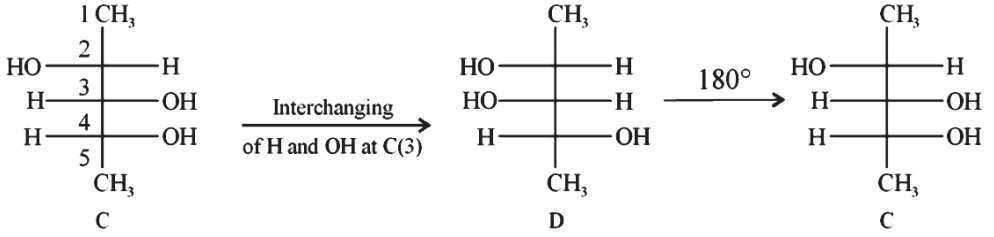
## 10.12 Chirotopicity

In a chiral molecule even, point is chiral. Mislow and Siegel introduced another concept which is called chirotopic or chirotopicity. According to them, every' point in a chiral molecule resides in a chiral environment. These points are called chirotopic points. In the simplest example of CHBrCIF for instance, all ligands and the spaces between them are chirotopic because the entire molecule is chiral.

In most cases, when a tetrahedral atom is appropriately substituted with four ligands, chirotopicity' and stereogenecity is uniquely linked. The carbon atom in CHBrCIF is thus both chirotopic and stereogenic while that in $CH_2BrCl$ is achirotopic ( i.e not chirotopic) and non-stereogenic. Molecules containing multiple chiral centres such as 2,3,4-trihydroxypentane can exist in various structures.




The molecule A is achiral due to the presence of a symmetry plane a passing through H, OH and is C(3) is achirotopic. Moreover, interchange of H and OH at C(3) leads to a different stereoisomer. So C(3) in A is stereogenic. This is an example of a molecule which has a stereogenic but achirotopic centre.



Since the molecule C is chiral and hence C(3) is chirotopic. But C(3) in C is nonstereogenic because a transposition of two ligands H and OH produces the same stereoisomer as shown above. So C(3) in C is non-stereogenic but chirotopic. This is an example of a molecule which has a non-stereogenic but chirotopic centre.

## 10.13 Stereoisomerism in molecules containing two or more chiral centres

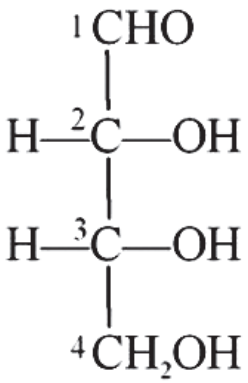
These molecules are of two types:

1) Molecules containing constitutionally non-equivalent centres such as AB, ABC type etc.

2) Molecules containing constitutionally equivalent centres such as AA, ABA type etc.

### 10.13.1 Molecules containing two or more non-equivalent chiral centres.

An acyclic molecule containing n non-equivalent chiral centres can exist as $2^n$ steresisomers which consists of $2^{n-1}$ diastereomers. All the stereoisomers arising from it are chiral and optically active. An aldotetrose (2,3,4-trihydroxybutanal) and an aldopentose (2,3,4,5-tetrahydroxy pentanal) provide examples. In 2,3,4-trihydroxybutanal shown below.



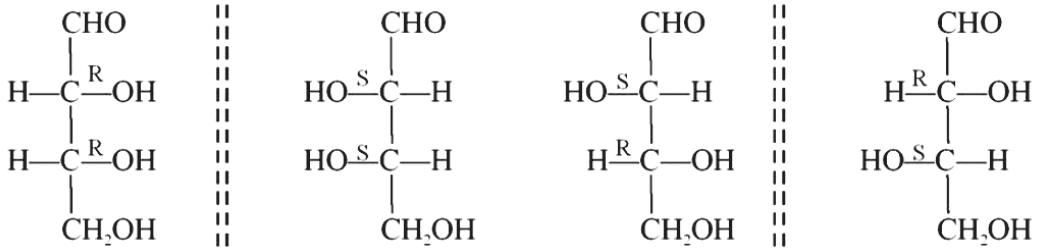

(one stereoisomer)

C(2) is constitutionally non-equivalent to C(3). Such type of molecule is described as AB type molecule where A and B stand for unlike chiral centres.

In this case, i) total number of optically active stereoisomer is = $2^2 = 4$

ii) total number of diastereomers = $2^{(2-1)} = 2$

These stereoisomers are shown below.

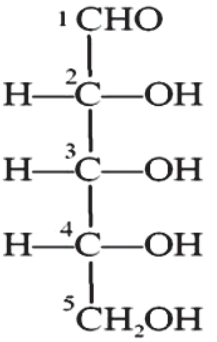



(±)-A (±)-B

So, 2,3,4-trihydroxybutanal with two non-equivalent chiral centres gives rise to four stereoisomers as two diastereomeric (±) pairs, i.e., (± )-A and (± )-B.

Each pair of enantiomer is diastereomic with any other pair. That means, total number of diastereomers = number of dl pair.

In 2,3,4,5-tetrahydroxypentanal shown below



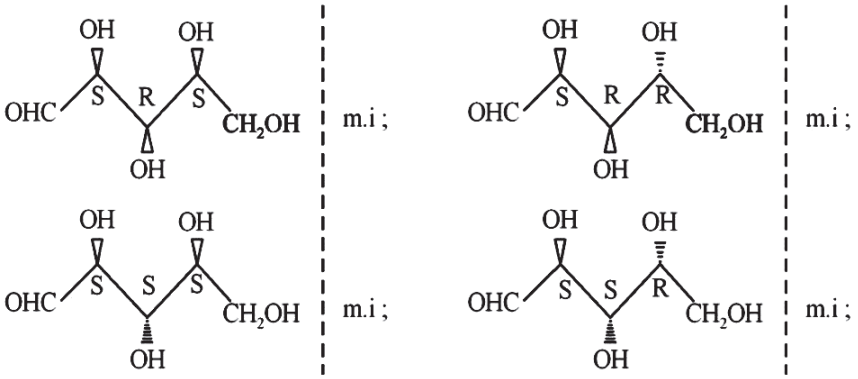

(one stereoisomer)

C(2) is constitutionally non-equivalent to C(3 ) and so are C(3) and C(4). This type of molecule can be described as ABC where A, B and C are unlike chiral centres. In this case,

(i) total number of optically active stereoisomers = $2^3 = 8$.

(ii) total number of diastereomers = $2^{(3-1)} = 4$

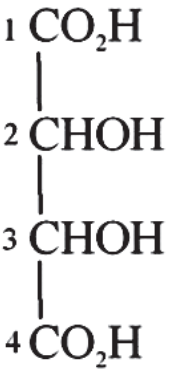
The stereoisomers are represented as.




### 10.13.2 Molecules containing two or more equivalent chiral centres

In this case, these will be lesser number of stereoisomers than expected because some stereoisomers are achiral meso and do not give enantiomers. When the number of chiral centres n is even, the number of optically active stereoisomers is $2^{n-1}$ and the number of meso isomer is $2^{\frac{n}{2}-1}$ The total number of steroisomer is thus $2^{n-1+2\frac{n}{2}-1}$. But when n is odd, the total number of stereoisomers is $2^{n-1}$. The number of meso isomer is $2^{\frac{n-1}{2}}$ . The number of optically active stereoisomers is $2^{n-1} - 2^{\frac{n-1}{2}}$.

These are illustrated with two examples, tartaric acid and pentanoic acid. In tartaric acid, C(2) is constitutionally equivalent to C(3).




(Tartaric acid)

This is AA type molecule where A stands for like chiral centres.

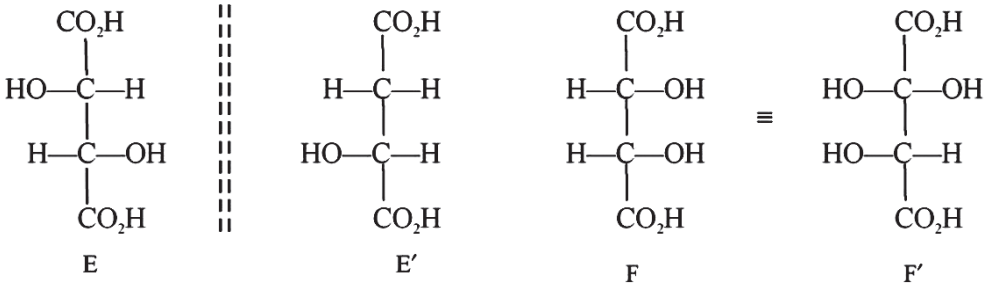
In this case, n = 2 (even) so,

(i) the number of optically active stereoisomers = $2^{2-1} = 2$.

(ii) the number of optically inactive meso isomer = $2^{\frac{2}{2}-1} = 1$

Therefore, the total number of stereoisomers = 3.

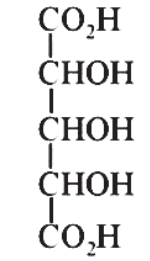
These are shown below.




The two stereoisomers E and E' are optically active because each of them has a C2 axis passing through the mid-point of central C-C bond and is chiral. They exist as a pair of enantiomers. The isomer F or F' has a plane of symmetry and is achiral. It is an achiral meso-tartaric acid.

Here, the total number of diastereomers = 1 (dl pair ) + 1 (meso isomer) = 2.

In pentaric acid (2,3,4-trihydroxyglutaric acid ), C(2) is constitutionally equivalent to C(4). This is described as ABA type molecule.



Pentaric acid

Here n = 3 (odd )

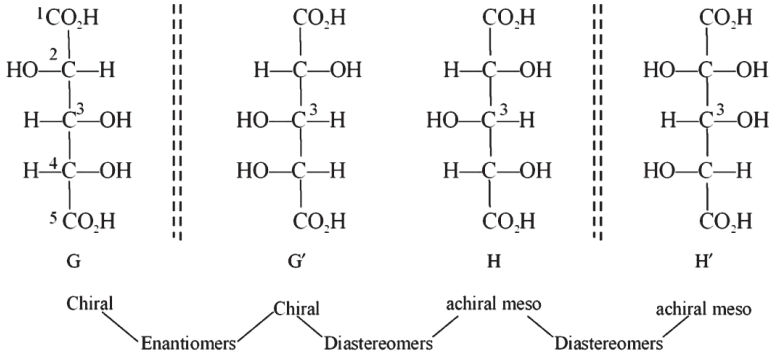
So (i) the total number of stereoisomers = $2^{3-1} = 4$

(ii) the number of meso isomers $= 2^{\frac{3-1}{2}} = 2$

Therefore, (iii ) The total number of optically active stereoisomers = 4- 2 = 2 ( 1 dl pair)

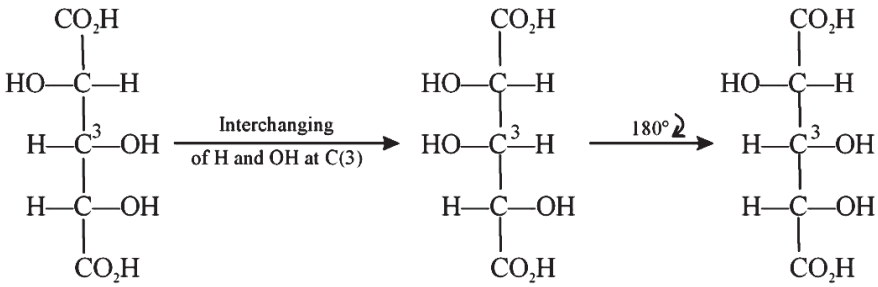
(iv) The total number of diastereomers = 1 (dl pair) + 2 (meso ) = 3.

The stereoisomers are depicted below.



## 10.14 Pseudoasymmetry

The C(3) in the steroisomers G, G', H and H' above is of particular interest. Since G and G' are chiral. So, C(3) in these isomers is chirotopic. But C(3) in G and G' is non-stereogenic because interchanging of H and OH at C(3) gives rise to the same stereoisomer as shown.




Therefore, C(3) in G and G' is chirotopic but non-stereogenic. The stereoisomers H and H' are achiral because of the presence of a a plane passing through H, C(3) and OH. C(3) in the achiral meso H and H' is thus achirotopic. Moreover, interchange of H and OH at C(3) converts one meso form into the other. So, C(3) in H and H' is stereogenic. Such an achirotopic but stereogenic centre is called pseudo-asymmetric centre.

## 10.15 Summary

- Four symmetry elements namely a proper axis of symmetry (Cn), a plane of symmetry (), an inversion centre (i) and an improper axis of symmetry (Sn) an their corresponding symmetry operation have been discussed.
- The molecules are classified into a number of symmetry point groups on the basis of symmetry operations that can be performed on them.
- Symmetry and molecular chirality have been discussed. Molecules which are not superimposable with their mirror images are called chiral and show a type of stereoisomerism known as enantiomerism. These molecules belong to the C1, Cn and Dn point groups. On the other hand, molecules which are superimposable with their mirror images are called achiral and belong to the point groups other than C1, Cn and Dn. The achiral molecules possess $\sigma$ plane, inversion centre, i or Sn axis. The

symmetry number ( $\sigma$ ) is used to calculate the entropy of a molecule. (Entropy =-RT In $\sigma$ ).

- Chirotopicity and stereogenecity are two distinct features of a chiral centre. The chirotopicity is defined by local symmetry while stereogenecity by disposition of bonds.
- Stereoisomerism in AB, ABC, AA and ABA ty pes of molecules are fully discussed with examples.
- Pseudoasymmetry in ABA type of molecule is explained.

## 10.16 Exercises

**A. Sample Questions**

1) Delineate the symmetry element(s) present in the following molecules and mention their point groups.

(i) 1,3-Dibromoallene, (ii) trans-l,2-Diiodoethylene, (iii) CH2BrCl, (iv) cis-1,2-Dichloroethylene, (v) staggered ethane

2) Give examples of

(i) a molecule containing a non-stereogenic but chirotopic centre

(ii) a molecule with a non-chiral stereogenic centre

(iii) a molecule having an achirotopic but stereogenic centre.

3. All asymmetric molecules are necessarily dissymmetric but dissymmetric molecules may not be asymmetric. Justify or Criticise.
4. What is symmetry, and why is it important in chemistry?
5. What are the four types of symmetry elements?
6. Explain the concept of a proper axis of symmetry (Cn) with an example.
7. Differentiate between horizontal ( $\sigma$ h), vertical ( $\sigma$ v), and diagonal ( $\sigma$ d) planes of symmetry with examples.
8. Define an improper axis of symmetry (Sn) and give an example of a molecule possessing it.

9. What is a point group in molecular symmetry?
10. Define enantiomers and diastereomers. How do they differ?
11. What is meant by the term "stereogenic center"?
12. How do epimers differ from other diastereomers?
13. What is chirotopicity, and how does it relate to stereogenicity?
14. How many stereoisomers can a molecule with two non-equivalent chiral centers have?

**B. Multiple Choice Question (MCQ)**

**1. Which symmetry operation is associated with the inversion center (i)?**

a) Reflection in a plane

b) Rotation around an axis

c) Movement of each atom through a center point to an equivalent position

d) Rotation followed by reflection

Answer: c) Movement of each atom through a center point to an equivalent position

**2. Which of the following point groups represents a molecule with only one C1 axis of symmetry?**

a) C1

b) C2

c) D3

d) C3v

Answer: a) C1

**3. Which of the following symmetry elements does an achiral molecule NOT possess?**

a) Cn axis

b) Plane of symmetry (s)

c) Inversion center (i)

d) Sn axis

Answer: a) Cn axis

**4. Which type of molecule belongs to the Dn point group?**

a) A molecule with only a single Cn axis

b) A molecule with both a Cn axis and n C2 axes perpendicular to it

c) A molecule with only reflection symmetry

d) A molecule with no symmetry elements

Answer: b) A molecule with both a Cn axis and n C2 axes perpendicular to it

**5. Which symmetry operation does the improper axis of symmetry (Sn) include?**

a) Only rotation

b) Rotation followed by reflection

c) Only reflection

d) Reflection followed by inversion

Answer: b) Rotation followed by reflection

**6. A molecule with only Cn and Dn symmetry elements is:**

a) Achiral

b) Chiral

c) Always optically inactive

d) Both a and c

Answer: b) Chiral

**7. Which of the following conditions is necessary for chirality?**

a) Presence of a plane of symmetry

b) Presence of an inversion center

c) Absence of improper symmetry elements ($\sigma$, i, Sn)

d) Presence of a horizontal mirror plane ($\sigma$h)

Answer: c) Absence of improper symmetry elements ($\sigma$, i, Sn)

**8. Which type of molecules generally exhibit optical activity?**

a) Molecules with a plane of symmetry

b) Molecules with an inversion center

c) Molecules belonging to the C1, Cn, and Dn point groups

d) Molecules with an Sn axis as the only symmetry element

Answer: c) Molecules belonging to the C1, Cn, and Dn point groups

**9. Diastereomers are stereoisomers that:**

a) Are mirror images of each other

b) Have identical physical and chemical properties

c) Do not have a mirror image relationship

d) Are always optically inactive

Answer: c) Do not have a mirror image relationship

# Unit 11 ❐ Stereochemical Descriptors and Nomenclature

## Structure



## 11.0 Objectives

By the end of this unit, students should be able to:

- Explain the concept of D/L nomenclature and its significance in stereochemistry.
- Apply R/S configuration rules to chiral centers using the Cahn-Ingold-Prelog (CIP) priority system.
- Define erythro and threo nomenclature for compounds and identify meso compounds, recognizing internal planes of symmetry.
- Define syn and anti nomenclature in aldol reactions based on the relative positioning of substituents.
- Assign E and Z configurations for C=C double bonds, conjugated dienes, trienes, C=N, and N=N systems based on priority rules.

## 11.1 Introduction

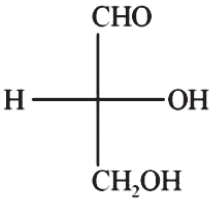
The three-dimensional arrangements of atoms or groups (i.e. ligands) around a stereogenic centre is called configuration. The three-dimensional arrangements of ligands in a chiral molecule that distinguishes from its mirror image is known as absolute configuration which can be determined by single crystal X-ray Crystallography.

If we do not have a crystal we cannot determine the absolute configuration but by correlating with other compounds of known configuration we can determine the relative configuration. So configuration at any stereogenic centre with respect to that of any other centre either in the same molecule or in a reference compound whose configuration is arbitrarily chosen as the standard is called the relative configuration.

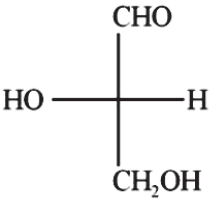
Three-dimensional structures of chiral molecules on two-dimensional plane are represented by F.P., wedge formulae, sawhorse and Newman projection formulae. These formulae actually show the chiral molecules in their relative and absolute configuration. Suitable configurational descriptor is therefore, required to be given to each structure to distinguish one from the other. The following are some configurational descriptor system.

## 11.2 D/L descriptors

According to D/L descriptors, if we have a molecule like glyceraldehyde, we can determine its absolute configuration. In order to determine its absolute configuration, the molecule is so written that the most oxidised carbon is placed at the top and the less oxidised carbon at the bottom. Then if the hetero atom, here OH group is on the right side, the molecule is given D configuration, if on the left, it is L configuration

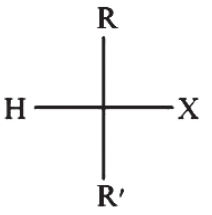



D-Glyceraldehyde

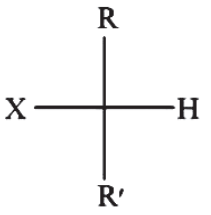



L-Glyceraldehyde

This is the initial descriptor system. It is not possible to predict the sign of optical rotation which is entirely an experimental fact. This system was extended by Rasanoff. In order to determine D/L descriptor of a molecule like RCHXR' where R and R' are two oxidised groups and x is a hetero atom, we are to proceed as follows. The carbon chain R-C-R' is written as in FP with the more oxidised group at the top and less oxidised group at the bottom. If the hetero atom X is placed on the right and H on the left as in glyceraldehyde it gives D configuration, if reverse it gives L configuration.

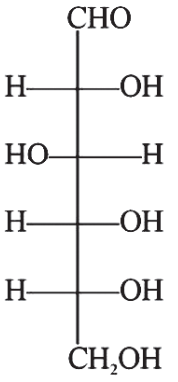



D-configuration

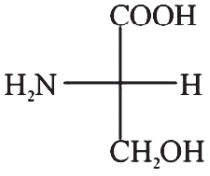



L-configuration

Example




D-glucose




L-Serine

The D/L descriptor system is still being used in carbohydrate and in amino acid chemistry. However, this D/L descriptor system of absolute configuration is not universal.

1 ) If we do not have any hetero atom, instead we may have an alkyl group or four alkyl groups, D/L descriptor system will not be applicable.

2) For two hetero atoms, there is no such rule that states which hetero atom is to be placed on the right or which one on the left while assigning D/L.

Rosanoff tried to extend it further to the absolute configuration of compound but that is not free from several limitations.

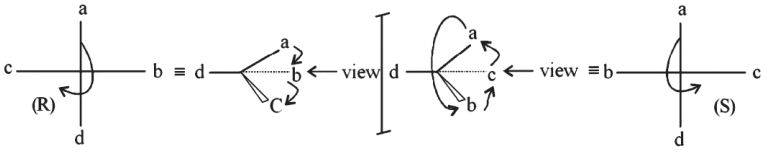
## 11.3 R/S descriptors :

A universal and generalised descriptor system based on three-dimensional structures of chiral molecules was introduced by Cahn, Ingold and Prelog. This is known as CIP system of descriptors. In this system, the absolute configuration of a chiral molecule is designated as either R [from rectus, Latin word meaning right (clockwise)] or S [sinister means left (anticlockwise)].

In order to assign absolute configuration to a molecule Cabcd, it is written in a tetrahedral fashion. In tetrahedral fashion, all four bonds cannot be in the same plane. If one bond is up, then one bond has to be down and the rest two bonds can be in the plain.

The ligands a, b, c and d are then assigned to a priority sequence following the priority sequence rule below. After assigning relative priorities the chiral centre is viewed from the side opposite to the lowest priority ligand.

Let the priority sequence of the ligands be a > b > c > d




If the priority sequence of the ligands a→b→c describes a clockwise turn, the configuration is R but if it describes an anticlockwise turn, the configuration is S. This is the CIP chirality rule.

**CIP rules for priority sequence:**

1) Proximity rule : Nearer end of a chiral axis precedes the farther end.
2) Atomic number rule : Higher atomic number precedes lower atomic number

   S > F > 0 > N > C > H

3) Atomic mass number rule : Higher atomic mass number precedes lower atomic mass number.

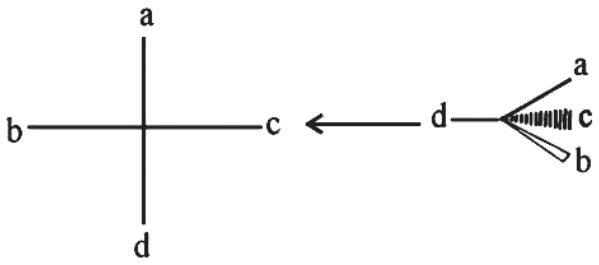
4) Cis precedes trans or Z precedes E

5) R precedes S

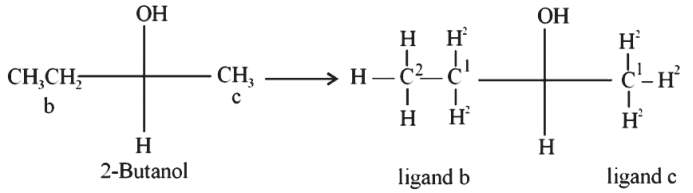
6) r* precedes s*

7) H precedes lone pair and phantom atom.

According to CIP rule, ligands attached to the chiral centre are to be sequenced first. If the first atom does not provide any decision one has to proceed outwards away from the chiral centre and then see where is the difference. Once a difference is found one has to stop there and then to assign priority. A chiral compound C*abcd with Fischer projection and the corresponding wedge formula is shown below.



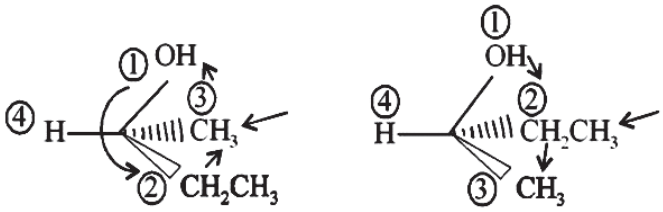

Let the ligand ‘a’ has the highest priority and the ligand 'd' the lowest. One has to assign priority to both the ligands ‘b’ and ‘c’. This is illustrated with an example of 2-Butanol.




(1) C (1) C No difference

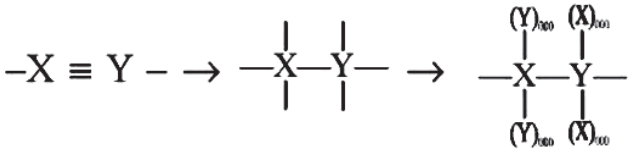
(2) C, H, H (1) H, H, H C > H

The second carbon atom in ethyl - $CH_2$- $CH_3$ has higher priority than the second hydrogen atom in methyl – $CH_3$ group. Therefore, -$CH_2CH_3$ > -$CH_3$.

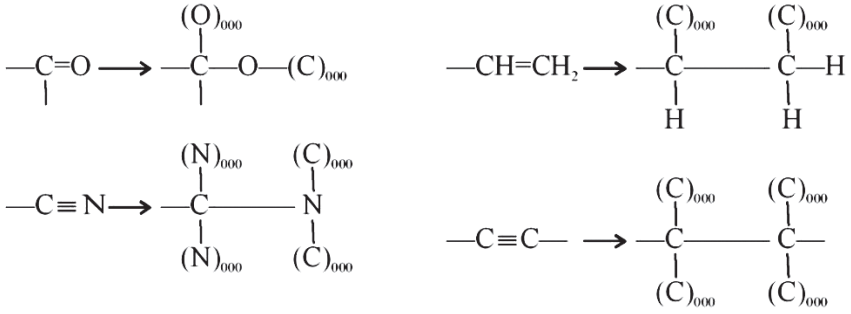



(S)-2-Butanol (R)-2-Butanol

Now we consider the assignment of priorities to ligands containing multiple bonds. A multiple bond can be disconnected to give one which as linked with two real atoms e g

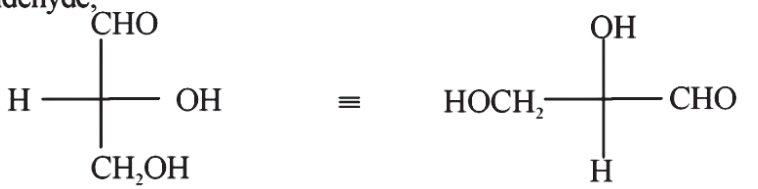



The bonds achieved by disconnection of the multiple bonds are then satisfied with replica atoms of the same type as shown above. Each replica atom is called a phantom atom which is enclosed in parenthesis and considered to be linked with three imaginary atoms having atomic number zero. The following are some illustrative examples.

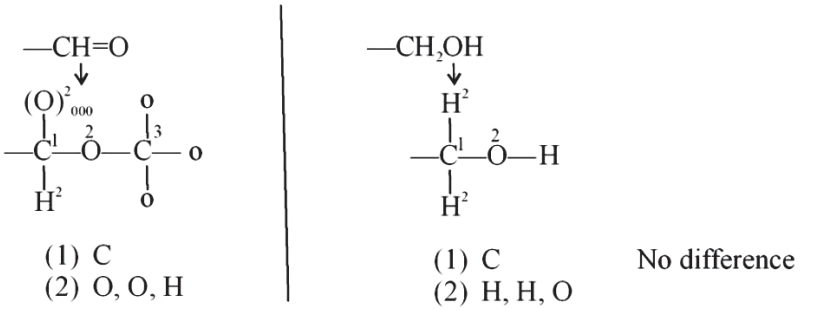


**Illustrative examples:**

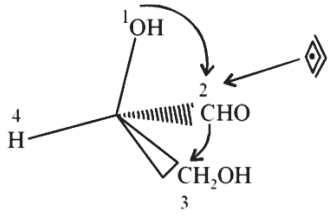
1) D-Glyceraldehyde,




In this case, the -OH group has the highest priority and H the lowest. Now we are to assign priority to both -CHO and $-CH_2OH$ groups i.e. -CH = O vs $-CH_2OH$

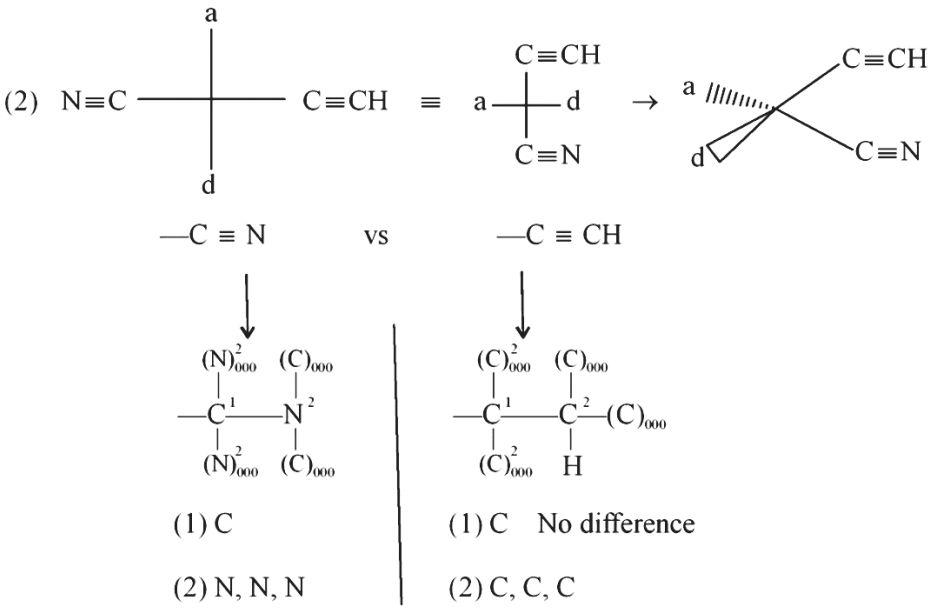



Since O > H; so –CHO > $–CH_2OH$

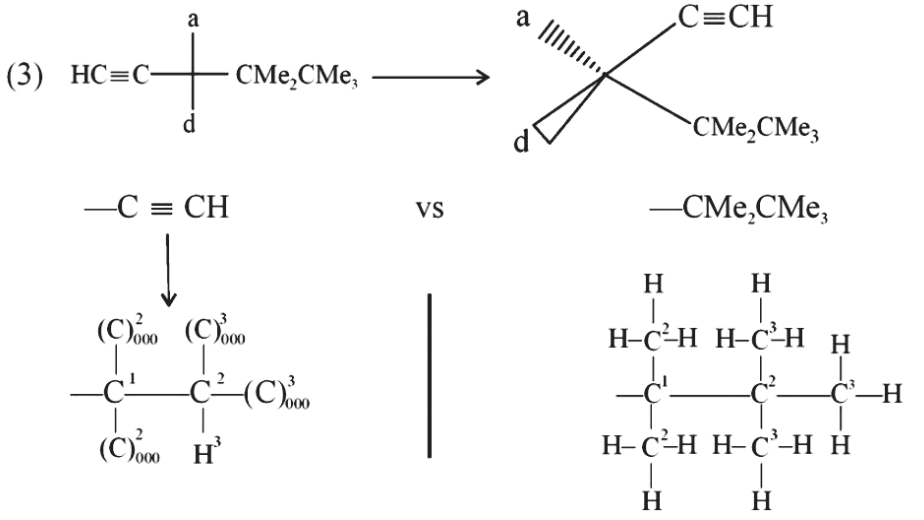




(R)-Glyceraldehyde

**Note:** There is actually no difference between phantom atom and normal atom. Phantom atom is attached to zero substituent.




As N > C, So – C ≡ N > – C ≡ CH



One proceeds along the branches of highest priority atoms

| | | |
|---|---|---|
| (1) C | (1) C | No difference |
| (2) C, C, C | (2) C, C, C | No difference |
| (3) C, C, H | (3) C, C, C | |

As C > H; So $—CMe_2CMe_3$ > – C ≡ CH

Some common ligands are given in order of increasing priority

–H, –D, $–CH_3$, $–C_2H_5$, –isobutyl, $–CH_2–CH=CH_2$,

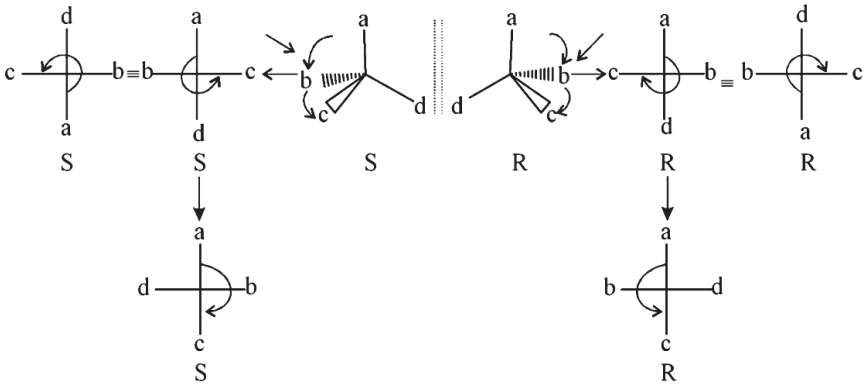
$–CH_2C_6H_5$, $–CH(CH_3)_2$, $–CH=CH_2$, $–C(CH_3)_3$,

–C≡CH, $–C_6H_5$, $–CMe_2CMe_3$, $–CH_2NH_2$,

–C≡N, $–CH_2OH$, –CHO, $–CO_2H$, $–NH_2$,

$–NHCH_3$, $–N(CH_3)_2$, $–NO_2$, –OH, F, Cl, Br, I.

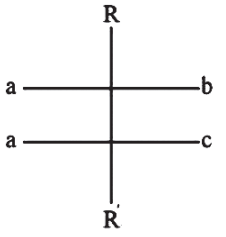
Once the priority sequence of the ligands is decided, assignment of configuration is done by the application of chirality rule which has already been discussed using wedge formula. Since molecules are normally represented by Fischer projection so wedge formula is converted into FP in which the lowest priority ligand ‘d' occupies either the top or the bottom position of the vertical bond. Then clockwise order of the remaining three ligands a→b→c corresponds to the R configuration and the anticlockwise order S configuration as shown below.



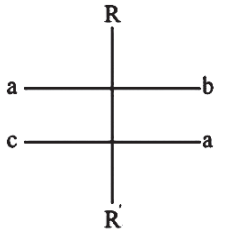
If the lowest priority ligand 'd' occupies either the left or the right position of the horizontal bond then the clockwise order of a→b→c give S and the anticlockwise order gives R configuration as shown above.

## 11.4 Erythro/Threo nomenclature

The erythro/threo nomenclature is a shorthand way of naming of diastereomers with two chiral centres of the type R-Cab-Cac-R' which have at least two ligands in common. If the two identical ligands are on the same side of the Fischer projection, the diasteresmer is called erythro form and if they are on the opposite side, the diastereomer is called threo form, in the analogy with tetrose sugars erythrose and threose.

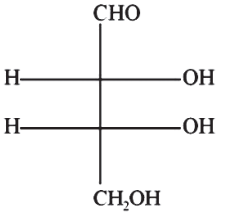



Erythro form

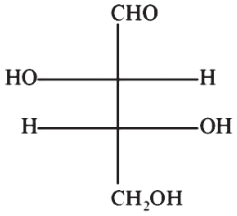



Threo form

Example:

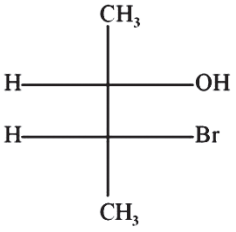



D-Erythrose

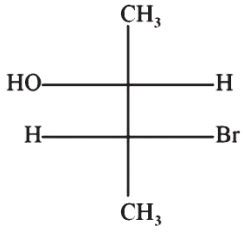



D-Threose

Other examples: 3-Bromo-2-butanol




erythro-3-Bromo-2-butanol




threo-3-Bromo-2-butanol

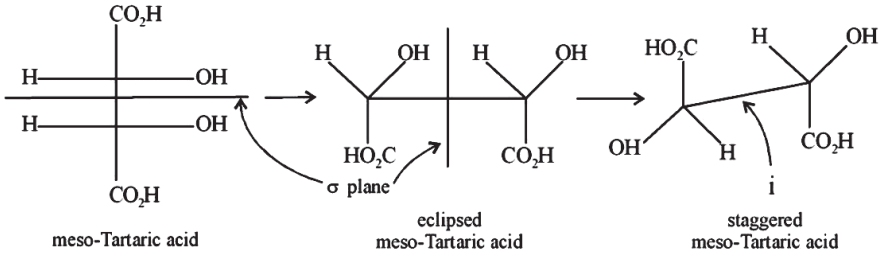
The erythro/threo nomenclause is simple and unambiguous. However, complications arise for the diastereomers of the type R-Cab-Ccd-R' which have no two ligands in common.

## 11.5 meso nomenclature

meso is used as prefix to specify the configuration or conformation for an achiral member of a set of diastereomers that include at least one chiral member.

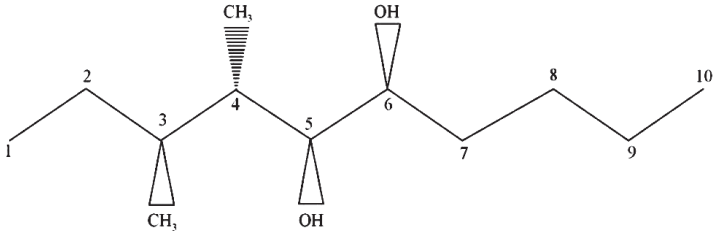
Example: meso-Tartaric acid. This is an AA type molecule and has already been discussed in section 4.5.

meso-Tartaric acid possesses a plane of symmetry a in the eclipsed conformation and a centre of symmetry / in the staggered conformation.

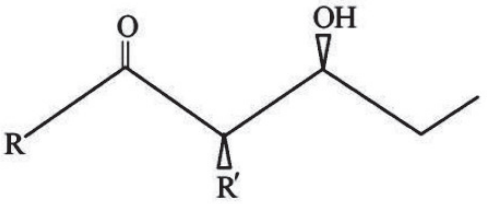



## 11.6 syn/anti nomenclature for aldols

Masamune et al (1980) proposed syn-anti designation to define relative configuration of molecules containing multiple chiral centres. According to this system of nomenclature, the molecule in question is written in zigzag fashion. If the two ligands on the adjacent chiral centres are on the same side of the molecular plane, the prefix syn is used, if they are on the opposite side, the prefix anti is used. Thus, the following compound would be 3,4-anti, 4,5-anti, 5,6-syn.

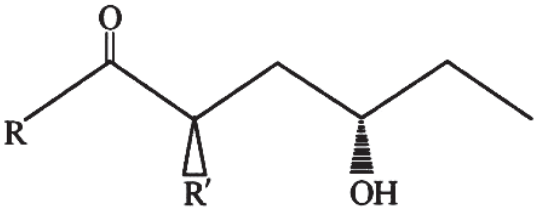


The system of nomenclature is particularly used for aldol-type compounds having multiple chiral centres. For example,




The relationship is syn.

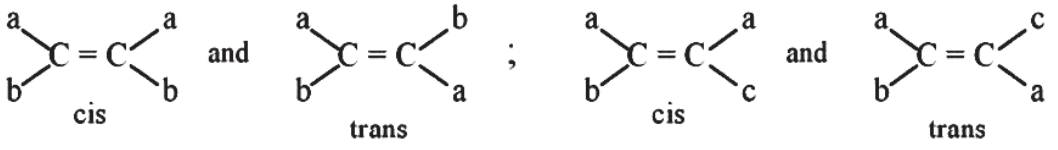
It is not necessary to have the adjacent chiral centres to assign a name. For example, The following compound.



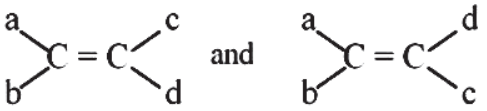

is 2,4-anti

## 11.7 E/Z descriptors

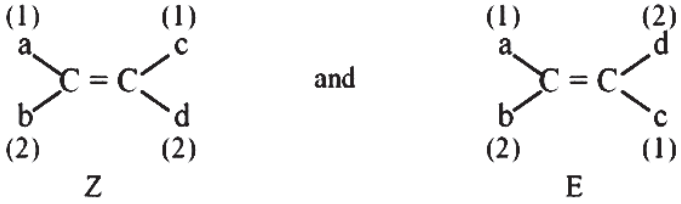
Alkenes of the type Cab = Cab or Cab = Cac where a, b, c and d are different ligands can exist in two diastereomeric forms which are known as cis and trans as shown.



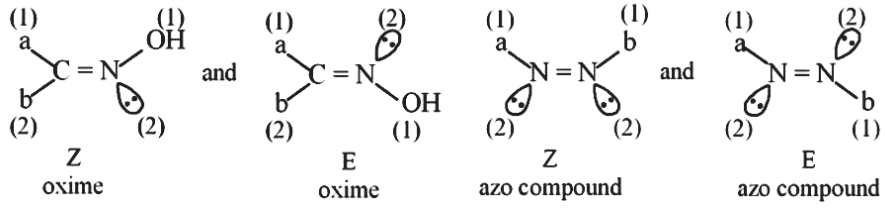

But alkenes of the type Cab = Ccd can exist in two diastereomeric form as shown



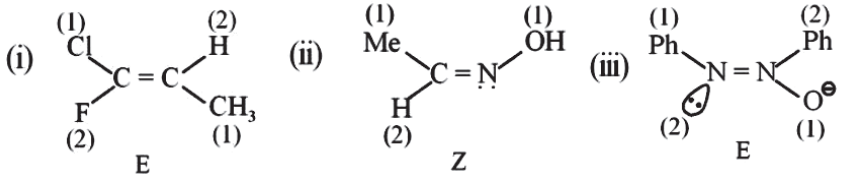

It is not possible to designate these diastereomers as cis or trans because no two ligands at the two ends of the double bonds are the same. This problem has been solved by applying CIP sequence rule. If the CIP priority of ligands is a > b and c> d, then among the two arrangements shown above one in which the higher priority ligands a and c are on the same side of the double bond is designated as Z (Zusammen, German word, meaning together ) and if they are on the opposite side of the double bond, the diastereomer is designated as E (Entgegen, German word, meaning opposite). Thus,




In the case of oximes and azo compounds, the lone pair of electrons on nitrogen has been considered to be the lowest priority ligand. Thus,

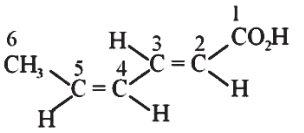



**Examples:**

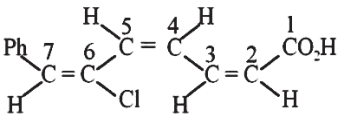


## 11.8 E/Z nomenclature for conjugated diene and triene

When a molecule possesses more than one double bond, the configuration is assigned by numbering the longest carbon chain such that the suffix is given at the lowest locant. It is then used in conjunction with the E/Z descriptor. This is illustrated with some examples

1) 

(2E, 4Z)-2,4-Hexadienoic acid

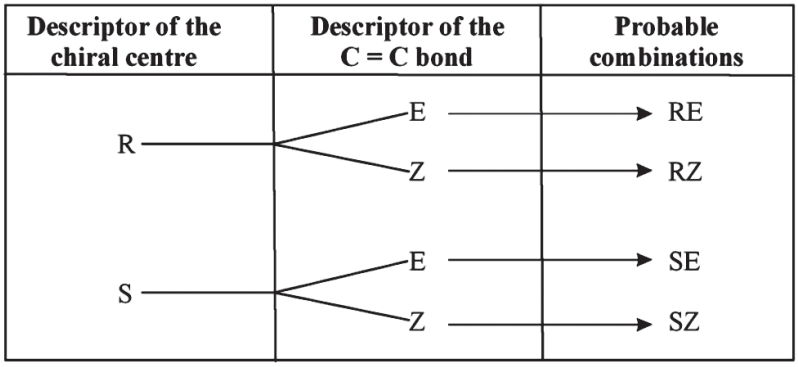
2) 

6-Chloro-7-phenylocta-(2Z,4Z,6E)-2,4,6-trienoic acid

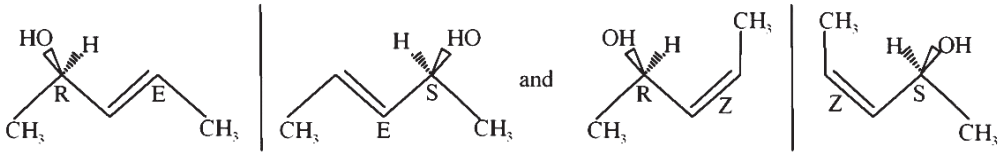
## 11.9 Combination of R/S and E/Z isomerism

If a molecule contains one or more chiral centres together with one or more olefinic double bonds, the number of stereoisomers can be predicted from the number of possible combinations of all the descriptors.

Pent-3-en-2-ol (CH3CHOHCH = CHCH3) provides an illustrative examples which has an olefinic double bond adjacent to a chiral centre. The probable combination of the descriptors are shown below.




As the number of probable combinations is four so the number of stereoisomers is four the configurations of which are RE, RZ, SE and SZ. These four stereoisomers can exist as two pairs of enantiomers as shown.



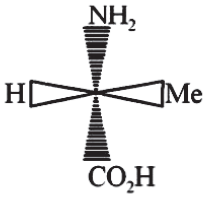

## 11.10 Summary

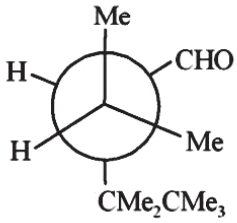
- Enantiomers are geometrically equivalent and are isometric. Enantiomers having a single chiral centre thus differ only in absolute configuration. The absolute configuration are denoted by the R/S or D/L systems.
- Diastereomers are anisometric and differ in their relative configuration. They are designated as erythro/threo, meso, syn/anti, E/Z etc.

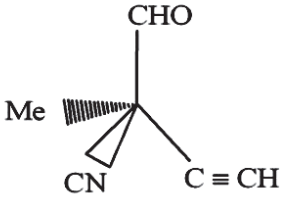
## 11.11 Exercises

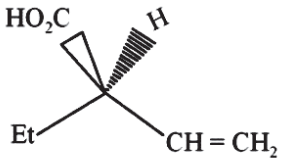
### A. Sample Questions

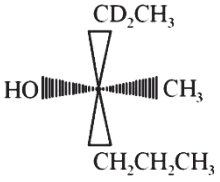
1) Assign R/S descriptors to each stereocentre of the following compound:

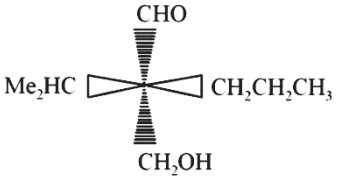
(i) 


; (ii) 


(iii) 


; (iv) 

(v) 

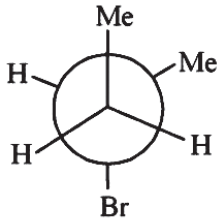
; (vi) 


2) Draw Fischer projection formula of a compound with (Reconfiguration having a stereogenic centre carrying the following ligands.

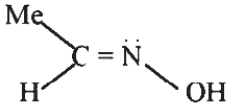
$$-C\equiv CH,\ \ -OMe,\ -C\equiv N \text{ and } -CMe_3.$$

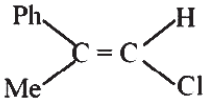
3) Draw the Fischer projection formula of (R )-2-deutero propanoic acid.

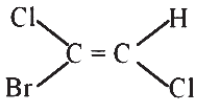
4) Indicate the following with R/S notation.

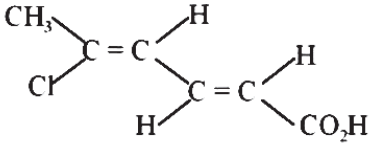



5) Assign configurational descriptor (E/Z) of the following :

i) 


ii) 


iii) 

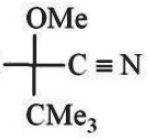

iv) 

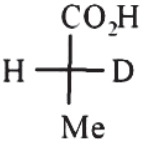

6) Draw all possible isomers of CH3CH(OH)CH=CHCl and designate them as R or S.

7) Draw (R,Z)-4-methyl-2-hexene and (S,E)-2-methyl-2-hexene and indicate their relationship.

**Answers :**

1 ) (i) R, (ii ) S, (iii) S, (iv) R, (v) S, (vi ) S

2) 


3) 


4) R

5) ( i ) E, ( ii ) Z, ( iii ) Z, ( iv) (2E, 4Z)-5-chloro-2,4-hexadienoic acid

6) see text

7) for the first part see text diastereomers

**B. Additional question**

4. What is the difference between absolute and relative configuration?
5. What limitations did Rosanoff face when extending the D/L descriptor system?
6. What is the basis of the CIP system for assigning R/S configuration? Explain with an example
7. What are phantom atoms, and how are they used in priority determination?
8. What is the main criterion for distinguishing between erythro and threo isomers?
9. What is a meso compound, and why is it achiral despite having chiral centers?
10. How do enantiomers and diastereomers differ in their geometric properties?

**C. Multiple Choice Question (MCQ)**

1. What is the basis for assigning D and L configurations in sugars and amino acids?

a) Optical rotation direction

b) Position of the hydroxyl (-OH) group on the reference carbon

c) Atomic number of substituents

d) Molecular weight of the compound

**Answer:** b) Position of the hydroxyl (-OH) group on the reference carbon

3. The erythro and threo nomenclature applies to:

a) Aldehydes and Ketones

b) Diastereomers with two adjacent chiral centers

c) Alkenes with double bonds

d) Aromatic compounds

**Answer:** b) Diastereomers with two adjacent chiral centers

4. A meso compound is:

a) Optically active

b) A racemic mixture

c) Optically inactive due to an internal plane of symmetry

d) A type of geometric isomer

**Answer:** c) Optically inactive due to an internal plane of symmetry

5. A compound with E configuration has:

a) Higher priority groups on the same side of the double bond

b) Higher priority groups on opposite sides of the double bond

c) A chiral center

d) Only one stereocenter

**Answer:** b) Higher priority groups on opposite sides of the double bond

6. Which type of system can also exhibit E/Z isomerism besides C=C bonds?

a) C=C (alkynes)

b) C=N (imines) and N=N (azo compounds)

c) Aromatic rings

d) Saturated alkanes

**Answer:** b) C=N (imines) and N=N (azo compounds)

7. Which of the following molecules can exhibit both R/S and E/Z isomerism?

a) 2-butanol

b) 3-methyl-2-pentene

c) 2,3-dibromo-2-butene

d) 2-chloropropane

**Answer:** c) 2,3-dibromo-2-butene

# Unit 12 ❐ Optical activity of chiral compounds

## Structure



## 12.0 Objectives

By the end of this unit, students should be able to:

- Differentiate between specific rotation and molar rotation
- Define racemic mixtures and explain their optical inactivity.
- Explain the principle of resolution and its importance in obtaining pure enantiomers.

- Define optical purity and enantiomeric excess (ee) and explain their relationship.
- Define invertomerism and explain its significance in chiral trialkylamines.

## 12.1 Introduction

We have mentioned earlier that a chiral molecule rotates the plane of a plane polarised light and is optically active. Enantiomers are identical in most of their physical and chemical properties in an achiral medium but behave differently in a chiral medium.

Optical rotation refers to the ability of a chiral substance to rotate the plane of polarized light. This phenomenon is observed when plane-polarized light passes through a solution of a chiral compound. Each enantiomer of an enantiomeric pair thus rotates the plane of a plane polarised light to an equal extent but in opposite direction because a plane polarised light is made up of two oppositely circularly polarised light and thus provides a chiral medium. The enantiomer that rotates the plane of a plane polarised light in a clockwise direction is called dextrorotatory (dextre, Latin word meaning right) and is designated as (+) or prefix dextro. The other enantiomer that rotates the plane of a plane polarised light in an anticlockwise direction is called laevorotatory (Laevus, Latin word meaning left ) and is designed as (-) or prefix laevo.

## 12.2 Specific rotation

The magnitude of optical rotation is measured in an instrument called 'polarimeter'. A solution of definite concentration of a chiral compound in an achiral solvent is taken in a polarimeter tube having definite length. According to Biot's law, the observed angle of rotation aobs is proportional to the concentration C of the optically active compound, and the path length / of the tube. Thus,

$$\alpha_{obs} \propto C./$$

$$\text{or, } \alpha_{obs} = [\alpha].Cl$$

$$\text{or, } [\alpha] = \frac{\alpha_{obs}}{C.l}$$

The value of proportionality constant [α] depends on the concentration of the solution

C and the path length of the tube l when C is expressed in g/ml and / in dm, the proportionality constant [α] is called the specific rotation. The specific rotation value depends on the wave length of the light used and the temperature of the experiment. So it is expressed as $[\alpha]_D^{25^\circ}$ where D is the wavelength of D-line sodium lamp (589 nm ) at 25°C.

## 12.3 Molar rotation

Molar rotation is a measure of how much a substance rotates plane-polarized light, normalized for its molar mass. It helps compare the optical activity of different compounds, independent of their concentration or density.

Molar rotation denoted by [ϕ| is defined as the product of specific rotation and molecular weight divided by 100 :

$$\text{That is, } [\phi] = \frac{[\propto]\ M.W}{100}$$

$$= \frac{\propto_{obs}}{Cg/ml.\ l\ dm} \times \frac{M.W}{100}$$

$$= \frac{\propto_{obs}}{\frac{C}{M.W}\frac{g}{100ml.} \times 1\ dm}$$

$$= \frac{\propto_{obs}}{C\ moles/100ml \times 1\ dm.}$$

## 12.4 Racemic compound

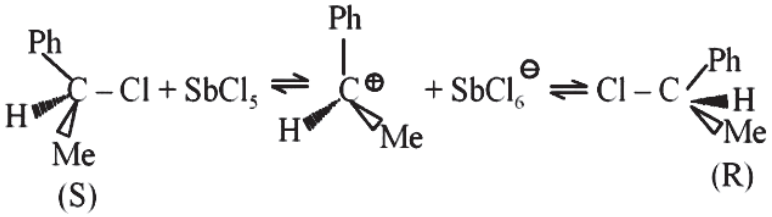
An equimolar mixture of the two enantiomers of a compound is called a racemic compound. It is also called racemic mixture, racemic modification or (±)-pair. Racemic compound is a true compound in stoichiometric sense and differ in properties from those of their enantiomers. Racemic compound shows zero optical rotation. Sodium ammonium tartrate forms racemic compound when crystallised from an aqueous solution above 27°C.

## 12.5 Racemisation

Racemisation is the process by which an optically active compound (containing one enantiomer in excess) converts into a racemic mixture (a 50:50 mixture of enantiomers), resulting in the loss of optical activity. Racemisation is a chemical process of converting an enantiomer into a racemic compound.

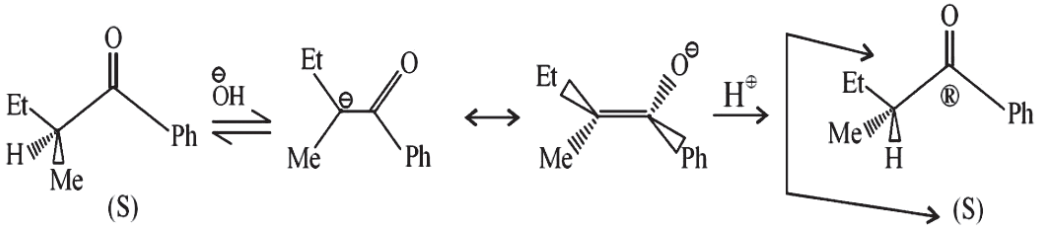
### 12.5.1 Though carbocation intermediate formation :

A carbocation formed by removal of an electron-withdrawing group is stabilised by resonance. Since a carbocation is sp2 hybridised, it is planar and can recombine with an anion from both faces leading to racemisation. Example:




### 12.5.2 Through carbanion intermediate formation:

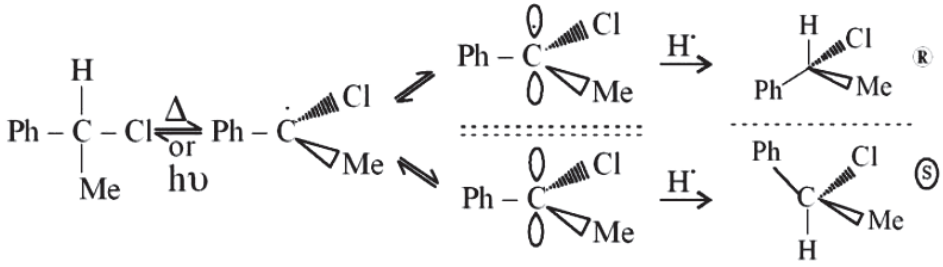
Achiral molecule undergoing racemisation must have an acidic proton at the chiral centre. This proton is removed by a base to generate a carbanion intermediate which undergoes inversion through a planar transition state. Recombination of H® from both faces results in racemisation. Example:




### 12.5.3 Through radical intermediate formation:

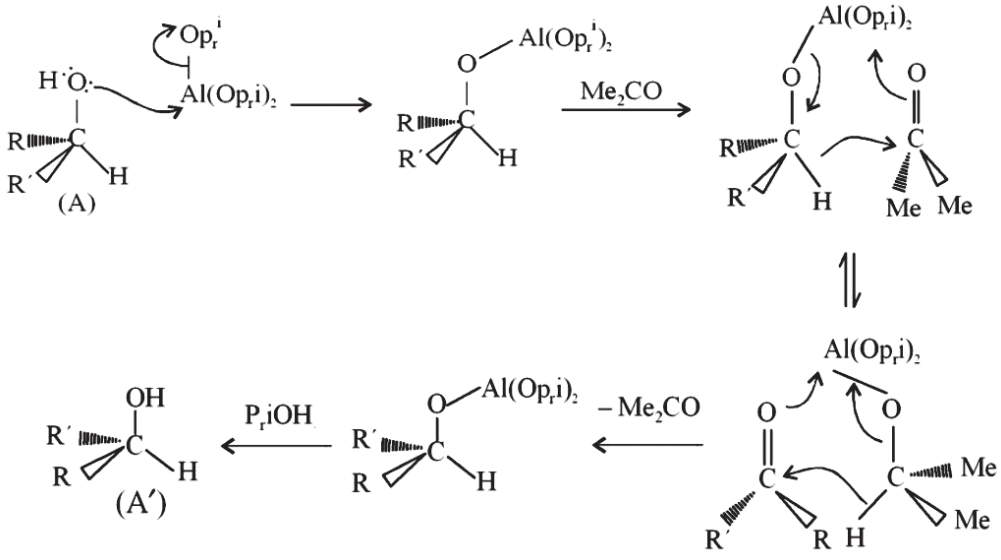
A molecule containing a hydrogen atom at the chiral centre undergoes homolysis under

the influence of heat or light to give a carbon radical. It has a planar structure. Recombination of the previously detached IT from both faces leads to racemisation. Example:



### 12.5.4 Through reversible formation of achiral intermediates:

An optically active secondary' alcohol RR'CHOH racemises by heating with aluminium isoproproxide in presence of traces of acetone.



A and A ' are enantiomers to each other.

In this case, the ketone RR 'CO fanned as an achiral intermediate initiates reversible

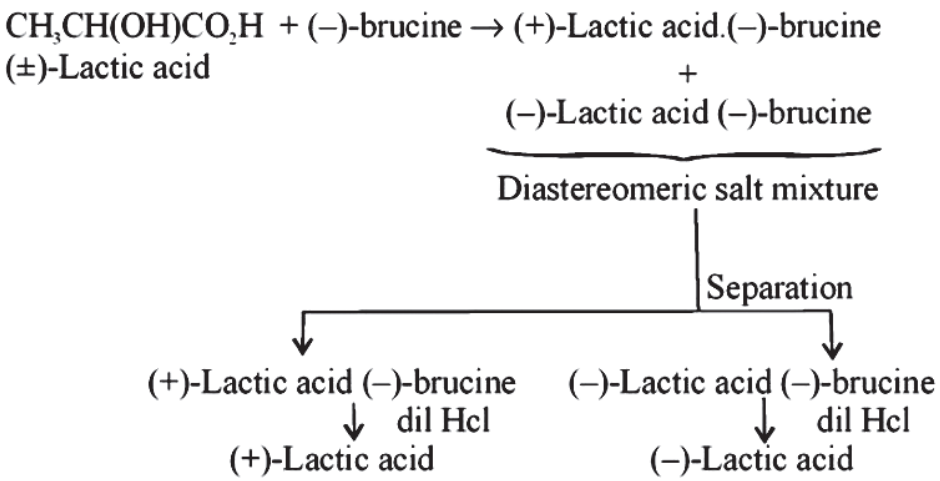
oxidation and reduction reactions and sets up an equilibrium between the enantiomeric products A and A .

## 12.6 Resolution

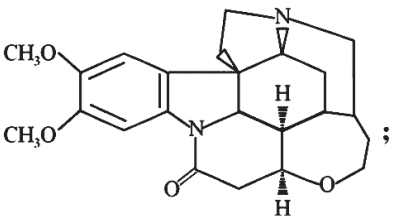
Resolution is the process of separating a racemic mixture into its individual enantiomers to obtain a pure optically active compound. Since enantiomers have identical physical and chemical properties in achiral environments, special techniques are required to achieve this separation. The methods are discussed below.

### 12.6.1 Resolution of racemic acid:

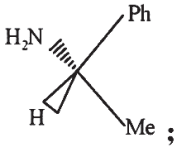
The racemic acid e.g. (± )-lactic acid is treated with an optically active base e.g. (-)-brucine ( resolving agent ) to give a mixture of diastereomeric salts. They are separated by fractional crystallisation or chromatography. Subsequent decomposition of each of the diastereomeric salts with dilute mineral acid would give rise to enantiomerically pure acid. This is illustrated as follows:



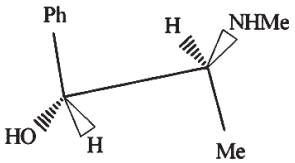
Some common 'resolving agent' for acid.




Brucine ;



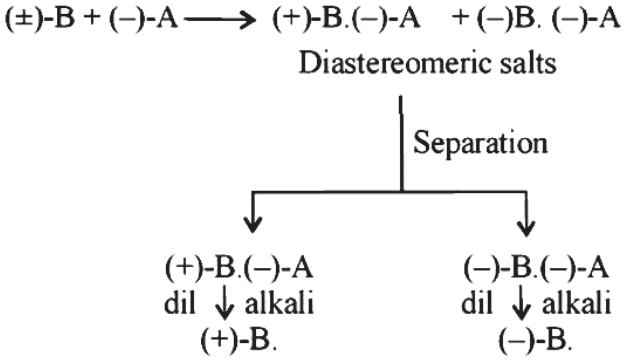

(–)-1-phenyl-ethylamine ;



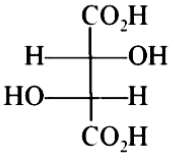

(–)-Ephedrine

### 12.6.2 Resolution of racemic base:

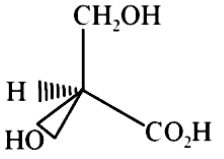
The racemic base is treated with an optically active acid to afford a mixture of two diastereomeric salts. They are separated by fractional crystallization. Subsequent decomposition of each of them with dilute alkali would furnish enantiomerically pure base. If (±)-B is a racemic base and (-)-A is an enantiomer of acid A, the overall strategy for resoloution is outlined below.



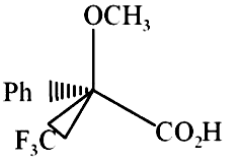

A few common resolving agent for bases




(+)-Tartaric acid ;



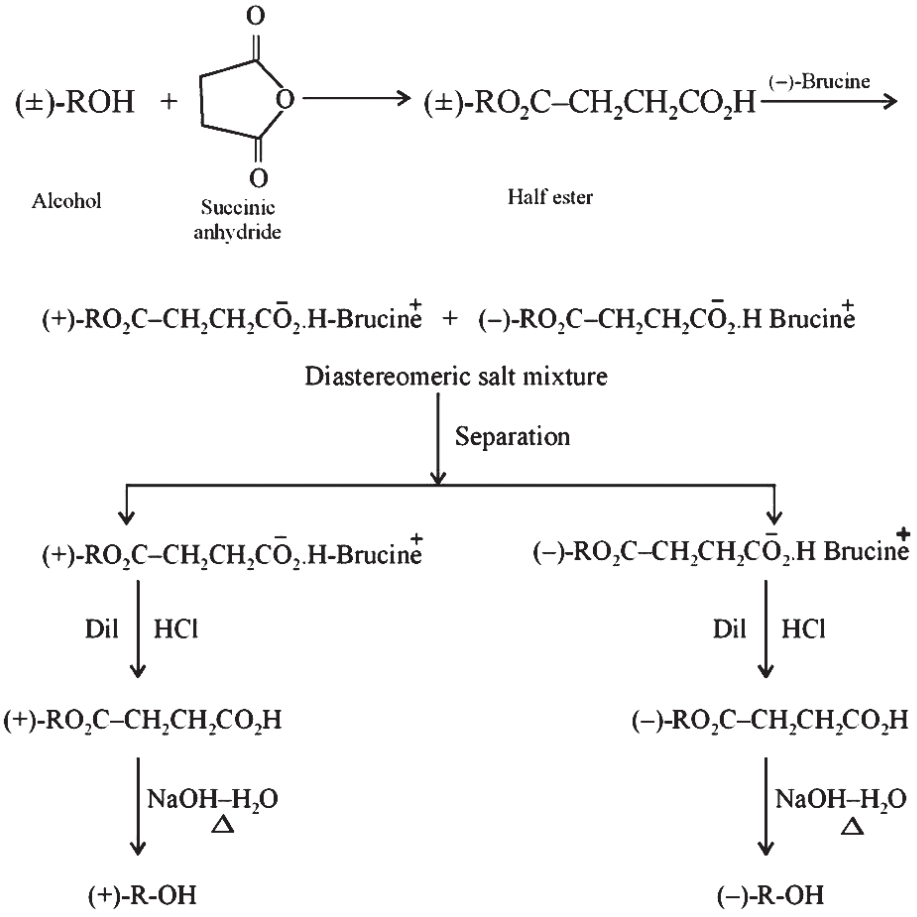

(–)-Malic acid ;




Mosher's acid

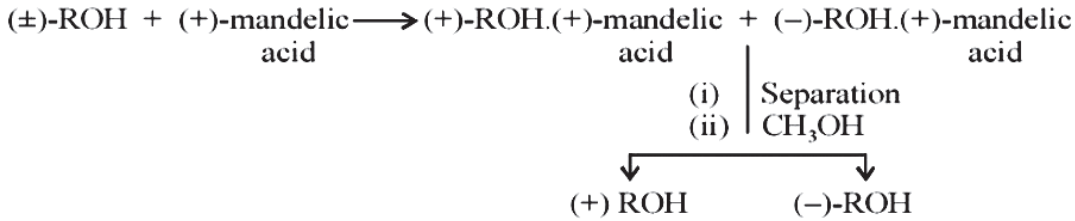
### 12.6.3 Resolution of racemic alcohol:

Racemic alcohol is converted into the half ester of succinic or phthalic acid by heating with succinic or phthalic anhydride in presence of pyridine. The half ester of the acid is then treated as racemic acid and resolved accordingly The following is an illustrative example.




The pure diasteromeric salt after separation is treated with hot aqueous alkali to set the resolved alcohol free.

Now a days, racemic alcohols are converted into a mixture of diastereomeric esters by reaction with enantiomerically pure acid (resolving acid). The diastereomeric ester mixtures after separation by chromatography are cleaved with methanol to give enantiomerically pure alcohol.




## 12.7 Optical purity and enantiomeric excess

The enantiomers obtained by resolution of racemic compound may not be 100% optically pure (that means 100% (+)-or 100% (-)-enantiomer ). In such cases, the excess of one enantiomer in the partially resolved material can be expressed as a percentage of the total. This is called optical purity. The optical purity of a nonracemic sample may thus be defined as the percentage ratio of its observed specific rotation to that of maximum specific rotation (rotation of a pure enantiomer). So,

$$OP = \frac{[\alpha]_{obs}}{[\alpha]_{max}} \times 100$$

Another term used is enantiomeric excess (ee). It is defined as the percentage excess of one enantiomer over the racemate. If x+ mole of (+)-enantiomer and x_ moles of (-)-enantiomer form a nonracemic sample where x+ > x_, the excess of (+)-enantiomer in the sample will be (x+- x_) moles.

Therefore, $(x_+ + x_-)$ moles of nonracemic sample contain = $(x_+ - x_-)$ moles of (+)-enantiomer

$\therefore$ 100 ,, ,, ,, ,, $= \frac{x_+ - x_+}{x_+ + x_+} \times 100$ ,,

That is, % excess of (+)-enantiomer = $\frac{x_+ - x_-}{x_+ + x_-} \times 100 = ee$

The optical purity (OP) is usually equal to enantiomeric excess (ee ) and therefore,

$$OP = \frac{[\alpha]_{obs}}{[\alpha]_{max}} \times 100 = ee = \frac{x_+ - x_-}{x_+ + x_-} \times 100$$

Since $x_+ + x_- = 1$, so, $ee = (x_+ - x_+)100$

$= \%$ of $x_+ - \%$ of $x_-$

$= \%$ of $x_+ - (100 - \%x_+)$

or, $ee + 100 = 2\ \%\ x_+$

or, $\%$ of $x_+ = \frac{ee+100}{2}$

and, $\%$ of $x_- = 100 - \left(\frac{ee+100}{2}\right)$

$= \frac{100-ee}{2}$

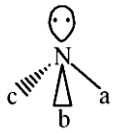
The optical purity and enantiomeric excess can be determined by measuring the specific rotation of the nonracemic sample and the corresponding specific rotation of the pure enantiomer. It is to be noted that the enantiomers isolated from natural sources are 100% optically pure.

Illustration: A mixture composed of 90% R enantiomer and 10% S enantiomer has 90% - 10% = 80% ee.

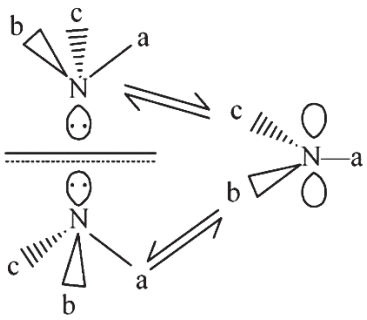
If the specific rotation of a nonracemic sample is (+) ve, the (+ )-enantiomer will be in excess in the sample.

## 12.8 Invertomerism of chiral trialkylamines

Molecules with a tricoordinate chiral atom such as Xabc (where X = C, N, P etc ) can be treated in a similar way as tetracoordinate chiral atom, Xabcd which has already been discussed. Tetrahedral geometry of Xabc appears as trigonal pyramid the base of which is formed by the ligands a, b, c and the apex by the lone pair of electrons of X. Example: A trialkylamine




An Sp3 hybridised pyramidal tertiary amine of the type Xabc undergoes inversion through a Sp2 planar transition state giving a pair of non-superimposable mirror images thereby showing enantiomerism.




The process is known as a pyramidal inversion and the enantiomers are called invertomers. Invertomerism is a process of isomerism involving invertomers.

## 12.9 Summary

- Chiral molecules are optically active. If a chiral molecule rotates the plane of a plane polarised light in a clockwise direction it is called dextrorotatory. If anticlockwise, it is laevorotatory. Specific rotation [α] is defined by

  $$[\propto]_D = \frac{\propto_{obs}}{c.l}$$

  Where αobs is the observed rotation, c is the concentration in gm/ml and / is the cell path length in dm.

- Molar rotation (ϕ) = $\frac{[\propto]_D M}{100} W$ Where M is the molecular weight of the chiral compound.
- Racemisation is a chemical process of converting an optically active compound into a

racemic mixture. It involves a reversible change of configuration at a chiral centre. Depending on the nature of substrates and reaction conditions racemisation may take place through the formation of carbocation, carbonion, free radical or even stable achiral intermediate e.g. ketone.

- Resolution is a process of separating the pure enantiomers from racemic mixture. It involves the formation of diastereomeric compounds with optically pure reagents (resolving reagent) and their separation and subsequent decomposition.
- The optical purity (OP) of a nonracemic sample is defined as the percentage ratio of its specific rotation to that of a pure enantiomer. The enantiomeric excess (ee) of a nonracemic sample is defined as the percentage excess of one enantiomer over the racemate.
- Invertomers are enantiomers that undergo inversion particularly at nitrogen atom. This phenomenon is known as invertomerism.

## 12.10 Exercises

### A. Sample Questions

1) When (+)-2-butanol is treated with aluminium isopropoxide in the presence of traces of acetone it gradually loses its optical activity. Explain.
2) Given that observed rotation for (R)-2-bromobutane is -23.1°. If the specific rotation of a nonracemic sample of 2-bromobutane is -9.2°, what is the percentage composition of each enantiomer in the sample?
3) If a pure R isomer has a specific rotation of-142° and a sample contains 77% of R and 23% of S isomers what is the observed specific rotation of the mixture?
4) An optically pure sample of (R)-(-)-2-butanol shows a specific rotation of-13.60. What relative molar proportion of (S)-(+)-butanol and (R)-(-)-2-butanol would give a specific rotation of +6.8°?
5) R1 R2 R3 N can be obtained in optically pure form. Justify or criticise.
6) Calculate [?]D of 1M solution of a compound A in a 1 dm cell when the observed rotation is +3.5°. Given the molecular weight of A is 120.

7) The specific rotation of a compound of molecular weight 70 is +30° ; what is its molar rotation?

**Answers:**

1) See text, 2) (R) is 68.9% and (S) is 31.1%, 3) -76.38, 4 ) 75% (+ ) and 25% (-)-forms., 5) See text, 6 ) +29.16° , 7 ) +21°

**B. Additional question**

1. What is optical rotation?
2. What is the difference between dextrorotatory and laevorotatory enantiomers?Example
3. How is specific rotation defined? Why is the specific rotation value expressed with reference to the D-line of a sodium lamp at 25°C?
4. What is molar rotation, and why is it useful? How is molar rotation calculated?
5. What is a racemic compound? Why does a racemic mixture show zero optical rotation? Give an example of a racemic compound formation.
6. What is racemisation? How does carbocation intermediate formation lead to racemisation?
7. How does radical intermediate formation contribute to racemisation?
8. What is resolution in the context of optical isomerism? Why is it difficult to separate enantiomers using standard physical methods?
9. Describe the process of resolving a racemic acid.
10. How can racemic bases be resolved?
11. Explain the method used for the resolution of racemic alcohols.
12. What is optical purity? Define enantiomeric excess (ee). How are optical purity and enantiomeric excess related?
13. If a sample contains 75% of one enantiomer and 25% of the other, what is its enantiomeric excess?
14. What is invertomerism? Explain how pyramidal inversion occurs in trialkylamines.

15. What type of hybridization does a pyramidal tertiary amine undergo? How does pyramidal inversion affect the chirality of amines?

**C. Multiple Choice Questions (MCQ)**

**Q1.** Optical rotation is measured using:

a) Polarimeter

b) Spectrophotometer

c) Refractometer

d) Chromatograph

**Answer:** a) Polarimeter

**Q2.** If an optically active compound has [a]D = +30°, what will be the observed rotation when measured at twice the concentration in the same solvent?

a) +30°

b) +60°

c) +15°

d) -30°

**Answer:** b) +60°

**Q3.** Molar rotation is defined as:

a) Specific rotation × Molecular weight

b) Specific rotation ÷ Molecular weight

c) Specific rotation × Density

d) Specific rotation ÷ Density

**Answer:** a) Specific rotation × Molecular weight

**Q4.** A racemic mixture is optically:

a) Active

b) Inactive

c) Dextrorotatory

d) Levorotatory

**Answer:** b) Inactive

**Q5.** Which mechanism does NOT usually cause racemisation?

a) SN1 reaction

b) SN2 reaction

c) Enolate formation

d) Free radical intermediates

**Answer:** b) SN2 reaction

**Q6.** Which method is commonly used for the resolution of a racemic mixture?

a) Formation of meso compounds

b) Chromatographic separation on achiral stationary phase

c) Formation of diastereomeric salts

d) Heating the racemic mixture

**Answer:** c) Formation of diastereomeric salts

**Q7.** If a sample has 80% of one enantiomer and 20% of the other, the enantiomeric excess (ee) is:

a) 60%

b) 50%

c) 40%

d) 80%

**Answer:** a) 60%

**Q8.** A sample shows an enantiomeric excess (ee) of 100%. What does this indicate?

a) Racemic mixture

b) Only one enantiomer is present

c) Equal amounts of both enantiomers

d) No optical activity

**Answer:** b) Only one enantiomer is present

**Q9.** Invertomerism occurs due to:

a) Free rotation around a single bond

b) Pyramidal inversion at nitrogen

c) Tautomeric shift

d) Ring strain

**Answer:** b) Pyramidal inversion at nitrogen

**Q10.** If the observed specific rotation of a sample is +10° and the pure enantiomer has a specific rotation of +20°, what is the optical purity?

A) 50%

B) 20%

C) 10%

D) 100%

**Answer:** A) 50%

# Unit 13 ❐ Stereoaxis-Induced Chirality

## Structure



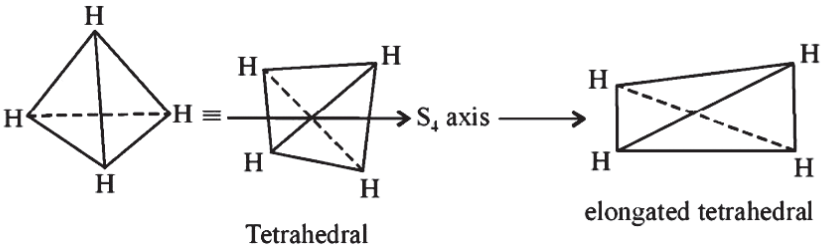
## 13.0 Objectives

In this unit learner will know about :

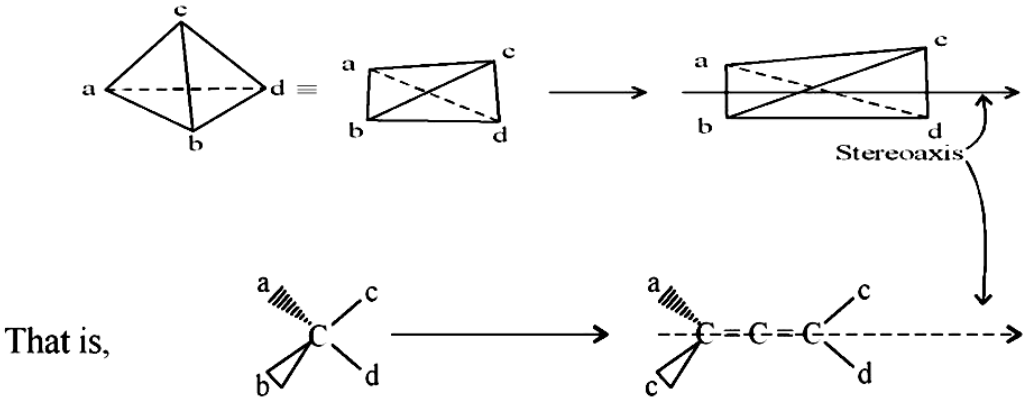
- The chirality arising out of stereoaxis.
- The concept of prostereoisomerism.
- Different types of comformations and this nomenclatures.
- Conformational analysis of some alkanes and substituted alkanes.

## 13.1 Introduction

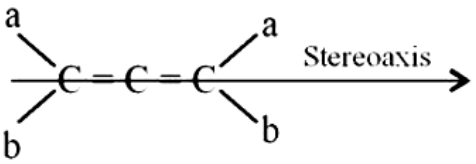
It has been found that there are several compounds which do not have any chiral centre but yet chiral and exist in enantiomeric forms. In such cases, chirality arises out of stereoaxis or chiral axis and is known as axial chirality. A tetrahedral framework of methane has an S4 axis. If this framework is stretched along the S4 axis, it is converted into an elongated tetrahedral framework as shown.




The elongated tetrahedral framework can accommodate the linear groupings C=C=C or C-C possessed by a large number of molecules such as allenes, alkylidene cycloalkanes, spiro compounds or biphenyls. A tetrahedral molecule of the type C*abcd having C1 symmetry is thus converted into an elongated framework with C1 symmetry as shown.



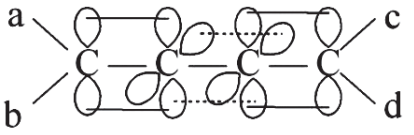

The framework also maintains chirality if a = c &/or b = d, but a ≠ b.



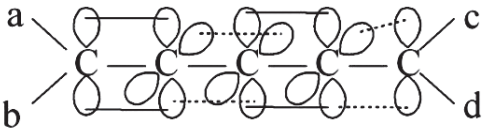

The nonplanar arrangement of two sets of substituents about an axis as above is called a stereoaxis. Some compounds possessing stereoaxis belong to the class of cumulated double bond system, allenes and the other class as biphenyls.

## 13.2 Stereoisomerism of substituted cumulenes

A cumulene [ab (C =)$_n$cd] is a hydrocarbon with three or more cumulative (consecutive ) double bonds. The simplest member is butatriene (H2C = C = C = CH2) which is simply called cumulene. In cumulene, the end carbon atoms are sp2 hybridised and the rest of the carbon atoms are sp hybridised as shown.

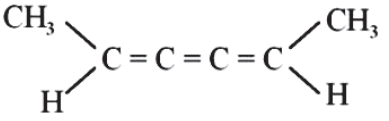



n = 3, odd number of double bonds



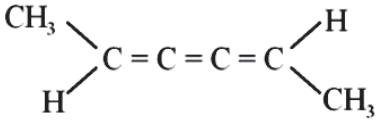

n = 4, even number of double bonds

In this case, successive plane of the double bonds are othogonal to each other. Thus when an odd number of cumulative double bonds exist in a compound orbital overlap causes the end groups to lie in the same plane and cis-trans isomerism is observed. For example, hexa-2,3,4-triene exists as cis-trans isomers.



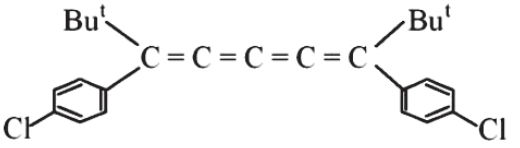

Cis (Z)

and



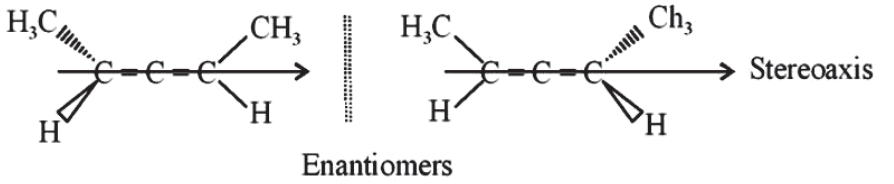

trans (E)

The cis-trans isomers readily interconvert under the influence of heat or light. When an even number of cumulated double bonds are present in a compound the end groups are orthogonal to each other and an enantiomerism is observed. The following compound exhibits enantiomerism.



## 13.3 Stereoisomerism of substituted Allenes

Allenes contain an even number of cumulative double bonds so that the end groups are orthogonal to each other. Thus properly substituted allenes exhibit enantiomerism due to presence of a stereoaxis. When an allene has two different substituents on each terminal carbon (C1 and C3), it lacks a mirror plane and becomes optically active. These enantiomers rotate plane-polarized light in opposite directions Example: Pentane-2,3-diene




Enantiomers

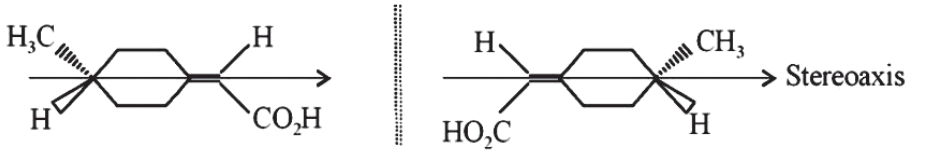
Unlike alkenes, allenes do not exhibit cis-trans isomerism because the double bonds are orthogonal to each other.

## 13.4 Chirality in substituted alkylidene cycloalkane

Alkylidene cycloalkanes are cycloalkane derivatives where a methylene (=CH2) or substituted alkylidene (-CHR or -CR1R2) group is attached to the ring via a double bond. The presence of this double bond introduces restricted rotation, leading to different types of stereoisomerism.

Certain alkylidene cycloalkanes can be chiral even without a traditional chiral center. This occurs when: i) The molecule lacks a plane of symmetry, ii) The double bond creates a rigid helical shape.

**Example:** 4-Methylcycloalkylideneacetic acid




Enantiomers

## 13.5 Chirality in properly substituted spiro compound

Spiro compounds are bicyclic structures where two rings share a single common atom (the spiro center). Their general notation is Spiro[n.m]alkane, where n and m represent the number of atoms in the two rings (excluding the spiro carbon).

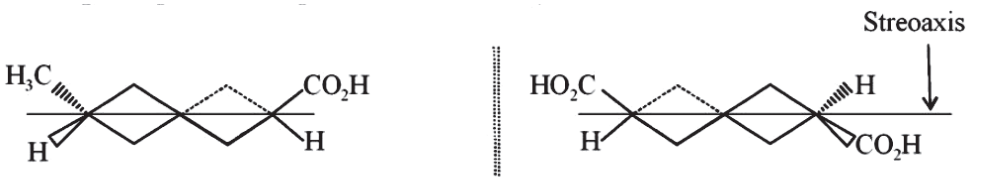
A spiro compound can be chiral without having a conventional chiral center (i.e., a carbon with four different groups). This occurs due to restricted rotation and asymmetry in the molecular structure. A spiro compound is chiral when:

i) The two rings are structurally different, creating a helical or axial chirality.

ii) The spiro center is tetrahedral and attached to two rings that prevent superimposability.

iii) There is an absence of a plane of symmetry or an inversion center in the molecule.

**Example:** Spiro[3,3]heptane-2,6-dicarboxylic acid




Enantiomers

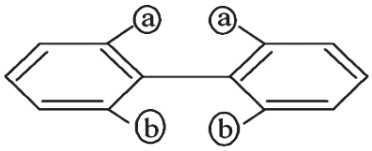
## 13.6 Chirality in Biphenyl system

Biphenyl is a compound in which two phenyl rings are connected by a single bond called pivotal bond as shown below:

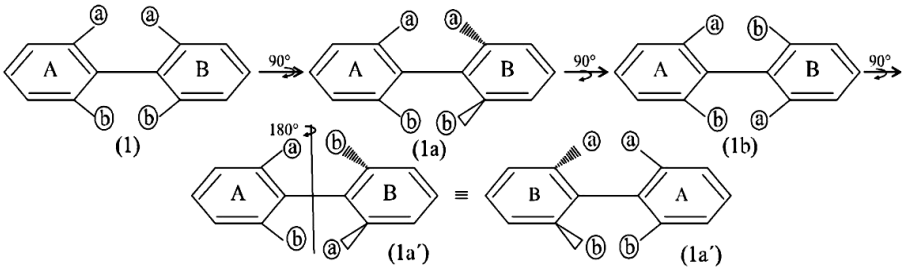
Biphenyl

When the rings are coplanar the system is stabilised due to extended conjugation between the two benzene rings. But if the ortho positions in biphenyl are substituted by bulky

substituents as shown in the following figure, there develops a steric crowding which affects the stability of the molecule.

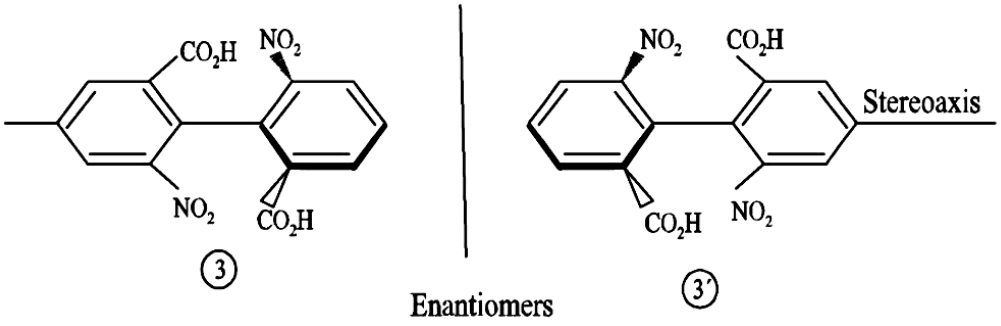


In that case, to reduce the steric repulsion one ring rotates with respect to the other and ultimately the two rings become orthogonal to each other as shown below.



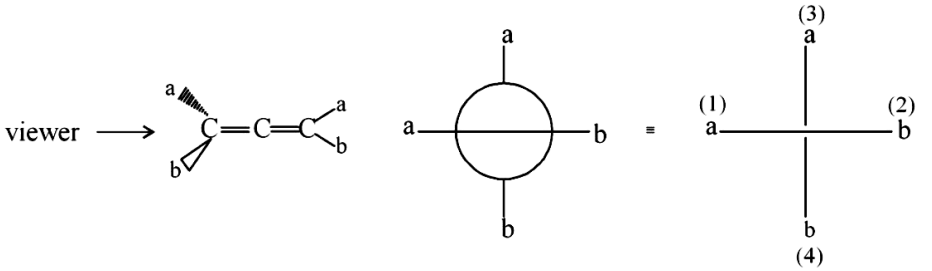

The ring B rotates with respect to the ring A giving rise to two conformational isomers la and la' which are mirror images of each other and exist as a pair of enantiomers. Each of the conformational isomers is known as atropisomer (Greek, 'a' meaning ‘not’ and tropos meaning 'turn’) Atropisomerism is therefore, a type of conformational isomerism in which conformers i.e. atropisomers are isolable due to restricted rotation about a single bond.

In order to assume axial chirality each of the substituted phenyl ring must not have a vertical plane of symmetry. So, 2,2 -Dinitro-6,6 -diphenic acid 3 is chiral and exists as a pair of enantiomers. (3,3’ ).

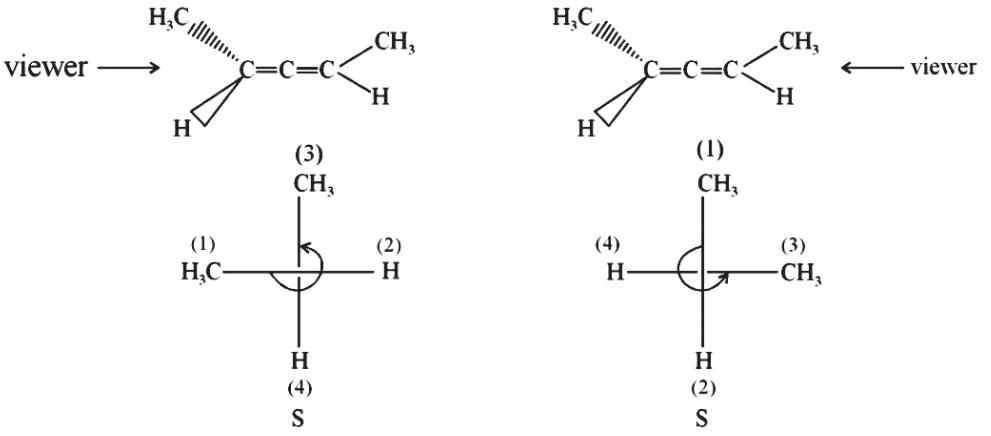


## 13.7 Configurational descriptors:

In order to assign Ra / Sa configurational descriptor to an axially chiral molecule such as properly substituted allene, the molecule is viewed along the chiral axis from the near carbon with two ligands in a horizontal position to the far carbon with two ligands in a vertical position and projected to a Newman projection as shown below.

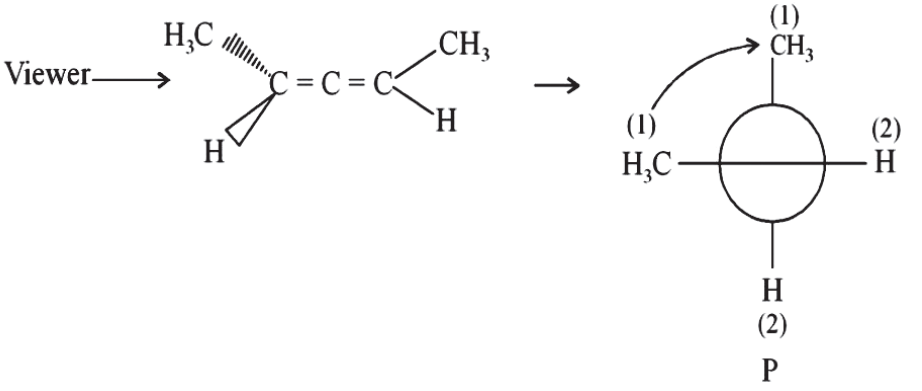



The near ligands a and b are numbered 1 and 2 and the far ligands a and b are numbered 3 and 4 following the priority sequence. The standard sub rule (O ) which says that near ligands precede far ligands is then applied to it. The sequence 1?2?3 describes an anticlockwise turn and so the configuration is S. It leads to the same configurational descriptor which is S in this case when viewed from the other end. Example:



## 13.8 Helix nomenclature

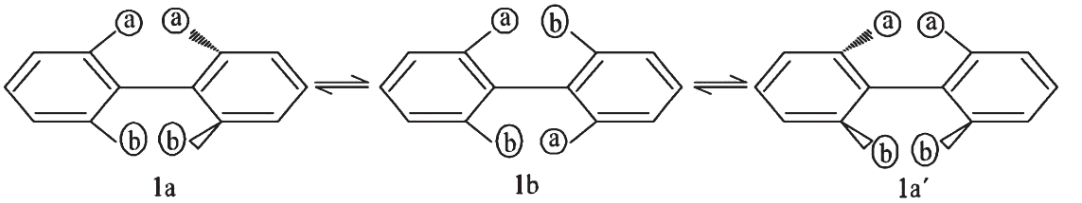
A restricted rotation about a stereoaxis due to steric congestion may lead to helicity. The stereoaxis may thus be looked at as a type of helicity. To designate a stereoaxis by helix nomenclature, the first priority ligand attached to the near carbon and that to the far carbon are considered. If the turn from the first priority ligand in the near to that in the far is clockwise, the descriptor is P (plus), if anticlockwise, it is M (Minus ). Thus,




The chiral designation of the above molecule is aS (P) where 'a' is used for axial chirality. S denotes CLP nomenclature. P is the helix nomenclature.

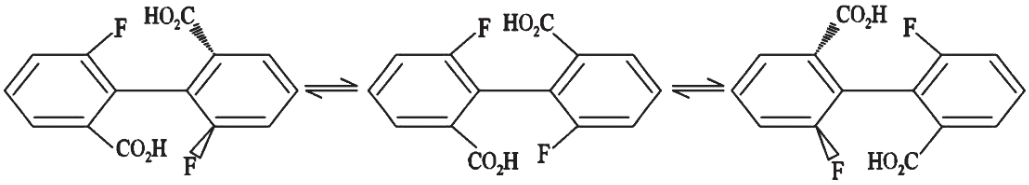
## 13.9 Racemisation of chiral biphenyls

In biphenyls the atropisomers la and la ' are capable of interconversion by rotation about C-C bond joining the two aryl rings.




The rate of interconversion depends on the temperature and and the energy barrier separating the atropisomers. It is to be noted that the bulkier the ortho substituents are, the higher is

the energy barrier. High energy barrier prevents rotation at an ambient temperature resulting in isolation of atropisomers. But the atropisomers may racemise at high temperature. The rate of racemisation increase with increasing temperature. When the ortho substituents e.g. F, OCH3 etc. have small van der Waals radii, the smaller substituent can easily surpass each other through planar transition state and the compound gets racemised. Example: 2,2 '-Difluoro-6,6 '-diphenic acid racemises readily.




## 13.10 Summary

- Chiral molecules that do not possess chiral centre but show stereoisomerism may be attributed to the presence of chiral axis. The axial chirality has been explained on the basis of elongated tetrahedron. A large number of molecules such as properly substituted allenes, alkylidenecycloalkanes, spiranes and biphenyls exhibit enantiomerism due to axial chirality. In order to assign configurational descriptors to axially chiral molecules, the molecule is viewed from either end of the chiral axis and the ligands near to the viewer are numbered 1 and 2 while the ligands at the far end are numbered 3 and 4 following CIP priority rule. If the order 1→2→3 is clockwise the configuration is R. If anticlockwise, it is S.
- Appropriately substituted cumelene containing an odd number of double bonds shows cis-trans isomerism but with an even number of double bonds exhibits enantiomerism.
- Stereoisomerism in properly substituted biphenyls due to hindered rotation around C— C bond joining the aryl rings is called atropisomerism. Assignment of configurational descriptor to chiral biphenyls is done in a similar way as for other axially chiral molecules. If the ortho substituents in biphenyl have small van der Waals radii they can easily pass each other through planar transition state and the compound gets racemised.

## 13.11 Exercises

### A. Sample Questions

1) What are the necessary structural features for a biphenyl compound to be dissymmetric? Explain with a suitable example.

2) Explain the stereoisomerism of 6,6'-dinitrodiphenic acid.

**Answers :**

1) Two features:

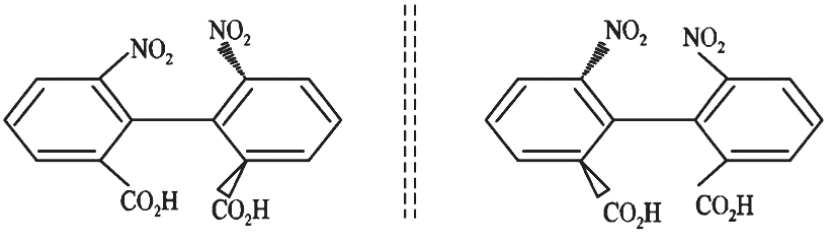
i ) ortho positions of both rings must be substituted by bulky groups

so that planes of the two aryl groups are non-coincident.

ii) it should not have vertical plane of symmetry.

For example see text

2)




### B. Additional question

1. What is axial chirality, and how does it differ from traditional chirality? What are some examples of molecules that exhibit axial chirality?
2. "Cumulenes with an odd number of consecutive double bonds exhibit cis-trans isomerism, while those with an even number exhibit enantiomerism". Explain
3. Under what conditions does an allene become optically active?
4. What structural conditions make alkylidene cycloalkanes chiral despite lacking a traditional chiral center?

5. What are spiro compounds, and what are the structural requirements for a spiro compound to be chiral?
6. What is atropisomerism, and how does it occur in biphenyl compounds?
7. How do you assign the descriptors P and M in helix nomenclature? Explain with an example.
8. How does racemization occur in chiral biphenyls? What factors influence the rate of racemization in biphenyl systems?
9. Why do bulkier ortho-substituents prevent racemization at room temperature?
10. What is the difference between atropisomerism and traditional conformational isomerism?

**C. Multiple Choice Question (MCQ)**

Stereoisomerism of Substituted Cumulenes with Even and Odd Number of Double Bonds

**Q1.** Which of the following statements is true regarding the stereoisomerism of cumulenes?

A) Cumulenes with an even number of double bonds are chiral if appropriately substituted.

B) Cumulenes with an odd number of double bonds are chiral if appropriately substituted.

C) Cumulenes do not exhibit stereoisomerism.

D) All cumulenes are optically inactive.

**Answer: A)** Cumulenes with an even number of double bonds are chiral if appropriately substituted.

**Q2.** Allenes exhibit chirality due to:

A) The presence of a chiral center.

B) The perpendicular orientation of the p-bonded planes.

C) Free rotation around the central carbon.

D) Their linear structure.

**Answer: B)** The perpendicular orientation of the p-bonded planes.

**Q3.** Allenes can exhibit chirality when:

A) They have an even number of carbon atoms.

B) The terminal carbon atoms have identical substituents.

C) The two p-bonded planes are perpendicular, and the terminal carbons have different groups.

D) They contain a traditional chiral center.

**Answer: C)** The two p-bonded planes are perpendicular, and the terminal carbons have different groups.

**Q4.** A spiro compound is chiral when:

A) It has identical rings on both sides of the spiro center.

B) The two rings are different, leading to asymmetry.

C) There is free rotation around the spiro carbon.

D) It contains an internal plane of symmetry.

**Answer: B)** The two rings are different, leading to asymmetry.

5. Biphenyl compounds exhibit atropisomerism when:

A) They contain a chiral center.

B) They have bulky ortho-substituents preventing free rotation around the single bond.

C) They have identical rings that rotate freely.

D) They have a planar conformation.

**Answer: B)** They have bulky ortho-substituents preventing free rotation around the single bond.

# Unit 14 ❐ Topicity

## Structure



## 14.0 Objectives

By the end of this unit, students should be able to:

- Understand the Concept of Prostereogenic Centers
- Identify prochiral molecules and recognize the importance of such centers in stereochemical transformations.
- Define and differentiate between homotopic, enantiotopic, and diastereotopic ligands and faces.

- Assign pro-R and pro-S descriptors to distinguish prochiral ligands in a molecule.
- Define propseudo asymmetric centers and explain their role in stereochemistry.

## 14.1 Introduction

Stereochemistry helps us understand how atoms arrange in 3D space, affecting a molecule's properties. While some molecules are inherently chiral, others can become chiral through specific changes—these are called prostereogenic centers.

The concept of (pro)n-chirality helps identify such centers by analyzing the arrangement of ligands and faces. A key idea here is topicity, which classifies ligands as homotopic, enantiotopic, or diastereotopic and molecular faces as Re or Si. This unit introduces these fundamental concepts, providing an essential framework for understanding stereochemical transformations in organic chemistry.

## 14.2 Topicity

Topicity describes the geometric relationship between two or more ligands in a molecule. These ligands are called homomorphic (Greek homos meaning same and morphe meaning form ) if they are identical in all respect when separated from the rest of the molecule. That means, the homomorphic ligands must have same constitution and the relationship between the ligands is called topicity. Topicity also describes the relationship between two faces of a double bond (C =O / C = C) in a molecule. There can be two types of topicity homotopic and heterotopic.

## 14.3 Homotopic ligands and faces

In stereochemistry, homotopic ligands or faces are identical in all respects and remain indistinguishable under any condition. They do not create chirality when one is replaced with a different atom or group.

Homotopic Ligands:

Two or more ligands attached to the same atom are homotopic if:

- They are identical and interchangeable by symmetry (e.g., a rotation or reflection).

- Replacing one with a different group does not create a new stereocenter or change the molecule's symmetry.

**Example:** The two hydrogen atoms in CH4 (methane) are homotopic because replacing one with another atom (e.g., chlorine) does not lead to chirality.

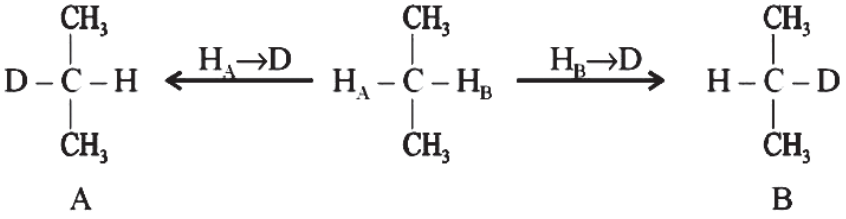
**Homotopic Faces:**

When a planar group (e.g., a carbonyl or alkene) has two indistinguishable faces, they are called homotopic faces. Example: In formaldehyde (H2C=O), both faces of the carbonyl group are homotopic because they are symmetric and indistinguishable.

Two criteria viz. substitution addition and symmetry criteria are applied to determine the topic relationships of ligand and faces.

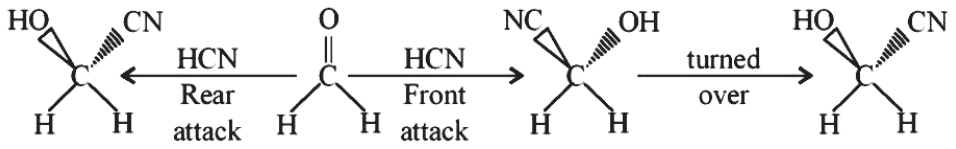
### 14.3.1 Substitution-addition criteria :

Two homomorphic ligands are homotopic if substitution of the first one and then the other by an achiral ligand not already present there produces the same product. Thus the two methylene hydrogen atoms in propane are homotopic since their respective substitution say by deuterium D leads to the same CH3CHDCH3.




A and B are the same since their constitution is same and there is no question of stereoisomerism because there is no stereogenic centre. So HA and HB are homotopic ligands.

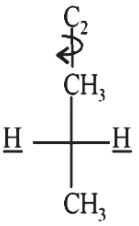
Two corresponding faces of a double bond (C=0 /C=C) are homotopic if addition of the same achiral reagent to either face produces the same product. Thus addition of HCN to either face of formaldehyde gives rise to the same cyanohydrin as shown below.



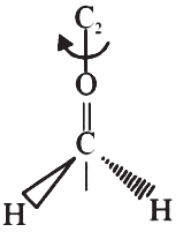

The two faces of the C = O double bond of formaldehyde are thus homotopic.

### 14.3.2 Symmetry criteria :

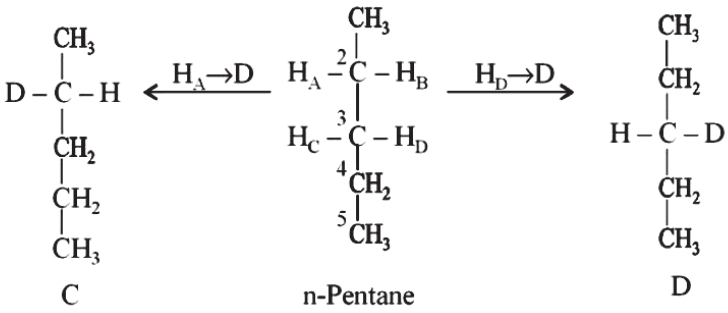
Homotopic ligands are connected by Cn and faces by C2 axis. Thus, two underlined hydrogens in propane are homotopic since they interchange their positions by the operation of a C2 axis.




Homotopic faces are also interchangeable by the operation of a C2 axis.

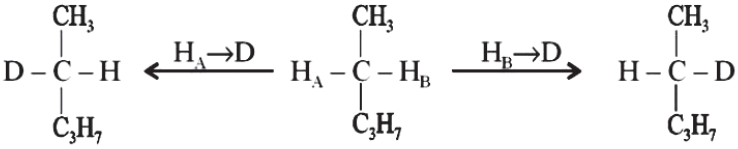



Thus two faces of the carbonyl group are homotopic. Two homomorphic ligands are heterotopic if substitution of the first one and then the other by a new achiral ligand produces different isomers. Depending on the nature of isomerism of the substituted products the heterotopic ligands can be classified as constitutionally heterotopic and stereoheterotopic. Constitutionally heterotopic ligands after substitution lead to a pair of constitutional isomers as for example H's at C(2 ) and H's at C(3) in n-pentane.



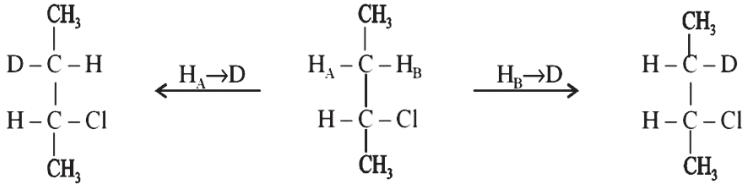

C n-Pentane D

Here, HA and HD so also HA and Hc are constitutionally heterotopic because they after substitution separately by another ligand lead to constitutional isomers. Here C and D are constitutional isomers. On the other hand, stereoheterotopic ligands after substitution generate different stereoisomers (stereoisomer should have a stereogenic centre) namely, enantiomers, diastereomers, E/Z or cis/trans-isomers. If enantiomers are produced after substitution, the ligands are called enantiotopic ligands as for example HA and HB at C(2 ) in n-pentane above.



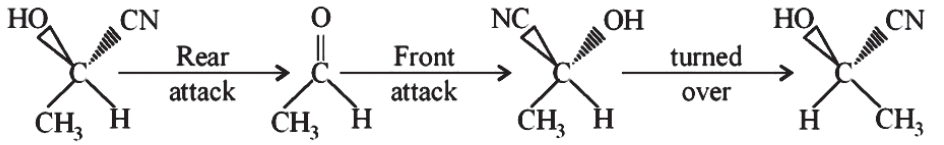

E n-Pentane F

E and F are enantiomers of each other. So HA and HB are enantiotopic ligands. If diastereomers are produced after substitution the ligands are called diastereotopic ligands. For example HA and HB in 2-chlorobutane.




G 2-Chlorobutane H

G and H are diastereomers of each other and hence HA and HB in 2-chlorobutane are diastereotopic ligands. The faces of a double bond (C = O / C = C) are heterotopic if addition of an achiral reagent to one or the other face will give stereoisomeric products ( i.e. enantiomers, diastereomers etc. ). Thus respective addition of HCN to the front and back faces of acetaldehyde produces a pair of enantiomeric lactonitriles as shown.



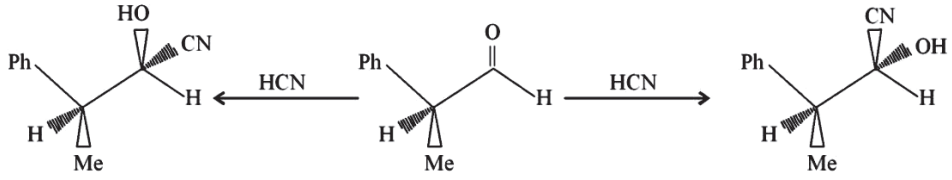

(S)
I

Acetaldehyde

(R)
J

I and J are enantiomers of each other suggesting that the two faces of carbonyl group in acetaldehyde are enantiotopic faces.

Similarly, addition of HCN to the front and back faces of a chiral aldehyde such as (S)-2-phenylpropanal gives ripe to two diastereomeric cyanohydrins K and L indicating that the two carbonyl faces are diastereotopic as shown.




K

(S)-2-Phenylpropanal

L

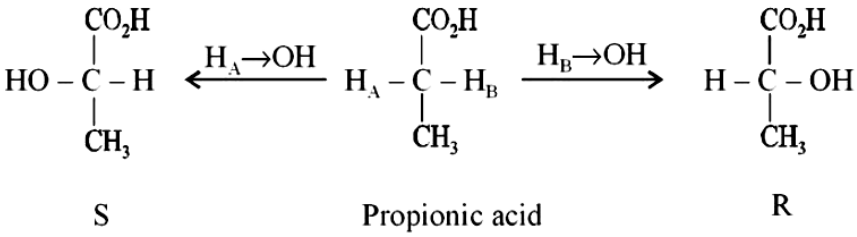
In symmetry term, enantiotopic ligands and faces are interconnected by a, i or Sn. That means an improper elements of symmetry is present in the molecule. Thus HA and HB in n-pentane interchange their positions through a plane indicating that they are enantiotopic. The two faces of C = O in acetaldehyde are interchangeable by a operation. So the two faces in acetaldehyde are enantiotopic. Diastereotopic ligands and faces are not related by any symmetry element.

## 14.4 Prostereoisomerism and prochirality

If replacement of one or the other of the two stereoheterotopic ligands by an achiral ligand or addition of an achiral reagent to one and the other faces of a carbonyl group in a molecule produces a stereogenic centre then the original centre or the faces are called prostereogenic centre or faces. The stereogenic centre may be or may not be chiral. If chiral then the prostereogenic centre is called prochiral centre and faces are called prochiral center and faces. These can be illustrated as follows.

### 14.4.1 Prochiral centre :

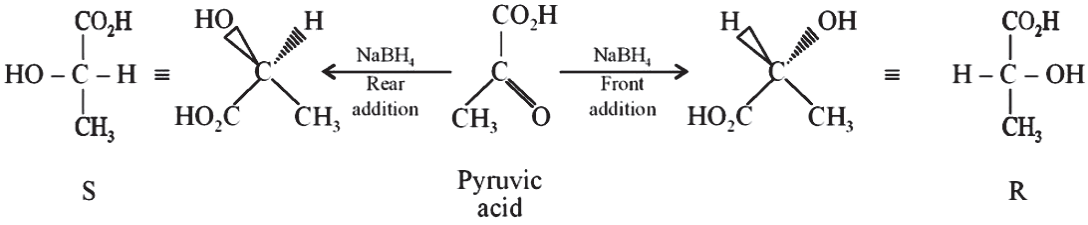
Respective replacement of stereoheterotopic ligands HA and HB in propionic acid by an achiral ligand OH produces a pair of enantiomeric lactic acids.




The C(2) centre in propionic acid is called prochiral centre.

### 14.4.2 Prochiral faces :

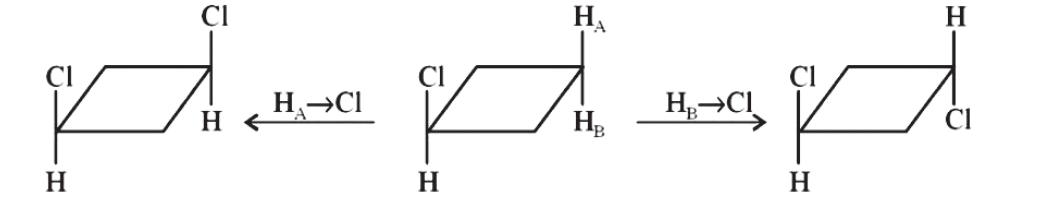
Respective addition of hydride (e g., from $NaBH_4$) to the two faces of carbonyl group of pyruvic acid can also produce enantiomeric lactic acids as shown.




Thus the carbonyl group in pyruvic acid is called prochiral and has two stereoheterotopic faces. So, prochirality refers to the existence of stereoheterotopic ligands or faces in a

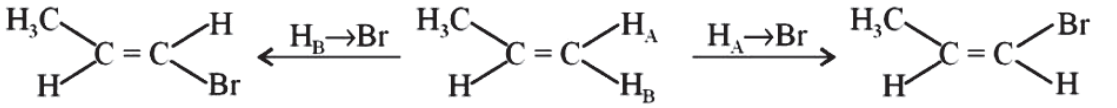
molecule such that proper substitution of one such ligand or addition to one such face in an achiral precursor generates chiral products. In some cases, respective replacement of one or other of the two heterotopic ligands or addition of one or other of the two heterotopic faces generates achiral diastereomers that contain stereogenic but not chiral element as shown in the following cases.

1) Respective substitution of heterotopic ligands HA and HB in chlorocyclobutane by an achiral ligand Cl leads to cis-and trans-l,3-dichlocyclobutane which are achiral diastereomers.




Cis- 1,3-dichlorocyclobutane Chlorocyclobutane trans-1,3-dichlorocyclobutane

2) Respective replacement of heterotopic ligands HA and HB in propene by an achiral ligand bromine produces (Z) and (E )-propenyl bromide which are also achiral diastereomers. The achiral diastereomers have no chiral centres or other chiral elements and hence are devoid of chirality. Thus, chlorocyclobutane and propenyl bromide exhibit prostereoisomerism but no prochirality




E-Propenylbromide propene Z-Propenyl bromide

## 14.5 Configurational descriptors for stereoheterotopic ligands

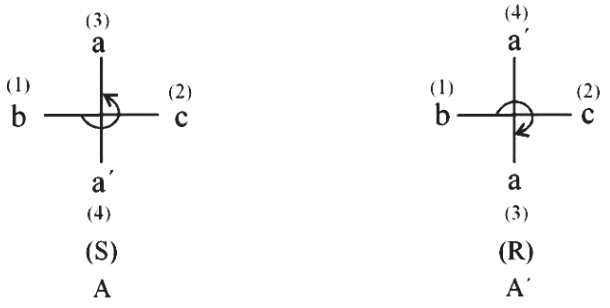
As the configurational descriptors R, S, E, Z etc are used to distinguish stereoisomers from one another, it is desirable to provide descriptors for stereoheterotopic ligands and faces. Descriptors for stereoheterotopic ligands are discussed below:

### 14.5.1 Molecules having a single prochiral centre:

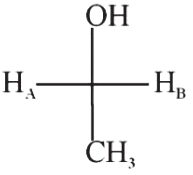
Molecules with a single prochiral centre such as Caabc can be represented by Fischer projection formula A as shown.


In order to assign descriptor to any one of the paired ligands (a, a), a hypothetical priority is given to one of the homomorphic ligand ‘a’ over the other ‘a’. It is assumed that the ligand b’ has higher priority' than the ligand 'c' while priority of the ligand ‘a’ may have higher, lower or in between with respect to the ligand b and ligand c. In the present case, let us assume that the ligand a has the lower priority than either of the ligand b or c.

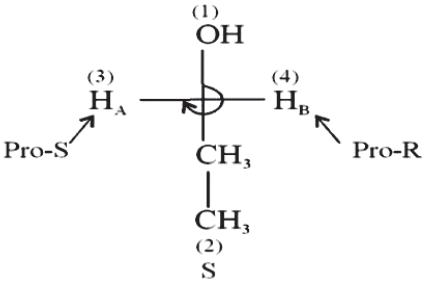
The priority order is thus b > c > a > a ' and A can exist as A and A '.




The chirality rule is then applied to A and A '. The configuration of the newly created hypothetical chiral centre in A is S and that in A ' is R. The ligand ‘a’ is called Pro-S in A and Pro-R in A '. The other ligand a ' is pro-R in A and pro-S in A ' by default. Let us take ethanol as an example.



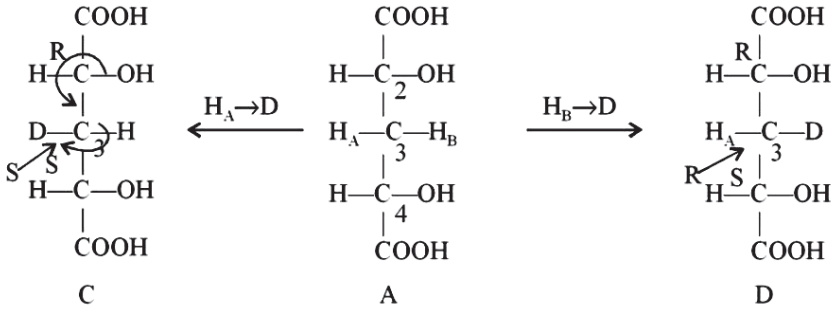
The hydrogen atoms HA and HB are enantiotopic. If hypothetical priority is given to HA over HB, the priority order is OH > CH3 > HA > HB. The hypothetical configuration of the newly created chiral centre would thus be 'S' as shown.




Hence, HA is pro-S, by default HB is pro-R.

### 14.5.2. Molecules containing pseudoasymmetric centre :

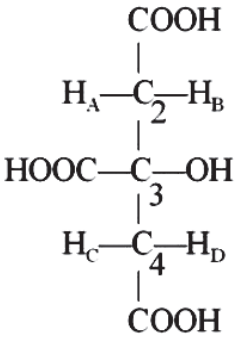
The two hydrogen atoms HA and HB at C(3) of 2,3-dihydroxyglutaric acid A are diastereotopic because their respective replacement by D gives rise to a pair of diastereomers C and D as shown below.




The C(3) in C and D is the pseudoasymmetric centre having S and R configuration respectively. The C(3) pseudoasymmetric centre is called pro-pseudoasymmetric centre. HA is thus pro-S and HB is pro-R.

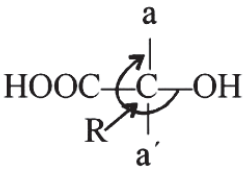
### 14.5.3. Molecules having more than one prochiral centre :

Citric acid has three prochiral centres C(2 ), C(3) and C(4 )

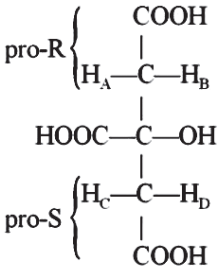



citric acid

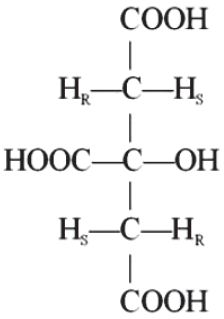
and both enantiotopic and diastereotopic H's. C(3) is prochiral because it bears two homomorphic ligands — CH2COOH, Citric acid can therefore, be represented as




The priority order is OH > COOH > a > a '. So the ligand a i.e. -CH2OOH is pro-R and a ' is pro-S. That is,

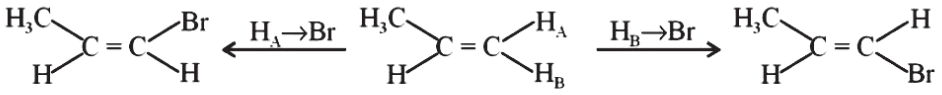



The topic descriptors to each of the H's can be assigned as HA is pro-S, HB ( proR ), Hc ( pro-S) and HD ( pro-R ). The subscripts of the group is now added to the individual subscripts of H's. The all four H's are thus labelled as




### 14.5.4. Molecules having prostereogenic but prochiral centre(s) :

Several prostereogenic molecules that do not have prochiral centre or centres but possess diastereotopic ligands give rise to achiral diastereomers on substitution. Such ligands are called pro-Z, pro-E, pro-cis, pro-trans etc. depending on the nature of the diastereomers produced. This is illustrated with propene as an example.

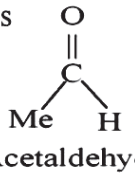



cis-(Z)-propenyl-bromide — propene — trans-(E)-propenyl-bromide

### 14.5.5. Descriptors for stereoheterotopic faces :

Enantiotopic faces of a molecule is two-dimensionally chiral. If one looks at the plane of a n face and finds that the three ligands arranged in a priority order is clockwise, the face is called Re (Rectus meaning right ), if anticlockwise, the face is called Si (Sinister meaning left). Example:

i) C=O faces

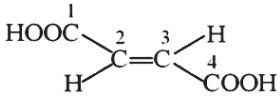



Acetaldehyde

Priority order is O > Me > H.

So Re (front) and Si (rear).

ii) C=C faces



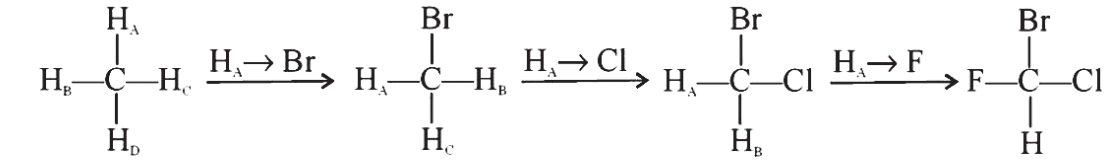

Fumaric acid

2 Re, 3 Re (front)

2 Si, 3 Si (rear)

## 14.6 Summary

- Prostereoisomerism is a property of some molecules due to which they are capable of producing stereoisomers. Such type of molecules possess either enantiotopic or diastereotopic ligands or aces.
- Molecules containing enantiotopic ligands or faces can give rise to two enantiomers and are prochiral. The homomorphic ligands at the prochiral centre are designated as proR and pro-S. The prochiral faces are designated as Re and Si face. The ligand at prostereogenic centre are assigned with pro-r and pro-s descriptors.
- When an achiral molecule on such transformation, gives a chiral molecule as mentioned above the original molecule is called prochiral. If there occurs two or more such transformations, the original molecule is called pro-pro, pro-pro-pro and so on. Example

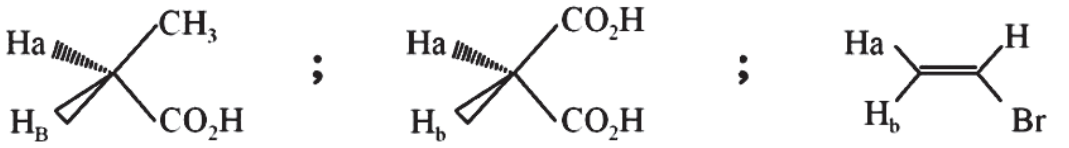



pro-pro-prochiral pro-prochiral prochiral chiral

## 14.7 Exercises

### A. Sample Questions

1. Classify the indicated pairs of atoms as homotopic, enantiotopic or diastereotopic:




2. Give an example of a molecule the heterotopic ligands of which are prostereogenic but not prochiral.

3. Define prostereogenic centers and explain their significance.
4. What is topicity, and how does it classify ligands and molecular faces?
5. Explain the difference between homotopic and heterotopic ligands.
6. What is the role of symmetry criteria in determining homotopic ligands and faces?
7. Differentiate between constitutionally heterotopic and stereoheterotopic ligands with examples.
8. What is the difference between enantiotopic and diastereotopic ligands?
9. Explain how the faces of a carbonyl group in formaldehyde are homotopic.
10. In propane, why are the two methylene hydrogen atoms considered homotopic?
11. Explain the enantiotopic nature of hydrogen atoms in n-pentane.
12. Why do the two faces of the carbonyl group in acetaldehyde lead to different enantiomers upon reaction with HCN?
13. Describe how a prochiral center is generated in propionic acid.
14. How does the substitution of ligands in chlorocyclobutane lead to diastereomers?
15. Why is citric acid considered to have multiple prochiral centers?

**B. Multiple Choice Question (MCQ)**

1. What does the term "topicity" describe in stereochemistry?

   A) The absolute configuration of a chiral center

   B) The relationship between identical ligands in a molecule

   C) The method of determining the polarity of molecules

   D) The ability of a molecule to rotate plane-polarized light

   **Answer: B)** The relationship between identical ligands in a molecule

2. In citric acid, the prochiral center at C(3) has two homomorphic -CH2COOH groups. How are they designated?

   A) Pro-E and Pro-Z

   B) Pro-cis and Pro-trans

C) Pro-R and Pro-S

D) R and S

**Answer: C)** Pro-R and Pro-S

3. If replacing one of the two hydrogen atoms in ethanol leads to the formation of a chiral center, the hydrogens are called:

A) Homotopic

B) Enantiotopic

C) Diastereotopic

D) Constitutional

**Answer: B)** Enantiotopic

4. In formaldehyde (H2C=O), the two faces of the carbonyl group are:

A) Homotopic

B) Diastereotopic

C) Enantiotopic

D) Prochiral

**Answer: A)** Homotopic

5. Which of the following is an example of homotopic ligands?

A) The two hydrogen atoms in CH4 (methane)

B) The two hydrogen atoms in 2-chlorobutane

C) The two hydrogen atoms in propane at different carbon positions

D) The two chlorine atoms in trans-1,2-dichloroethene

**Answer: A)** The two hydrogen atoms in CH4 (methane)

6. Which of the following best defines a prostereogenic center?

A) A carbon atom with four different groups attached

B) A center that can become chiral through a single substitution

C) A carbon-carbon double bond with different substituents

D) A center that remains chiral even after substitution

**Answer: B)** A center that can become chiral through a single substitution

7. What does the term "prochiral" refer to?

A) A molecule that is already chiral

B) A molecule that cannot become chiral

C) A molecule that can become chiral by replacing one of its identical ligands

D) A molecule with only one stereocenter

**Answer: C)** A molecule that can become chiral by replacing one of its identical ligands

8. The pro-R and pro-S descriptors are used to distinguish:

A) Homotopic ligands

B) Stereogenic centers

C) Enantiotopic ligands in a prochiral molecule

D) Configurations of chiral centers

**Answer: C)** Enantiotopic ligands in a prochiral molecule

9. Which of the following descriptors is used to differentiate enantiotopic faces in a planar system?

A) R/S

B) E/Z

C) Re/Si

D) Pro-R/Pro-S

**Answer: C)** Re/Si

10. In a trigonal planar molecule, how do you determine whether a face is Re or Si?

A) Assign priorities to the three substituents using the Cahn-Ingold-Prelog rules and check the clockwise or counterclockwise order

B) Check whether the molecule has a stereogenic center

C) Measure the bond angles between the ligands

D) Identify if the molecule is chiral or achiral

**Answer: A)** Assign priorities to the three substituents using the Cahn-Ingold-Prelog rules and check the clockwise or counterclockwise order

# Unit 15 ❐ Conformational analysis

## Structure

## 15.0 Objectives

After going through this unit learners be able to-

- Understand Conformational Nomenclature of organic compounds.
- Analyze Energy Barriers in Conformational Changes in organic compounds.
- Compare the Stability of Conformers.
- Perform Conformational Analysis of Simple Alkanes.
- Study the Conformations of Substituted Compounds.
- Explore the Conformations of Conjugated Systems.

## 15.1 Introduction

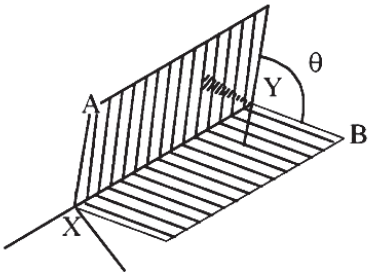
It was believed in early days that there was free rotation about single bond in saturated acyclic compounds. In reality, the rotation is not completely free but restricted because of steric interactions between atoms/groups attached to the single bond. Thus when two tetrahedral carbons are joined to each other, there is rotation about carbon carbon single bond and as they rotate there creates different geometries of the same molecule and all such geometries are called conformations. That is, an infinite number of geometrical arrangements that are arising out of rotation about carbon carbon single bond in a molecule are called conformations.

Since the energy a molecule (potential energy) depends on the geometry' it possesses so one conformation differ in energy from the other. Thus, as we rotate carbon carbon single bond the energy of the system changes with the change of dihedral angle (0) or

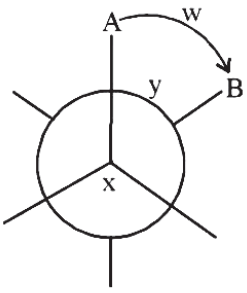
torsion angle (co). We have already mentioned dihedral angle in section 3.1.

## 15.2 Torsion angle (ω)

Although torsion angle (ω) is similar to dihedral angle (0) but it has slightly different implication. Dihedral angle is the angle between two intersecting planes A-X-B and X-Y-B in a nonlinear molecule of the type A-X-Y-B while torsion angle is the angle subtended by A and B across the bond X-Y as shown below.



Dihedral angle



Torsion angle

Dihedral angle has magnitude only but torsion angle has both magnitude and direction. The conformations of a molecule are separated by low energy barrier and are easily interconvertible. They are observed spectroscopically but never separated from one another.

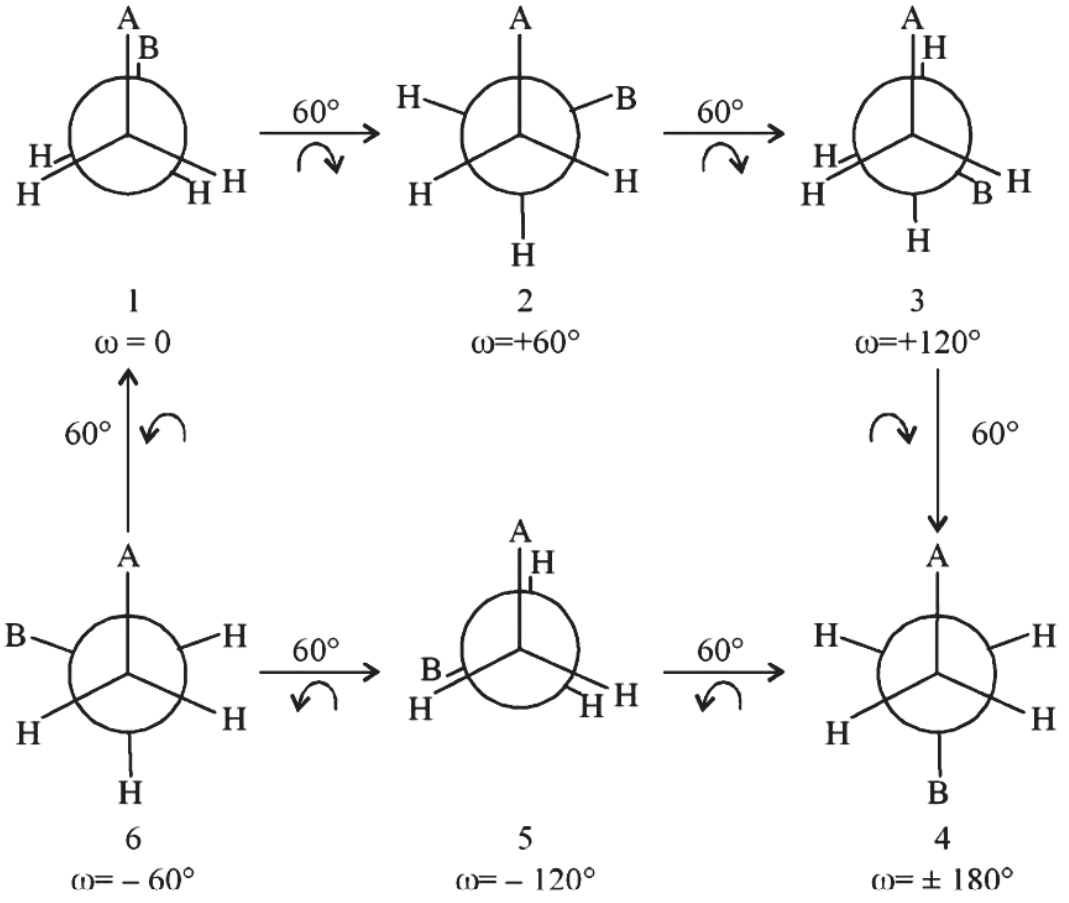
## 15.3 Conformation

The conformations that correspond to energy minima are called conformers. That is, the conformations which lie in the minima in the energy profile diagram are called conformers. In fact, staggered conformations with energy minima are called conformational isomers or conformers.

Conformational energy (AG°): Difference in potential energy between the most stable conformer and the designated less stable one of a molecule is called its conformational energy. The conformational energy i.e. the energy difference between the gauche and anti conformer of n-butane in liquid stable is about 2.4 KJ mol-1.

It is useful to designate the various conformations obtainable from 1,2-disubstituted

ethane of the type A-$CH_2$-$CH_2$-B (where A and B are alkyl groups or halogen atoms) by rotation around C-C bond from w = 0° to ±180°. A and B are the fiducial groups.



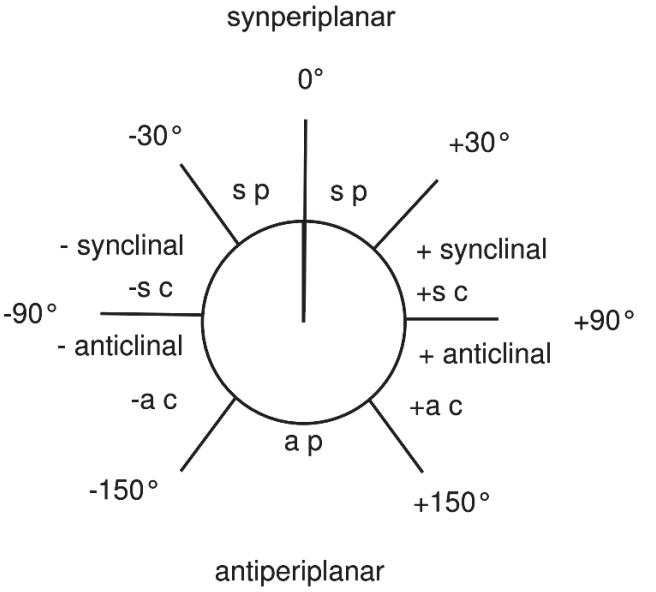

The conformations 1, 3, and 5 having torsion angles 0° (zero), +120° and -120° respectively are called eclipsed and 2, 4, and 6 with torsion angles +60°, +180° or -180° and -60° are called staggered. The staggered conformations 2 and 6 are conveniently considered to be gauche and 4 anti. So the conformational designation syn or eclipsed is used with co = 0° and anti or staggered with co = ±180°.

## 15.4 Conformational nomenclature

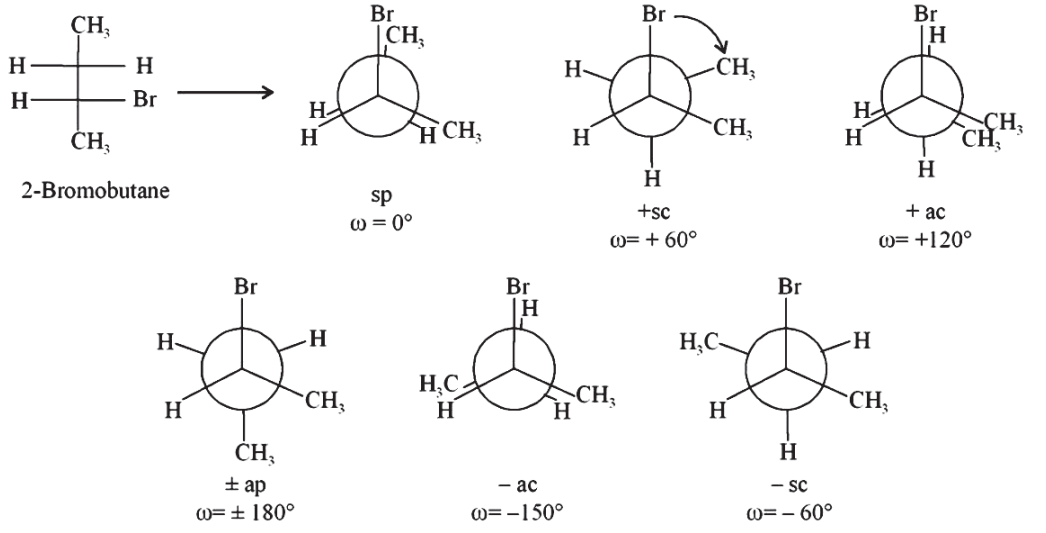
The name of conformations such as eclipsed, gauche or skew and anti are used with torsion angles 0°, 60° and 180° respectively. In most cases, the value of torsion angle is no longer a multiple of 60° but can have intermediate values. Klyne and Prelog ( 1960 )

described a general system of nomenclature for conformations based on torsion angles, which may not necessarily be a multiple of 60°. But since the exact values of torsion angles are not known for most of the molecules in their gaseous or liquid states so the torsion angles are not known for most of the molecules in their gaseous or liquid states so the torsion angles are expressed within a range. Klyne Prelog nomenclature for conformations based on approximate torsion angles ( to) are listed in the following Table and Figure Specifying Torsion Anglesthereof.

| Torsion angle (ω) | Conformation designation | Symbol |
|---|---|---|
| 0° to + 30° | + synperiplanar | + sp |
| + 30° to + 90° | + synclinal | + sc |
| + 90° to + 150° | + anticlinal | + ac |
| + 150° to + 180° | + antiperiplanar | + ap |
| + 180° to – 150° | – antiperiplanar | – ap |
| – 150° to – 90° | – anticlinal | – ac |
| – 90° to – 30° | – synclinal | – sc |
| – 30° to 0° | – synperiplanar | – sp |




Example : Designation of conformations of 2-bromobutane is given below



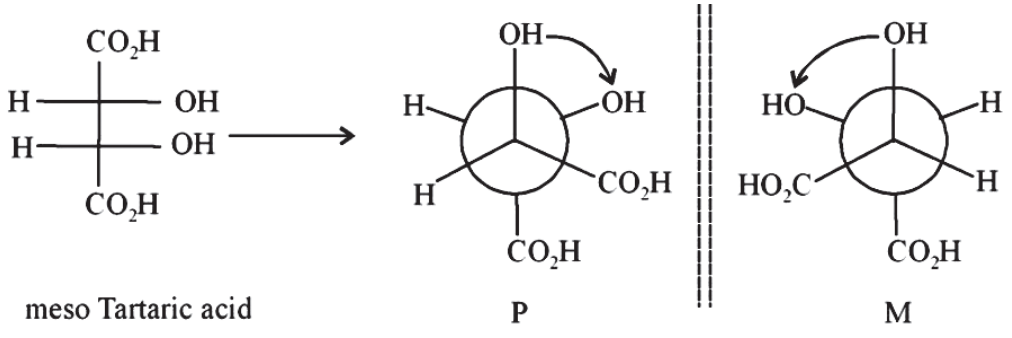
## 15.5 P/M descriptors

The P/M descriptors are used to describe the helicity (twist) of axially chiral molecules. These descriptors are particularly useful for differentiating enantiomers in molecules that exhibit axial chirality, such as biaryls, allenes, and certain conformational isomers of acyclic molecules.

In the case of meso-tartaric acid, which is normally achiral due to an internal plane of symmetry, conformational isomerism can lead to chiral conformations. The two enantiomeric conformations of meso-tartaric acid can be assigned P (plus) or M (minus) descriptors based on their helical twist:

- **P (Plus) Descriptor:** If the molecule follows a right-handed (clockwise) helical twist when viewed from a reference point.
- **M (Minus) Descriptor:** If the molecule follows a left-handed (counterclockwise) helical twist when viewed from a reference point.

This is illustrated bellow with two enantiomeric conformational isomers of meso tartaric acid .




## 15.6 Energy barrier to rotation

The difference in the maximum energy of the transition state between the two interconverting conformers and the minimum energy of the conformer is known as the energy barrier to rotation, that is, one conformer has to surpass the rotational energy barrier to convert into the other.

## 15.7 Concept of torsional and steric strain

A molecule exists in a dynamical equilibrium in a number of conformations which differ from one another in potential energy and in torsion angles. These distinct molecular species separated by energy barriers are called conformational isomers or conformers. The energy of a conformer depends on its geometry it possesses. The parameters that have connection with molecular geometry are bond length, bond angle, torsion angle and internuclear distance between nonbonded atoms or groups in the conformer. Any deviation of these parameters from ideal geometry causes the conformer to increase energy called steric energy or steric strain. The total steric strain (Es) of a conformer can thus be expressed as the sum of all these four energy functions as:

$$Es = E(/) + E(\alpha) + E(\omega) + E(r)$$

where, E(/) = strain due to bond stretching or compression

$E(\alpha)$ = strain due to bond angle deviation

$E(\omega)$ = torsional strain

E(r) = strain due to nonbonded interaction.

### 15.7.1 Torsional strain :

Excess strain developed in a molecule due to deviation of the torsion angles from their ideal value over that of the lowest energy conformer is known as torsional strain. The torsional strain is believed to originate from the electronic factor. That is, the bonding and nonbonding electrons on adjacent atoms repel each other to different extent depending on torsion angles. The bond pair-bond pair repulsion along with the steric interaction between the substituents on the adjacent atoms at a particular torsion angle develops a strain which is called torsional strain. The torsional strain is maximum at $\omega = 0°$, 120° and -120° for the eclipsed conformations and minimum at $\omega$ = 60°, 180° and -60°for the staggered conformations.

### 15.7.2 Strain due to nonbonded interaction:

When two nonbonded atoms approach each other the interaction between them is attractive though small at long distances. This is called van der Waals force of attraction (or London force). The attractive force increases in magnitude with decrease in distance between the

atoms and becomes maximum when the distance is minimum. Every atom has an effective size called van der Waals radius and the minimum distance at which the van der Waals force of attraction is maximum is equal to the sum of the van der Waals radii of the two atoms. If the distance between the two atoms is less than the sum of their van der Waals radii, the force of attraction is converted into force of repulsion called the vander waals force of repulsion. This is also known as steric repulsion between nonbonded atoms and increase the potential energy of the system.

## 15.8 Relative stability of conformers

The relative stability of conformers depends on various factors, including Steric effect, dipole interactions and intramolecular hydrogen bonding,

### 15.8.1 Steric effect :

Steric effect arises from the close approach of two non-bonded atoms or groups in a system giving rise to considerable van der Waals forces (attractive or repulsive). When the distance between them is less than the sum of their van der waals radii, they repel each other sterically by van der Waals force of repulsion and the conformer (conformational isomer ) is thereby destabilised on steric ground. But if the distance between them is equal to the sum of their van der Waals radii, they attract each other by van der Waals force of attraction and the conformer is thereby stabilised.

### 15.8.2 Dipole-dipole interaction :

Unlike poles stabilise a conformer by force of attraction while like poles destabilise a conformer by force of repulsion. Dipole-dipole interaction stabilises the anti conformer.

### 15.8.3 Hydrogen-bonding :

A hydrogen bond is formed between an electron-rich heteroatom such as oxygen, nitrogen etc. and an electron-deficient hydrogen as shown below.

$$\overset{\delta-}{X}-\overset{\delta+}{H}\ldots:\overset{\delta-}{Y}$$

Hydrogen bond

Intramolecular H-bonding stabilises the gauche conformer

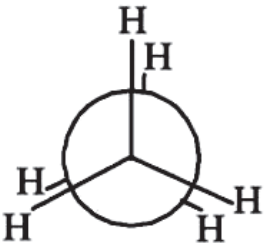
## 15.9 Conformational Analysis

We have mentioned earlier that as we rotate carbon carbon single bond energy of the system changes with the change of dihedral angle (0) or torsion angle (to) in a conformer.

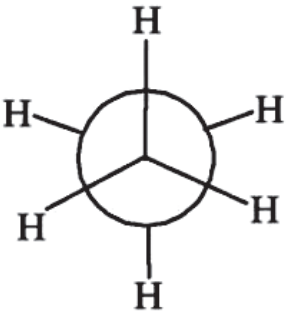
Conformational analysis also deals with the reactivity of various conformations. Conformational analysis of ethane, propane, n-butane, 2-methylbutane and 2,3-dimethylbutane will be discussed qualitatively in terms of torsional strain and nonbonded interaction while conformational analysis of acyclic molecules containing heteroatom will be discussed qualitatively in terms of dipole-dipole interaction and intramolecular H-bonding in addition to steric and torsional strain.

### 15.9.1 Conformational analysis of Ethane, CH3CH3

Ethane is the simplest of all the system. It has two extreme conformations, eclipsed and staggered as shown below.

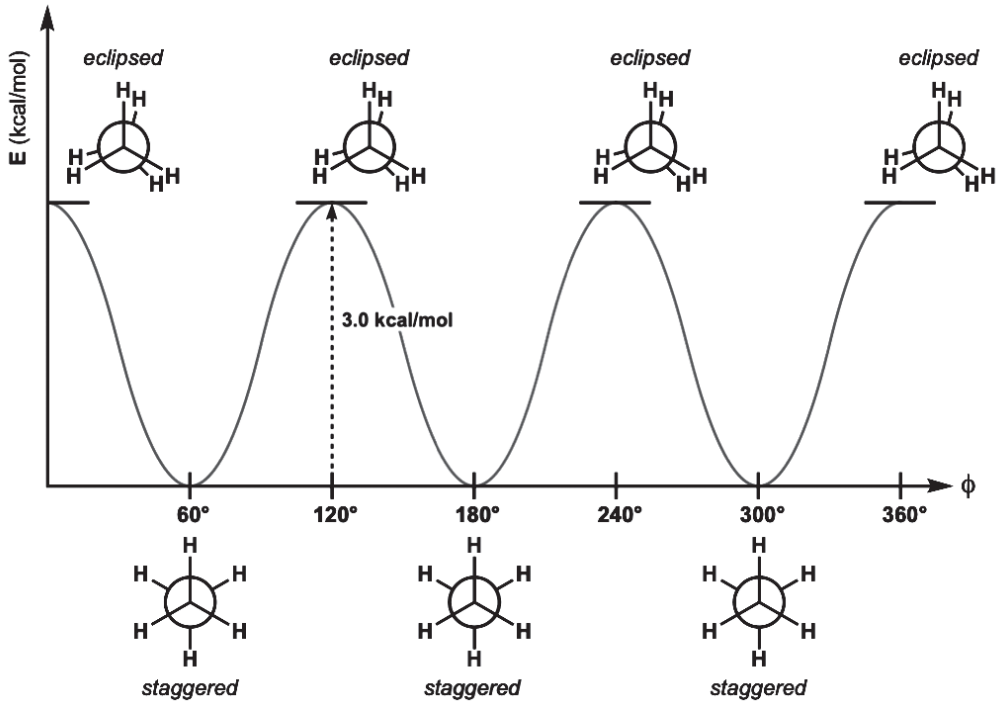



Eclipsed




Staggered

Variation of potential energy of conformation as a function of torsion angle is shown in the following Energy profile diagram.




The energy barrier of rotation in ethane is around 3 Kcal.mol-1or 12 kJ mol-1. The molecule will prefer to exist in the staggered form because it has lower energy than the eclipsed form. So 99% of the molecule will exist in the staggered form but does not prohibit the molecule from undergoing rotation. The contributions to the energy barrier of rotation are due to;

i) steric reason,

ii) bond opposition strain, and

ii) unfavourable overlap of bond orbitals.

i) The distance between the nonbonded pairs of hydrogen atoms in eclipsed conformation is 230 pm which is just within the van der Waals radii of hydrogen atoms (240 pm ). This accounts for only 10% of the total energy barrier.

ii) The bond opposition strain arising out of bond pair-bond pair repulsion in the eclipsed form contributes a little to the energy barrier in ethane.

iii) The major contribution to the energy barrier comes from the unfavourable overlap interaction between the filled $\sigma_{C-H}$ bond orbitals in the eclipsed conformation and favourable interaction between filled $\sigma_{C-H}$ bonding and empty $\sigma^*_{C-H}$ antibonding orbitals in the staggered conformation.

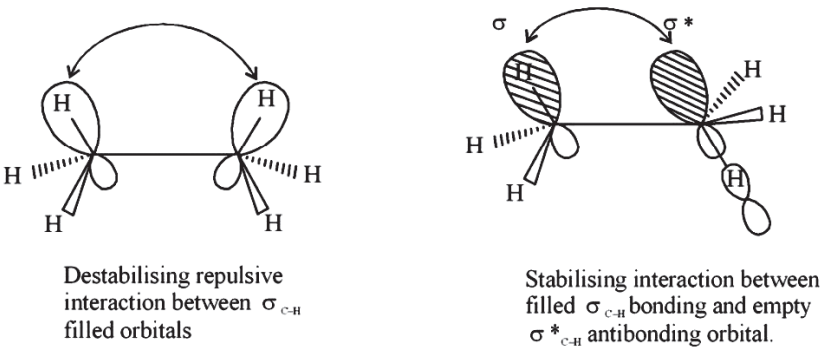
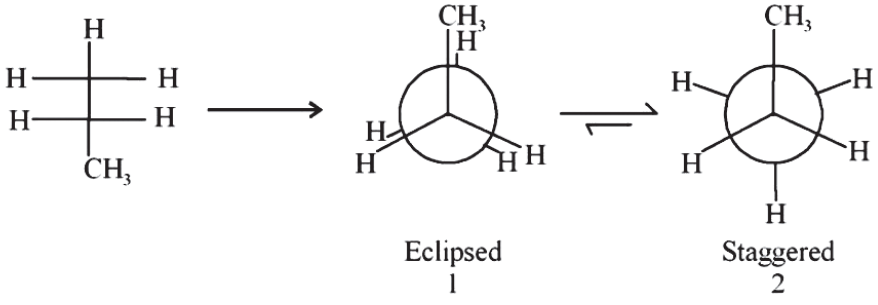



**Figure:** Orbital interactions

The real picture is probably a combination of all three effects. In the energy profile diagram of ethane there are three equivalent energy maxima corresponding to three H/H eclipsing interactions in the eclipsed conformation and three equivalent energy minima corresponding to six H/H gauche interactions in the staggered conformation. As the H/H gauche interactions are generally not taken into consideration, so a value of 4 kJ mol-1 is attributed to each of the H/H eclipsing and has been said to be due to torsional strain.

### 15.9.2 Conformational analysis of Propane (CH3CH2CH3):

The eclipsed and staggered conformations of propane that exist in equilibrium are shown as



The energy profile diagram of propane is very similar to that of thane but the energy barrier for rotation in propane is slightly higher than in ethane.

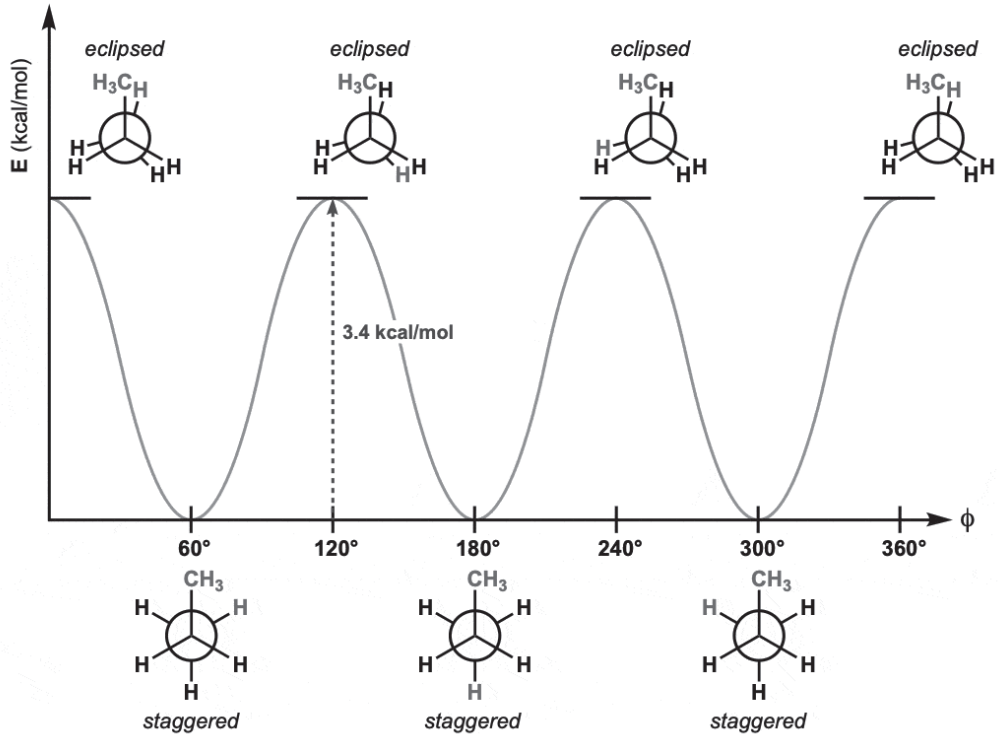



Fig: Energy profile diagram of propane

As the H/H gauche and CH3/H gauche in the staggered conformation of propane are not considered so the energy barrier in propane is due to two H/H eclipsing and one CH3/H eclipsing interaction in the eclipsed form. Since a value of about 4 kJ mol-1 is attributed to each of H/H eclipsing so an energy value of about 6 kJ mol-1 is attributed to CH3/H eclipsing interaction in eclipsed propane.

### 15.9.3 Conformational analysis of n-Butane ($CH_3$ - $CH_2$ – $CH_2$ - $CH_3$):

Conformational analysis means first of all we have to identity each form and then to analyse the energy barrier of rotation.

Conformations: Rotation about C(2)-C(3) bond in n-butane in 60° interval gives six conformations 1-6, which are represented in its potential energy diagram as shown below.

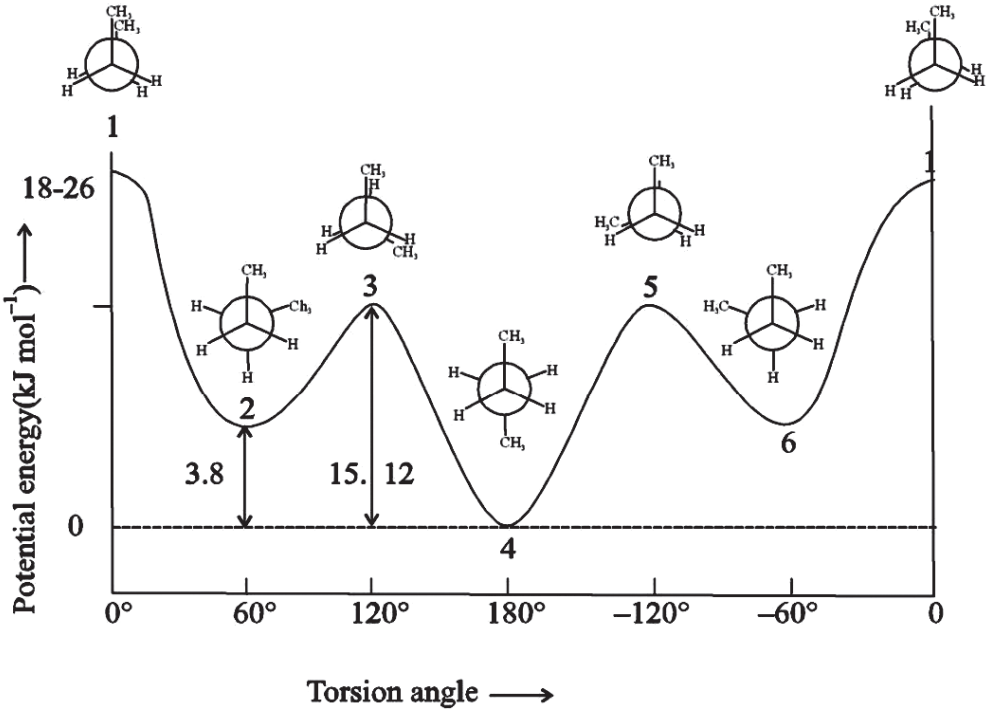



**Figure:** Potential energy diagram of n-butane (gas phase)

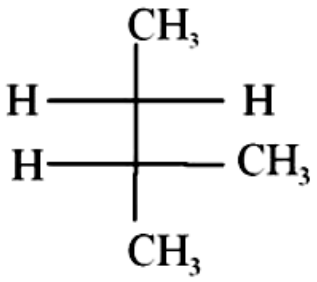
There are two different types of eclipsed forms, one corresponding to the fully eclipsed 1 in which two methyl can eclipse each other and one corresponding to the partially eclipsed 3 or 5 where methyl and hydrogen can eclipse each other. The fully eclipsed form 1 belongs to C2V point group and is achiral. The partially eclipsed conformer (conformational isomer) 3 forms non-superimposable mirror image with 5 and hence 3 and 5 exist as a pair of enantiomers. Similarly, there are two different types of staggered forms, one 4 in which methyl methyl are totally anti to each other at OJ = 180°, the other 2 or 6 in which methyl methyl torsion angle is +60° or-60°. These staggered conformations are called gauche conformations. The gauche form 2 with +60° is called P-gauche and the other 6 M-gauche.

The anti form belongs to C2i, point group and is achiral. The gauche conformations with +60° and -60° have a C2 axis each passing through the mid-point of C(2 )-C(3) and bisecting the dihedral angle between two methyls and belong to C2 point group. They are therefore, chiral and exist as a pair of enantiomers.

**Energy barrier to rotation :**

The potential energy diagram of n-butane exhibits three maximum energy conformations 1, 3 and 5 of which 1 with two eclipsed methyls and two pairs of eclipsed H's has the highest energy. As the two methyls are eclipsing each other so there will be a strong van der Waals repulsive interaction. Moreover, there is bond opposition strain but methyl methyl steric interaction contributes a major portion of energy to the eclipsed form. The experimental value amounts to 18-26 kJ mol-1. The conformers 3 and 5 are enantiomeric to each other. In each enantiomeric form 3 or 5, there are two CH3/H eclipsing and one H/H eclipsing which raises the energy barrier to about 16 (6×2+4×l ) kJ mol-1. The experimental value is 15.12 kJ mol-1. The conformer with to = 180° has minimum energy because it is devoid of CH3/CH3 van der Waals repulsive interaction. Its potential energy is arbitrarily taken as zero and is the most stable conformer. The gauche conformers with to = +60° or -60° have potential energy of about 3.8 kJ mol-1 due to van der waals repulsive interaction between two methyl groups about that of the anti conformer and is commonly known as the gauche butane interaction. At room temperature (25°C), n-butane (gaseous phase ) contains 70% of the anti conformer 4 and 15%. P-gauche and 15% M-gauche.

**15.9.4 Conformational analysis of Methylbutane:**




Rotation around C(2 )- C(3) bond in 2-methylbutane in 60° intervals generates six conformations 1-6 which are represented in the following energy profile diagram.

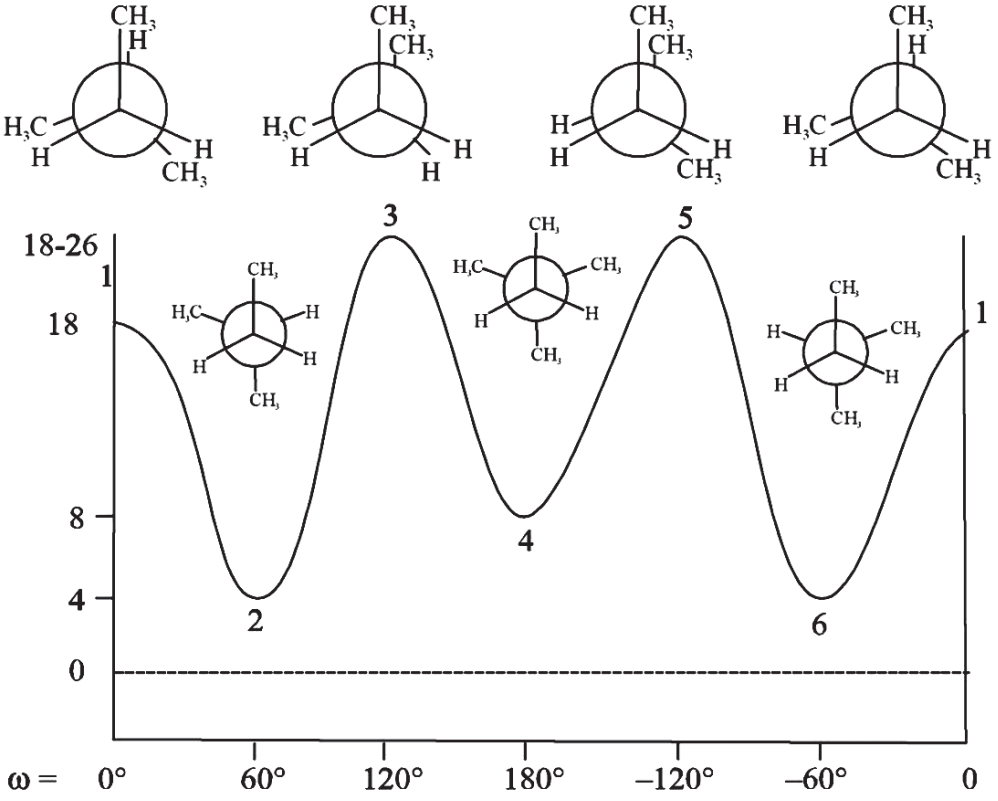



**Figure:** Energy profile diagram of 2-methylbutane

Each of the eclipsed conformations 1, 3 and 5 are at the energy maxima but conformations 3 and 5 involving $CH_3/CH_3$, $CH_3/H$ and H/H eclipsing will however, have higher energy than 1 involving three $CH_3/H$ eleclipsing only. On the other hand, each of the staggered conformations 2 and 6 involving one CH3/CH3 gauche butane interaction will be at lower energy than the anti form 4 involving two CH3/CH3 gauche butane interactions.

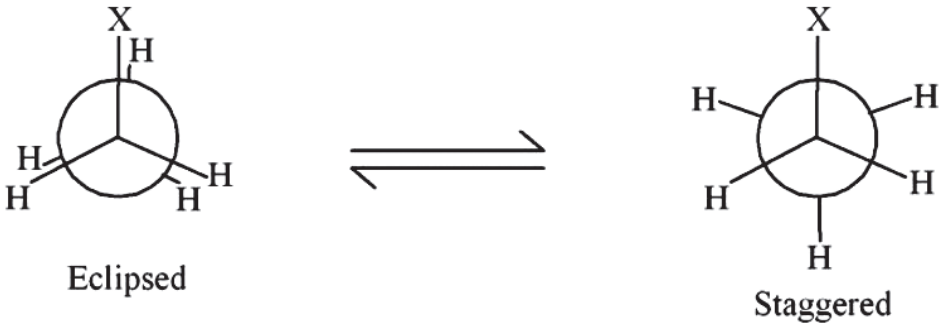
So considering steric factor P.E. of the conformations: 3 = 5 > 1 > 4 > 2 = 6

### 15.9.5 Conformation of haloalkanes :

The conformations of a large number of haloalkanes have been studied by IR, Raman and microwave spectroscopy some of which are discussed below.

### 15.9.5.1 Conformational analysis of ethyl halides: $CH_3CH_2X$ (X = Cl, Br, I)

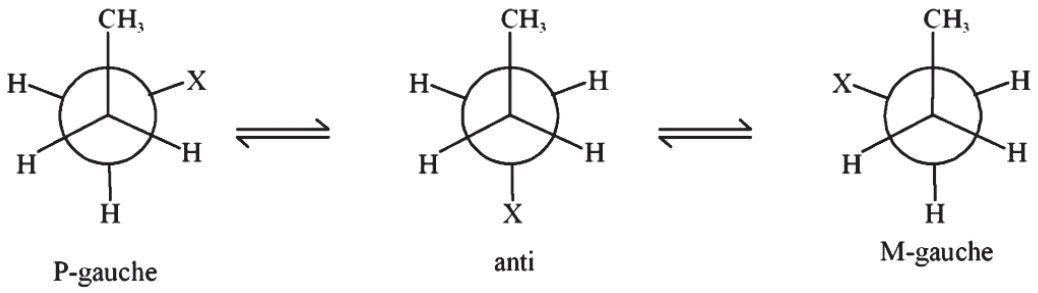
Conformations of alkyl halides $CH_3CH_2X$ where X = Cl, Br, I is similar to that of ethane and exist in eclipsed and staggered forms as shown below.




In this case, the energy barrier to rotation can be explained as follows. The C-X bond length in ethyl halides increases as the size of X increases. With the size increasing the bond length also increases which in turn takes the halogen atom further away from the hydrogen. As a result, van der Waals interaction does not alter appreciably. The energy barrier (14-15 kJ mol-1) in ethyl halides thus almost remains constant. The slightly higher values of energy' barrier relative to that of ethane is due to increased van der Waals radii of halogen compared to hydrogen.

### 15.9.5.2 Conformation of 1-halopropane:

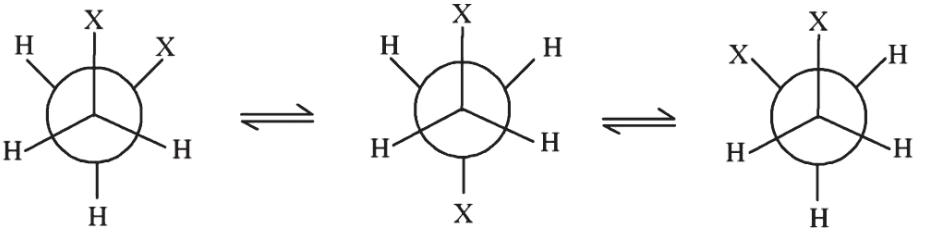
An achiral anti and two enantiomeric gauche conformers of CH-CH2CH2X exist in equilibrium as shown below



The gauche form is preferred over the anti because of stabilising interaction between the partially negatively charged X and positive end of CHV This has been confirmed by electron diffraction studies. Such stabilisation is absent in the anti conformer because of larger distance between X and CH3.

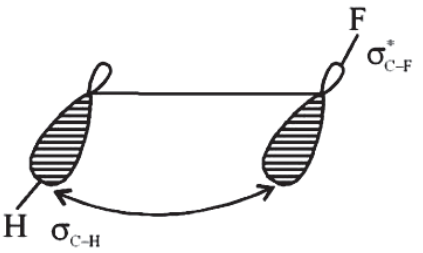
**15.9.5.3 Conformational analysis of 1,2-dihaloalkanes:**

1,2-Dihaloethane, X-$CH_2$-$CH_2$- X ( X = Cl, Br) can exist in gauche and anti conformations as shown below.

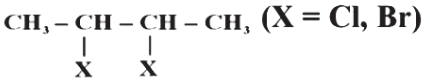



In this case, the anti form is preferred over gauche in the gaseous state. The reason for less preferred gauche is not purely steric but also due to strong dipole-dipole repulsion between C-X dipoles in the gauche conformation. In the liquid state or in polar solvents, however, dipole-dipole repulsion decreases appreciably because of high dielectric constant of the medium and the population of the gauche conformers increases accordingly. At room temperature, 1,2-dichloroethane contains 73% of the anti and 23% of the gauche as against 70% anti and 30% gauche for n-butane. The anti and gauche conformers of 1,2-dichloroethane are however, almost equally populated in the liquid state.

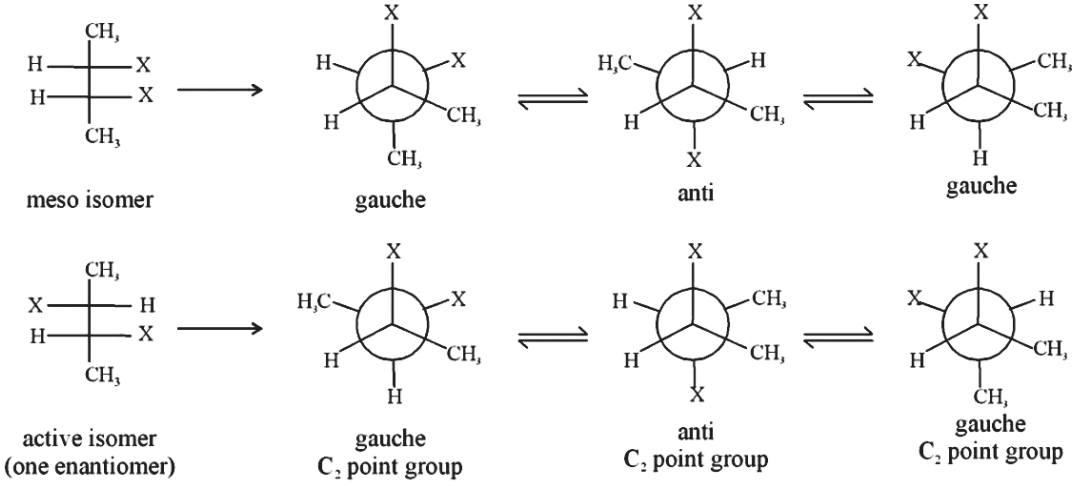
1,2-Dichloro and 1,2-dibromoethane exhibit a similar type of potential energy diagram as that of n-butane but the situation is different in 1,2-difluoroethane. In 1,2-difluoroethane the gauche conformer is more stable than the anti. This can be rationalised in terms of hyperconjugation. The destabilising dipole-dipole and van der waals repulsive interactions between two fluorine atoms are outweighed by stabilising hyperconjugative interactions. Interaction of the type $FCH_2 - CH_2F \leftrightarrow \bar{F}CH_2 = CHF\overset{+}{H} \leftrightarrow \overset{+}{H}CHF = CH_2\bar{F}$ which is equivalent to overlap of $\sigma_{C\text{-}H}$ with $\sigma^*_{C\text{-}H}$ (Gauche effect ) as shown below:


### 15.9.5.4 Conformations of 2,3-dihalobutane




The diastereomeric meso and active isomers of 2,3-dihalobutane exist in several conformations as shown below.

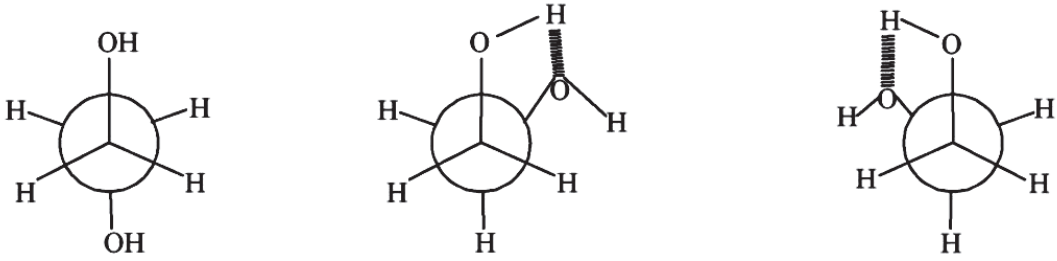



In this case, the most populated anti conformer of the meso isomer is stabilised by two $CH_2$/X van der Waals force of attraction. On the other hand, dipole-dipole repulsive force between two X atoms destabilises the most populated gauche forms of the active isomer. The meso isomer is therefore, more stable than the active isomer of 2,3-dihalobutane.

### 15.9.6 Conformations of 1,2-diol and 1 ,2-holohvdrin :

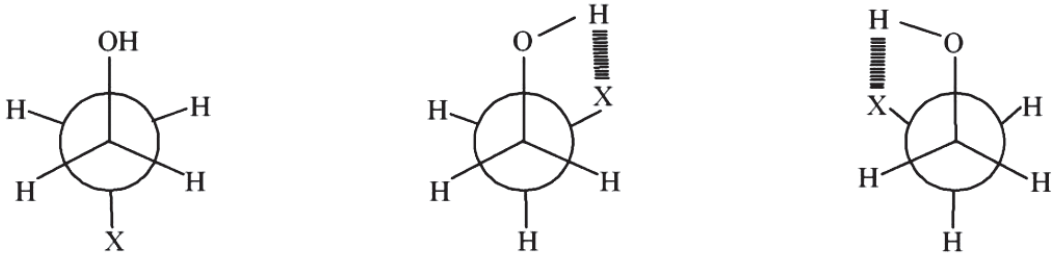
Molecules of the type HO-CH2-CH2-X where X = OH, halogen give a number of conformations the gauche form of which is found to be more stable than the anti. In this case, apart from the steric and torsional strain, additional interactions like intramolecular H-bonding and dipole-dipole repulsion need to be considered. Intra-molecular H-bonding tend to stabilise the gauche conformation while dipole-dipole repulsion forces the molecule to assume an anti conformation.

#### 15.9.6.1 Ethylene glycol




Anti P-gauche M-gauche

**15.9.6.2 Halosubstituted ethanol**, HO - $CH_2$ - $CH_2$ - X (X = cl, Br, F)

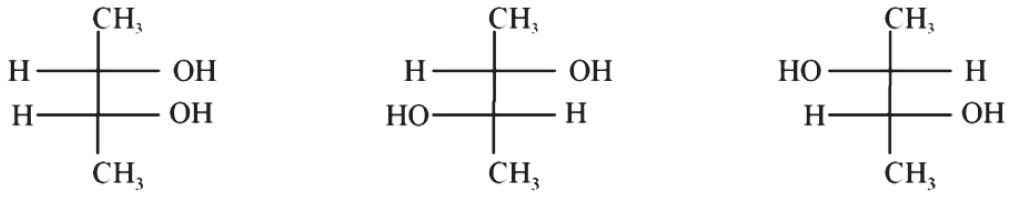



Anti P-gauche M-gauche

Ethylene glycol or halohydrin such as halogen substituted ethanol adopts gauche conformations because of strong intramolecular H-bonding.

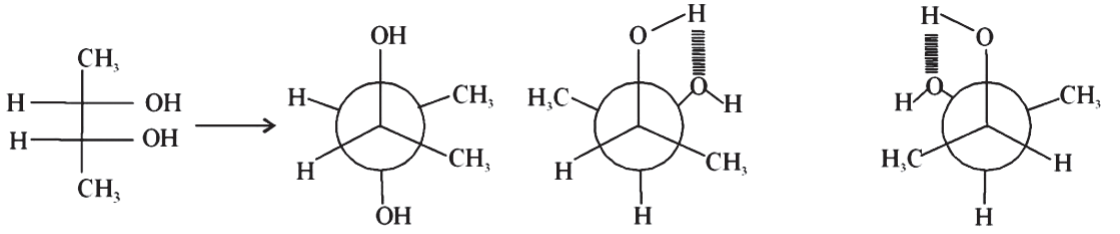
### 15.9.6.3 Butane-2,3-diol

Butane-2,3-diol exists in two diastereomeric forms, the meso and the optically active isomers as shown below.



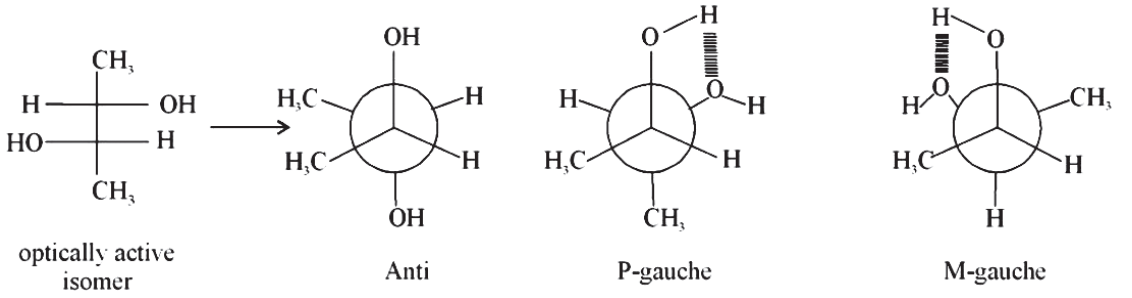

meso isomer Optically active isomers

The meso isomer has three preferred conformations of which the enantiomeric gauche forms predominate over the anti due to the formation of intramolecular H-bond and are equally populated.




meso isomer Anti P-gauche M-gauche

The optically active isomer (one enantiomer shown) also consists of three preferred conformations of which the gauche forms predominate over the anti due to intramolecular H-bonding but are unequally populated . The intramolecularly H-bonded gauche form with two methyls anti is favoured over that with two methyls gauche.




The gauche conformer with two methyls anti of the active isomer is preferred over the gauche conformer of the meso isomer.

## 15.10 Summary

- Due to rotation about carbon carbon single bond the torsion angle changes continuously generating various conformations. These conformations are designated according to the specific value of torsion angle. Thus conformations are named as eclipsed, gauche and anti with torsion angle to = 0°, 60° and 180° respectively. In most cases, the torsion angle value is no longer a multiple of 60° but can have intermediate values. Klyne and Prelog used a general system of nomenclature for conformations based on torsion angle which may not necessarily be a multiple of 60°. This system of nomenclature has been discussed in the text.
- Conformations that correspond to energy minima are called conformational isomers or conformers and that correspond to energy maxima are the transition states between two conformers. Rotation about a single bond involve overcoming a rotational energy barrier to interconvert one conformer into the other.
- Conformational analysis of some acyclic hydrocarbons are discussed qualitatively in terms of torsional strain and nonbonded interaction while those with hetero atoms are discussed qualitatively in terms of dipole-dipole interaction and intramolecular H-bonding along with steric and torsional strain.

## 15.11 Exercises

### A. Sample Questions

1) Explain the terms dihedral angle and torsion angle. Draw +sc conformation of 1-chloropropane

2) What do you mean by conformational isomers, conformer and diastereomers? Illustrate with examples.

3) What is gauche butane interaction? Draw the staggered conformations of 2-methylbutane for rotation about the C(2)-C(3 ) bond. Why do they have different energies? Explain.

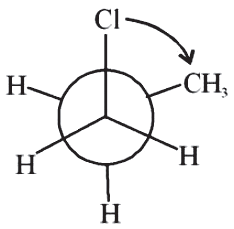
4) Explain why 2-chloroethanol exists exclusively in the gauche conformations in liquid state.

5) What is the most populated conformer of optically active 2,3-dichlorobutane? Is it an asymmatric or dissymmetric molecule? Explain.

6) The conformational free energy of 1,3-butadiene is 12 kJ mol-1 but the energy barrier is about 28 kJ mol-1. Explain.

**Answer**

1) For the 1st part see text

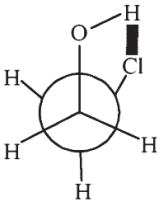


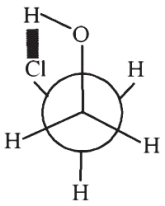

+ sc for ω = +30° to +90°

2) See text,

3) See text

4) because of strong intramolecular H-bonding




5) dissymmetric

6) s-trans is preferred over s-cis by about 12 kJ mol-1 owing to steric repulsion in the s-cis form. This is conformational free energy of 1,3-butadiene. The energy barrier to rotation about C(2 )- C(3) single bond ( i.e. interconversion of the s-cis and s-trans forms) is about 28 kJ mol-1

**B. Additional question**

1. What is the difference between dihedral angle and torsion angle?
6. What is conformational energy, and how is it related to molecular stability?
7. How does the energy difference between gauche and anti conformers of n-butane affect its stability?
8. What are the different types of staggered and eclipsed conformations in 1,2-disubstituted ethane?
11. What is the energy barrier to rotation in a molecule?
12. Define and differentiate between torsional strain and steric strain.
13. Why does the eclipsed conformation of ethane have higher energy than the staggered conformation?
16. Describe the energy profile diagram for the conformational analysis of ethane.
17. What are the different conformations of n-butane, and which one is the most stable?
18. Why do gauche conformations of n-butane have higher energy than the anti conformation?
21. How does dipole-dipole interaction influence conformational stability?

22. Explain how intramolecular hydrogen bonding stabilizes the gauche conformation.

23. What stabilizing interaction is present in the gauche conformer of 1-halopropane?

**C. Multiple Choice Questions (MCQs)**

1. What are different geometries of the same molecule due to rotation around a carbon-carbon single bond called?

   A) Configurations

   B) Resonance structures

   C) Conformations

   D) Tautomers

   **Answer: C)** Conformations

2. What is the main difference between a dihedral angle and a torsion angle?

   A) Torsion angle has both magnitude and direction, while dihedral angle has only magnitude

   B) Dihedral angle has both magnitude and direction, while torsion angle has only magnitude

   C) Both are the same with different names

   D) Torsion angle applies only to cyclic compounds

   **Answer: A)** Torsion angle has both magnitude and direction, while dihedral angle has only magnitude

3. What is the name of the conformation when the torsion angle is 0°?

   A) Staggered

   B) Gauche

   C) Eclipsed

   D) Anti

   **Answer: C)** Eclipsed

4. In n-butane, which conformation has the highest energy?

A) Anti

B) Gauche

C) Fully eclipsed

D) Staggered

**Answer: C)** Fully eclipsed

5. What type of strain arises due to repulsion between nonbonded atoms in a molecule?

A) Torsional strain

B) Steric strain

C) Bond angle strain

D) Resonance strain

**Answer: B)** Steric strain

6. Which conformation is most stable in ethane?

A) Eclipsed

B) Staggered

C) Gauche

D) Syn

**Answer: B)** Staggered

7. Which conformation of n-butane is present in the highest percentage at room temperature?

A) Gauche

B) Fully eclipsed

C) Anti

D) Eclipsed

**Answer: C)** Anti

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