PREFACE

In a bid to standardise higher education in the country, the University Grants Commission (UGC) has introduced Choice Based Credit System (CBCS) based on five types of courses: core, generic discipline specific elective, and ability/ skill enhancement for graduate students of all programmes at Elective/ Honours level. This brings in the semester pattern, which finds efficacy in tandem with credit system, credit transfer, comprehensive and continuous assessments and a graded pattern of evaluation. The objective is to offer learners ample flexibility to choose from a wide gamut of courses, as also to provide them lateral mobility between various educational institutions in the country where they can carry acquired credits. I am happy to note that the University has been recently accredited by National Assessment and Accreditation Council of India (NAAC) with grade "A".

UGC (Open and Distance Learning programmes and Online Programmes) Regulations, 2020 have mandated compliance with CBCS for all the HEIs in this mode. Welcoming this paradigm shift in higher education, Netaji Subhas Open University (NSOU) has resolved to adopt CBCS from the academic session 2021-22 at the Under Graduate Degree Programme level. The present syllabus, framed in the spirit of syllabi recommended by UGC, lays due stress on all aspects envisaged in the curricular framework of the apex body on higher education. It will be imparted to learners over the six semesters of the Programme.

Self Learning Materials (SLMs) are the mainstay of Student Support Services (SSS) of an Open University. From a logistic point of view, NSOU has embarked upon CBCS presently with SLMs in English. Eventually, these will be translated into Bengali too, for the benefit of learners. As always, we have requisitioned the services of the best academics in each domain for the preparation of new SLMs, and I am sure they will be of commendable academic support. We look forward to proactive feedback from all stake-holders who will participate in the teaching-learning of these study materials. It has been a very challenging task well executed, and I congratulate all concerned in the preparation of these SLMs.

I wish the venture a grand success.

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Vice-Chancellor

Netaji Subhas Open University

Subject: Honours in Chemistry (HCH)
Choice Based Credit System (CBCS)
Course : Organic Chemistry-I
Course Code : CC-CH-04

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UG : Chemistry
(HCH)

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Unit 1 ❑ Hybridisation

Structure

1.0 Objectives

- After going through this unit a learner will acquire knowledge about various bonding and physical properties of molecules such as :
- Valance Bond Theory, hybridisation and orbital pictures for bonding.
- Different electronic displacements, effects and resonance energy.
- Qualitative idea about molecular orbital pictures, HOMO, LUMO etc.
- Physical properties like bond distances, bond angles, bond angle strain, polarisation and influence of hybridization on these bond properties.

1.1 Introduction

Organic Chemistry is a highly organized discipline. It is the study of the relationship between the structures of molecules and their reactions. We will beginour study with the type of bonding and structural aspects of the molecules. Compounds can be broadly divided into two asses, ionic and covalent compounds. Ionic compounds are composed of positively and negatively charged ion; which are held together by electrostatic forces. In contrast to the ionic compounds in covalent compounds, the molecules are formed by the sharing of electron air(s) between the constituent atoms. The bonds formed by sharing of

pair(s) of electron sare alled covalent bonds. Since in organic compounds, the bonds formed bycarbon atom are ovalent in nature. The intensity of covalency in the bonds of organic compounds are responsible for some of the physical properties such as melting and boiling points, solubility, and reactivity. Chemical bonds also influence other properties such as crystal symmetry and leavage of bonds. Stronger bonds between atoms make them more difficult to separate and in general, stronger chemical bonds result in higher melting and boiling points, and smaller co-efficients of expansion. We will study some features of the covalent bonding in light of Valence bond theory. We will then explain shapes of molecules using the concept of hybridization, resonance, hyperconjugation and so on.

1.2 Bonding, Structure and Properties

1.2.1 Brief discussions

Bonding is the way the atoms are held together. The bonding and structure of substances determine their properties. The structure is the way the atoms are arranged relative to each other. There are two major types of structure giant and molecular. Giant structures go on indefinately, whereas molecular structures are made up of groups of atoms. Three main factors are important in deciding the properties of a substnace.

i. The type of basic particles it contains.

(such as sodium chloride), then it will conduct electricity when molten in water. To be solouble in water, the substance must contain either ions of polar.

ii. The way the basic particles are bonded together.

The bonding may be ionic, covalent, metallic or weak intermolecular forces. The stronger the bonds, the higher the melting/boiling point and the hardness of the substance. For example silica, SiO_2, has strong covalent bonds linking every atom to several others forming a giant covalent structure. The atoms in silica are very hard to separate, and therefore it is very hard and difficult to melt. Carbon dioxide on the other hand has strong covalent bonds between the C and O atoms, but only weak intermolocular forces between each CO_2 molocules are therefore easily separated and so CO_2 has a low melting/boiling point.

iii. The way the particles are arranged relative to one another.

The particles may be arranged in 1-dimensional plains (such as in polymers). 2-dimensional sheet (like clays) or in many different kind of 3-dimensional arrangements. Graphite is arranged in 2-dimensional sheets, and so its layers can move past each other (think of writing using a graphite pencil). Diamond, on the

other hand, has a giant 3-dimensional structure and is the hardest natural substance.

1.2.2 Valence bond theory

Valence bond theory (VBT) was proposed by Heitler and London in 1927 and it was extended by Pauling and Slater (1931).

The VBT is based on the following concepts.

i) The pairing and electrons

ii) Neutralization of opposite electron spins.

iii) Overlapping of orbitals to give a common electron density to the combining atoms which results in the formation of a chemical bond.

Postulates of VBT:

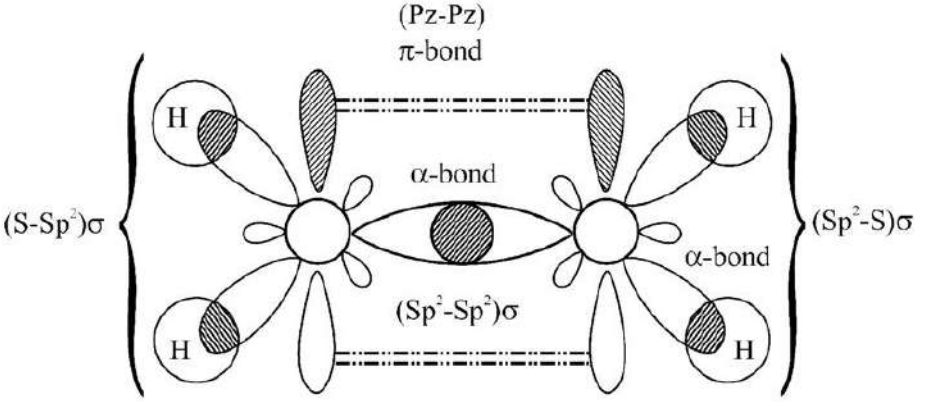
i) The overlapping of two half-filled valence orbitals of two different atoms result in the formation of the covalent bond.

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 (σ) and a pi bond. (π).

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



Limitations of VBT :

i) It fails to explain the tetravalency of carbon.

ii) This theory does not discuss the electrons' energies.

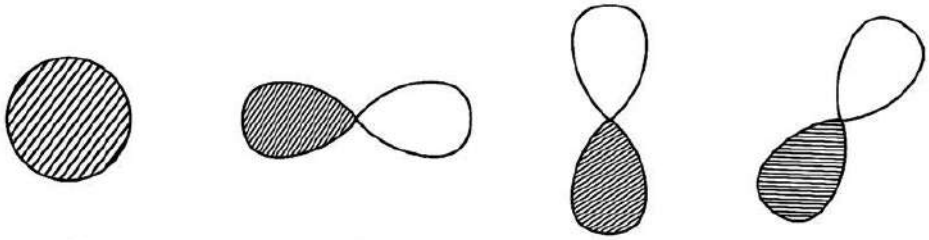
iii) The assumptions are about the electrons being localized to

iv) It fails to explain the magnetic and spectroscopic properties of molecules.

1.2.3 Concept of hybridisation

The process of mixing of pure orbitals to give a set of new equivalent orbitals is termed as hybridization. For the fact that all the C — H bonds in molecules like methane are identical.

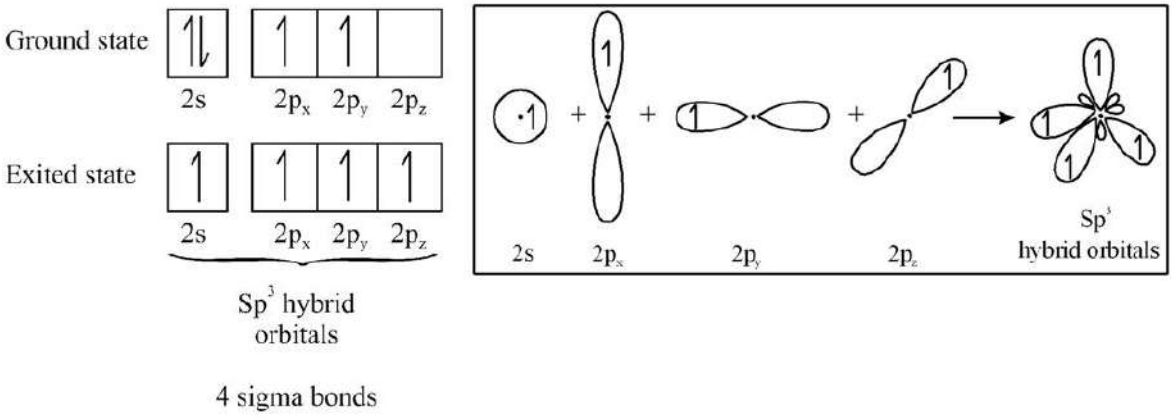
The individual orbitals (pure orbitals) look something like this.



2S $2p_x$ $2p_y$ $2p_z$

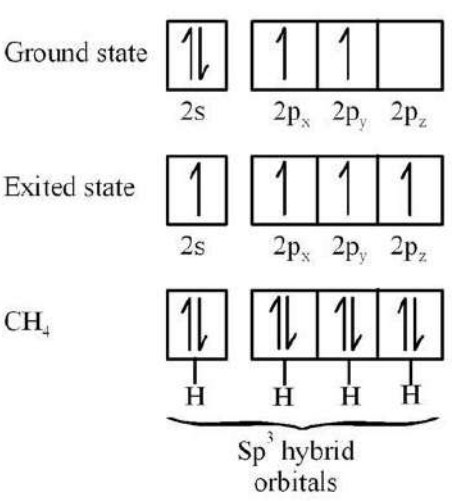
Types of Hybridisation : sp^3—Hybridisation

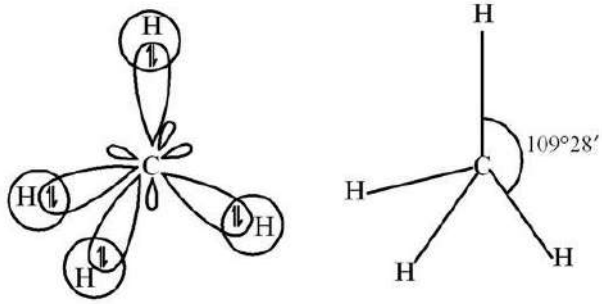
In sp^3 hybridization, one 2s and three 2p orbitals of excited carbon intermix together and form 4 hybrid orbitals which are oriented in tetrahedral geometry in space around the carbon atom. Each sp^3 hybrid orbital is occupied by one electron.



single bonds with other atoms in tetrahedral geometry. The bond angles are usually equal to or nearer to 109°28′.

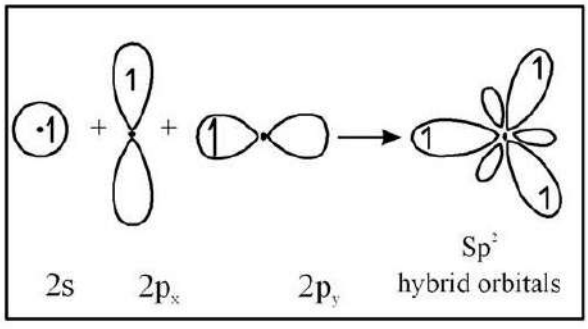
e.g. methone molecule. CH_4.

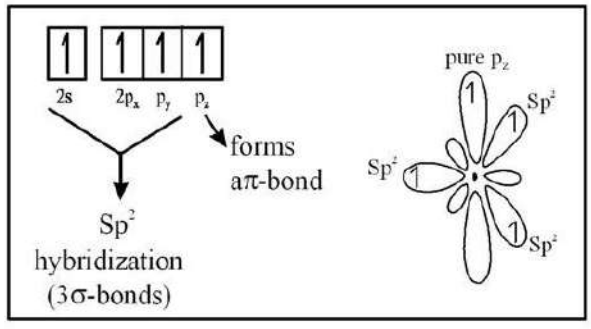




sp^2-Hybridisation

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

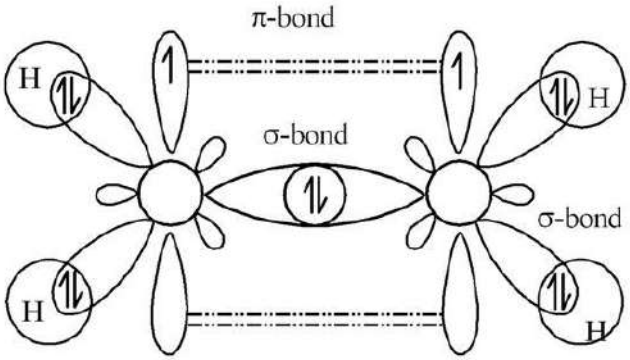


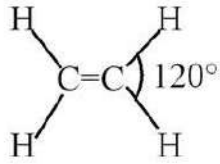


Each sp^2 hybrid orbital is occupied by one electron. The remaining pure 2p orbital with one electron lies at right angle to the plane of hybrid orbitals.

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

e.g. ethylene molecule, C_2H_4.

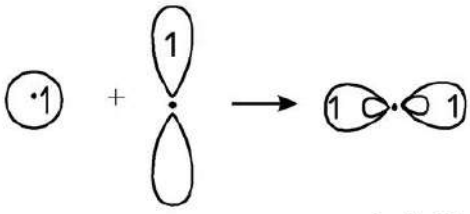




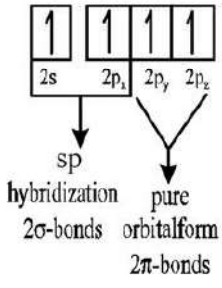
planar geometry

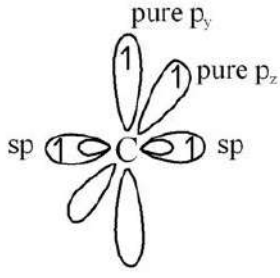
sp-Hybridisation

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

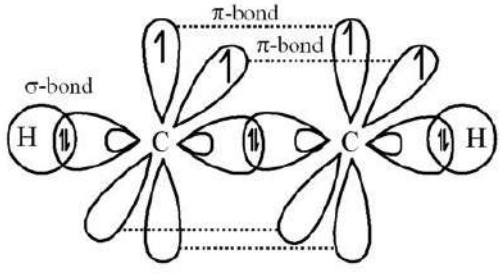


s orbital p orbital sp hybrid orbitals





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



180°

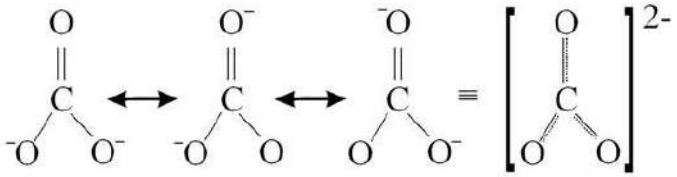
H—C≡C—H

Linear geometry

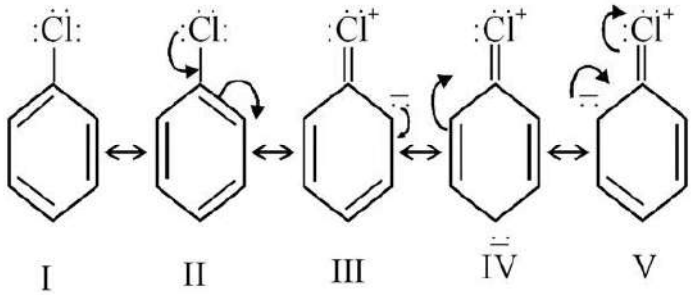
1.2.4 resonance

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 streucture, then the true structure is said to be resonance hybrid and phenomenon is called resonance.

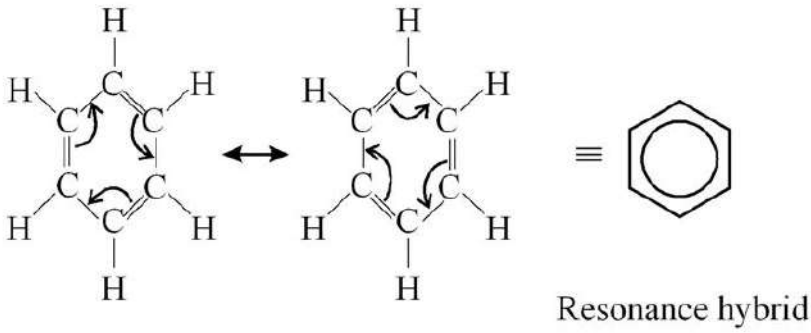
All contributing structures are known as canonical forms or resonance structures. The resocance of carborate ion is shown below.



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



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



Canonical forms

Resonance hybrid

1.2.5 Hyperconjugation (no bond resonance or Baker-Nathan Effect)

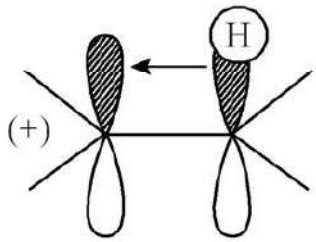
The delocalization of σ-electrons or lone pair of electrons into adjacent p-orbital or P-orbital is called hyperconjugation.

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

Conditions for hyperconjugation: There must be a α-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 a-hydrogen.

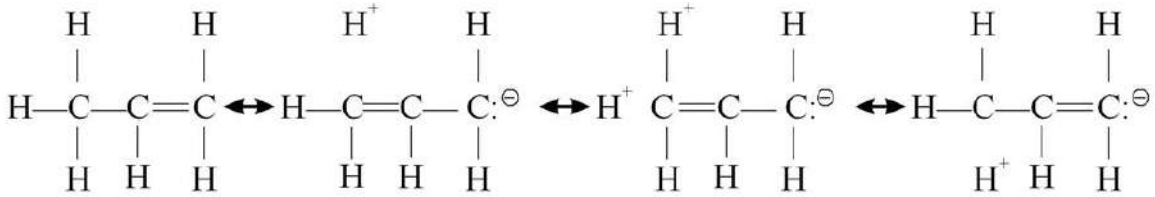
Illustration of Hyperconjugation: A 'α' bond can stabilize an adjacent or neighboring carfbocation by donating electrons to the vacant p orbital. The positive charge is delocalized or spread out. This stabilizing effect is known as hyperconjugation. It opernates through C-H and C-C bonds.



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

The electrons of C-H 'σ' bond spends sometime at the vacant 'P' orbital of Carbocation.

e.g., In propene, the σ-electrons of C-H bond of methyl group can be delocalized into the π-orbital of doubtly bonded carbon as represented below.



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

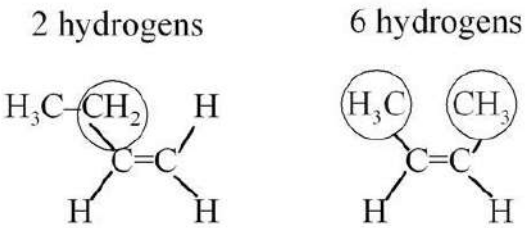
In the contributing structures: (II), (III) & (IV) or propene, there is no bond between

an α-carbon and one of the hydrogen atom. Hence the hyperconjugation is also known as ***"no bond resonance".***

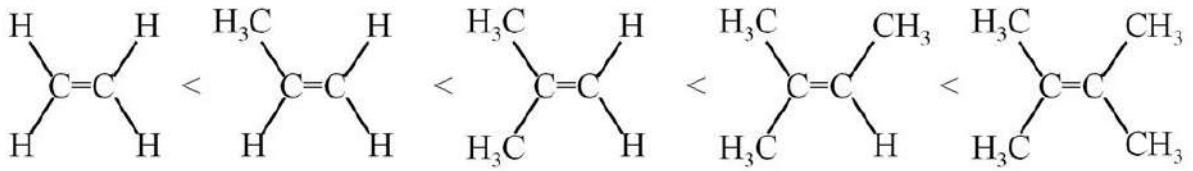
This type of hyperconjugation is also referred to as ***sacrificial hyperconjugation*** since one bond is missing.

i) **Stability of alkenes:** A general rule is that, the stability of alkenes increase wrong 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.



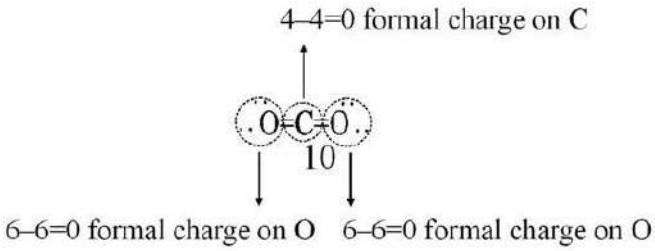
The increasing order of stability of alkenes with increases in the number of methyl groups on the double bond is depicted below.



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

1.2.6 Formal charges and double bond equivalent (DBE) :

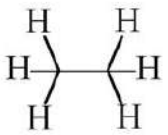
In chemistry, a formal charge (FC) is the charge assigned to an atom in a molecule, assuming that electrons in all chemical bonds are shared equally between atoms, regardless of relative electronegativity.



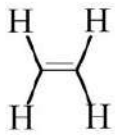
- **Formal charge** = [No. of valence electroris] — [electrons in ione pairs + 1/ 2 the number of bonding electrons]
- **Formal Charge** = [No. of valence electrons on atom] – [non-bonded electrons + number of bonds].

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:

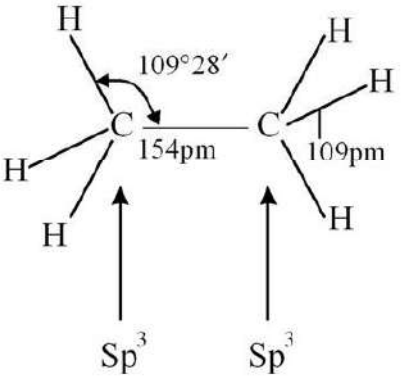
Ethane (C_2H_6) : DBE = C–(H/2) + (N/2) + 1 = 0 Ethylene (C_2H_4) : DBE = C–(H/2) + (N/2) + 1 = 2 – (4/2) + (0/2) – (4/2) + (0/2) + 1 = 1 Cyclohexane (C_6H_{12}) : DBE = C – (H/2) + (N/2) + 1 = 6 – (12/2) + (0/2) + 1 = 1

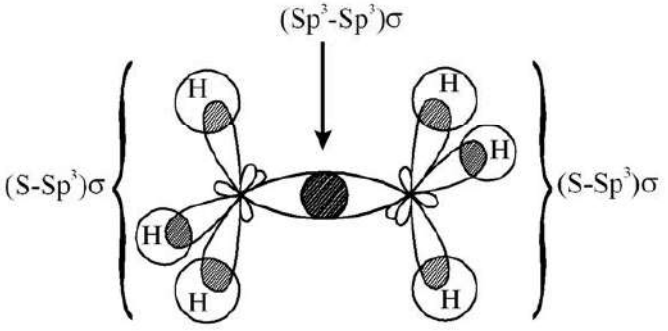
Benzene (C_6H_6) : DBE = C – (H/2) + (N/2) + 1 = 6 – (6/2) + (0/2) + 1 = 4

1.2.7 Orbital pictures

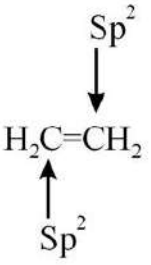
A molecular orbital diagram, or molecular orbital picture, is a qualitative descriptive tool explaining chemical bonding in molecules in terms of molecular orbital theory in general and the linear combination of atomic orbitals method in particular.

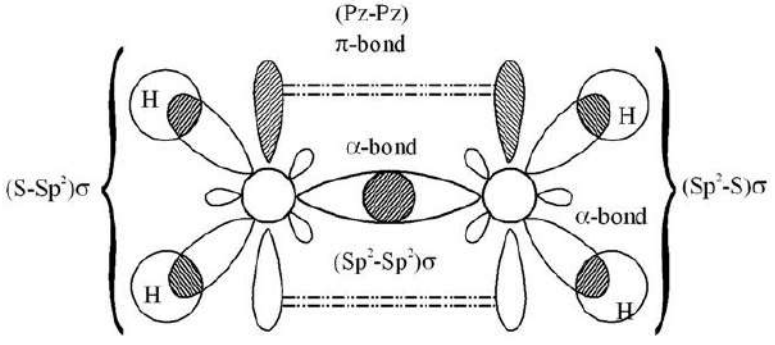
i) Ethane, CH_3-CH_3 **orbital picture**



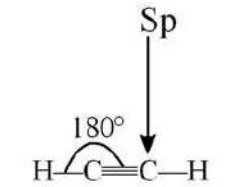


ii) Ethylene, CH_2=CH_2 **orbital picture**

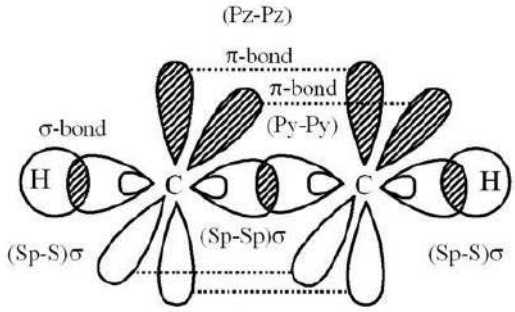




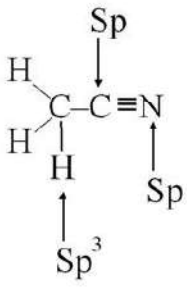
iii) Acetylene **orbital picture**

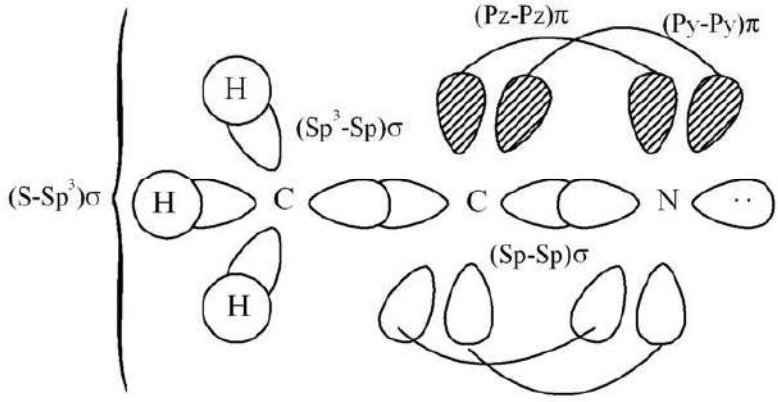


Linear structure of acetylene molecule

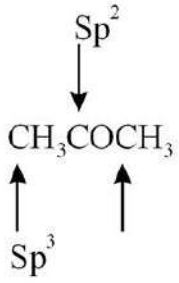


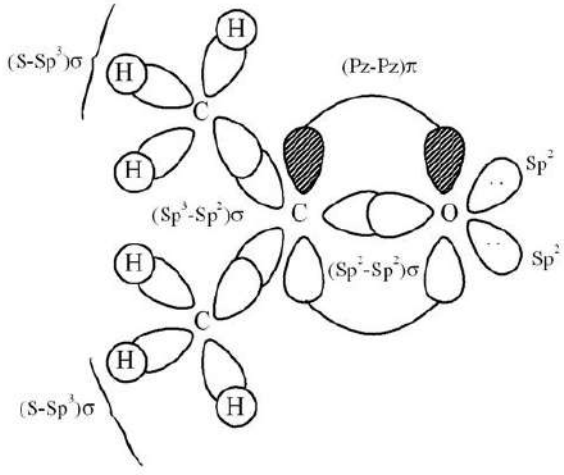
iv) Acetonitrile, CH_3CN



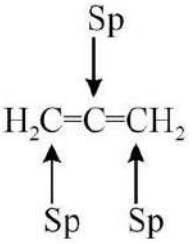


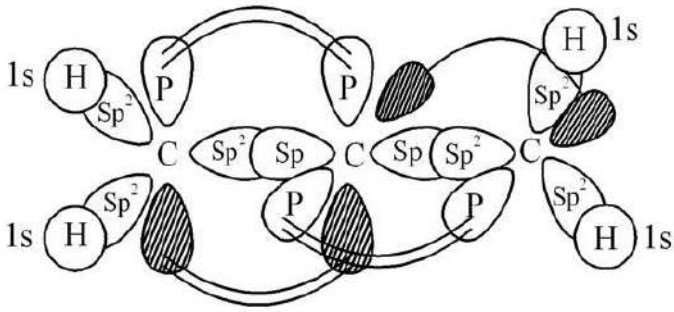
v) Acetone, CH_3COCH_3



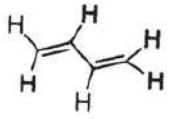


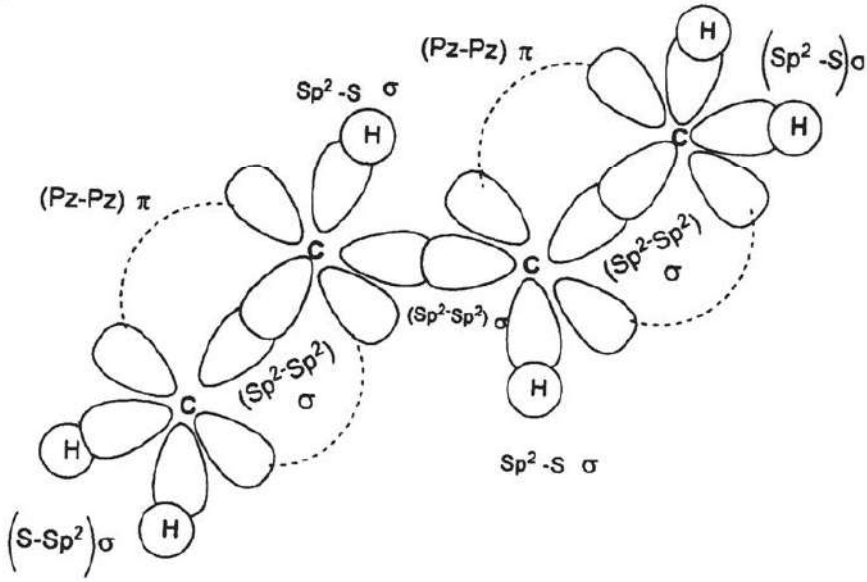
vi) Allene, $CH_2=C=CH_2$





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





1.2.8 Electronic displacements

Inductive effect, field effect, mesomeric effect, resonance energy; bond polarization and bond polarizability; electromeric effect; steric effect, steric inhibition of resonance.

Reactivity of Organic Compounds:

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

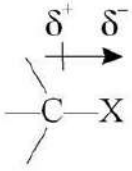
b) Mesomeric effect or resonance

c) Electromeric effect

d) Steric inhibition of resonance

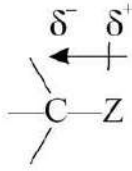
1.2.8.1 Inductive effect: An inductive effect is an electronic effect due to the polarisation of a bonds within a molecule or ion. This is typically due to an electronegatvity difference between the atoms at either end of the bond.

.. .. - α" 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"

Negative inductive effect (-I)



Electron density is greater near "C" than "Z"

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

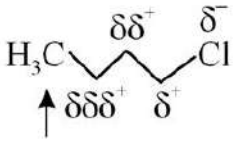
More electronegative group exhibits stronger -I effect.

+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

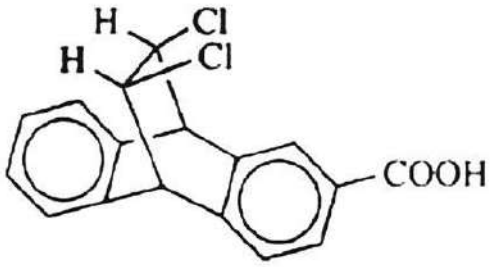
The overall polarity of a molecule by the individual bond polarities are measured by

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).

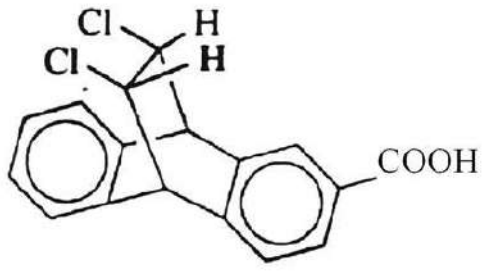
In most cases, inductive and field effects operate together and difficult to separate them. The following system is designed to show only the field effects.

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)

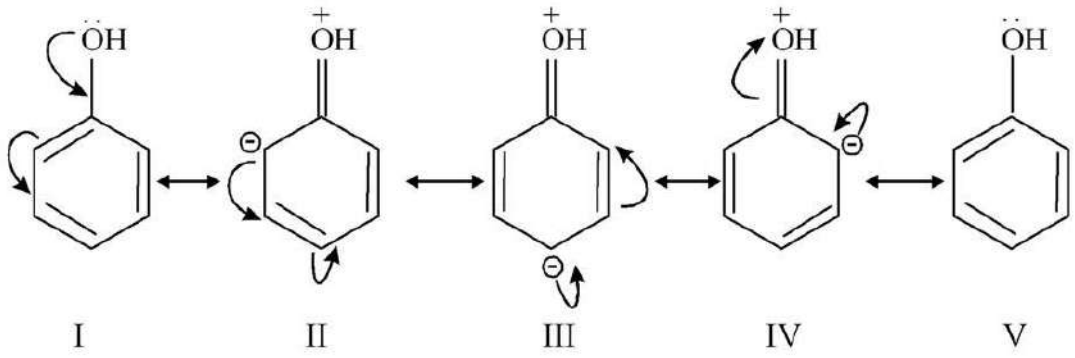
1.2.8.2 Mesomeric effect (Resonance effect): The mesomeric effect (or resonance effect) is the movement of π electrons toward or away from a substituent group.

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 n 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

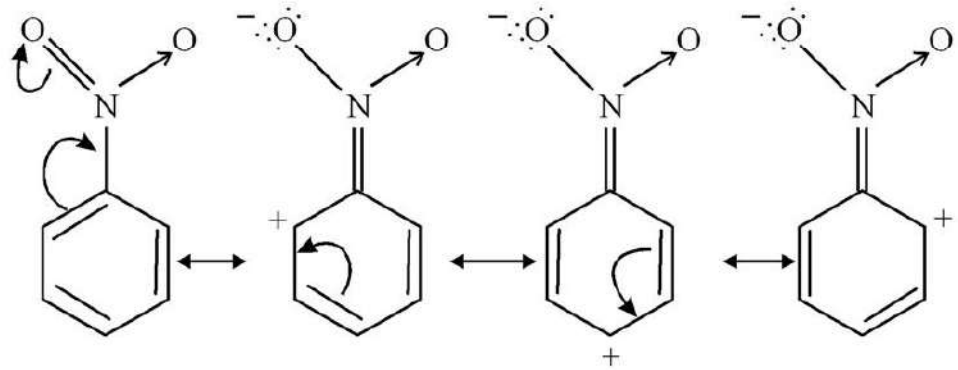


Other + M substituents are $-OR_2$, $-NH_2$ –OCOR, $-NR_2$, and –NHCOR.

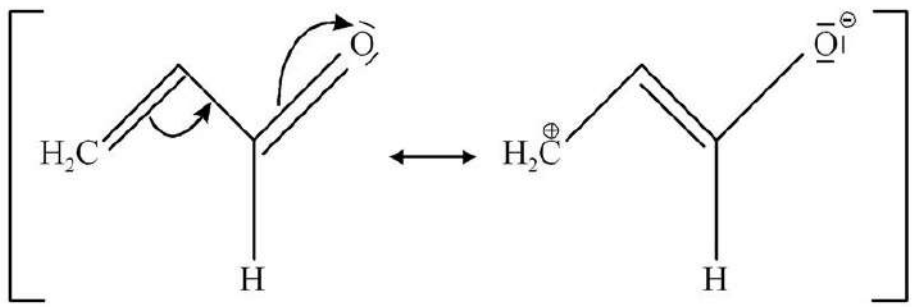
–R or –M effect:

If the π 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 α,β- 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.

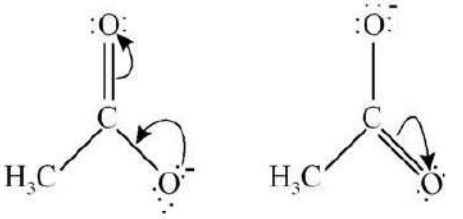
Rules of Resonance:

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 (Identical canonical form). Indentical canonical form (I and II)

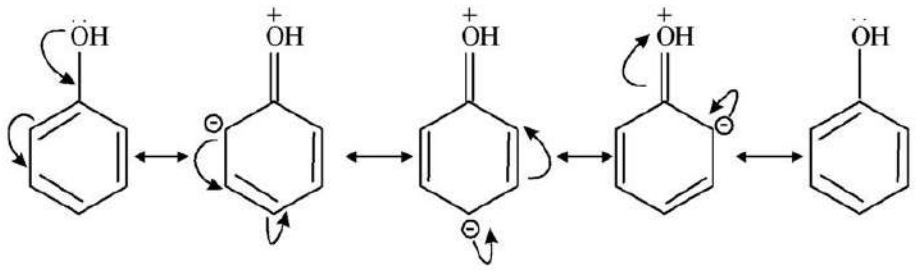


I II

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).

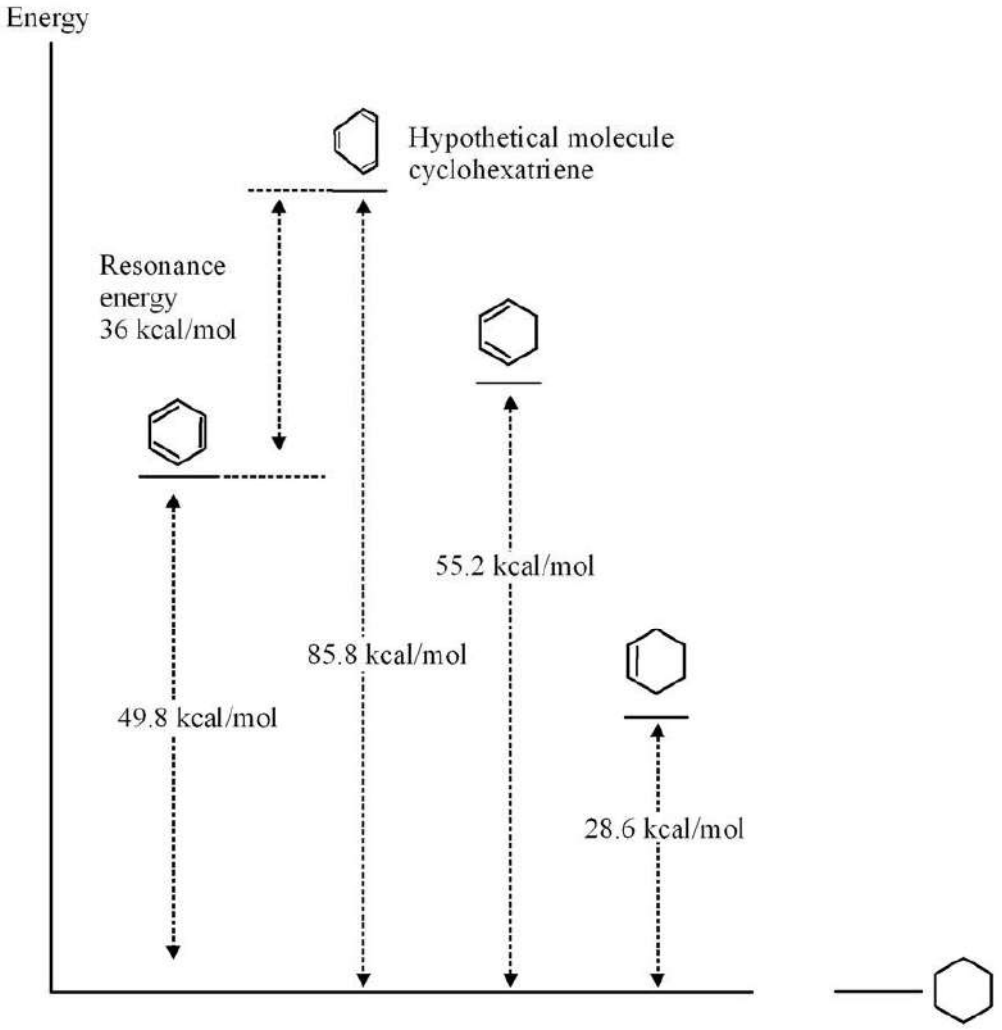
vii)



I II III IV V

viii) 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, ΔH_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 ΔH_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.

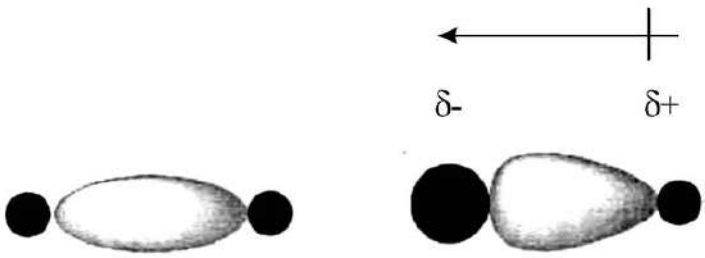
More the resonance energy, greater is the stabilization. It is calculated from heat of hydrogenation data.

1.2.8.3 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-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 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, α, is experimentally measured as the ratio of **induced dipole moment** p to the electric field E that induces it:

$$\alpha = p/E$$

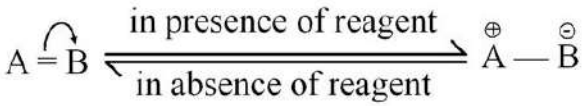
The units of α are $C.m^2.V^{-1}$.

Example: Large, negatively charged ions, such as L 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 L and Br.

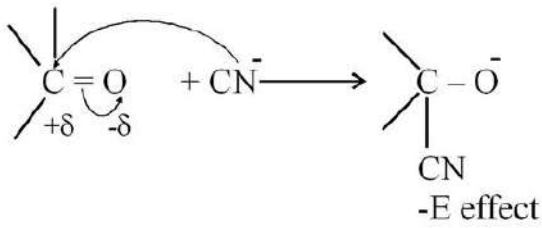
Note:

- 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 (p). The higher the dipole moment results the more polar compound.

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

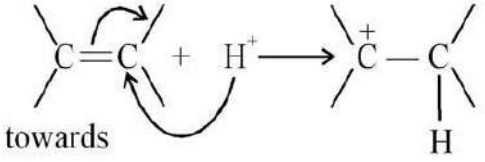


This is a temporary effect because the molecule gains its original electronic nature upon removal of the reagent and takfes place between two atoms joined by a multiple bond (double or triple bond



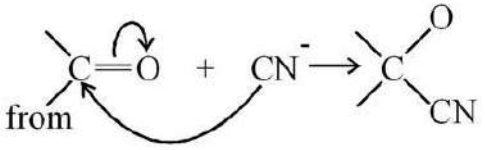
The electromeric shift of electrons takes place only at the moment of reaction. Like I effect it is also classified as +E and –E.

Positive electromeric effect (+E)



Transfer of electrons takes place the attacking reagent

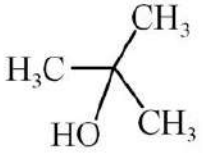
Negative electromeric effect (–E):



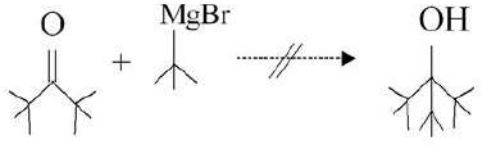
Transfer of electrons takes place the attacking reagent Transfer of electrons takes place away the attacking reagent.

1.2.8.5 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.

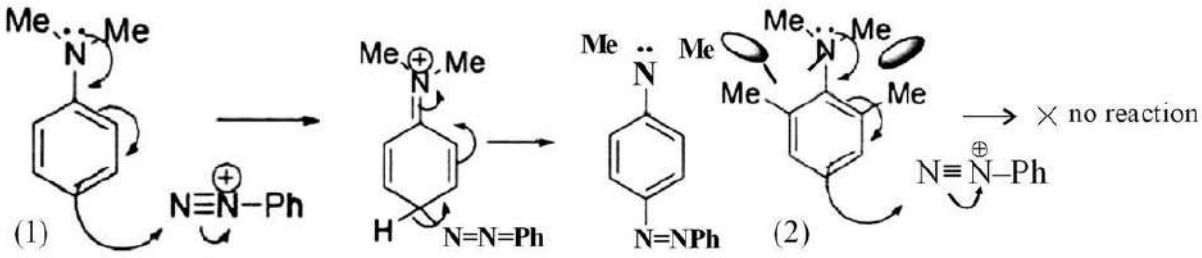


- An example would be a reaction called a Grignard addition, which occurs between a ketone and a magnesium-bromide reagent (called the Grignard reagent).

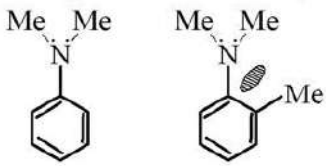


The Grignard reagent does not work due to steric effects

1.2.8.6 Steric inhibition of resonance: The effective delocalization of electrons via n orbitals can only take place when the 'P' or π orbitals involed 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 π system is inhibited and transfer of electronic charge does not take place.



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

1.3 Molecular Orbital (MO) Theory

qualitative idea about molecular orbitals, bonding and antibonding interactions, idea about σ, σ*, π, π, n - MOs; basic idea about Frontier MOs (FMO); concept of HOMO, LUMO and SOMO; interpretation of chemical reactivity in terms of FMO interactions.

1.3.1 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.

1.3.2 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.

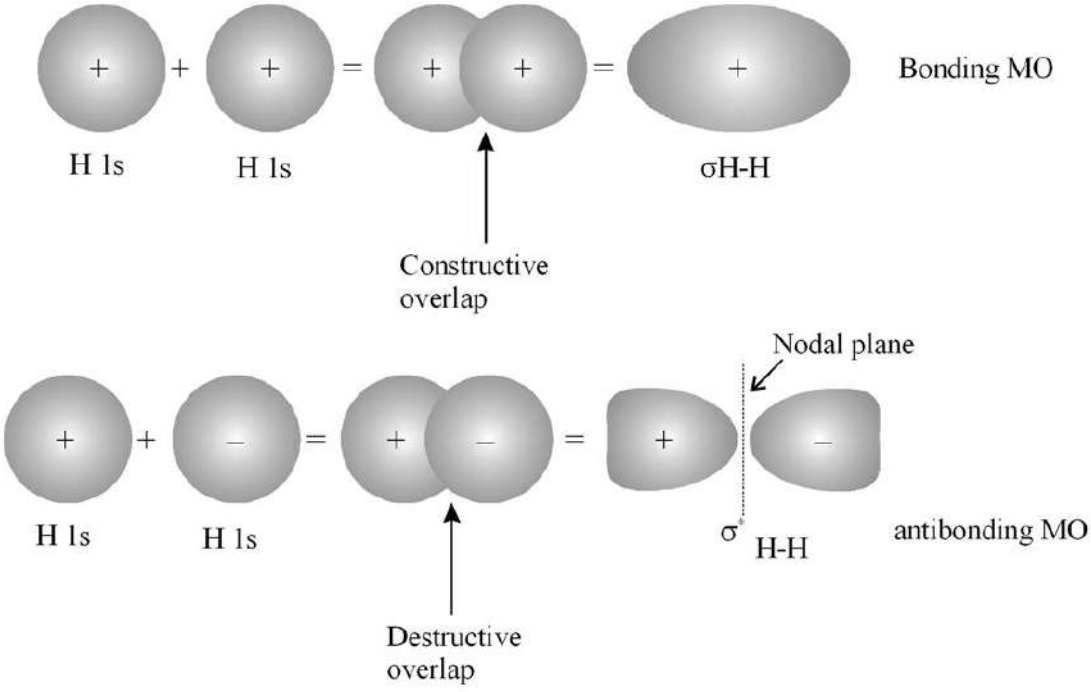
Second principle: Bonding molecular orbitals are lower in energy that the parent orbitals, and the antibonding orbitals are higher in energy.

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

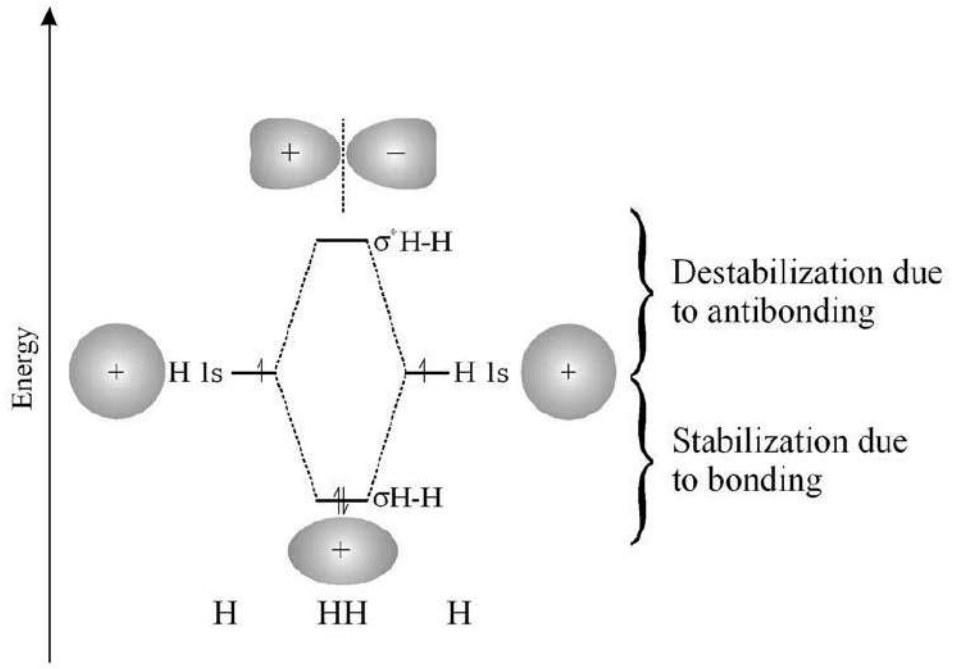
Fourth principle: Atomic orbitals combine to form molecular orbitals most effectively when the atomic orbitals are of similar energy.

1.3.3 Example:

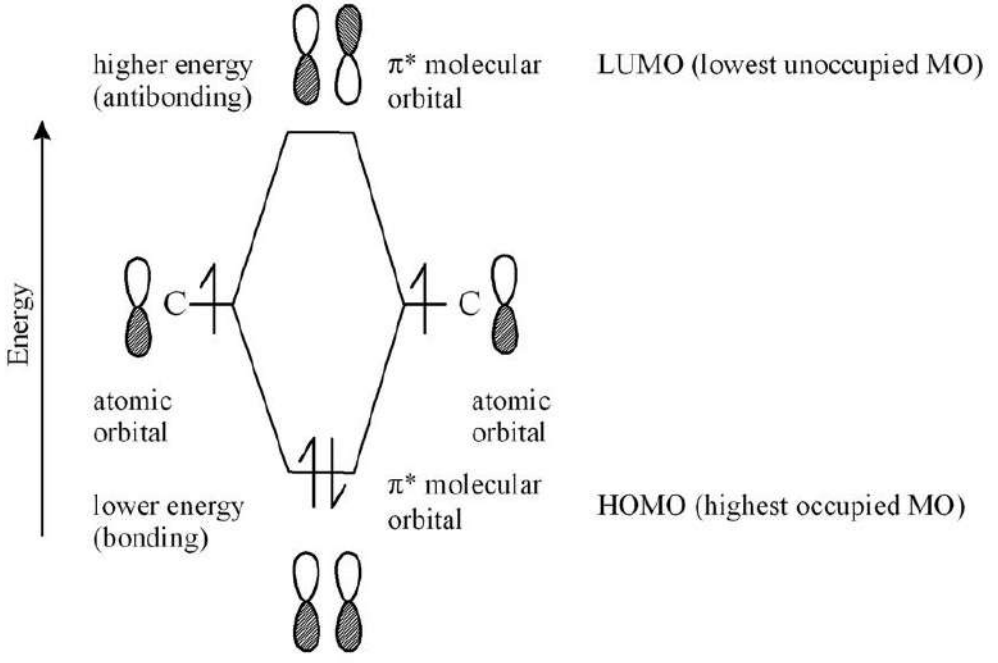
- **H_1 molecule (principle 1)**



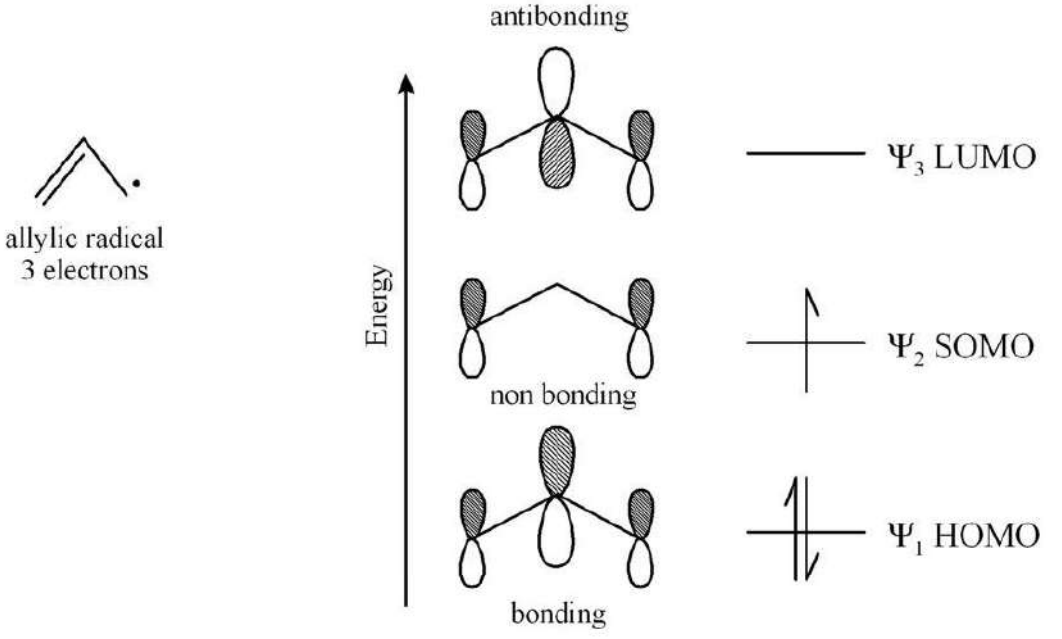
- **H_2 molecule (principle 2 & 3)**



- **Energy diagram for two π MO in a typical π-bond: e.g CH_2=CH_2 molecule**

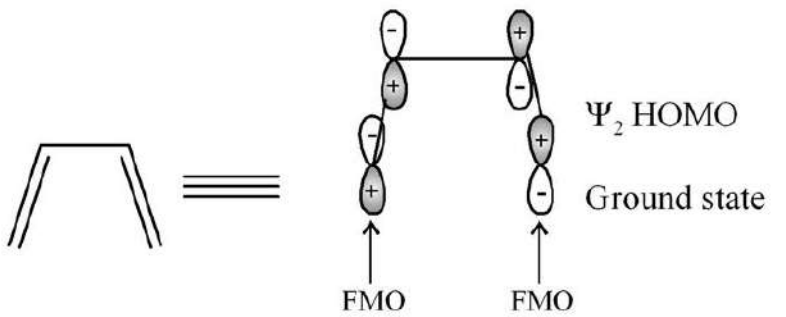


- **Energy diagram for allylic radical (bonding, nonbonding and antibonding π MOs):**



1.3.4 Frontier Molecular Orbital Theory (FMO) :

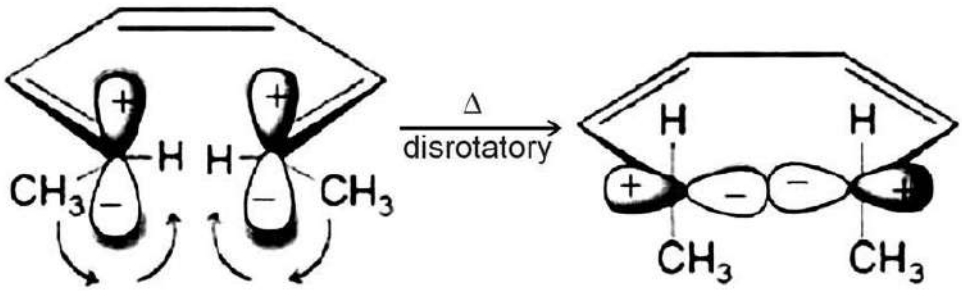
A powerful practical model for describing chemical reactivity is the frontier molecular orbital (FMO) theory, developed by Kenichi Fukui in 1950's. The important aspect of the frontier electron theory is the focus on the highest occupied and lowest unoccupied molecular orbitals (HOMO and LUMO).



Interpretation of chemical reactivity in terms of FMO interactions:

Thermal electrocyclic ring closure of (2E,4Z,6E)-2,4,6-octatriene yields a single product with methyl groups on the ring.

To explain the stereochemistry observed in above electrocyclic reactions, we must examine the symmetry of the HOMO of the ground state electronic configuration. Rotation occurs in a disrotatory or conrotatory fashion so that like phases of the p orbitals on the terminal carbons of this molecular orbital combine



counterclockwise clockwise
(2E,4Z,6E)-2,4,6-octatriene

cis-5,6-dimethyl-1,3-cyclobexadiene
cis-product

1.3.5 Sketch and energy levels of π MOs :

i) Acyclic p orbital system:

Ethylene system (CH_2=CH_2):

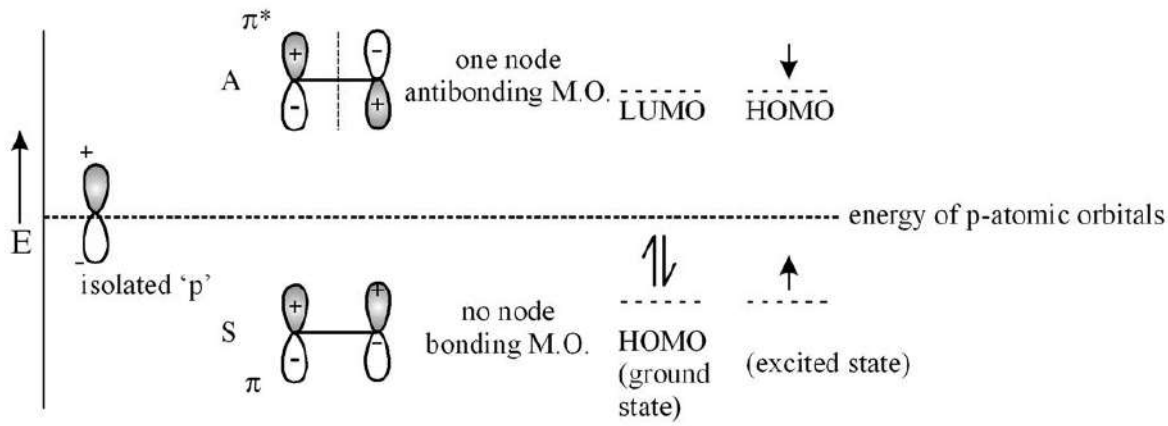


Fig-1: Energy levels of π MOs of C=C system

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 ($CH_2 = CH - CH = CH_2$) :

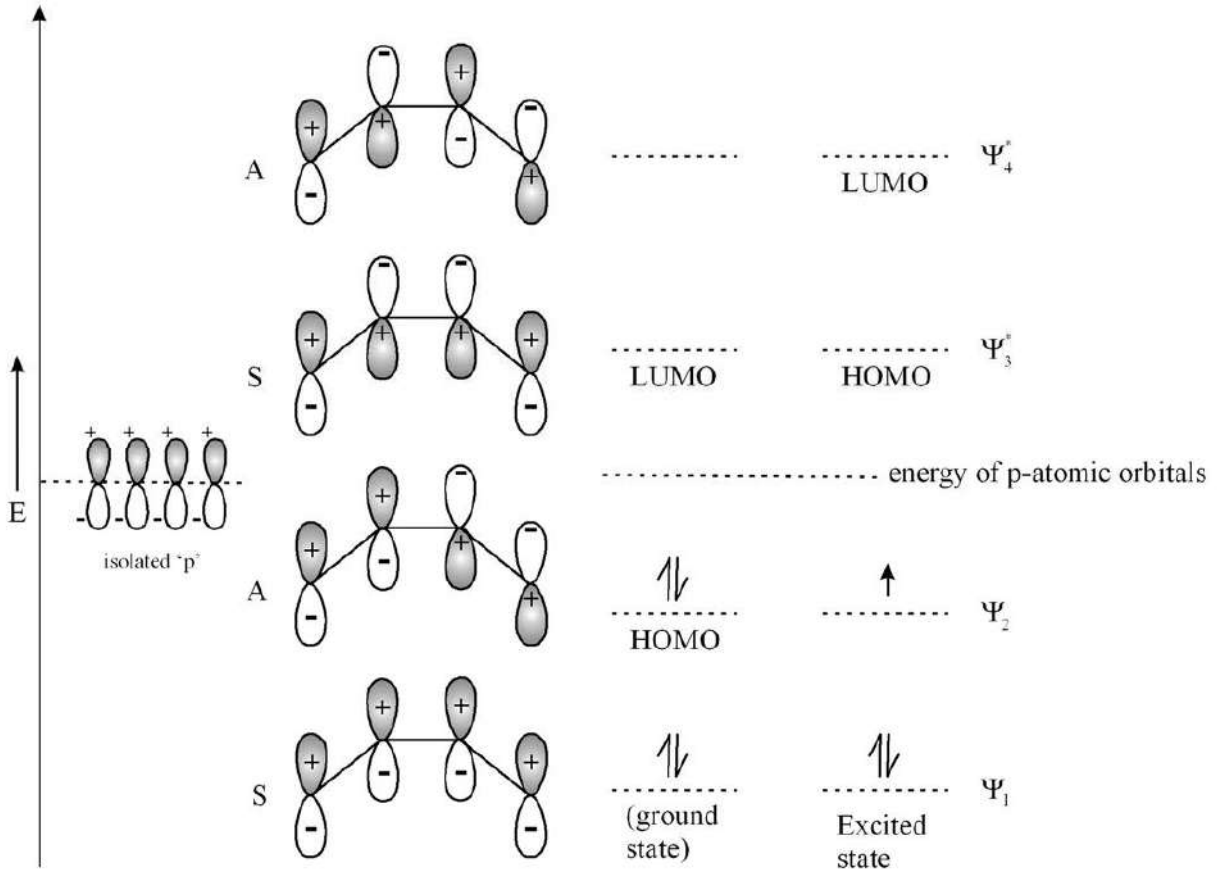


Fig. 2: Energy levels of π MOs of conjugated diene system

1,3,5-hexatriene ($CH_2 = CH - CH = CH_2 - CH = CH_2$)

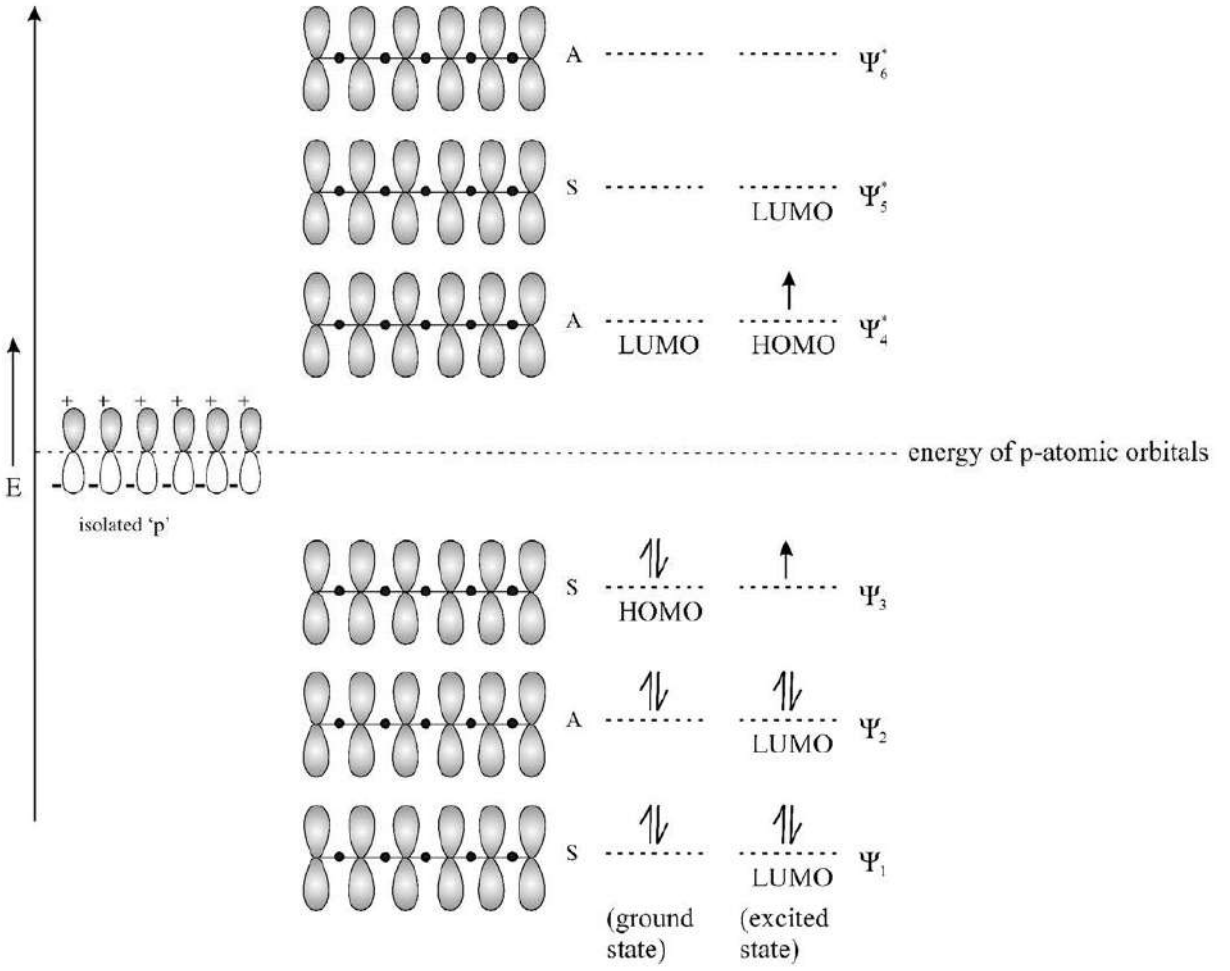


Fig. 3: Energy levels of π MOs of conjugated triene system

Allyl system:

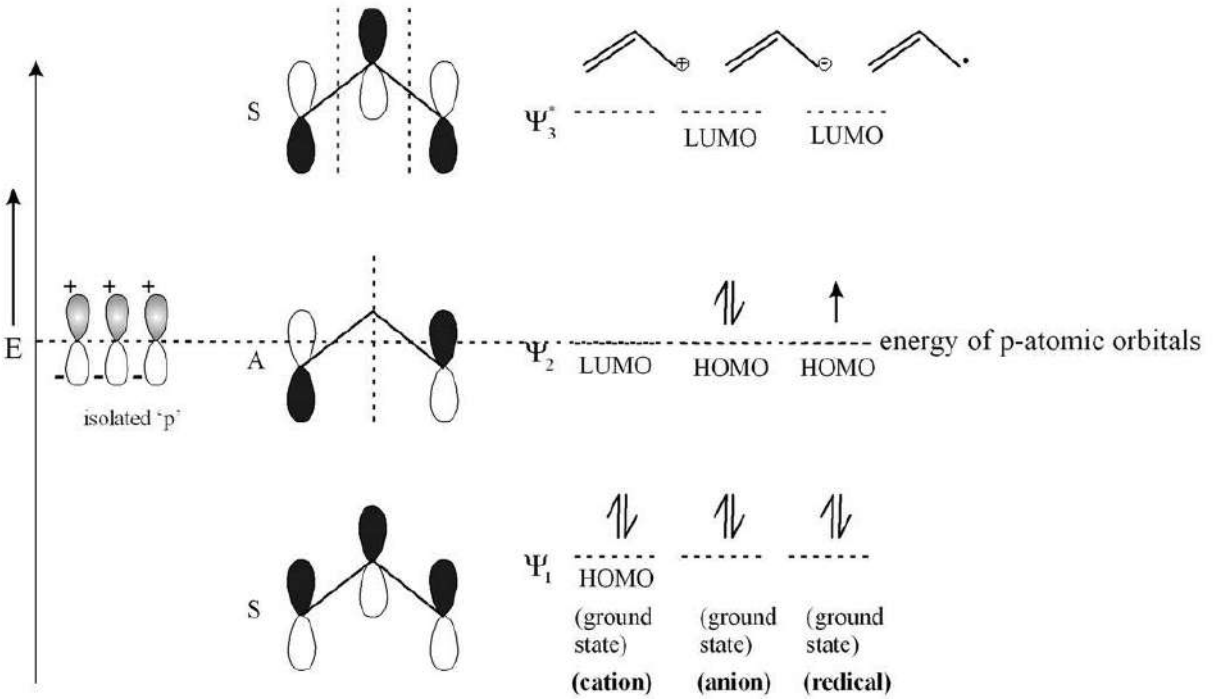


Fig- 4: Energy levels of π MOs of allyl system

Pentadienyl system:

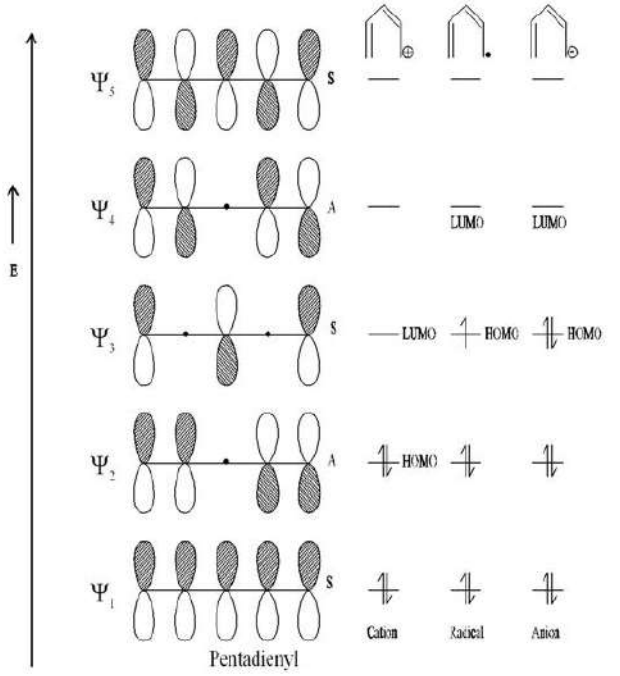
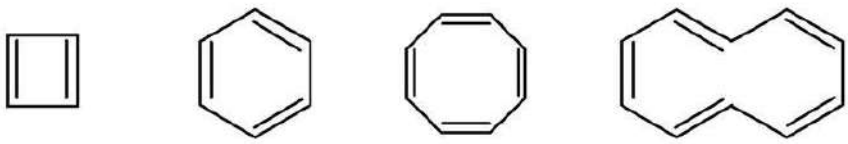


Fig- 5: Energy levels of π MOs of pentadienyl system

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 | cyldecapentaene [10] annulene

π-M.O.s of [4] annulene:

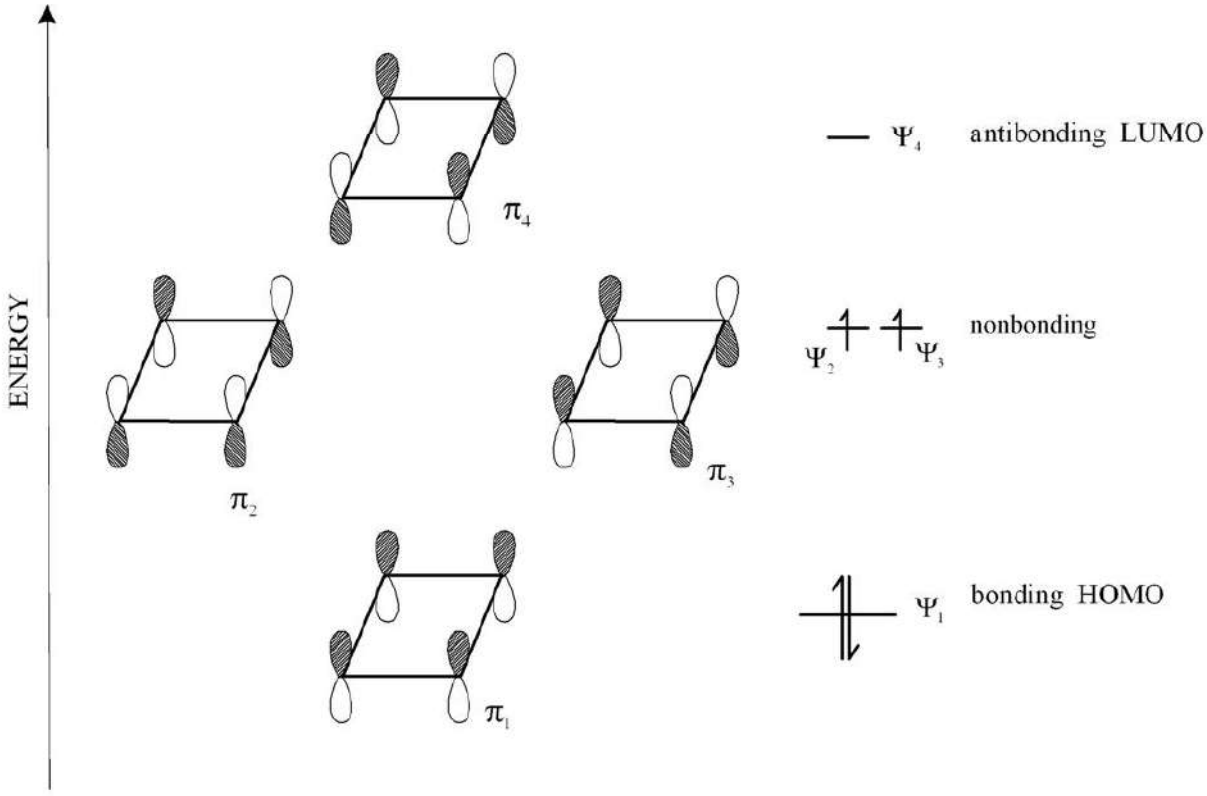
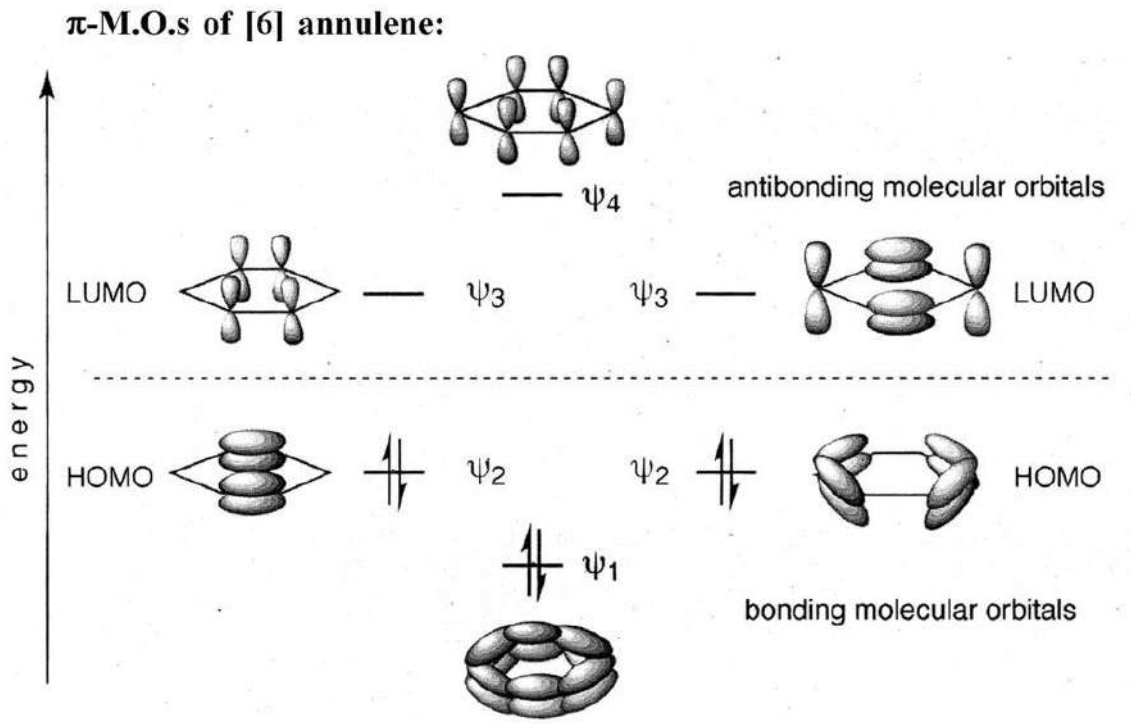


Fig- 6: Energy levels of π MOs of [4] annulene



The π molecular orbitals for benzene. The dashed line represents the energy of an isolated p orbital - all orbitals below this line are bonding, all above it are antibonding. Benzene has six electrons in its it system so all the bonding MOs are fully occupied

Fig- 7: Energy levels of π MOs of [6] annulene

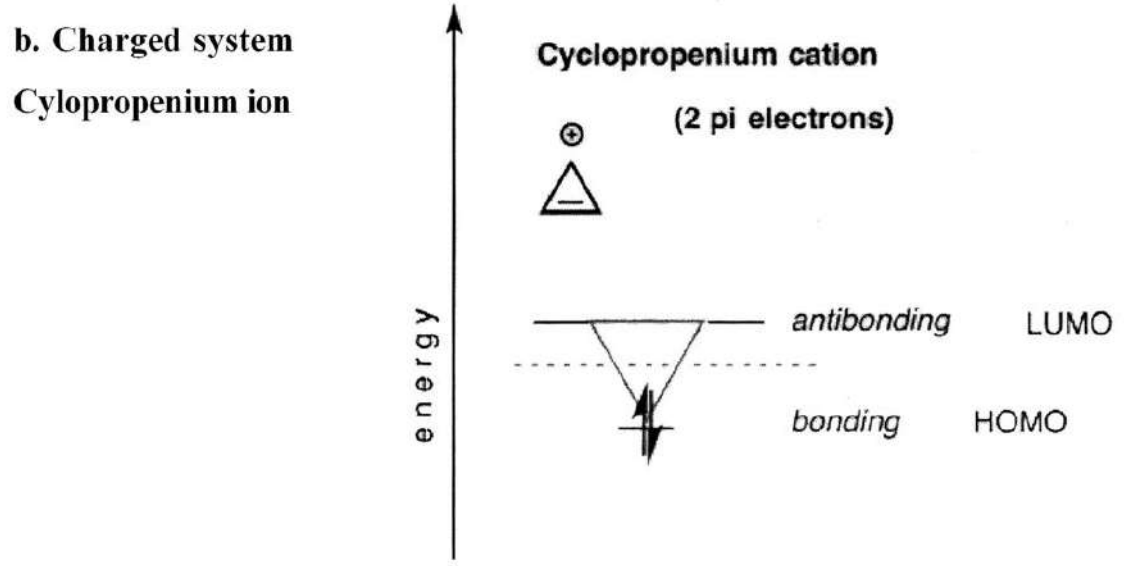


Fig- 8: Energy levels of π MOs of charged 3-membered ring system

Cyclopropenyl ion

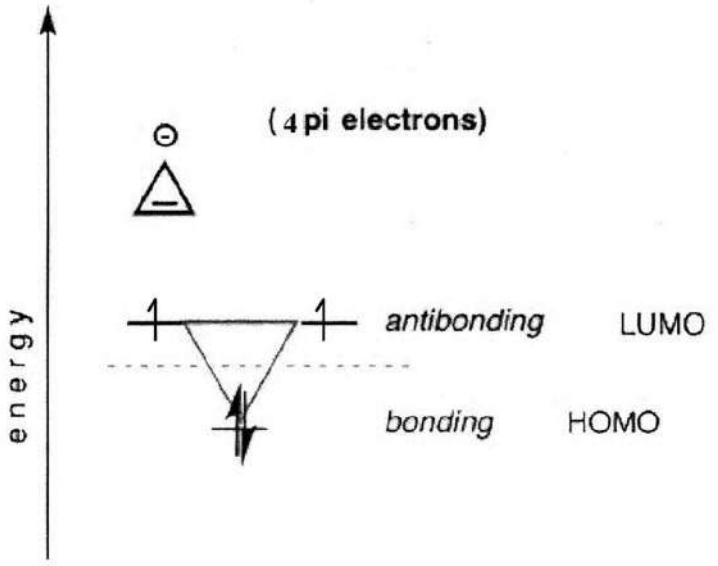


Fig- 9: Energy levels of π MOs of charged 3-membered ring system

Cyclobutenyl dication

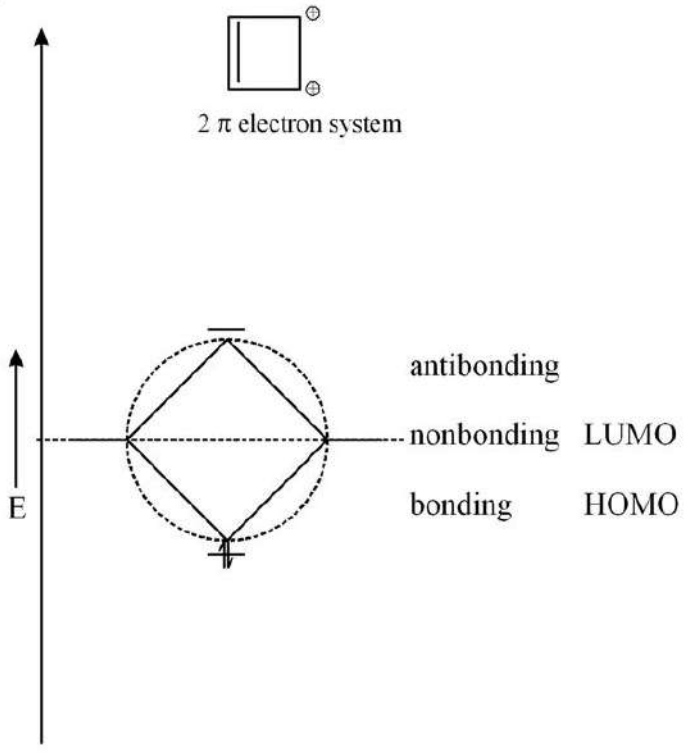


Fig-10: Energy levels of π MOs of charged 4-membered ring system

Cyclobutenyl dianion

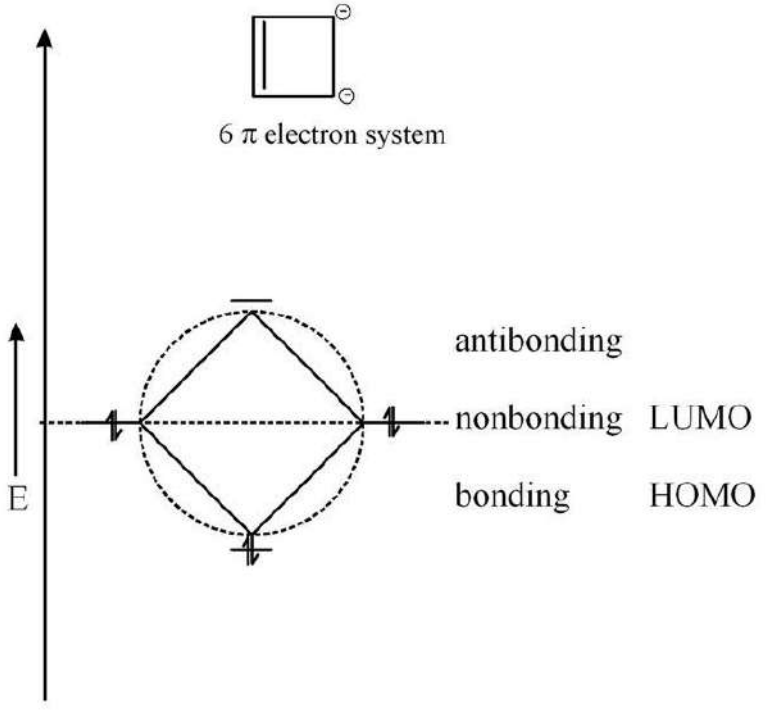


Fig-11: Energy levels of π MOs of charged 4-membered ring system

Cyclopentadienyl anion

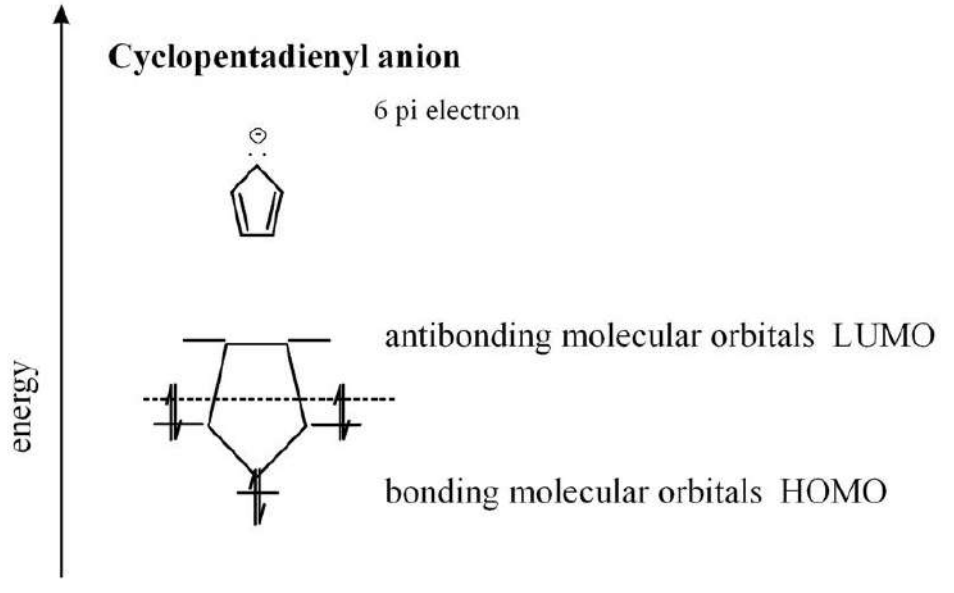


Fig-12: Energy levels of π MOs of charged 5-membered ring system (anion)

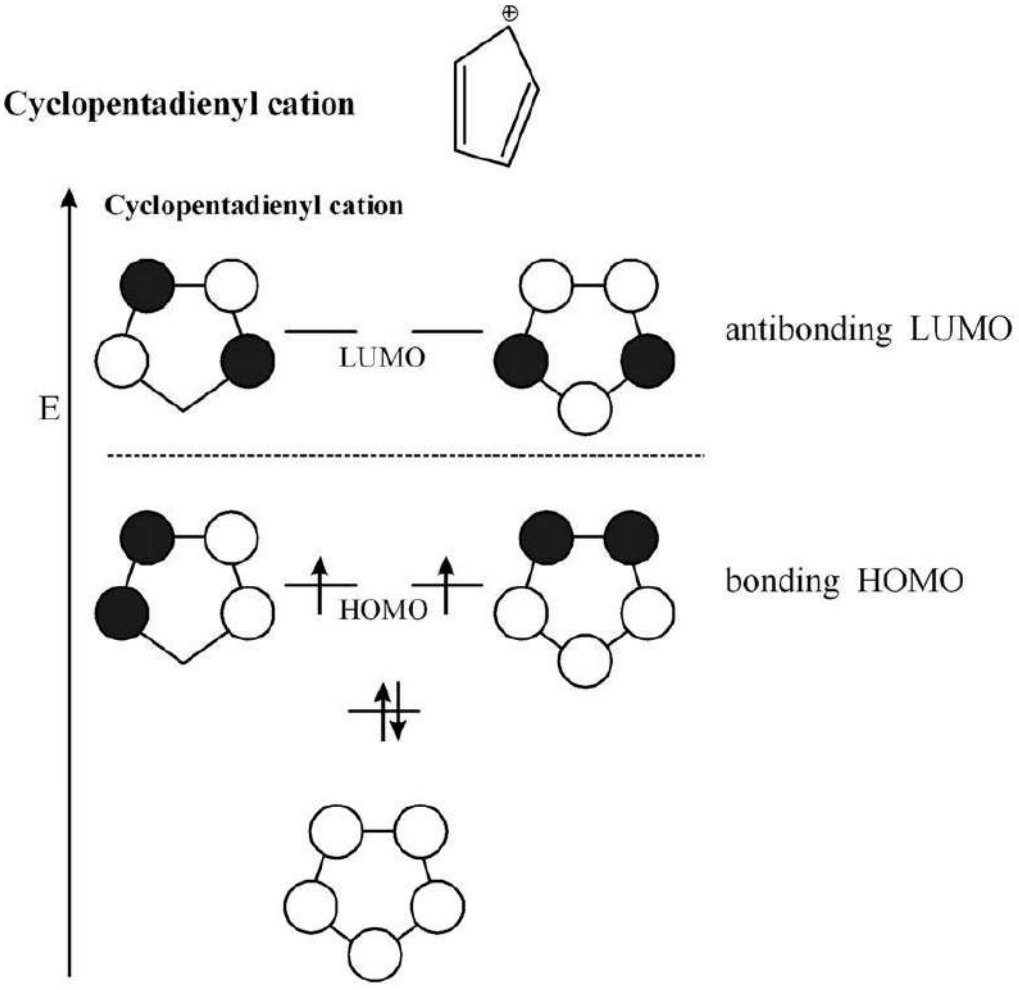


Fig-13: Energy levels of π MOs of charged 5-membered ring system (cation)

1.3.6 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):

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

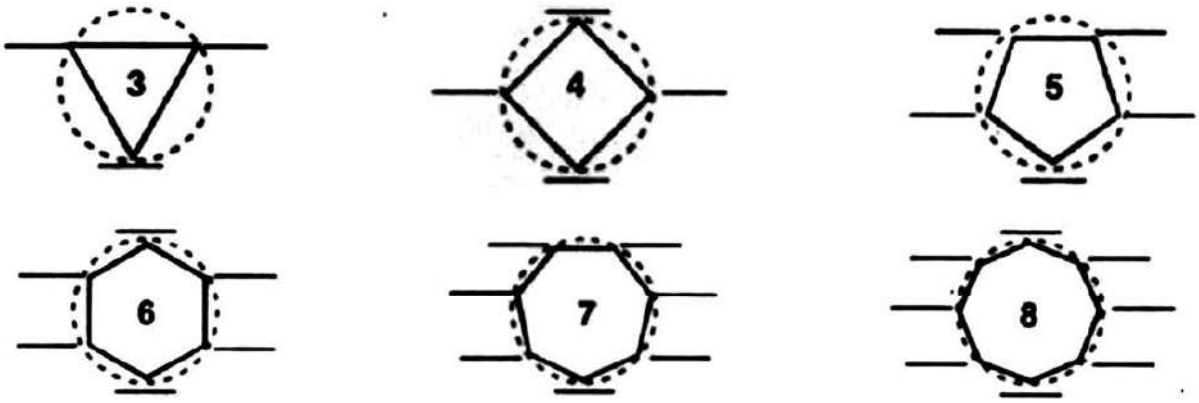
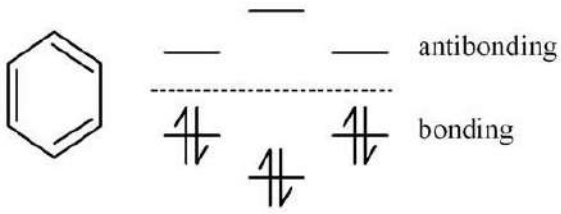


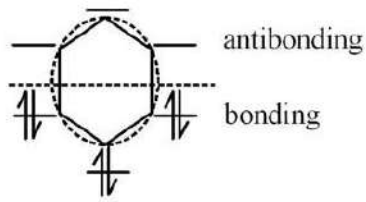
Fig 14.

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.

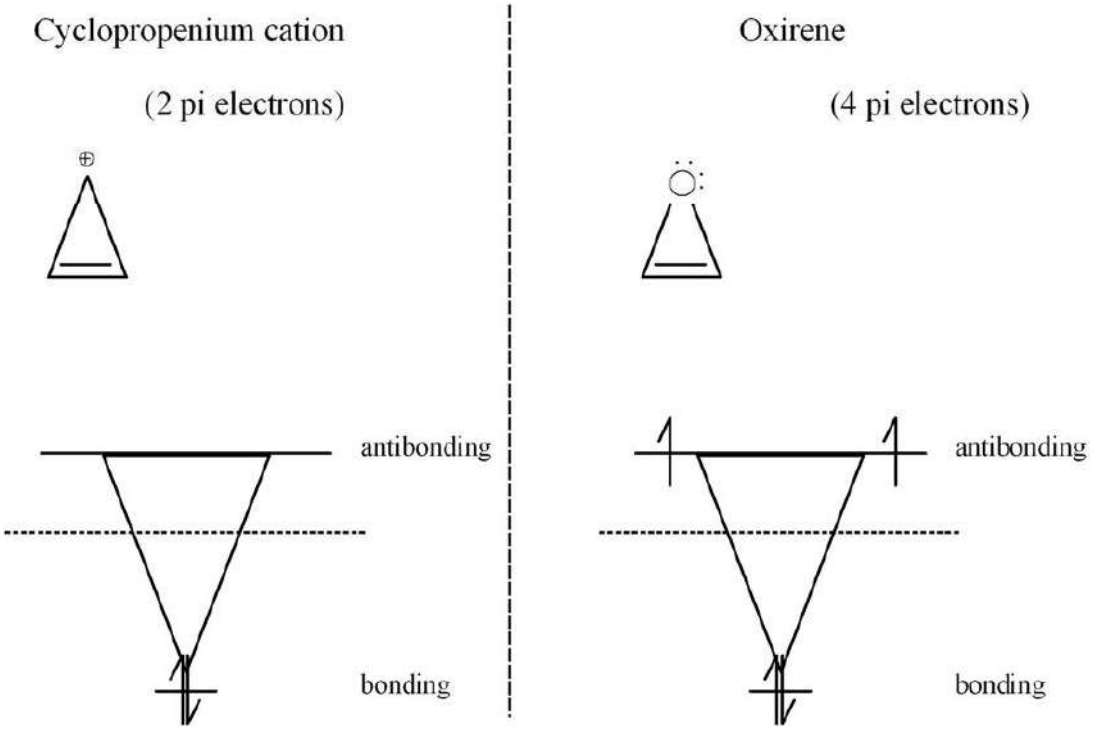
Frost diagram of various ring systems are given below.

3-Membered Rings

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

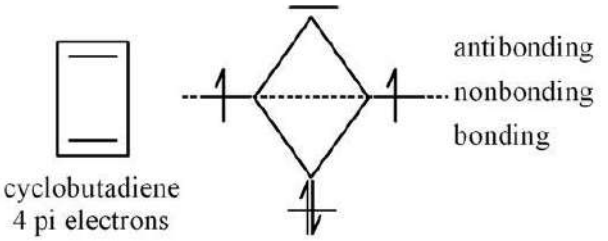
One example is the cyclopropenium cation, which is 2 pi electrons system.

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**.

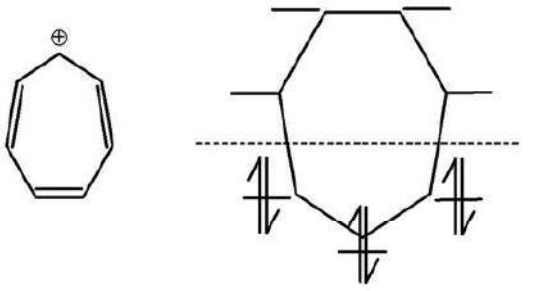


7-Membered Rings

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").

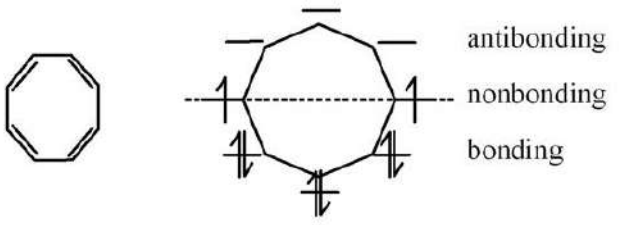
Cycloheptatrienyl cation (6 pi electrons)



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)



1.3.7 Huckel's Rule (4n + 2 rule)

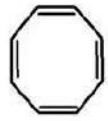
In 1931, Erich Hiickel postulated that monocyclic, (single ring) planar, delocalized n electron system having (4n + 2) n electrons where n equaled any whole number (n = 0, 1,2, 3,...etc) should be aromatic

For example, the benzene molecule, which has 3 π bonds or 6 π electrons, is aromatic.

- Number of π electrons = 4 n + 2
- 6 = 4n + 2 Benzene
- n = 1

Benzene

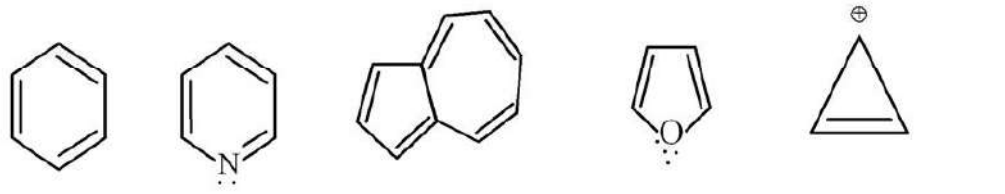
However, 1,3,5,7 cyclooctatetraene, which has 4 π bonds or 8 π electrons, is not only nonaromatic but is actually considered antiaromatic because it is even less stable than the open chain hexatriene.



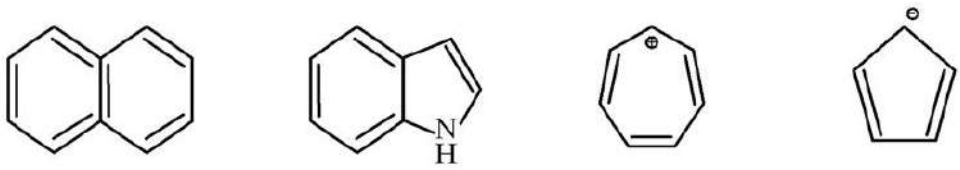
Cyclooctatetraene

- Number of π electrons = 4 n + 2
- 6 = 4n + 2 Benzene
- n = 1.5

Some aromatic molecules are shown below:



Benzene Pyridine Azulene Furan Cylcopropeoyl cation



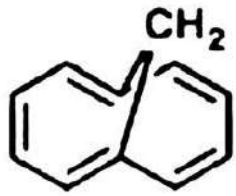
Naphthalene Indole Tropylium ion Cylcopentadienyl cation

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 CH_2 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 4nn electrons (n = 1, 2, 3,...etc) should be antiaromatic. Unlike aromatic compounds, antiaromatic compounds are highly unstable and highly reactive.

Example-1:

Cyclobutadiene

- 4π electrons
- Conjugated
- Planar

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.

- 8π electrons

- Conjugated
- Planar

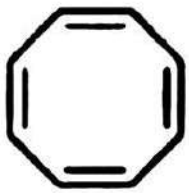
Pentalene

Antiaromatic

Nonaromatic compounds

The 4nπ 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*. Hqwever, 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

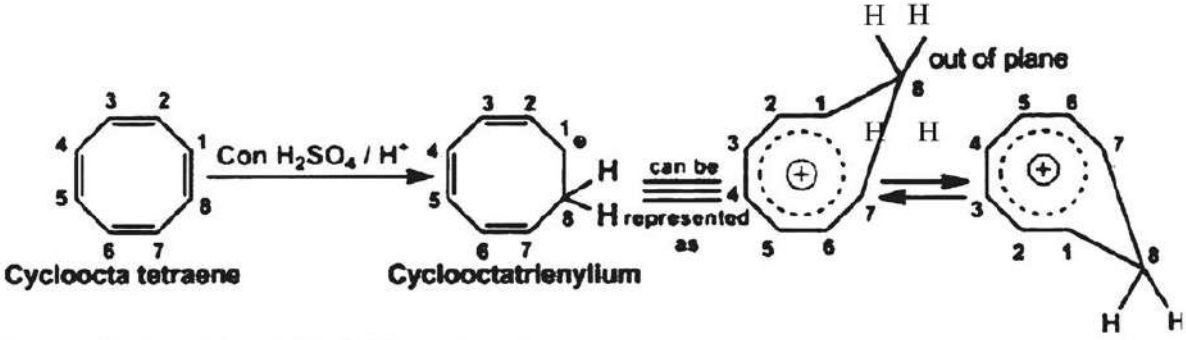
Tub-shaped, non-aromatic

Nonaromatic

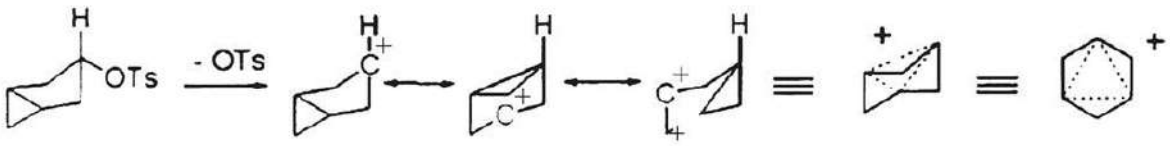
Homoaromatic compounds

A homoaromatic compound is defined as a compound that contains one or more sp^3 hybridized carbon atom in a conjugated cycle.

Example: Pronounced homoaromaticity is not normally associated with neutral molecules, but mainly with species bearing an electrical charge, e.g., the "homotropylium" cation, $C_8H_9^+$,



Example 2: 3-bicyclo[3.1.0]hexyl cation



Homoaromatic

1.3.8 Elementary idea about α and β:

The Huckel method or Huckel molecular orbital theory, proposed by Erich Huckel 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 α and β for buta-l,3-diene, cyclobutadiene, hexa-l,3,5-triene and benzene.

The delocalization energy is the extra stabilization that comes from letting the electrons spread over the whole molecule. The calculations are made using Huckel Molecular Orbital Theory (HMO) and this is part of physical quantam chemistry. Here we take simple form of the calculations. This method predict how many energy levels exist for a given molecule which are degenerale and it expresses the molecular orbital energies in terms of two parameters, called 'α' the energy of an electron in 2p orbital, and 'β', the interaction energy between two 2p orbitals.

Buta-l,3-diene:

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

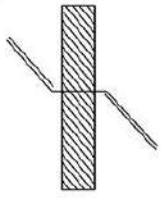


Fig. 1

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)

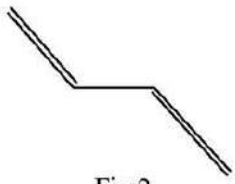


Fig:2

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

$= 4\alpha + 4.4\beta$

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-l,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 (nondelocalized, **Fig: 4**) bonds.

Fig: 4

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

$= 6\alpha + 6.99\beta$

Therefore the delocalization energy of hexa-l,3,5-triene

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

$= 1.01\beta$

1.3.9 Physical properties:

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:

$$- C - C > - C = C - > - C \equiv C -$$

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}.

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

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 homoatomic 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.

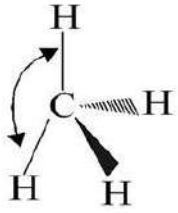
Some common bond lengths are given below.

	(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:

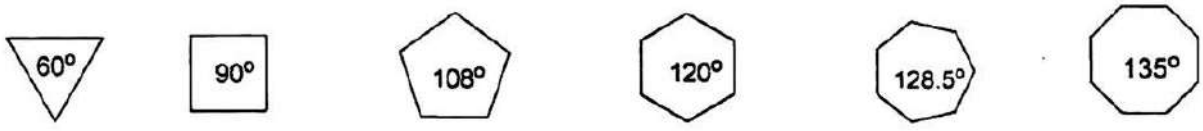
Number of regions of high electron density around central atom	Arrangement of regions of high electron density in space	Predicted bond angles	Example	Geometry of molecule
4	tetrahedral	109.5°	CH_4, methane	tetrahedral
			NH_3, ammonia	pyramidal
			H_2O, water	bent
3	trigonal planar	120°	H_2CO, formaldehyde	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

1.3.9.1 Concept of bond angle strain (Baeyer's strain theory): Cycloalkanes are very important in components of food, pharmaceutical drugs, and much more. Recall that in alkanes, carbon adopts the sp^3 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 asTing 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.



cyclopropane cyclobutane cyclopentane cyclohexane cycloheptane cyclooctane

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 (109.5°) 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 Baeyer, 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 as under. Cyclohexane > Cyclopentane > Cyclobutane > Cyclopropane.

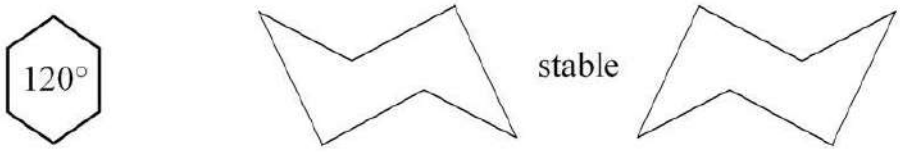
Thus, Baeyer made some false assumptions,

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.



flat ring
leass stable

puckered

chair conformation

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.

1.3.9.2 Melting point/boiling point and solubility of common organic compounds in terms of 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 vapor 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.

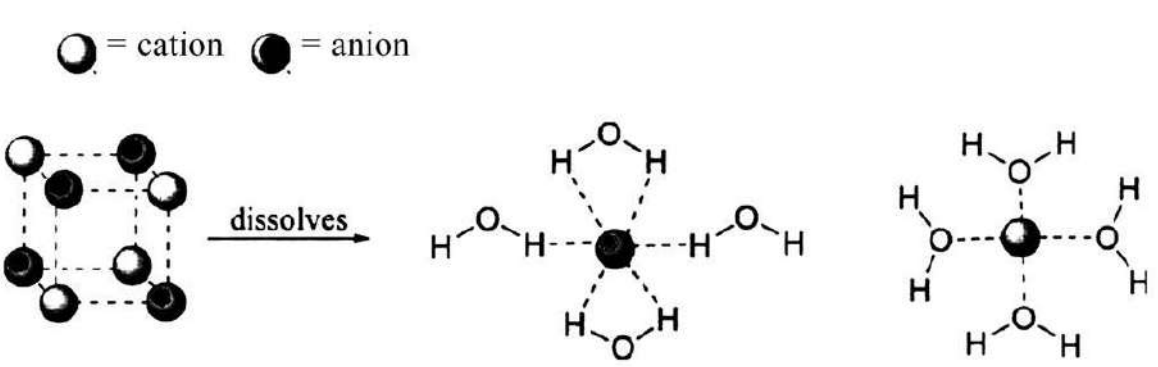
If the numbers of carbons are the same then the boiling point of different isomer depends on the surface area of the molecule. As Van der Waals attractive force is proportional to surface area, straight chain molecule such as normal pentane will have the strongest attractive force among themselves compare 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.

1.3.9.3 Intermolecular Forces & 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).

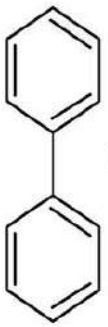
It is common to remember the rule regarding solubility is that 'like dissolves like'. Let's revisit this old rule, and put our knowledge of covalent and noncovalent bonding to work.

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.



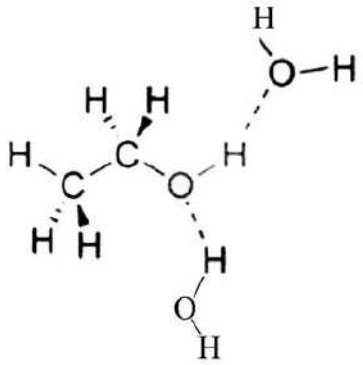
To the end, in place of sodium chloride crystals, we have individual sodium cations and chloride anions surrounded by water molecules - the salt is now in solution (i.e. solvation). Charged species as a rule dissolve readily in water: in other words, they are very hydrophilic (water-loving).

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

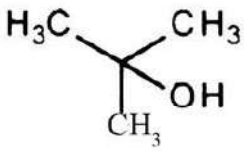


biphenyl, an organic molecule

Biphenyl does not dissolve at all in water. Why is this? Because it is a very non-polar 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.

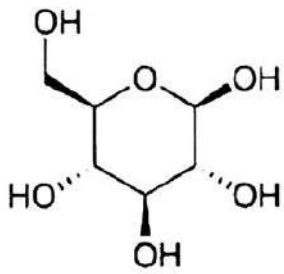


But, tert- butanol is immiscible in water. The longer-chain alcohols - pentanol, hexanol, heptanol, and octanol - are increasingly non-soluble. What is happening here? Clearly, the same favorable water-alcohol hydrogen bonds are still possible with these larger alcohols. The difference is that the larger 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

1.3.9.4 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:

$$\overset{\oplus}{\delta}\quad\overset{\ominus}{\delta}$$
$$H—F$$
$$\longrightarrow$$

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."

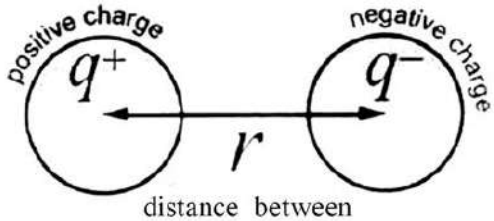
Factors on which the Polarity of Bonds Depends;

i) Relative electronegativity of participating atoms

ii) The spatial arrangement of various bonds in the atom

1.3.9.5 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, u., is the product of the magnitude of the separated charge and the distance of the separation:



$$\mu = q \cdot r$$

dipole moment — separated charge — distance between

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

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

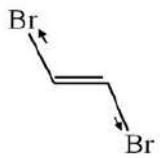
Again, $\mu_r = \sqrt{\mu_1^2 + \mu_2^2 + 2\mu_1^2\mu_2^2 \cos\theta}$

μ_1 = moment of one bond; μ_2 = moment of another bond; θ = angle between two vectors

Non polar bond:

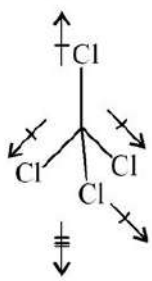
H–H, Br–Br and N–N $\mu = 0$

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

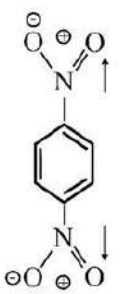


trans-1,2-dibromoethylene
$\mu = 0$

CCl_4, $\mu = 0$



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

σ-Moment and π-Moment: Electronegativity differences between the adjacent atoms joint by σ-bond develops σ-moment. A dipole moment is thus generated is known as σ-moment or inductive moment. The dipole moment generated by the delocalization of π-electrons is called as π-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.

$$NH_2\text{-}CH_2\text{-}COOH \longleftrightarrow \overset{\oplus}{N}H_2\text{-}CH_2\text{-}CHO\overset{\ominus}{O}$$

zwitter ion, As $\mu = e \times d$

here, e is high so μ is also high

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.

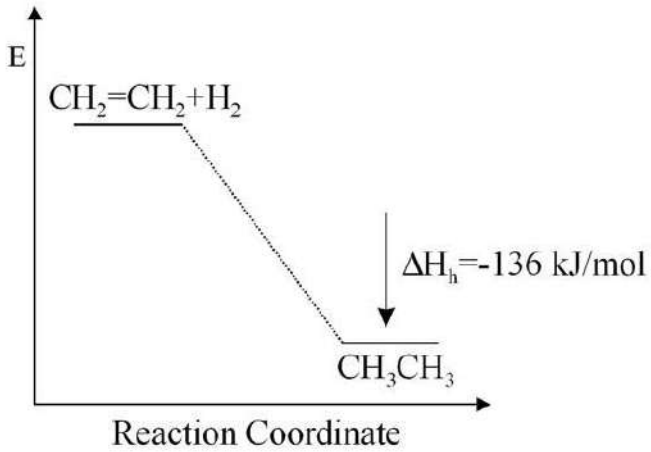
$CH_3\text{-}CH_2\text{-}COOH$
propanoic acid

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

1.3.9.6 Heat of hydrogenation, heat of combustion and heat of formation

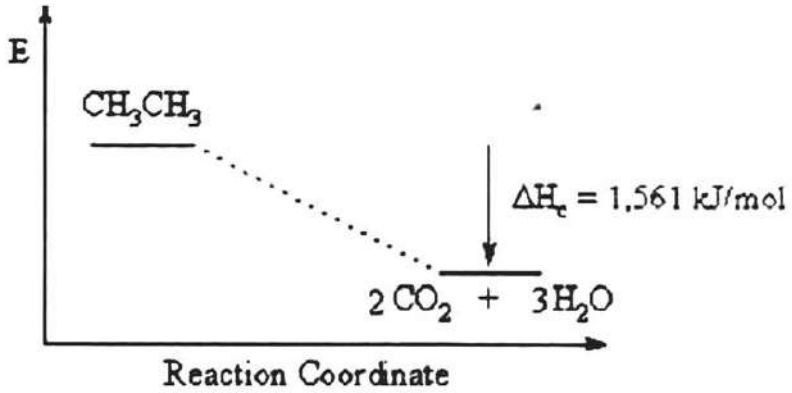
Heat of hydrogenation (ΔH_h) can be defined as the amount of heat released upon the addition of H_2 to one mole of a compound (e.g. an alkene or alkyne) to generate the corresponding alkane.

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



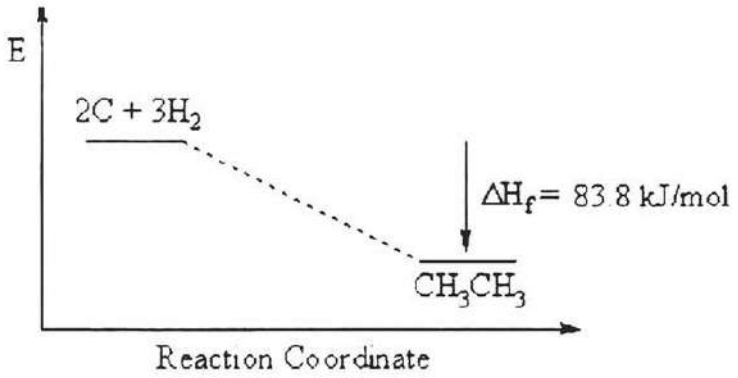
Heat of combustion (ΔH_c) can be defined as the heat released when one mole of a compound undergoes complete combustion in Chto produce CO_2 and H_2O.

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



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

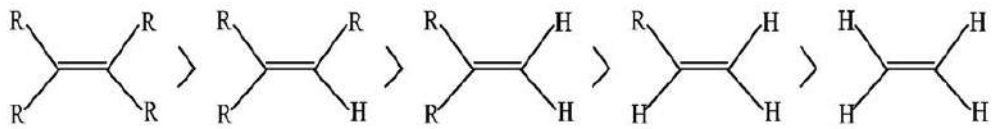
- These diagrams can be either **endothermic** or **exothermic** processes.



1.3.9.7 Relative stabilities of isomeric hydrocarbons :

The stability of alkene can be determined by measuring the heat of hydrogenation. Since the double bond is breakin'g 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 yery accurately. Stability is simply a measure of energy Lower of energy molecules are more stable than higher energy molecules. More substituted alkenens 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 :

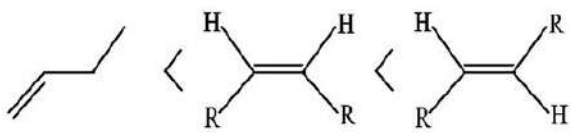
Stability increases .....heat of hydrogenation decreases



most stable least stable

Heat of hydrogenation increases.....stability decreases

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:



least stable most stable

–30.3 kcal/mol –28.6 kcal/mol –27.6 kcal/mol

highest heat of hydrogenation lowest heat of hydrogenation

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	$(CH_3)_3CC(CH_3)_3$	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.

1.4 Summary

Physical properties of organic compounds typically of interest include both quantitative and qualitative features. Physical properties are observable and can be measured. Quantitative information includes melting point, boiling point etc. Qualitative properties include odor, consistency, solubility, and color.

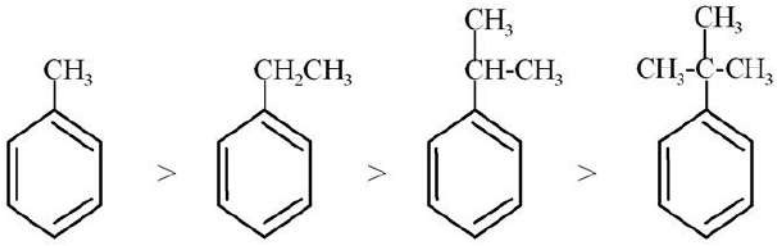
1.5 Questions/Answers :

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

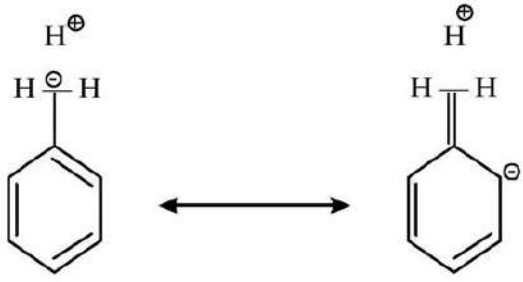
   Answer: Based on the overlapping of orbitals, two types of covalent bonds are formed. These are known as sigma (σ) and pi (π) bonds.

- 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 intemuclear 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 $\overset{\oplus}{E}$ attack on benzene nucleus.



For t-butyl benzene there is no α-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: See 1.2.6

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) $C_6H_{12}0_6$ 3) $C_3H_4Cl_2$ 4) C_8H_7N 5) $Cl_{13}H_{10}$ 6) C_4H_9NO

Answer: See 1.2.6

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, heta of hydrogenation of C_6H_6 should be –28.6 x 3 = –85.8 Kal/mole

But experimental value is -49.8 Kcal/mole

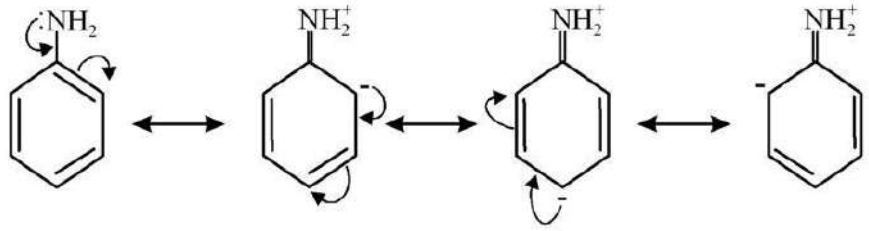
Thus, R.E of C_6H_6 = [– 85.8 – (– 49.8)] Kcal/mole

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

6. Draw the possible resonating structures of aniline.

See 1.2.4

Hint:



7. 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.

8. Compare the dipole moment between NF_3 and NH_3.

Answer: 1.3.9.5

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

Answer: See 13.9.5

10. 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_2CHCl, $CH{\equiv}C{-}Cl$

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 a moment). There is no opposition moment so it possesses high dipole moment.

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

But in vinyl chloride both the σ moment and π-moment acts in opposite direction. So they cancel partially.

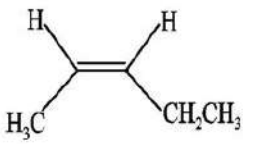
$$H_2C = \overset{\rightarrow}{CH}-\overset{\leftarrow}{Cl}$$

Net dipole moment (μ) = $\mu\sigma - \mu\pi$

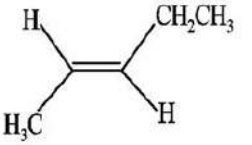
Due to more electronegative nature of alkyne triple bond, the value of $\mu\pi$ is greater for **CH≡C–C1**. So, it possesses lower dipole moment than vinyl chloride.

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

i)

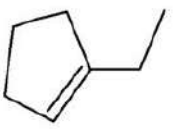


A

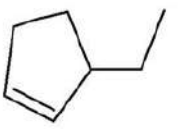


B

ii)



A

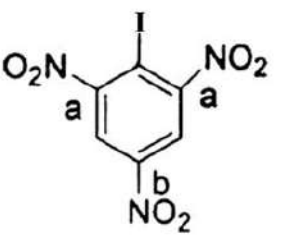


B

Answer: See 1.3.12.3

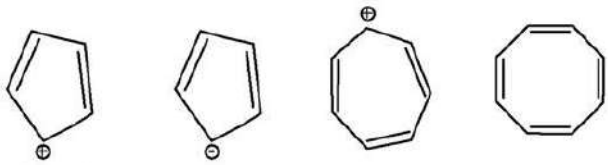
Hint: i) B; ii) A

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



Answer: See 1.3.9

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



Answer: See 1.3.7

14. Draw all the π MOs of allyl cation, allyl anion and allyl radical. Arrange them in order of increasing energy levels. Indentify HOMO and LUMO in each case.

Answer: See c: 1.3

15. Arrange the following compounds in order of their boiling point and explain.

n-pentane. iso-pentane and neo-pentaqe.

Answer: 1.3.9.2

16. Why ethanol is water soluble but tert-butanol is immiscible in water?

Answer: 1.3.9.3

I7. How do you differentiate cis-2-butene and trans.-2-butene by considering their physical properties?

Answer: 1.3.9.5

18. Arrange the following compounds in order of their stability and explain.

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

Answer: 1.3.9.7

19. State and explain Baeyer's strain theory.

Answer: 1.3.9.1

20. What are the Baeyer's false assumptions regarding relative the stability of cycloalkanes? Answer: 1.3.9.1

21. How will you separate ortho-nitrophenol and para-nitrophenol?

Answer: See 1.3.9.2 (Hint: Different boiling points due to hydrogen bonding effects. Separation can be done by distillation technique).

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

Answer: 1.3.9.2

Unit 2 ❑ General Treatment of Reaction Mechanism I

Structure

2.0 Objectives

Main objective of this unit is to provide basic knowledges about the reaction mechanism which will include the following :

- Mechanistic classification

- Representation of mechanistic steps
- Elementary idea about electrophiles and nucleophiles
- Reaction intermediates such as carbocation, carbanions, carbon radicals, carbenes etc.
- Generation and stability of these reactive intermediates.

2.1 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.

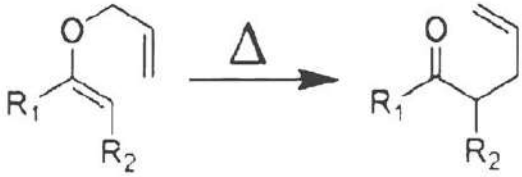
Collectively, an overall reaction and a reaction mechanism consist of multiple elementary processes. These elementary steps are the basic building blocks of a complex reaction, and cannot be broken down any further.

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.

$$CO + NO_2 \rightarrow CO_2 + NO$$

- **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 steps are the details one can obtain through the study of reaction mechanism.

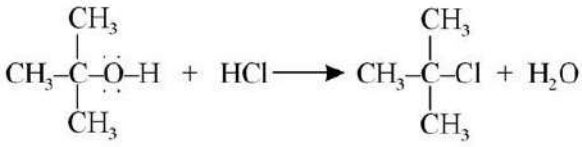
2.2 Mechanistic classification

2.2.1 Ionic reaction:

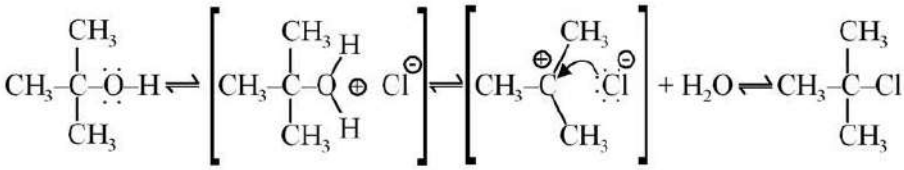
Reactions which involve charged species and the bonding together of electrophiles and nucleophiles are ionic or polar reactions.

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:



2.2.2 Radical reaction :

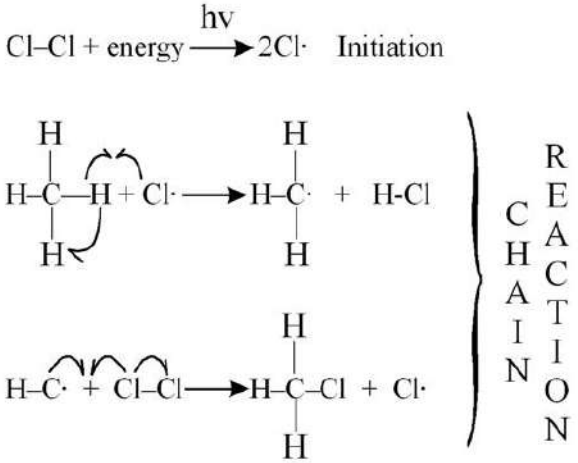
A free-radical reaction is any chemical reaction involving free radicals. This reaction type is abundant in organic reactions.

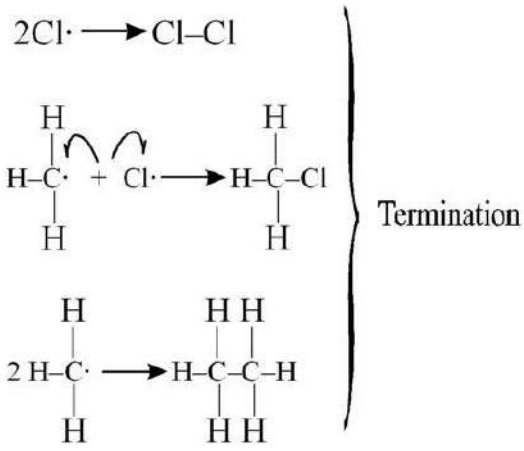
Many radical reactions are chain reactions with a chain initiation step, a chain propagation step and a chain termination step

Example: Chlorination of methane in presence of light energy.

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

Mechanism:





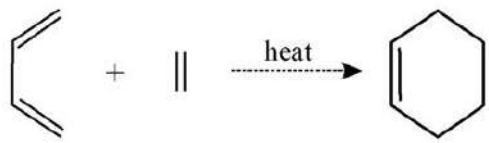
2.2.3 Pericyclic reaction :

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

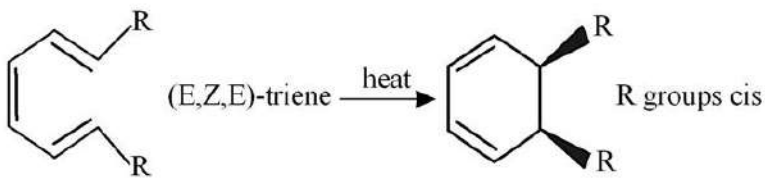
The word '**pericyclic**' comes from how the electrons flow round the outside of the ring.

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

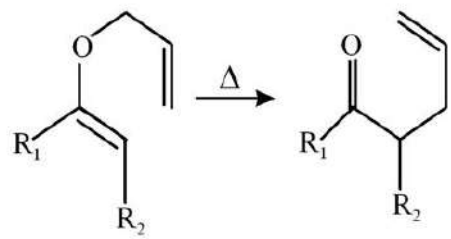
i) Diels-Alder reaction:



ii) Electrocyclic reaction:



iii) [3,3]-sigmatropic rearrangement:



2.3 Types of reaction

Three basic reactions are

i) Addition reactions

ii) Elimination reactions

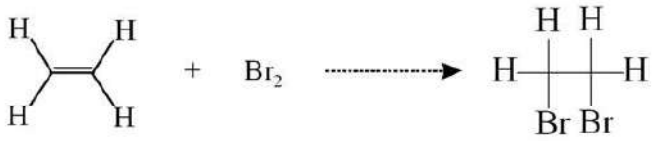
iii) Substitution reactions

2.3.1 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).

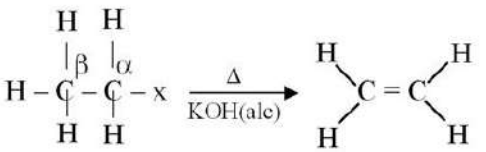
Example: When bromine is added to ethylene the red dolour of bromine disappears.



bownish-red colourless

2.3.2 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.



Haloalkane Alkene

2.3.3 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.

$$CH_3I + NaOH \longrightarrow CH_3OH + CH_3I$$

2.4 Nature of bond cleavage and bond formation

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

2.4.1 Homolytic cleavage :

A covalent bond breaks in such a way that each of the bonded atoms gets one of the shared electrons.

$$H_3C\text{-}CH_3 \longrightarrow \underset{\text{radicals}}{\dot{C}H_3 + \dot{C}H_3}$$

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

2.4.2 Heterolytic cleavage :

A covalent bond breaks in such a way that one of the bonded atoms gets both of the shared electrons.

$$H_3C\text{-}OH \longrightarrow \overset{+}{C}H_3 + \overline{O}H$$

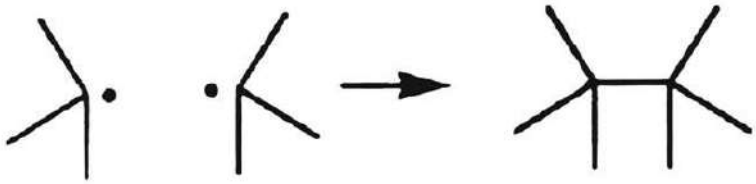
Resulting species are called cations and anions.

2.4.3 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

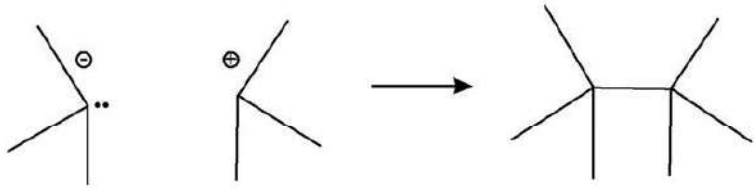


2.4.4 Heterogenic bond formation :

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



2.5 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.

2.5.1 Reagent classification :

Basically two types—

i) Electrophiles

ii) Nucleophiles

2.5.1.1 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

2.5.1.2 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.

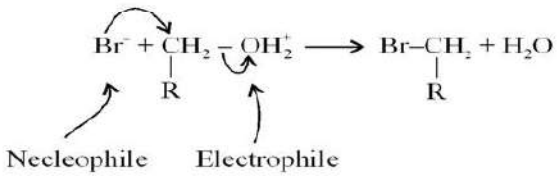
Example: NH_3 HO^- H_2O

2.5.2 Curly arrow rules in representation of mechanistic steps :

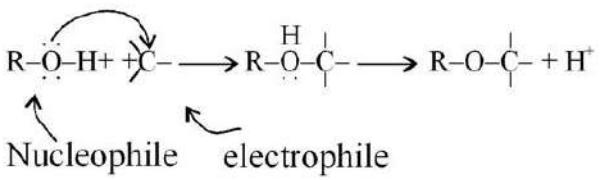
- Electrons always flow from nucleophile to electrophile

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

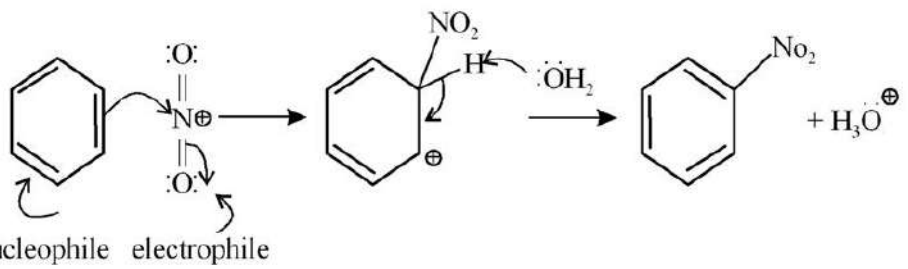
i)



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).

2.6 Reactive intermediates

2.6.1 Introduction :

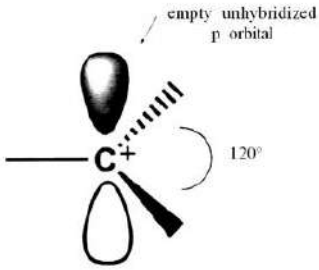
A reactive intermediate or an intermediate is a short-lived, high-energy, highly reactive molecule.

- 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:

2.6.2 Carbocations :

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



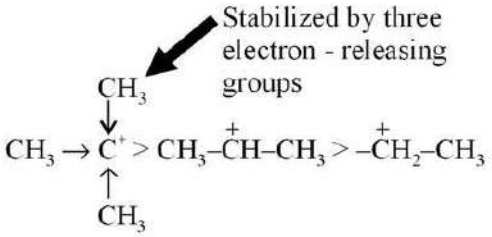
Structure of Carbocations: Generally, in the carbocations the positively charged carbon atom is bonded to three other atoms and has no nonbonding electrons. It is sp^2 hybridized with a planar structure and bond angles of about 120°. There is a vacant unhybridized p orbital which in the case of CH_3^+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

Stability of Carbocations :

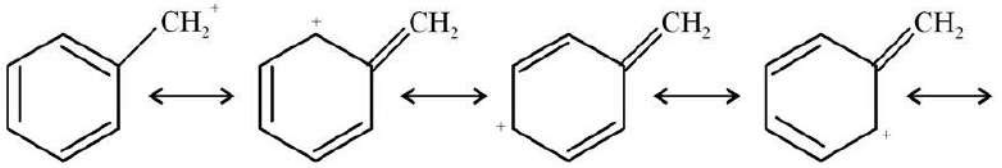
Stability of carbocations $3° > 2° > 1° > CH_3^+$

Thus one finds that addition of HX to three typical olefins decreases in the order $(CH_3)_2C = CH_2 > CH_3–CH = CH_2 > CH_2 = CH_2$.

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.



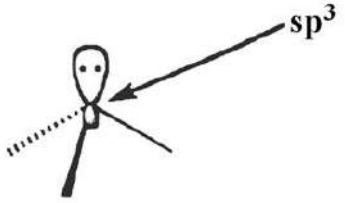
- **Electron release:** Disperses charge, stabilizes carbocation.
- Benzyl cation is highly stabilized by the following type of resonance.



2.6.3 Carbanions

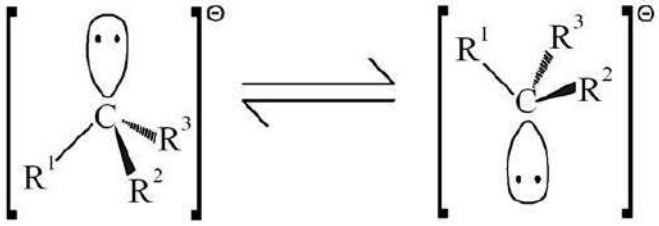
Negatively charged trivalent carbon atom.

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

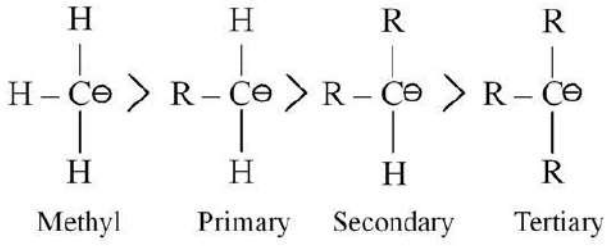
- Carbanions would thus have pyramidal structures similar to those of amines.
- It is believed that carbanions undergo a rapid interconversion between two pyramidal forms.



Pyramidal inversion

Stability of Carbanions:

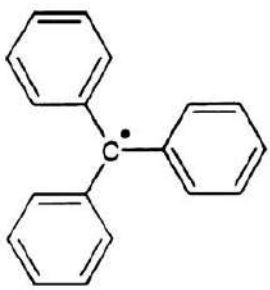
$3°, 2° < 1° < CH_3^-$



Properties of Carbanions: Carbanions are nucleophilic and basic and in this behaviour 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

2.6.4 Carbon radicals :

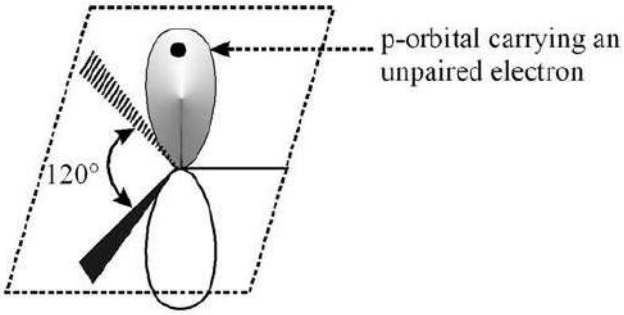
In this module an overview of carbon radicals are given. Some preliminary examples of their structure, properties, generation and reactions are provided.

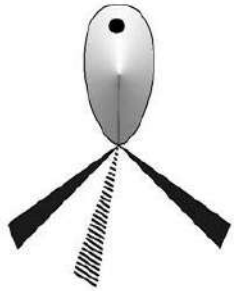


The first organic free radical identified was triphenylmethyl radical formed by abstraction of chlorine by silver metal. This species was discovered by Moses Gomberg in 1900 at the University of Michigan USA.

- A radical is a reactive intermediate with a single unpaired electron, having very short lifetime. It is represented by atom with one dot.

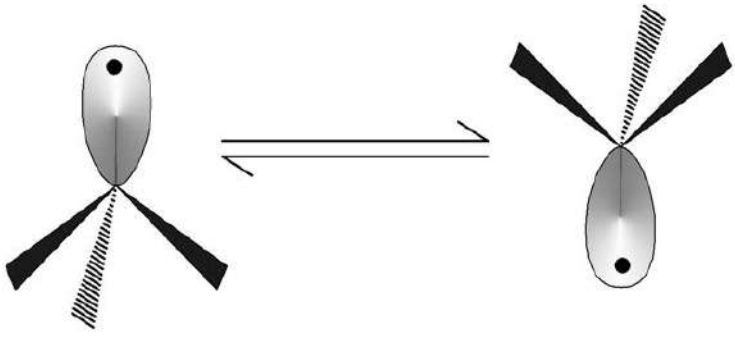
- Carbon radical is a neutraf carbon species with three single bonds and one unpaired electron. Structure: A carbon radical is sp^2-hybridized with an unpaired single electron occupying an unhybridized p-orbital, having trigonal pyramidal or planar geometry possessing an angle of 120° rigid pyrimidal geometry.





sp_z Hybridised carbon having rigid pyrimidal geometry

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



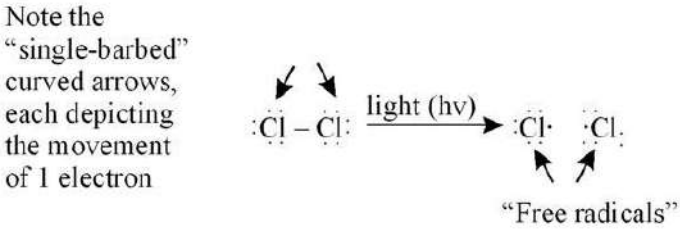
Flexible pyramidal geometry

- In most of the cases the pyramidal geometry is observed, especially when heteroatom's are π electron donating substituent or electronegative groups like **fluorine** 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.

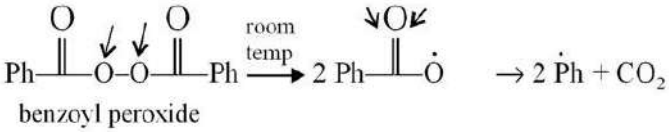
$$A — B \qquad A^{\cdot} + B^{\cdot}$$

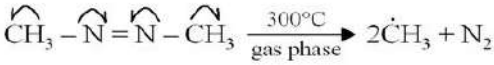
Example: formation of chlorine radicals in presence of light.



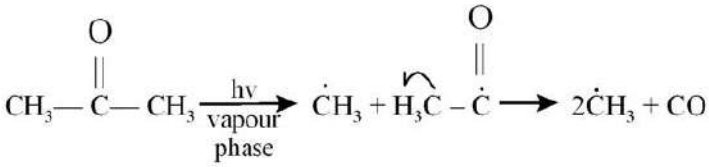
Free radicals may be generated by the following way.

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

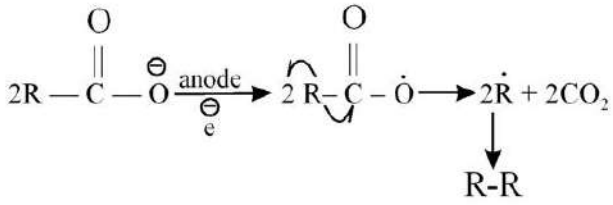




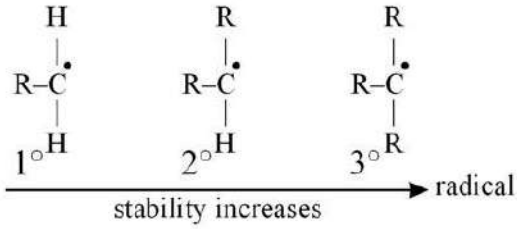
ii) **Photolysis:** Photochemical dissociation (visible or UV light) of covalent bonds may generate free radicals.



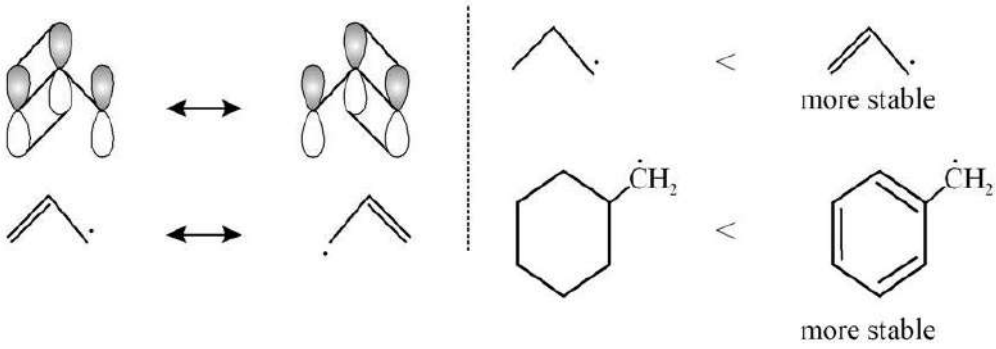
iii) **Redox reaction:** Single electron transfer reactions (SET) are very much useful to produce free radicals. One such reaction is the Kolbe electrolysis of the salts of carboxylic acids.



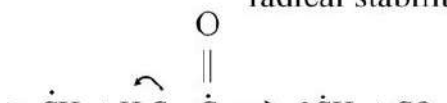
Stability: Like carbonium ions, a tertiary free radical is more stable than a secondary which in turn is more stable than a primary.

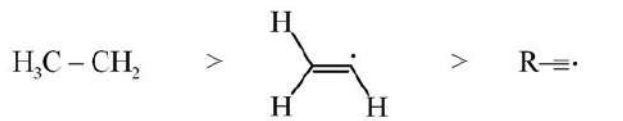


- Free radicals are stabilized by resonance.



- 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 decrease as the atom goes from $sp^3 \rightarrow sp^2 \rightarrow sp$





most stable sp^3 sp^2 least stable sp

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

most stable least stable

2.6.5 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.

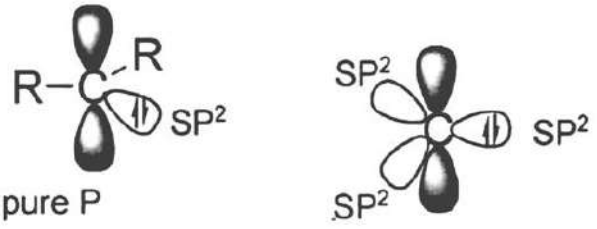
The simplest member of the class is methylene, a non isolable species of molecular formula H_2C:

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).

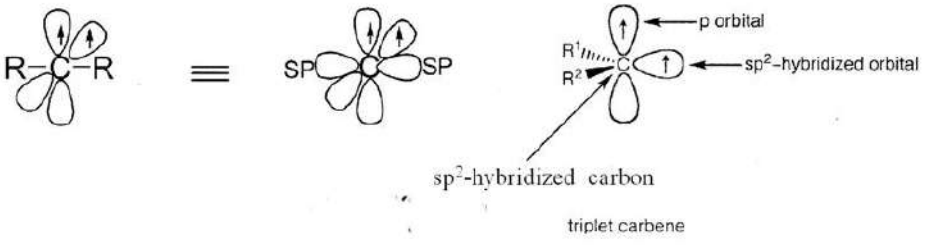
Singlet carbene: In singlet state a carbon atom is approximately SP^2 hybridized. Two of three Sp^2 hybrid orbitals are used in forming two covalent bonds where as the third orbital contains the unshared pair of electrons. The bond angle would be expected to be less than normal 120 °C due to L.P. - L.P.>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

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

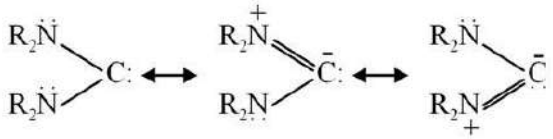


Triplet carbene: In triplet state a carbon atom is SP hybridized and it is linear. These two hybrid orbitals are involved in bond formation with two groups and the remaining two electrons are placed one each of the two unhybrid orbitals). SP^2 triplet carbene are also possible.

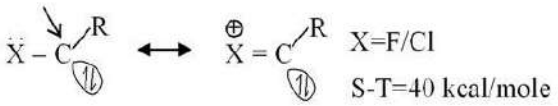
(Triplet state: diradical-like in nature, linear geometry)



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 'π' -donation into the vacant 'P' orbital.

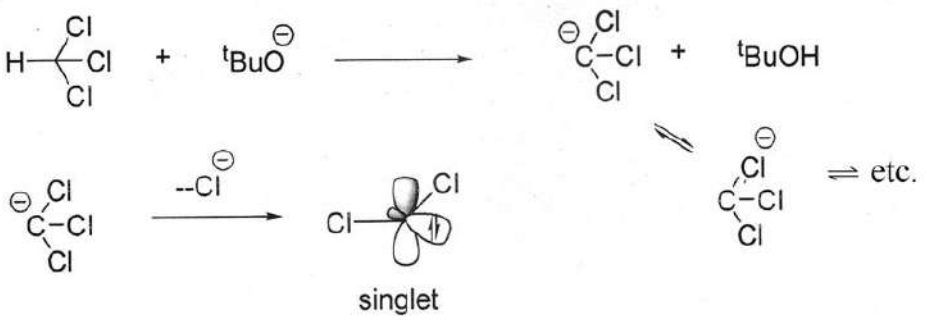


- For H_2C: or Li_2C:, triplet state is more stable than singlet state and the energy difference is 10-20 kcal/mole.
- Because of these properties, the parent carbene :CH_2 (or dialkyl carbene) has a triplet ground state.

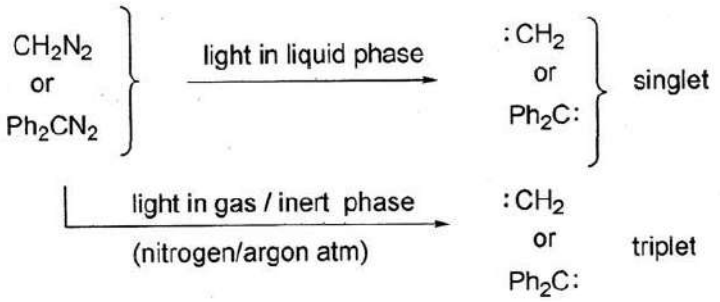
Properties: A singlet carbene may act as a Lewis bases and can donate it,s non-bonded electron pair. Again, by accepting two electrons in the vacant 'p' orbital it can acts as a Lewis acid. Triplet carbene acts as diradical.

Formation reactions of carbenes:

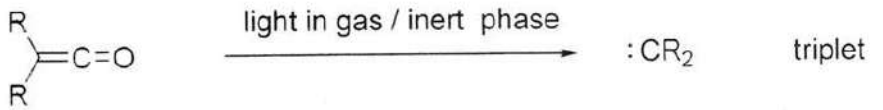
a) Reaction between $CHCl_3$ and strong base e.g. ^-OH or $^tBuO^-$



b) Photolysis or thermolysis of diazocompounds

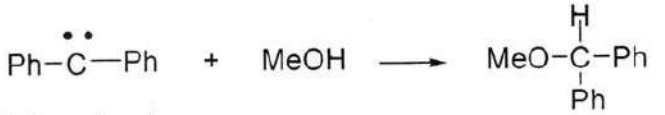


c) photolysis of ketenes:



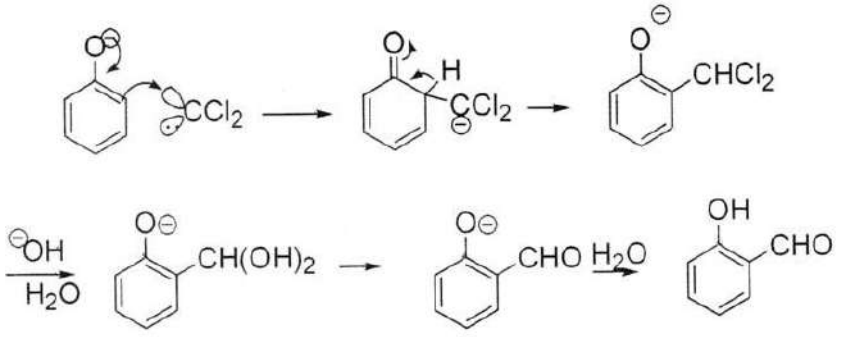
Reactions of carbene:

i) Acts as electrophile



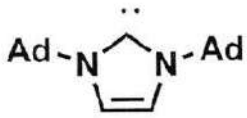
diphenyl carbene

In Reimer Tiemann Reaction:



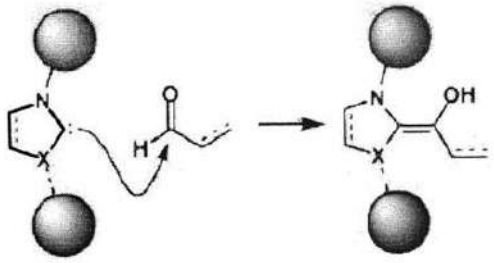
ii) Acts as nucleophile

N-Heterocyclic carbene (NHCs) acts as nucleophile.



(Ad = alkyl or aryl group

Example:



nucleophile

2.7 Summary

- Ionic reactions normally takes place in liquid solution. where solvent molecules assist the formation of charged intermediates.
- Two types of bond cleavage may occur e.g. Homolytic cleavage and Meterolytic cleavage.
- Electrophile accepts a pair of electrons whereas Nucleophile donates a pair of electrons to form a new covalent bond.
- Stability carbocations as well as carbon radicals is $3° > 2° > 1° > CH_3^+$
- Triplet carbenes are more stable than singlet carbenes.

2.8 Questions and Answers

1. What is the correct order of decreasing stability of the following cations?

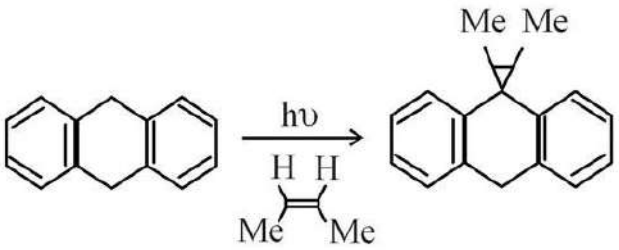
$CH_3\overset{\oplus}{C}HCH_3$ (I)

$CH_3\overset{\oplus}{C}(OH)CH_3$ (II)

$CH_3\overset{\oplus}{C}H{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}CH_3$ (III)

Ans. III > II > I

2. Which intermediate is involved in the reaction given below?



Ans. Carbene

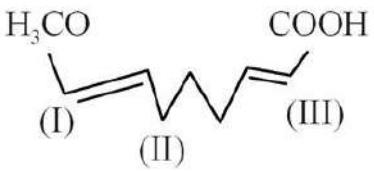
3. Which halogen nucleophile is weakest in polar, aprotic solvents?

Ans. I^-

4. Which among the following is not an electrophile? H_2O, Cl_2, HBr, Br_2

Ans. HBr.

5. In the given molecule where will electrophile will attack?



Ans. (I) position

Unit 3 ❑ Stercochemisty-1

Structure

3.0 Objectives

By the end of this unit learners will be able to know :

- About the bonding geometries of carbon and stereochemical representation of molecules.
- To point out the symmetry elements of a molecule.
- To designate R/S, E/Z, syn/anti descriptor of a molecule.
- About optically active compound's having chirality;
- Stereoisomers and their relations.

3.1 Bonding geometries of carbon compounds

3.1.1 Introduction :

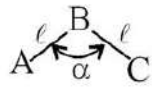
Stereochemistry is the chemistry in three dimensions and hence concerned with the geometry of molecule. Molecular geometry can be described by its bond length, bond angle, dihedral angle and other geometrical parameters that determine the position of each atom.

3.1.2 Geometrical parameters :

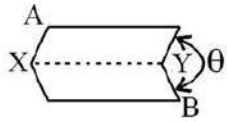
Bond length (ℓ) : The bond length of a diatomic molecule AB can be defined as the equilibrium value of the distance between the centres of the two atomic nuclei connected by one or more covalent bonds as shown.

A ℓ B

Bond Angle (α) : It is the angle subtended by the centres of three atomic nuclei connected together as in A-B-C.



Dihedral angle (θ) : 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 θ as shown. (see section 4.3.1)



Vander Waals radii of atoms or groups:

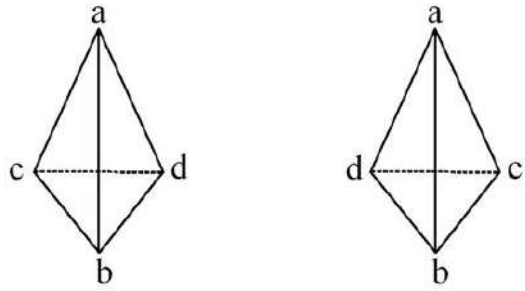
When two nonbonded atoms or groups (ligands) are close to each other there appears an attractive force between the electrons of one atom and the nucleus of the other and repulsive forces between the nuclei and between the electrons of the two atoms. The distance at which the attractive and repulsive 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_3 (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.

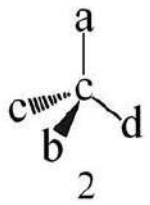
3.1.3 Tetrahedral nature of carbon and concept of asymmetry and represention of molecules :

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

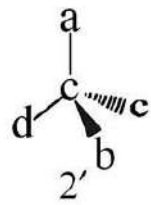


1 1′

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. 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.



2

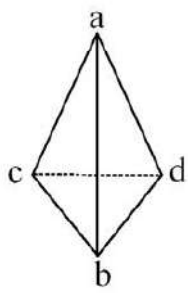


2′

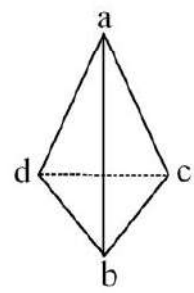
In 2 and 2′, bonds with uniform lines lie in the plane of the paper, the thick end of the wedge are in the front and the dotted lines are behind the plane. The structures 2 and 2′ are called flying wedge formula. They form non-superposable mirror images of each other. A Cabcd type of molecule that is not superposable on its mirror image is called chiral and exists as a pair of enantiomers. A molecule with one chiral centre is called asymmetric (see section 3.2.3) molecule.

Fischer projection formula :

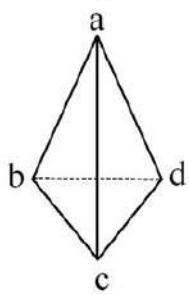
If the positions of the tetrahydral structures are slightly changed, 1 and 1′ assume the gesmetric figures 3 and 3′ in which b and d are horizontally placed.



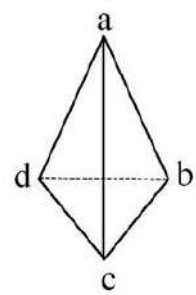
1



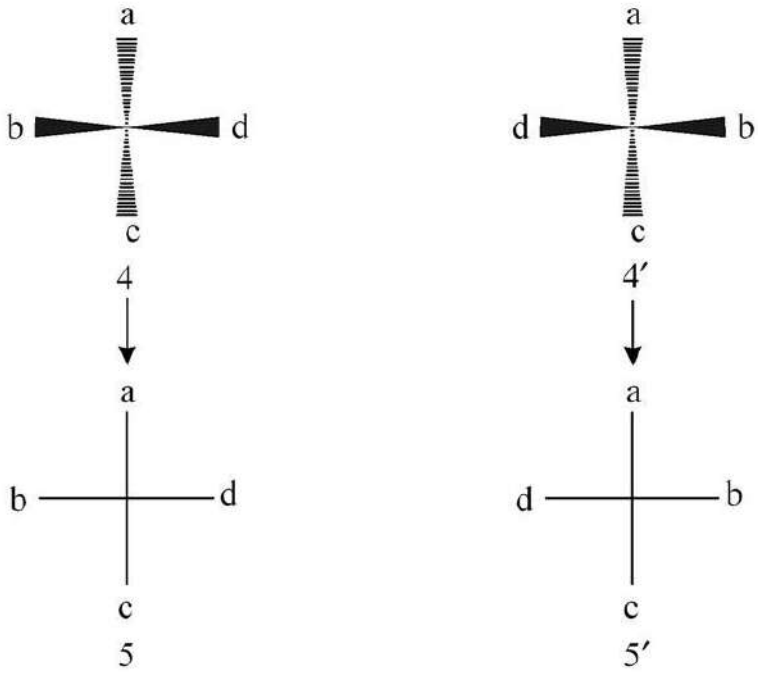
1′



3



3′

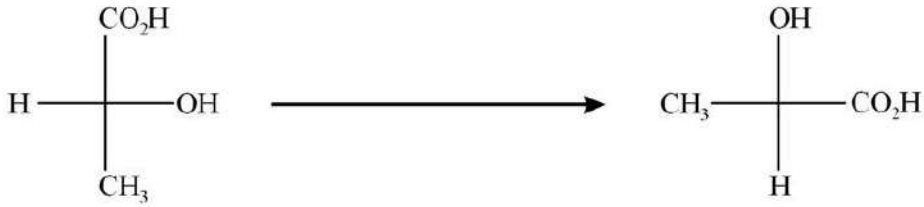


When the ligands a, b, c and d are joined to the central carbon atom by chemical bonds, 3 and 3′ give three-dimensional perspective formula 4 and 4′ on two-dimensional paper in which the horizontal ligands b and d are above the plane and towards the observer while the vertical ligands are below the plane 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.

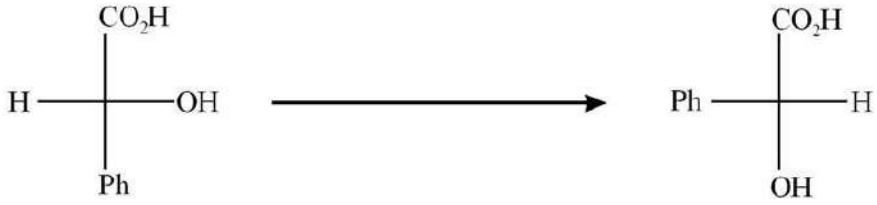
1. The projection formula cannot be lifted out of the plane of the paper.
2. The projection formula is not allowed to rotate through 90° or 270° although it is permissible to rotate through 180° or 360°.
3. Single exchange of a pair of ligands results in an enantiomeric structure while double exchange between two pairs leads to an equivalent structure.

Problem : How would you convert the following by exchange of ligands?

(i)



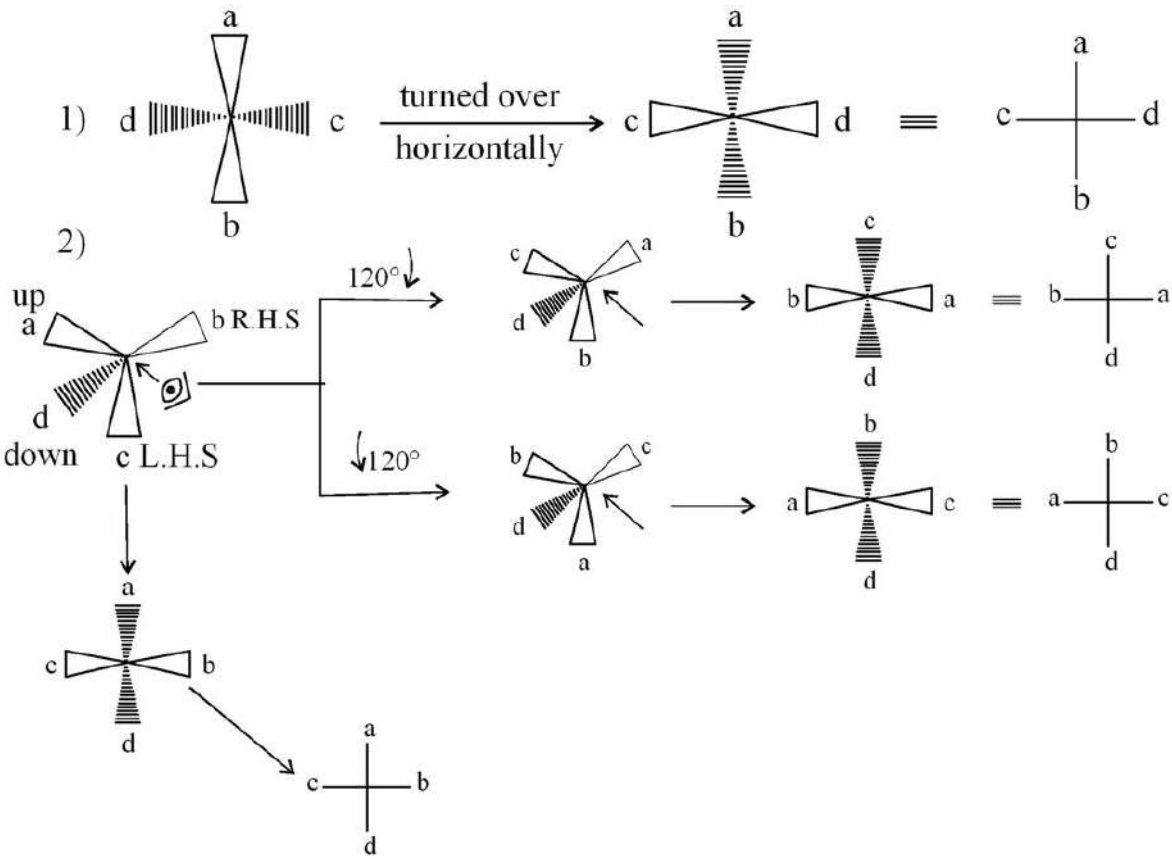
(ii)



Solution: i) double exchange between H ↔ CH_3 and HO ↔ CO_2H

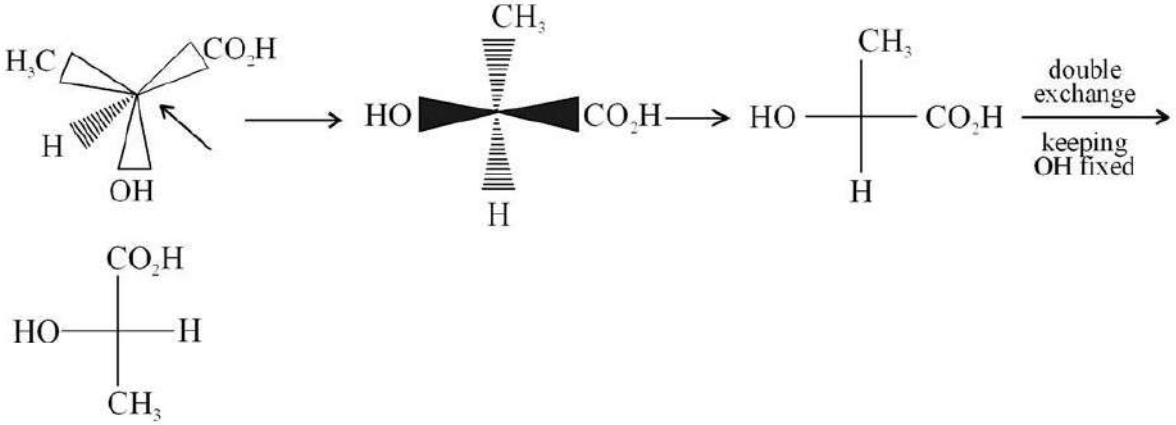
ii) double exchange of ligands.

● Conversion of 3D-perspective or Wedge formula having one chiral centre to Fischer projection (F.P) formula.

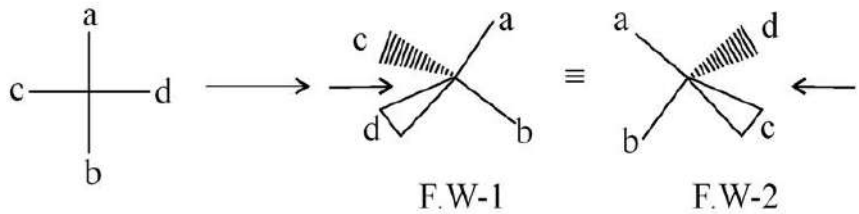


Problem : How would you transform the following 3D-perspective formula of lactic acid to F.P. ?

Solution:

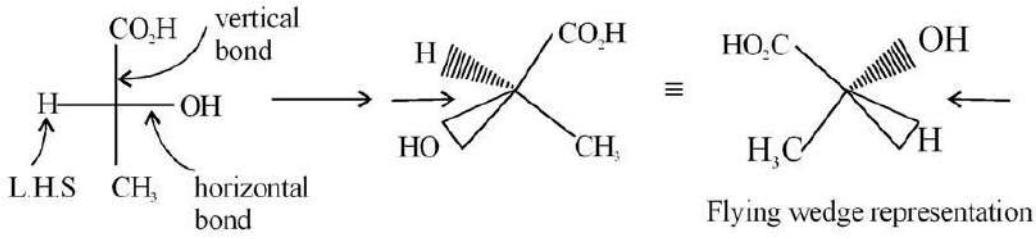


- Interconversion of F.P into F.W (flying wedge):



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.

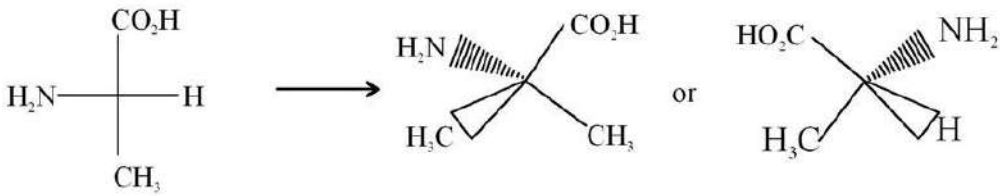
Illustration with an example.



F.P.

Problem : Convert alanine from its F.P. to F.W.

Solution:

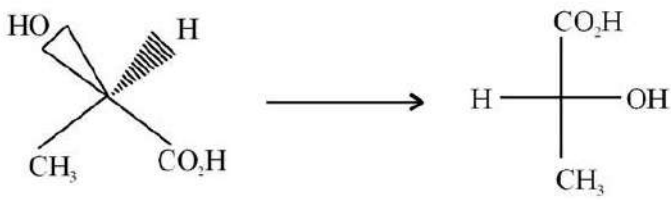


(alanine)

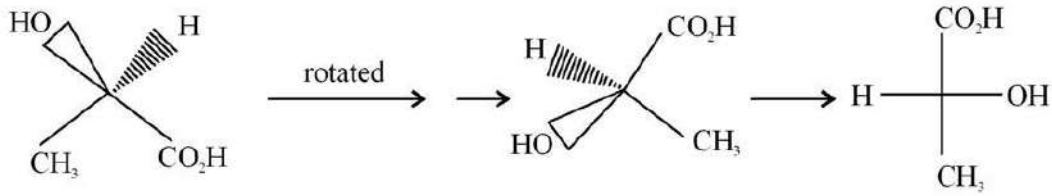
- Conversion of F.W to F.P.

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 :

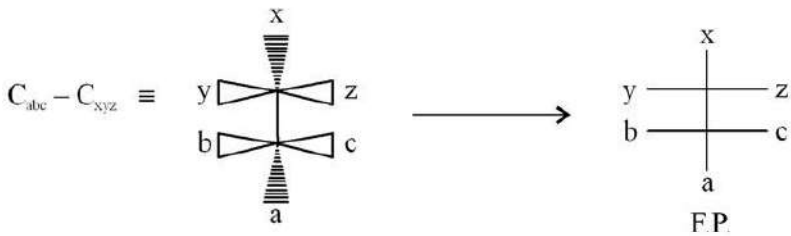


Solution:



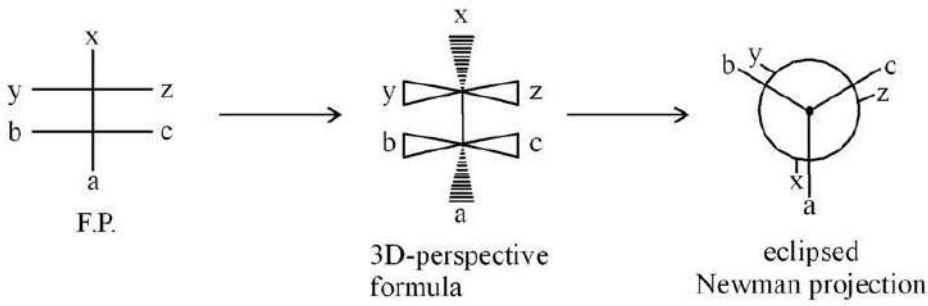
- **Fischer projection formula for molecules having two chiral centres.**

Fischer projection formula with two chiral centres such as C_{abc}—C_{xyz} 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.

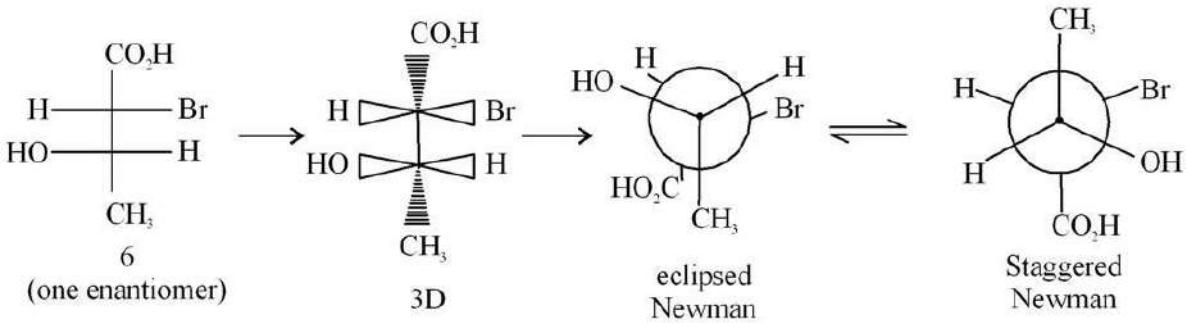
- Newman projection formula.



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.

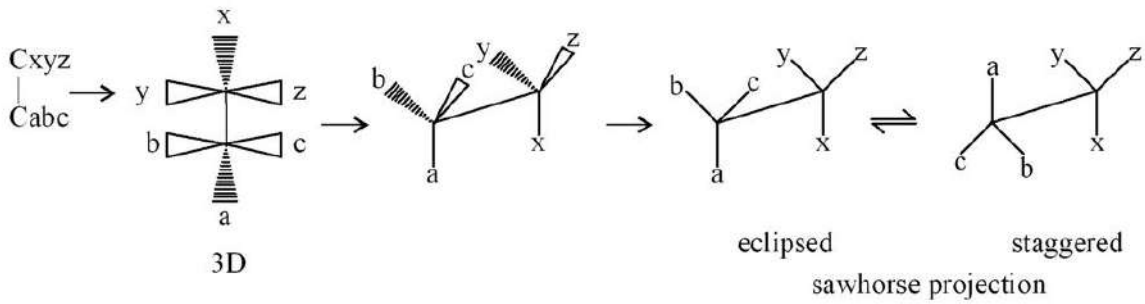
These are illustrated with 2-bromo-3-hydroxybutanoic acid 6



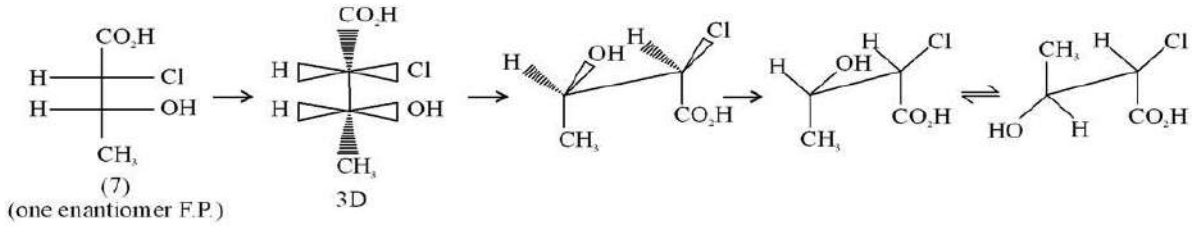
So, we can directly convert a molecule with two chiral centres in F.P. to the corresponding Newman projection.

- Sawhorse projection formula (sawhorse formula)

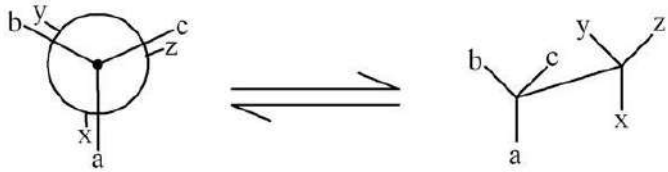
In this case, C–C bonds in 3D-perspective formula is viewed from an angle such that after projection C–C bond will appear as an oblique line called diagonal line. The bonds attached to each chiral centre are then projected into the same vertical plane as usual to give eclipsed or staggered sawhorse projection formula.



2-Chloro-3-hydroxybutanoic acid (7) can be cited as an example:

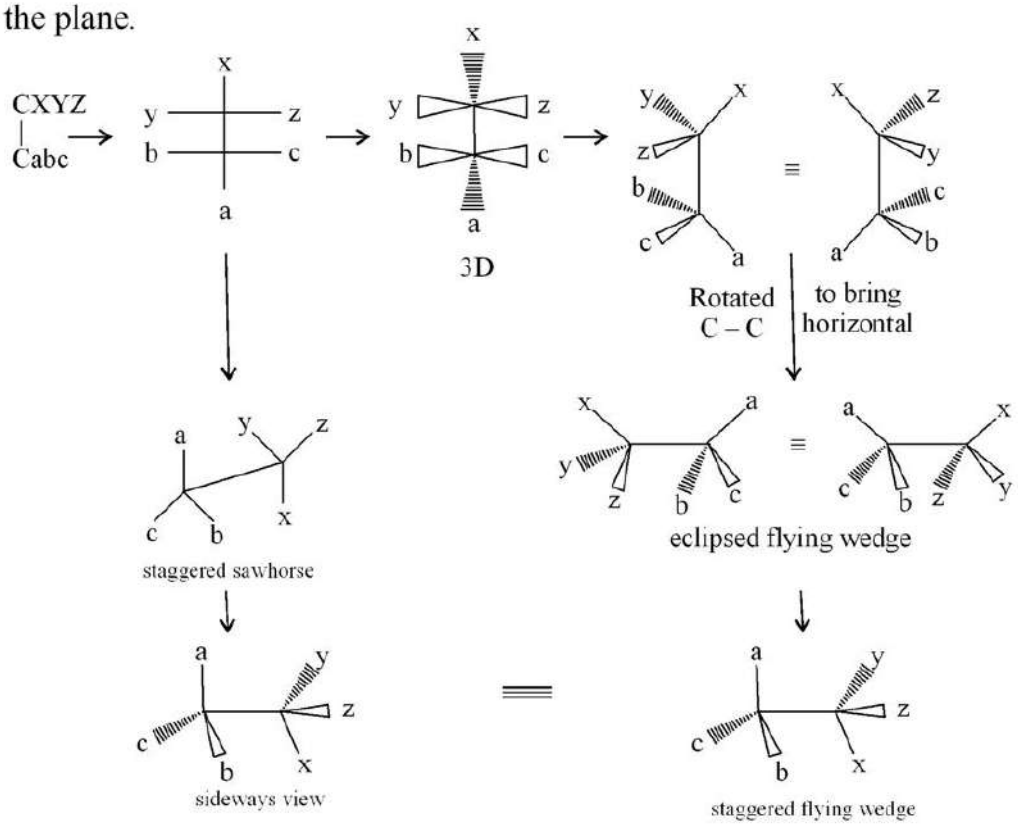


- Interconversion of Newman to sawhorse formula and vice versa.



- **Flying wedge formula with two chiral centres.**

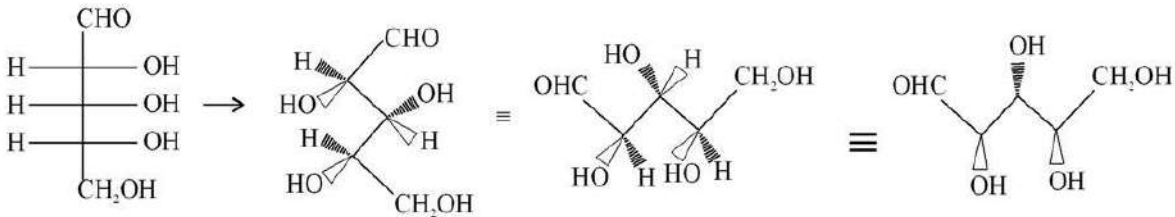
3D-perspective formula with two chiral centres can be represented by flying wedge formula in a similar manner as with one chiral centre. The vertical bonds are considered to be in the plane of the paper and one of the horizontal bonds will be above and another below the plane.



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

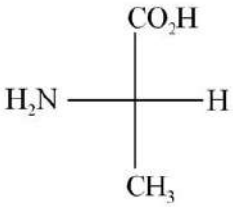


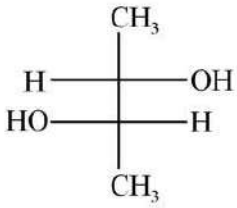
3.1.4 Summary :

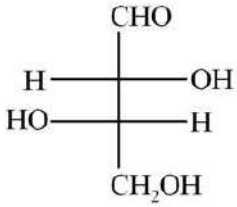
- Three basic parameters namely bond length, bond angle and dihedral angle which determine the geometry of a molecule have been defined.
- van der Waals radii of atoms or groups have also been defined.
- Tetrahedral nature of carbon and concept of asymmetry are discussed.
- Three-dimensional molecular structures on two-dimensional paper namely Fischer projection, flying wedge representation, Newman projection and sawhorse formula are delineated.

3.1.5 Questions :

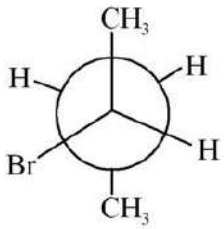
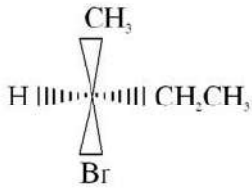
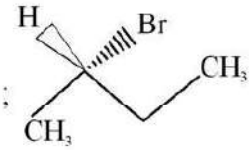
1. Interconvert the molecular structures as indicated.

(a)  to flying wedge

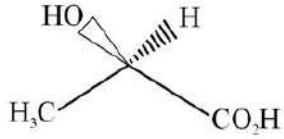
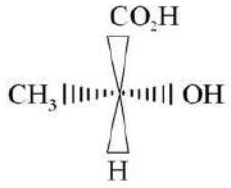
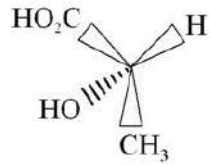
(b)  to Newman projection

(c)  to sawhorse formula

2. Determine whether the following structures are equivalent.

 ;  ; 

3. Give the Fischer projection for the following 3D-perspective formulae and state whether they are identical.

 ;  ; 

3.1.6 Answer :

1. (a) to (c). See text
2. Equivalent
3. See text.

3.2 Symmetry

3.2.1 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. Stereschemistry 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.

3.2.1.1 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.

Table 1

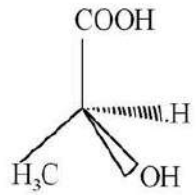
Symmetry elements	Symmetry Operations
1. Proper axis of symmetry (C_n)	1. Rotation about the axis (C_n)
2. Plane of symmetry (σ)	2. Reflection in the plane (σ)
3. Centre of symmetry or inversion centre (i)	3. Inversion through the centre (i)
4. Improper axis of symmetry (S_n)	4. Rotation about the axis followed by reflection in a plane perpendicular to the axis (S_n)

Proper axis of symmetry (C_n) : 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 $\frac{360^\circ}{n}$, an equivalent structure from the original results. It is denoted by C_n where n is the order of rotation. This operation is called C_n operation. Molecules with different order of proper axis are discussed below:

C_1 axis:

In a true sense, C_1 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.

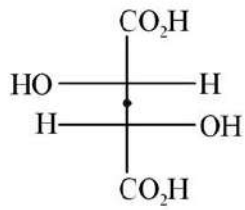
Example: Lactic acid,



C_2 axis:

Rotation of a molecule through 180° about C_2 axis produces a structure indistinguishable from the original.

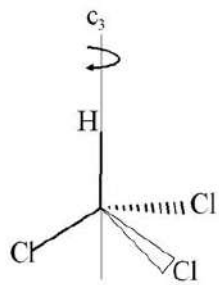
Example: Optically active tartaric acid.



C_3 axis:

Rotation of a molecule by 120° about C_3 axis will give rise to an equivalent molecule.

Example: Chloroform

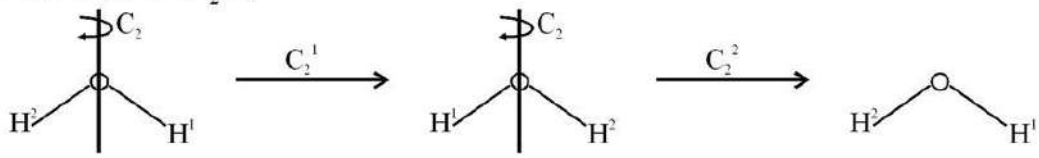


Similarly, rotation of a molecule by 90° about C_4 will give an equivalent structure an so on.

Identity operation, E

A proper axis of symmetry of order n, C_n generates n operations such as C_n^1, C_n^2, C_n^3 ... ... C^{n-1}, C_n^n. This n th operation, C_n^n is the identity operation i.e., $C_n^n = E$

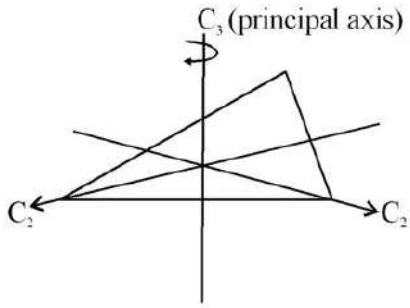
In the case of H_2O,



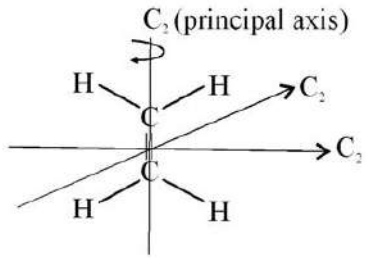
$C_2^2 = E$.

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 C_n 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 C_n 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.

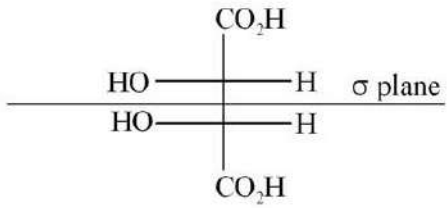


Rotation is a real operation and C_n operation is called the symmetry operation of the first kind.

Plane of symmetry (σ):

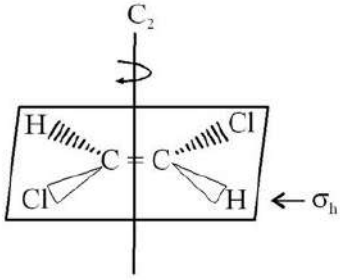
A plane of symmetry is a plane bisecting a molecule into two halves which are mirror images of each other. The reflection of the two halves across the plane produces a structure indistinguishable from the original one.

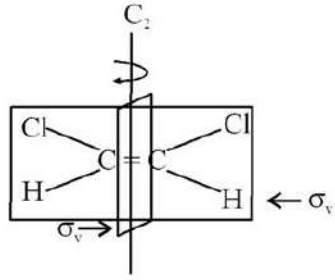
Example: meso-Tartaric acid

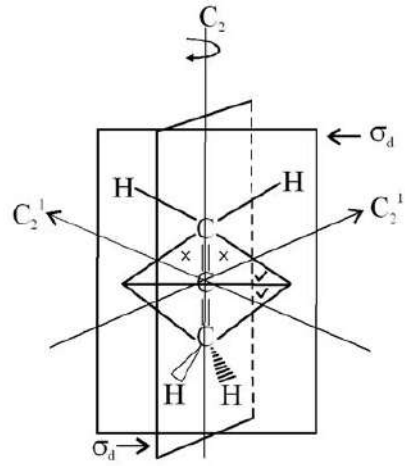


Identity operation: Two successive s operations lead to an identity operation. That is, $\sigma \times \sigma = E$.

When a molecule contains the principal axis, C_n along with symmetry plane, σ it is necessary to replace σ by σ_u, σ_v or σ_d as the case may be. When the symmetry plane σ is perpendicular to the principal axis, C_n it is called horizontal symmetry plane and is symbolised as σ_h. On the other hand, when the symmetry plane σ contains the C_n, it is called vertical symmetry plane and is denoted by σ_v. When σ_v bisects the angle between two C_2 axes, it is called diagonal symmetry plane and is designated σ_d.



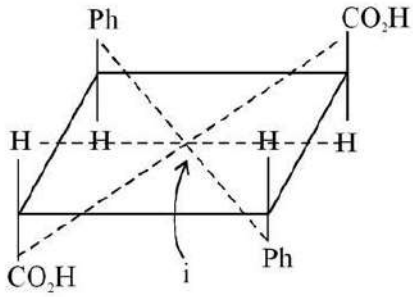




Centre of symmetry or inversion centre (i):

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 enquivalent atom or group. The inversion centre as also the inversion operation are denoted by 'i'.

Example: ∝-Truxillic acid



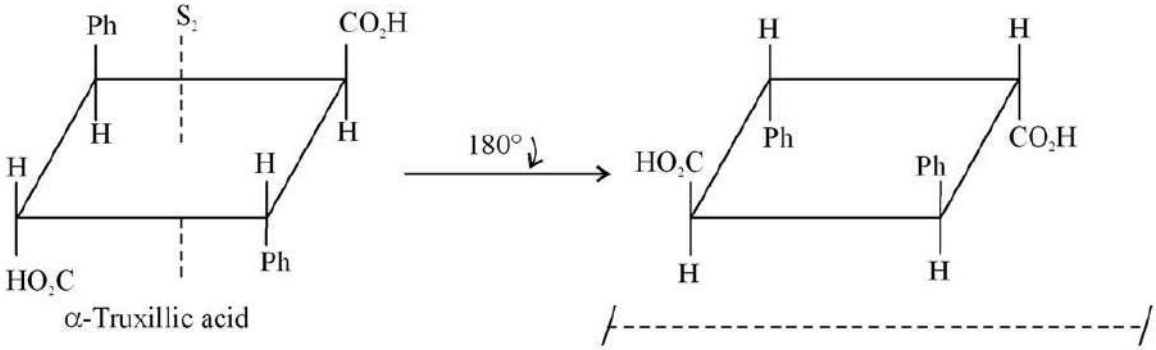
In an inversion operation there is mutual exchange of like pairs of ligands within the molecule.

Identity operation: Two successive i operations lead to an identity operation. That is, $i \times i = E$

Improper axis of symmetry (S_n):

An improper axis of symmetry of order n is an axis such that rotation of the molecule about this axis through $\frac{360^\circ}{n}$ followed by reflection in a plane perpendicular to the axis produces a structure indistinguishable from the original one. It is denoted by S_n. The operation due to improper axis is called S_n operation which can be represented, $S_n = \frac{360^\circ}{n} \times \sigma$ or $S_n = \sigma \times \frac{360^\circ}{n}$ when n = 2, $S_2 = 180^\circ \times \sigma = \sigma \times 180^\circ$.

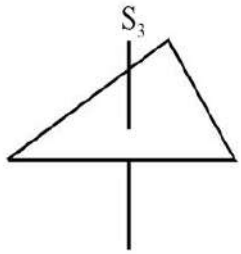
An example of molecule with an S_2 axis is α-truxillic acid.



α-Truxillic acid

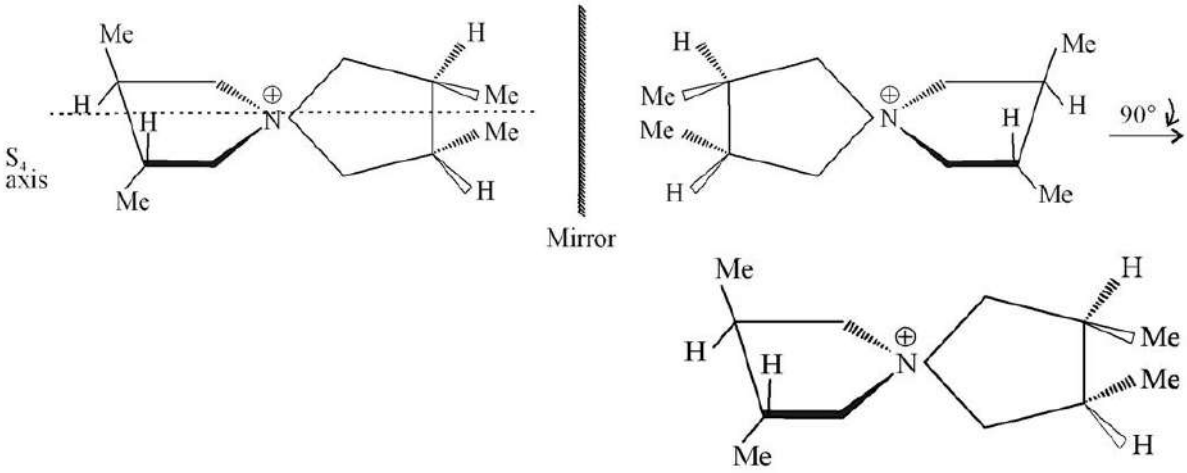
α-Truxillic acid

An example of molecule possessing an S_3 axis is cyclopropane.



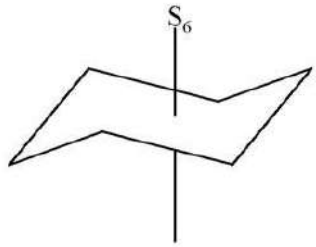
Molecules having an S_4 axis.

Example : 3,4,3′,4′-Tetramethyl-spiro-(1,1′)-dipyrrolidinium ion



A molecule with an S_6 axis

Example: Cyclohexane chair



It is to be noted that when a molecule possesses an S_n axis as the only symmetry element the order of n must be even. In that case, the S_n axis coexists with $C_n/2$ axis. When n is odd, the S_n axis cannot be the only symmetry element and will exist in conjunction with other symmetry elements like C_n axis and σ 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.

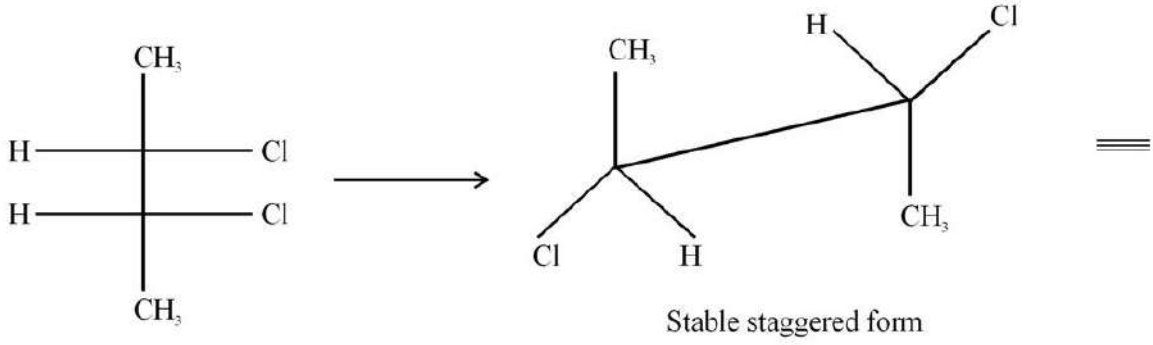
S_n operation is thus the successive C_n operation followed by σ operation across the plane perpendicular to the C_2 axis or the reverse.

$$S_n = C_n \times \sigma = \sigma \times C_n.$$

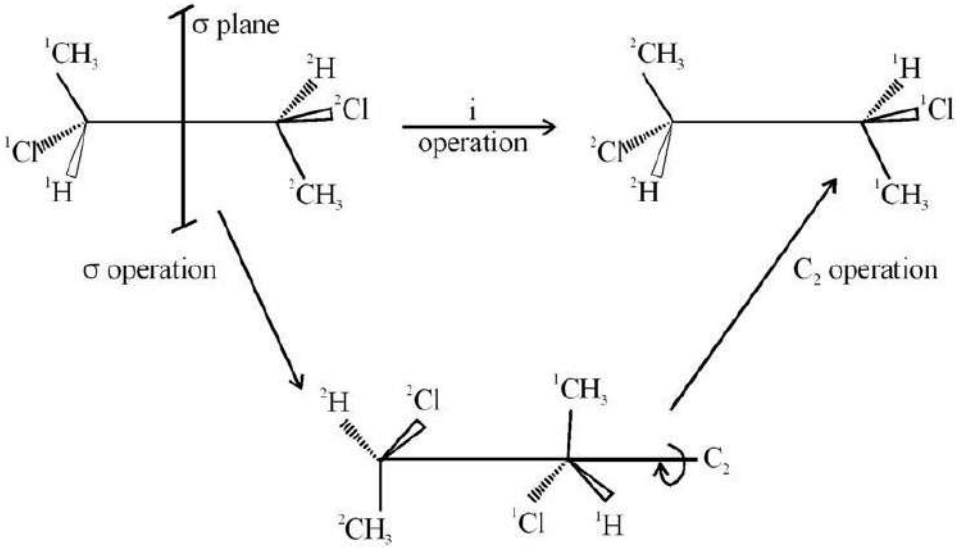
It can be shown that an S_2 operation is equivalent to an i operation and S_1 operation is equivalent to σ operation.

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.



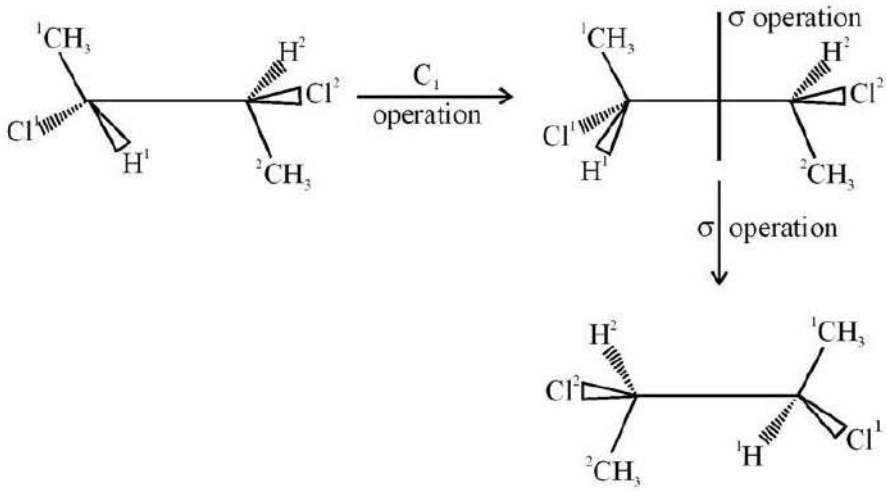
Stable staggered form



Thus, $S_2 = \sigma \times C_2 = i$

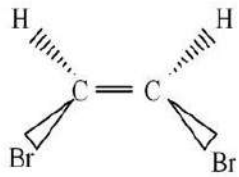
(ii) $S_1 = C_1 \times \sigma = \sigma \times C_1$

Illustration



3.2.2 Point group :

3.2.2.1 Introduction: Let us consider trans-1,2-dibromoethylene as a model compound.



It has four symmetry operations E, C_2, σ_n and i corresponding to the symmetry elements C_2, σ 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 symmetry operations. A group of molecules with the same set of symmetry operations is called a symmetry point group. The group of symmetry operations E, C_2, σ_n and i is called C_2h 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 σ of the molecule. We can combine the symmetry elements following some rules.

1) The presence of a C_2 axis and a σ plane perpendicular to it implies the existence of an S_2 axis (i.e. an inversion centre i).

2) σ_n cannot coexist with σ_d

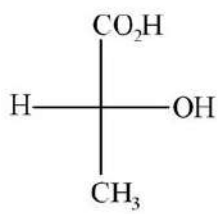
3) An S_n axis always coaxial with C_n axis.

3.2.2.2 Point groups of chiral molecules :

C_1 point group:

A molecule with only C_1 axis of symmetry belongs to C_1 point group.

Example: Lactic acid



The order of this point group is 1

Operators E

Sym. No. σ = 1

Molecules to this point group are chiral or asymmetric. They are optically active.

C_n point group: Molecules with only n-fold proper axis of symmetry belong to C_n point group and are chiral.

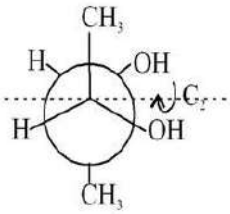
Order of this point group C_n is n.

Operators C_n^1, C_n^2, C_n^3 ... ... C_n^{n-1}, C_n^n ($\equiv$ E)

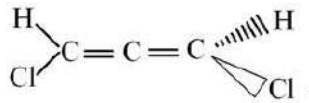
Symmetry number $\sigma = n$

Molecules belonging to this point group are dissymmetric and optically active.

C_2 point group. Examples



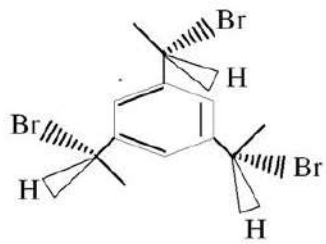
Butane-2,3-diol



1,3-Dichloroallene

The order of C_2 is 2, operators E, C_2, $\sigma = 2$.

C_3 point group, Example.



The order of C_3 is 3

Operators E, C_1^1, C_3^2

$\sigma = 3$

D_n point group:

When a molecule has a C_n axis as the principal axis and nc_2 axes lying perpendicular to the C_n axis it belongs to D_n point group.

That is, $D_n = C_n + nC_2$ ($\perp$)

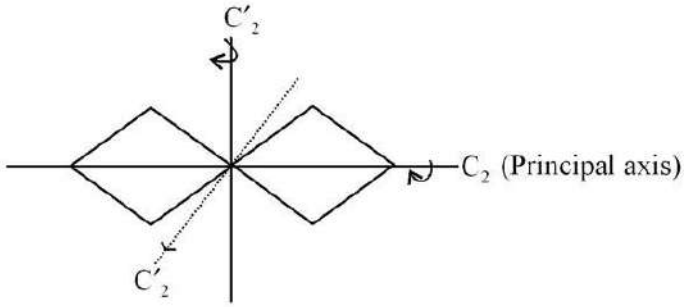
The order of a D_n point group is 2n

Operators E, C_n^1, C_n^2 ... ... C_n^{n-1}, $_nC_2$

$\sigma = 2n$

Molecules belonging to D_n point group are chiral or dissymmetric. These molecules are optically active.

D_2 point group: Example twist-boat conformation of cyclohexane

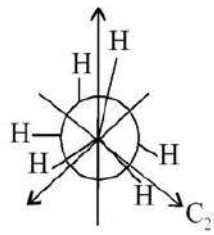


The order of D_2 is 4

Operators E, C_2, $2C_2^1$

$\sigma = 4$

D_3 point group: Example, skew form of ethane



C_3 axis passes through C–C bond, $3C_2$ axes passing through the mid-point of C–C bond and bisecting the dihedral angle.

The order of this point group D_3 is 6

Operators E, C_3^1, C_3^2, $3C_2$

Symmetry number $\sigma = 6$

3.2.2.3 Point groups of achiral molecules : Molecules belonging to point groups other than C_1, C_n and D_n generally have σ plane, inversion centre, i or S_n 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 σ 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_n^3 ... ... S_n^{n-1}, S_n^n ($\equiv$ E)

The order of this point group is n

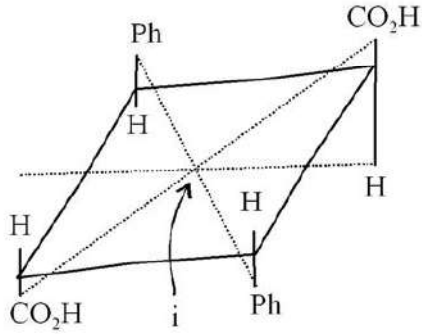
Operators E, S_n^1, S_n^2 ... S_n^{n-1}

Symmetry number, $\sigma = n/2$

But when n is odd, 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 δ_n. The molecule with odd order S_n axis are thus placed under C_{nh} point group.

S_2 point group: As $S_2 \equiv$ i, so this point group is also called C_i point group.

C_i point group: Example, α-Truxillic acid



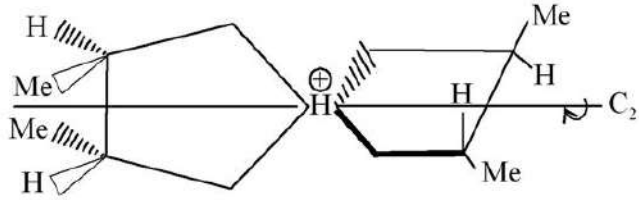
The order of C_i is 2

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 ($\equiv C_2^1$), S_4^3, S_4^4 ($\equiv E$)

Symmetry number, $\sigma = 2$

C_{nh} point group:

A molecule that has a C_n axis and σ_h belongs to C_{nh} point group. These molecules are achiral and optically inactive.

The order of C_{nh} is 2_n

Operators C_n^1, C_n^2, C_n^3 ... C_n^n ($\equiv E$), σ_n S_n^1, S_n^2 ... S_n^{n-1}.

Sytmmetry number, $\sigma = n$

C_{1h} point group:

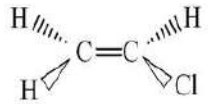
Since $C_{1h} = C_1 \times \sigma_h$

$= E \times \sigma_h$

$= \sigma$ (symmetry plane)

So, C_{1h} is called C_s (s stands for symmetry plane).

Example:



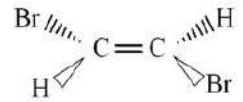
Vinyl chloride

The order of C_s is 2

Operators E, σ

Symmetry number, $\sigma = 1$

C_{2h} point group. Example



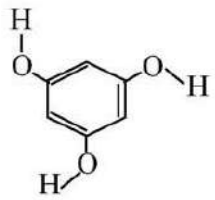
trans-1,2-Dibromoethylene

The order of C_{2h} is 4

Operators E, C_2, σ_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, σ_h, S_3^1, S_3^2

Symmetry number $\sigma = 3$

C_{nv} point group:

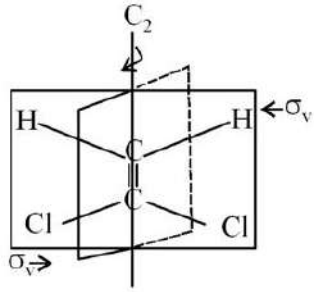
A molecule that has a C_n axis and $n\sigma_v$ planes belongs to C_{nv} point group.

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, $2\sigma_v$

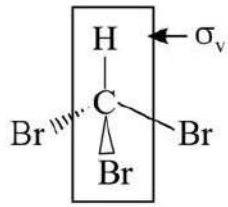
Symmetry number $\sigma = 2$

C_{3v} point group: Example: Bromoform

The order of C_{3v} is 6

Operators E, C_3^1, C_3^2, $3\sigma_v$

Symmetry number $\sigma = 3$



D_{nh} point group: $D_{nh} = D_n + \sigma_h$

$= C_n + nC_2 (\perp) + \sigma_h$

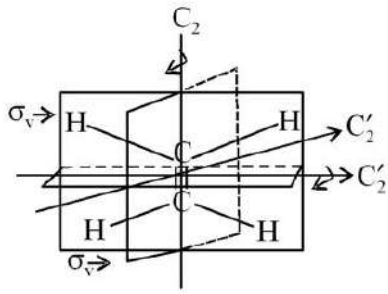
The existence of σ_h and nC_2 lying in the same plane ensures the presence of $n\sigma_v$. Also, $C_n \times \sigma_h = S_n$

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

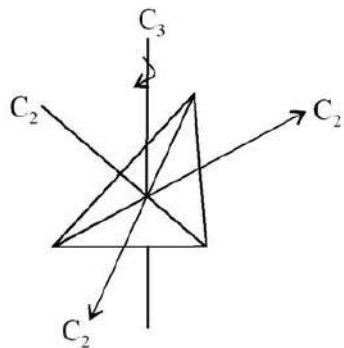


The order of D_{2h} is 8

Operators E, C_2^1, $2C_2^1$, $2\sigma_v$, σ_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, $3C_2$, $3\sigma_v$, σ_h, S_3^1, S_3^2

Symmetry number $\sigma = 6$.

D_{nd} point group: $D_{nd} = D_n + n\sigma_d$

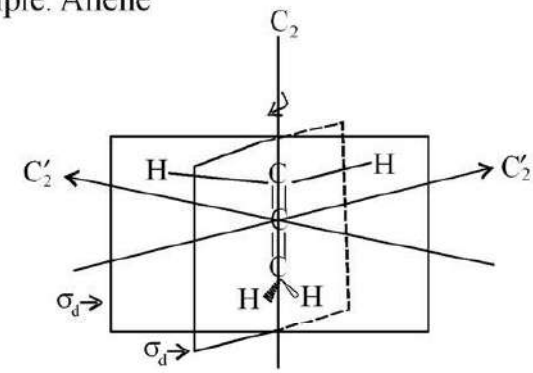
$= C_n + nC_2 (\perp) + n\sigma_d$

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

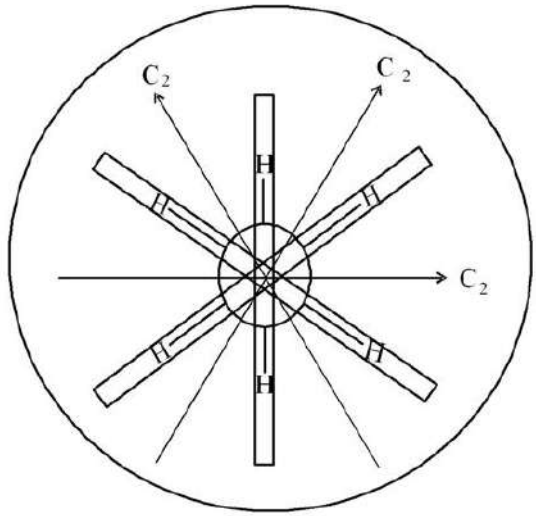


The order of D_{2d} is 8

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 $3\sigma_d$ planes each bisecting two C_2 axes.

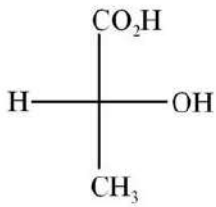
The order of D_{3d} is 12

Operators E, C_3^1, C_3^2, $3C_2$, $3\sigma_d$, i, S_6^1, S_6^5.

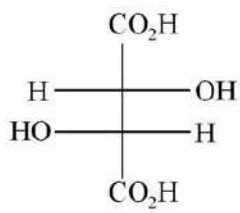
Symmetry number $\sigma = 6$.

3.2.3 Symmetry and Chirality :

A molecule can form only one mirror image which may or may not be superposable with the original. A molecule with proper axis of symmetry C_n is not superpasable with its mirror image. But a molecule with C_n, i or S_n axis is superposable with its mirror image. The property due to which a molecule is nonsuperposable with its mirror image is called chirality. Such a molecule is called chiral. A chiral molecule rotates the plane of a plane polanised 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 σ plane, i centre and S_n axis. All dissymmetric molecules are thus chiral and optically active. Molecules belonging to C_1, C_n and D_n point groups are chiral or dissymmetric. Asymmetry denotes the absence of symmetry elements C_n ($n > 1$) axis, σ plane, i centre or S_n axis in a molecule and such a molecule is asymmetric and optically active. Molecules, in particular, belonging to C_1 point group are asymmetric. For example, lactic acid is asymmetric but (+) tartaric acid is dissymmetric.



Lactic acid



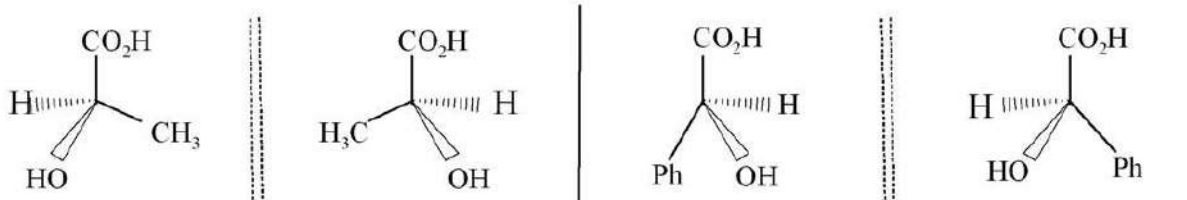
(+)-Tartaric acid

3.2.4 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

steresisomers that bear a nonsuperposable 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.

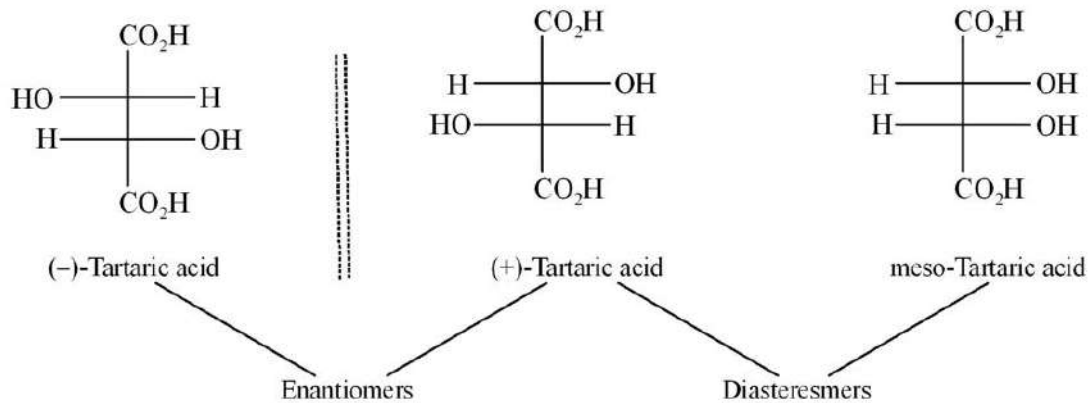


(+)-Lactic acid (–)-Lactic acid (+)-Mandelic acid (–)-mandelic acid

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 lacvorotatory.

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.

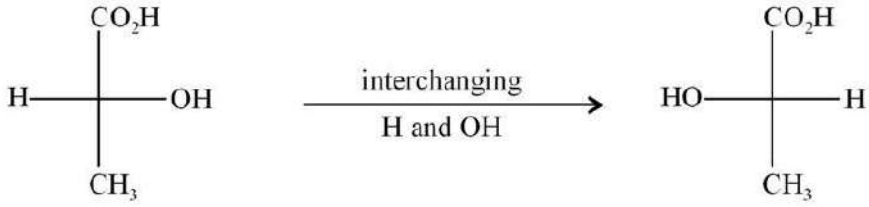


Each pair of enantiomer is diastereomeric with any other pair. Unlike enentiomers, diastereomers differ in most of their physical and chemical properties. They may be or may not be chiral. Chiral diastereomers are opically active and exist as (±)-pair.

3.2.5 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.

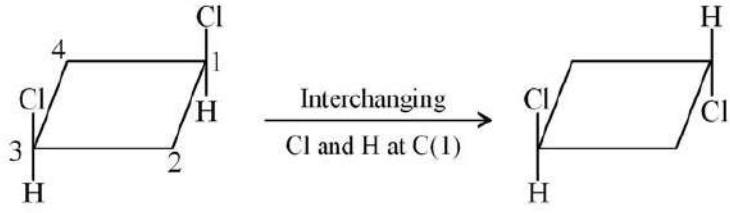
Let us take the example of lactic acid. In lactic acid, the chiral centre is attached with four different ligands H, OH, CH_3 and CO_2H. If we interchange the position of H and OH we will get a stereoisomer as shown below.



(one enantiomer) (another enantiomer)

The chiral centre is called the stereogenic centre. The phenomena involving inchanging 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.

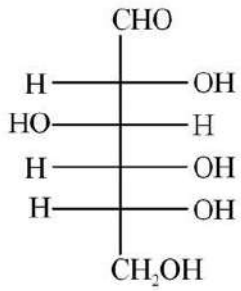


cis isomer trans isomer

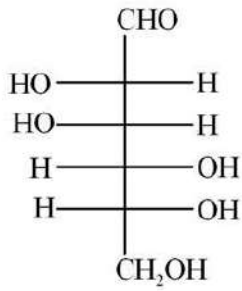
The carbon atoms C(1) and C(3) in both the diastereomers are achiral because each is linked to two identical CH_2 ligands but stereogenic.

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

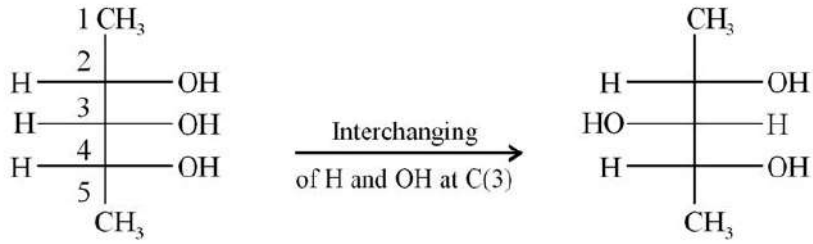


D-Mannose

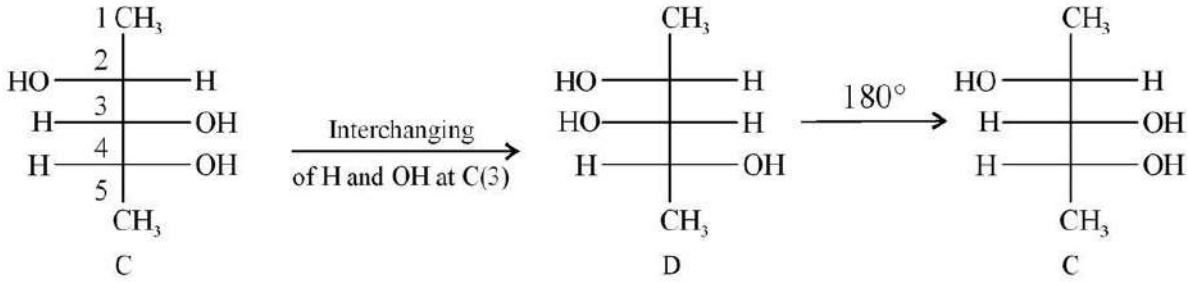
3.2.6 Chirotopicity :

In a chiral molecule every 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 CHBrClF 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 CHBrClF 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 σ 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 non-stereogenic 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.

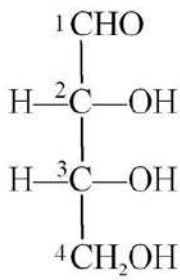
3.2.7 Stereoisomerism in molecules containing two or more chiral centres :

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.

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

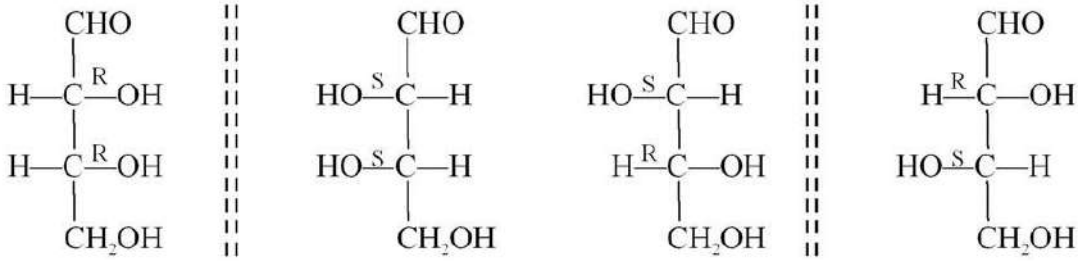
AB type molecule where A and B stand for unlike chiral centres.

In this case,

i) total number of optically active stereoisomeris = $2^2 = 4$

ii) total number of diastereomers = $2^{2-1} = 2$

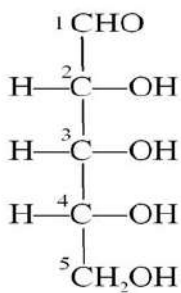
These steresisomers are shown below.



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.



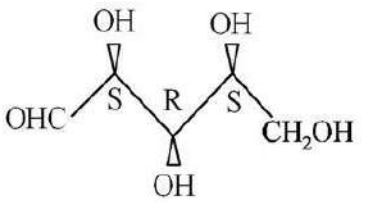
(one stereoisomer)

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,

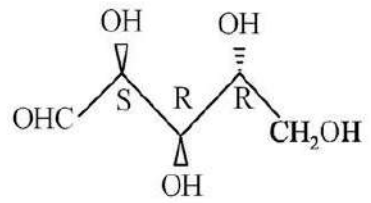
(i) total number of optically active stereoisomers = $2^3 = 8$.

(ii) total number of diastereomers = $2^{3-1} = 4$

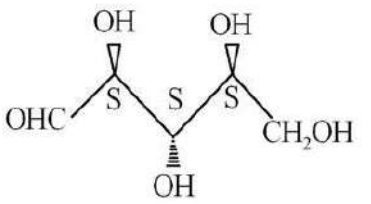
The stereoisomers are represented as.



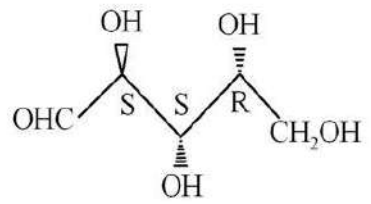
m.i ;



m.i ;



m.i ;



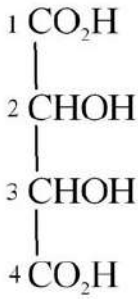
m.i ;

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.

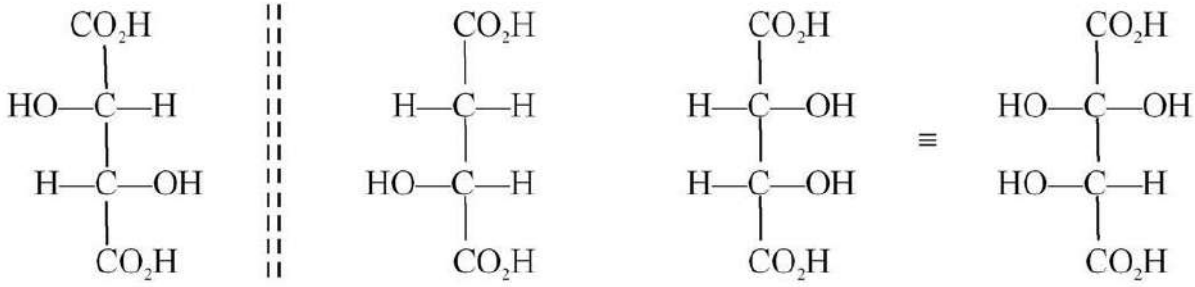
In this case, n = 2 (even) so,

(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.

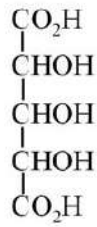
These are shown below.



The two stereoisomers E and E′ are optically active because each of them has a C_2 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)

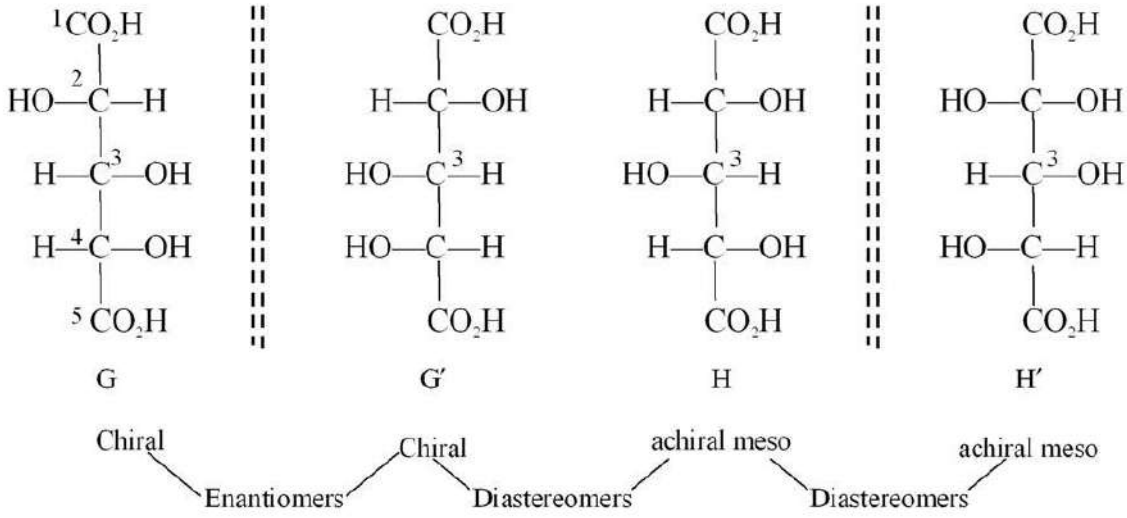
So (i) the total number of stereoisomers = $2^{3-1} = 4$

(ii) the number of meso isomers = $2^{\frac{3-1}{2}} = 2$

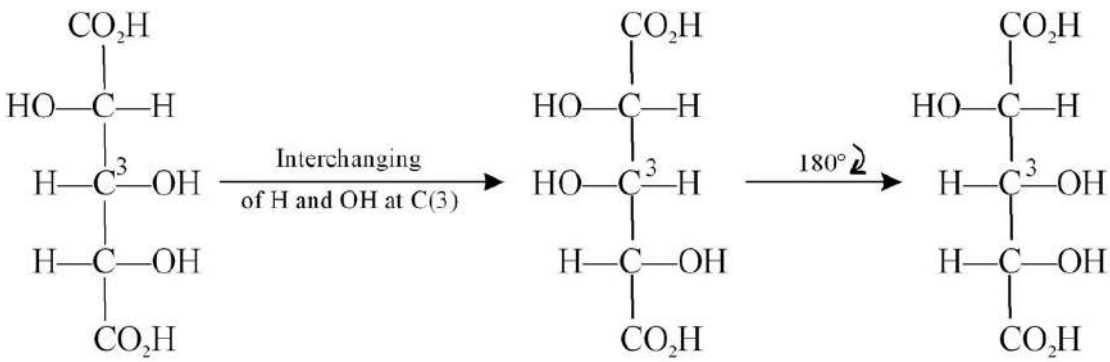
Therefore, (iii) The total number of optically active stereoisomers = 4 – 2 = 2 (1dl pair)

(iv) The total number of diastereomers = 1 (dl pair) + 2 (meso) = 3.

The stereoisomers are depicted below.



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 σ 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 pseudoasymmetric centre.

3.2.8 Summary :

- Four symmetry elements namely a proper axis of symmetry (C_n), a plane of symmetry (σ), an inversion centre (i) and an improper axis of symmetry (S_n) and 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 superposable with their mirror images are called chiral and show a type of steroimerism known as enantiomerism. These molecules belong to the C_1, C_n and D_n point groups. On the other hand, molecules which are superposable with their mirror images are called achiral and belong to the point groups other than C_1, C_n and D_n. The achiral molecules possess σ plane, inversion centre, i or S_n axis. The symmetry number (σ) is used to calculate the entropy of a molecule. (Entropy = $-RT \ln \sigma$).
- 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 types of molecules are fully discussed with examples.
- Pseudoasymmetry in ABA type of molecule is explained.

3.2.9 Questions

1) Delineate the symmetry element(s) present in the following molecules and mention their point groups.

   (i) 1,3-Dibromoallene, (ii) trans-1,2-Diiodoethylene, (iii) CH_2BrCl, (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.

3.2.10 Answer

1) (i) - (v) — See text
2) (i) - (iii) — See text
3) See text

3.3 Absolute and Relative configuration configuration

3.3.1 Introduction :

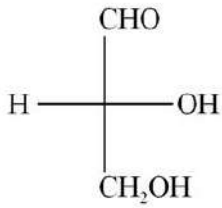
The three-dimensional arrangements of atoms or groups (i.e. ligands) around a stereogenic centre is called configuration. The three-dimensional arrangements of ligands in a chiral molecule that distinguishes from its mirror image is known as absolute configuration which can be determined by single crystal 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 chsosen as the standard is called the relative configuration.

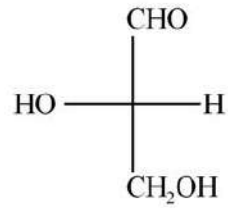
Three-dimensional structures of chiral molecules on two-dimensional plane are represented by F.P., wedge formulae, sawhorse and Newman projection formulae. These formulae acutally show the chiral molecules in their relative and absolute configuration. Suitable configurational descriptor is therefore, required to be given to each structure to distinguish one from the other. The following are some configurational descriptor system.

3.3.2 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 confriguration, 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.



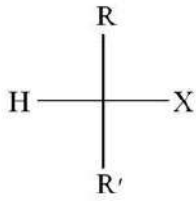
D-Glyceraldehyde



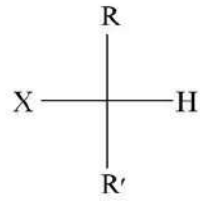
L-Glyceraldehyde

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.

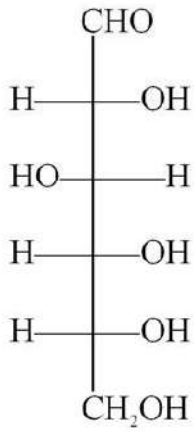


D-configuration

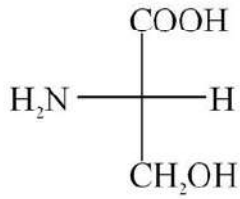


L-configuration

Examples:



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.

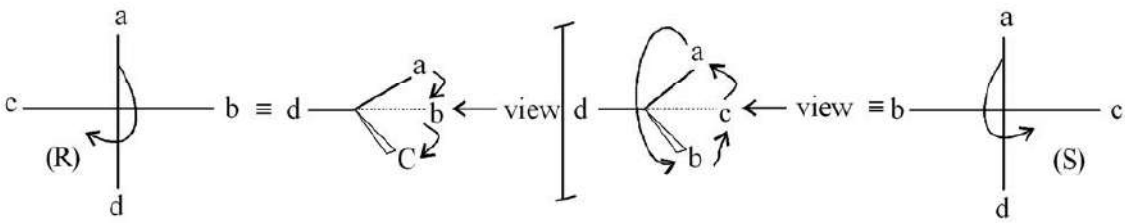
3.3.3 R/S descriptors :

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 loigands 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:

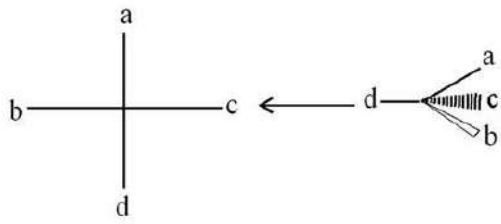
1) Proximity rule : Nearer end of a chiral axis precedes the farther end.
2) Atomic number rule : Higher atomic number precedes lower atomic number

   S > F > O > 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.

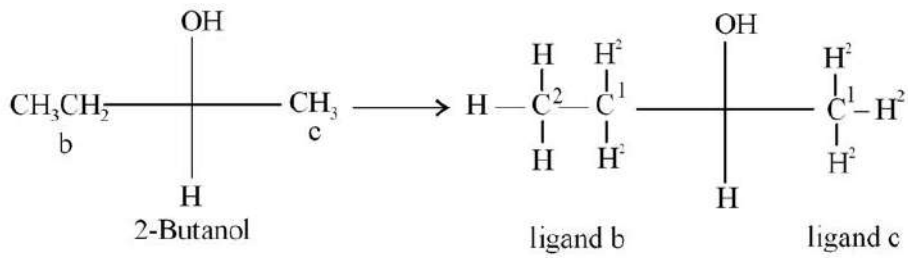
According to CIP rule, ligands attached to the chiral centre are to be sequenced first. If the first atom does not provide any decision one has to proceed outwards away from the chiral centre and then see where is the difference. Once a difference is found one has to stop there and then to assign priority.

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.

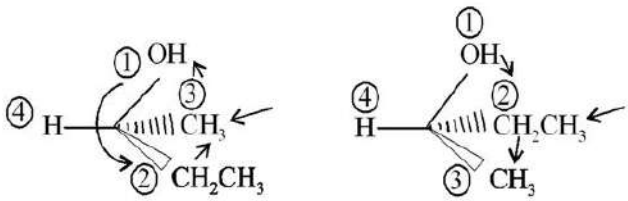


(1) C (1) C No difference

(2) C, H, H (1) H, H, H C > H

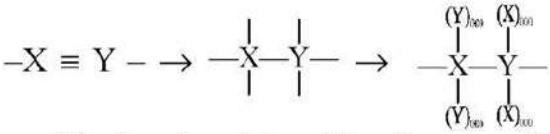
The second carbon atom in ethyl – CH_2 – CH_3 has higher priority than the second hydrogen atom in methyl – CH_3 group.

Therefore, $-CH_2CH_3 > -CH_3$.

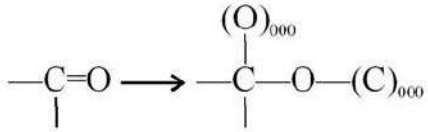


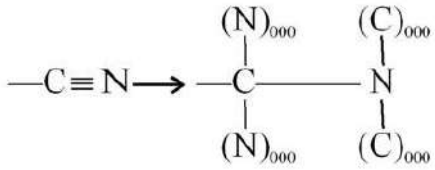
(S)-2-Butanol (R)-2-Butanol

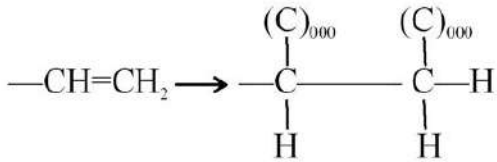
Now we consider the assignment of priorities to ligands containing multiple bonds. A multiple bond can be disconnected to give one which as linked with two real atoms e.g.

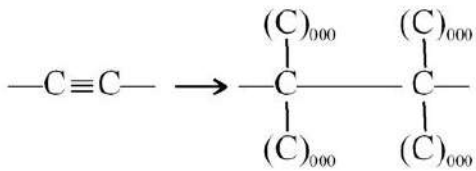


The bonds achieved by disconnection of the multiple bonds are then satisfied with replica atoms of the same type as shown above. Each replica atom is called a phantom atom which is enclosed in parethesis and considered to be linked with three imaginary atoms having atomic number zero. The following are some illustrative examples.



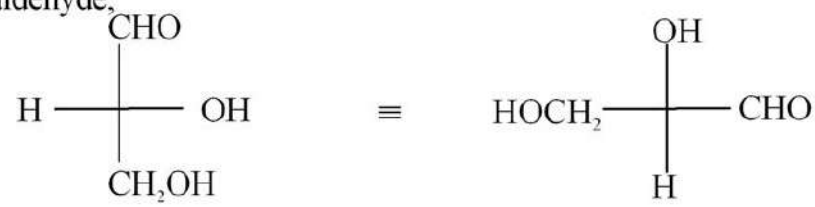




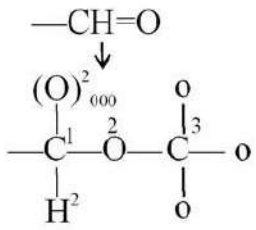


Illustrative examples:

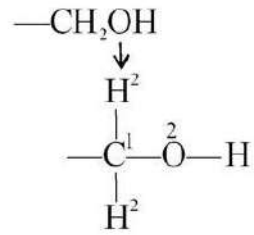
1) D-Glyceraldehyde.



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 $-CH_2OH$



(1) C
(2) O, O, H

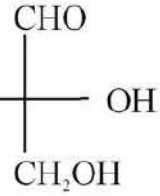


(1) C
(2) H, H, O

No difference

Since O > H; so –CHO > $-CH_2OH$

Thus,



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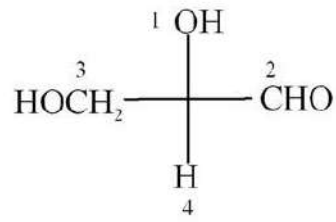
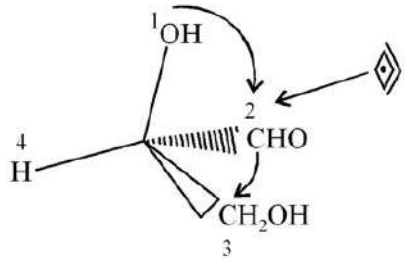
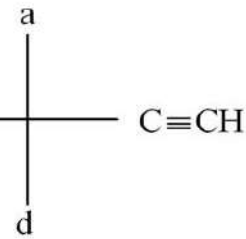




(R)-Glyceraldehyde

Note: There is actually no difference between phantom atom and normal atom. Phantom atom is attached to zero substituent.

(2)



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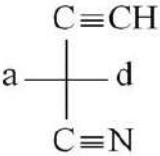

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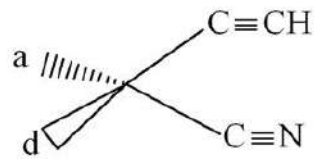
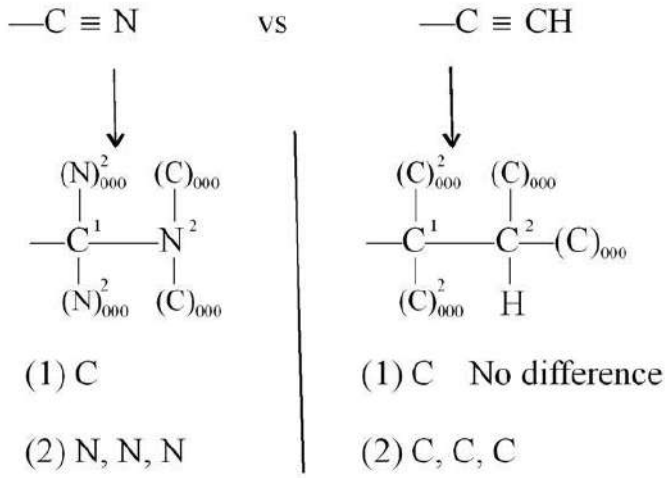
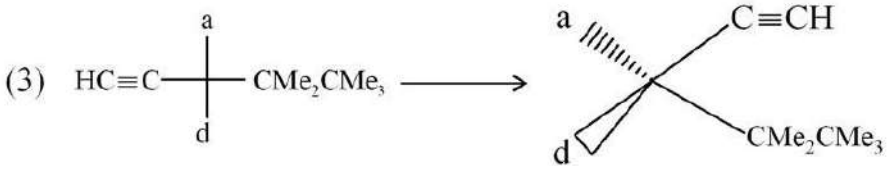
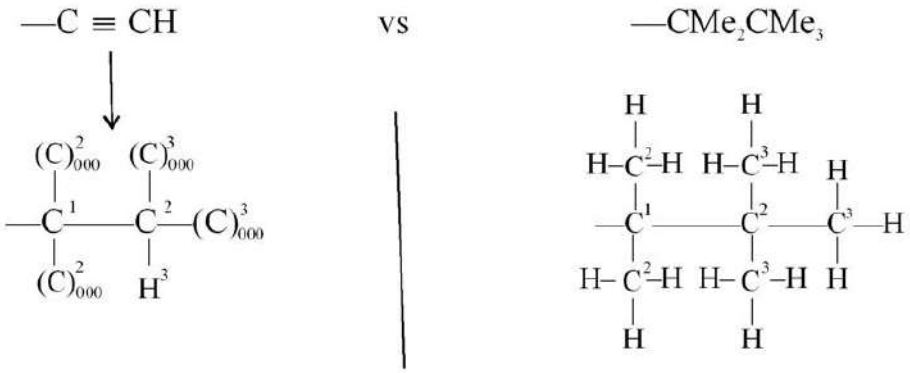




As N > C, So – C ≡ N > – C ≡ CH





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,

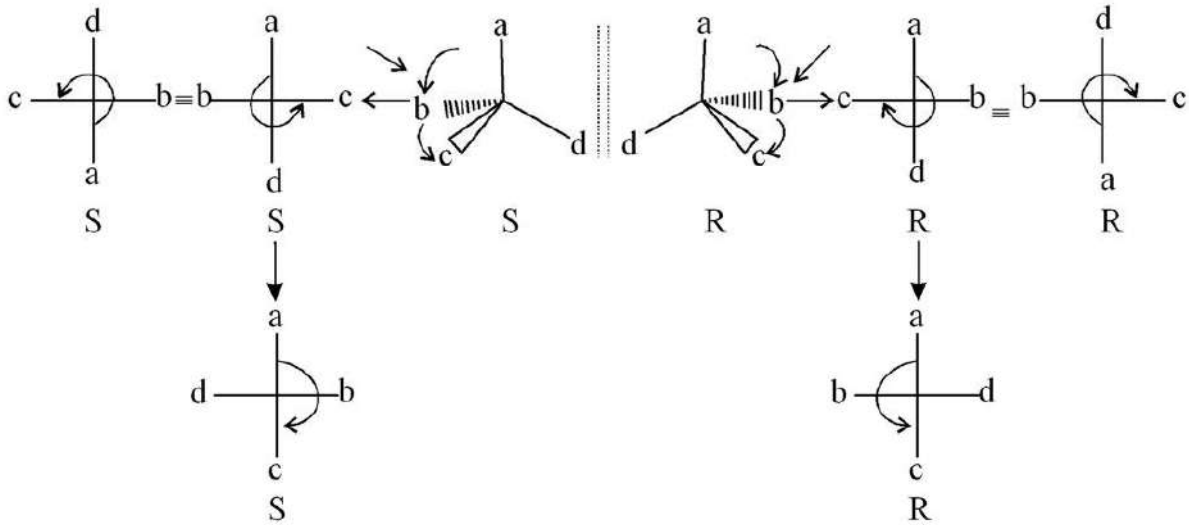
$-CH_2C_6H_5$, $-CH(CH_3)_2$, $-CH{=}CH_2$, $-C(CH_3)_3$,

$-C{\equiv}CH$, $-C_6H_5$, $-CMe_2CMe_3$, $-CH_2NH_2$,

$-C{\equiv}N$, $-CH_2OH$, $-CHO$, $-CO_2H$, $-NH_2$,

$-NHCH_3$, $-N(CH_3)_2$, $-NO_2$, $-OH$, F, Cl, Br, I.

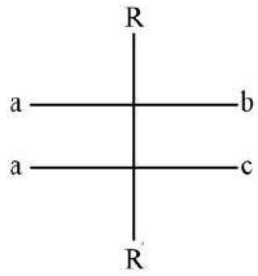
Once the priority sequence of the ligands is decided, assignment of configuration is done by the application of chirality rule which has already been discussed using wedge formula. Since molecules are normally represented by Fischer projection so wedge formula is converted into FP in which the lowest priority ligand 'd' occupies either the top or the bottom position of the vertical bond. Then clockwise order of the remaining three ligand $a \rightarrow b \rightarrow c$ corresponds to the R configuration and the anticlockwise order S configuration as shown below.



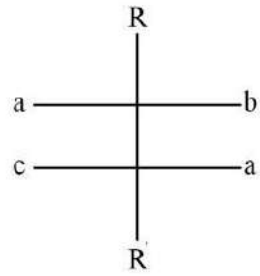
If the lowest priority ligand 'd' occupies either the left or the right position of the horizontal bond then the clockwise order of $a \rightarrow b \rightarrow c$ give S and the anticlockwise order gives R configuration as shown above.

3.3.4 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.

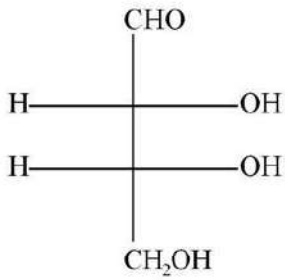


Erythro form

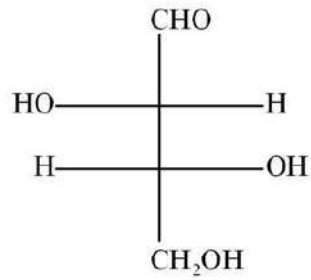


Threo form

Example:

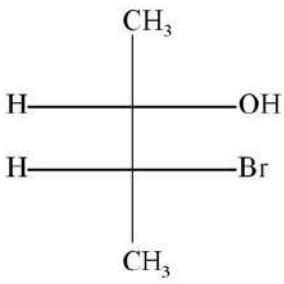


D-Erythrose

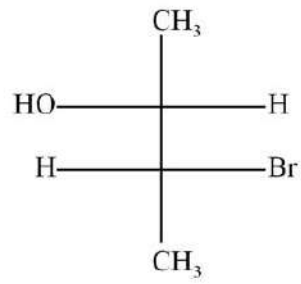


D-Threose

Other examples: 3-Bromo-2-butanol



erythro-3-Bromo-2-butanol



threo-3-Bromo-2-butanol

The erythro/threo nomenclause is simple and unambiguous.

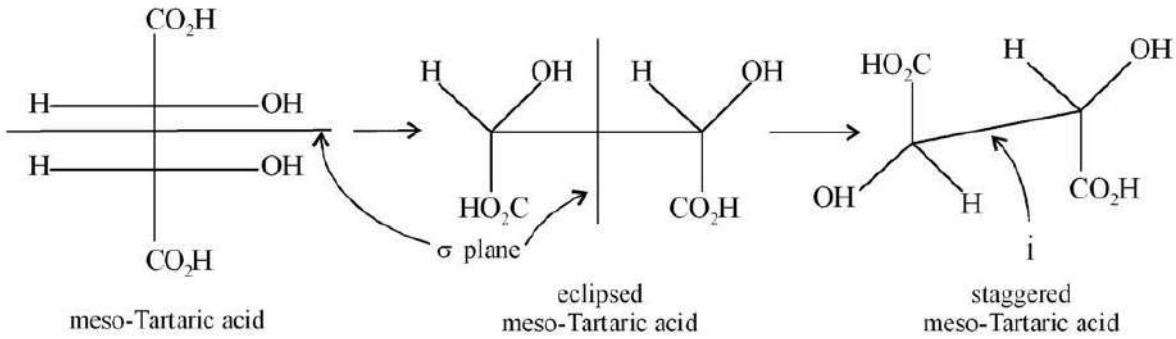
However, complications arise for the diastereomers of the type R–Cab–Ccd–R′ which have no two ligands in common.

3.3.5 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.

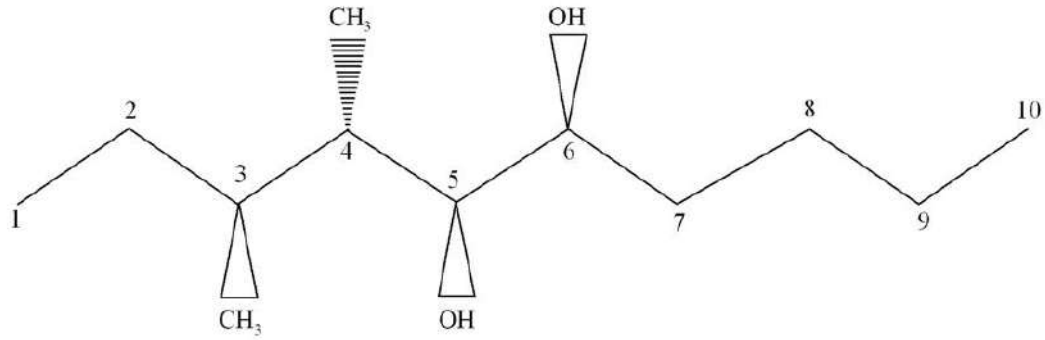
meso-Tartaric acid possesses a plane of symmetry σ in the eclipsed conformation and a centre of symmetry *i* in the staggered conformation.



meso-Tartaric acid | eclipsed meso-Tartaric acid | staggered meso-Tartaric acid

3.3.6 syn/anti nomenclature for aldols :

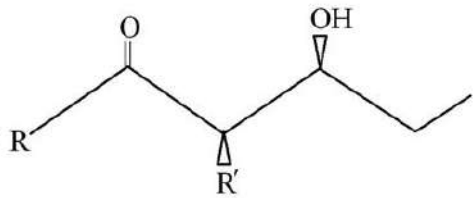
Masamune et al (1980) proposed syn-anti designation to define relative configuration of molecules containing multiple chiral centres. According to this system of nomenclature, the molecule in question is written in zigzag fashion. If the two ligands on the adjacent chiral centres are on the same side 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.

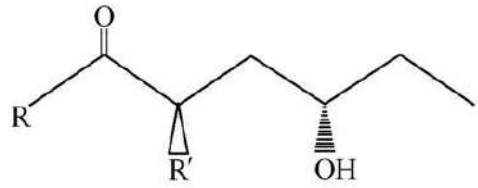
For example,



The relationship is syn.

It is not necessary to have the adjacent chiral centres to assign a name.

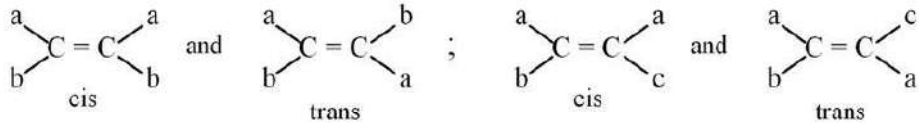
For example, The following compound.



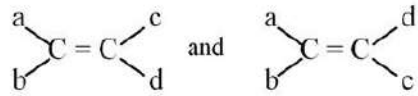
is 2,4-anti

3.3.7 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.



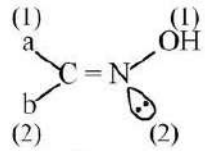
But alkenes of the type Cab = Ccd can exist in two diastereomeric form as shown



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,

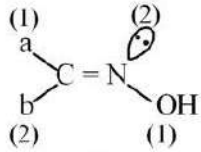
In the case of oximes and azo compounds, the lone pair of electrons on nitrogen has been considered to be the lowest priority ligand.

Thus,

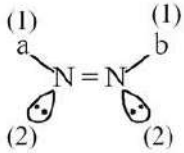


Z
oxime

and

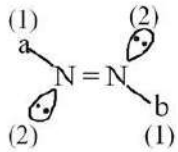


E
oxime



Z
azo compound

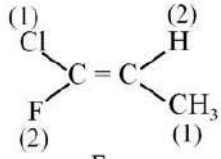
and



E
azo compound

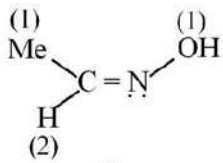
Examples:

(i)



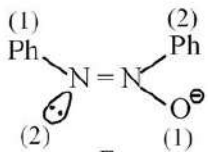
E

(ii)



Z

(iii)



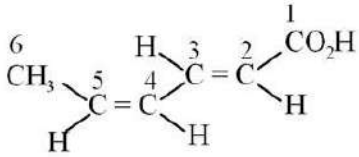
E

3.3.8 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.

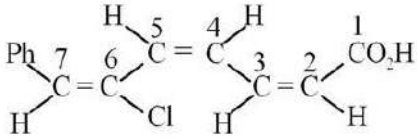
This is illustrated with some examples.

1)



(2E, 4Z)-2,4-Hexadienoic acid

2)



6-Chloro-7-phenylocta-(2Z,4Z,6E)-2,4,6-trienoic acid

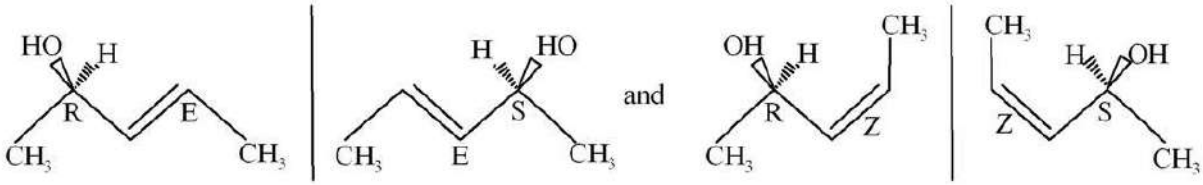
3.3.9 Combination of R/S and E/Z isomerism :

If a molecule contains one or more chiral centres together with one or more olefinic double bonds, the number of steresisomers can be predicted from the number of possible combinations of all the descriptors.

Pent-3-en-2-ol ($CH_3\overset{*}{C}HOHCH = CHCH_3$) provides an illustrative examples which has an olefinic double bond adjacent to a chiral centre. The probable combination of the descriptors are shown below.

Descriptor of the chiral centre	Descriptor of the C = C bond	Probable combinations
R	E	RE
	Z	RZ
S	E	SE
	Z	SZ

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.



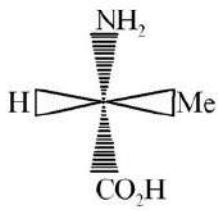
3.3.10 Summary :

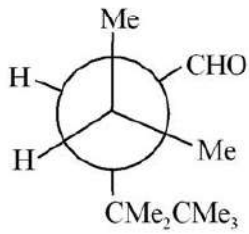
Enantiomers are geometrically equivalent and are isometric. Enantiomers having a single chiral centre thus differ only in absolute configuration. The absolute configuration are denoted by the R/S or D/L systems.

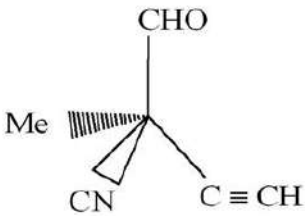
Diastereomers are anisometric and differ in their relative configuration. They are designated as erythro/threo, meso, syn/anti, E/Z etc.

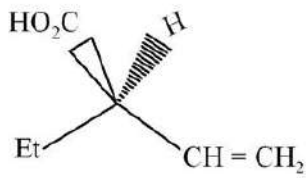
3.3.11 Questions :

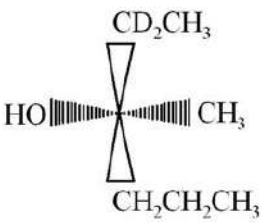
1) Assign R/S descriptors to each stereocentre of the following compound:

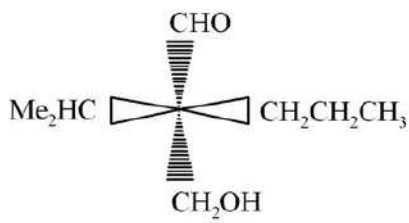
(i) 

; (ii) 

(iii) 

; (iv) 

(v) 

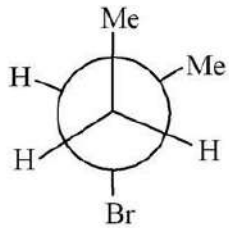
; (vi) 

2) Draw Fischer projection formula of a compound with (R)-configuration having a stereogenic centre carrying the following ligands.

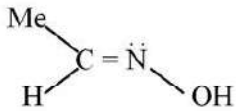
–C≡CH, –OMe, –C≡N and $-CMe_3$.

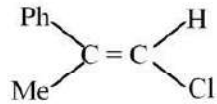
3) Draw the Fischer projection formula of (R)-2-deutero propanoic acid.

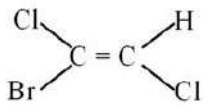
4) Indicate the following with R/S notation.

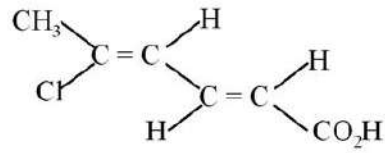


5) Assign configurational descriptor (E/Z) of the following :

i) 

ii) 

iii) 

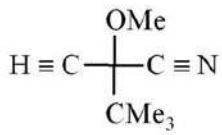
iv) 

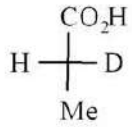
6) Draw all possible isomers of $CH_3CH(OH)CH{=}CHCl$ and designate them as R or S.

7) Draw (R,Z)-4-methyl-2-hexene and (S,E)-2-methyl-2-hexene and indicate their relationship.

3.3.12 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

3.4 Optical activity of chiral compounds, optical rotation, specific rotation and molar rotation

3.4.1 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. 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.

3.4.2 Specifc 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 α_{obs} is proportional to the concentration C of the optically active compound, and the path length *l* of the tube.

Thus, $\alpha_{obs} \propto C.l$

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 *l* of the tubel when C is expressed in g/ml and *l* 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.

3.4.3 Molar rotation denoted by [ϕ] is defined as the product of specific rotation and molecular weight devided by 100 :

$$\text{That is, } [\phi] = \frac{[\alpha]\ M.W}{100}$$

$$= \frac{\alpha_{obs}}{Cg/ml.\ 1\ dm} \times \frac{M.W}{100}$$

$$= \frac{\alpha_{obs}}{\frac{C}{M.W}\frac{g}{100ml.} \times 1\ dm}$$

$$= \frac{\alpha_{obs}}{C\ moles/100ml \times 1\ dm.}$$

3.4.4 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

$$[\alpha]_D = \frac{\alpha_{obs}}{c.l}$$

Where α_{obs} is the observed rotation, c is the concentration in gm/ml and *l* is the cell path length in dm.

Molar rotation $\phi = \frac{[\alpha]_D M}{100} W$

Where M is the molecular weight of the chiral compound.

3.4.5 Questions :

1) Calculate $[\alpha]_D$ 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.
2) The specific rotation of a compound of molecular weight 70 is +30° ; what is its molar rotation?

3.4.6 Answers :

1) +29.16°
2) +21°

3.5 Racemic compound

3.5.1 Introduction :

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.

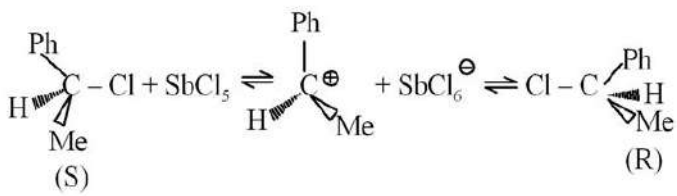
3.5.2 Racemisation :

Racemisation is a chemical process of converting an enantiomer into a racemic compound.

3.5.2.1 Though carbocation intermediate formation :

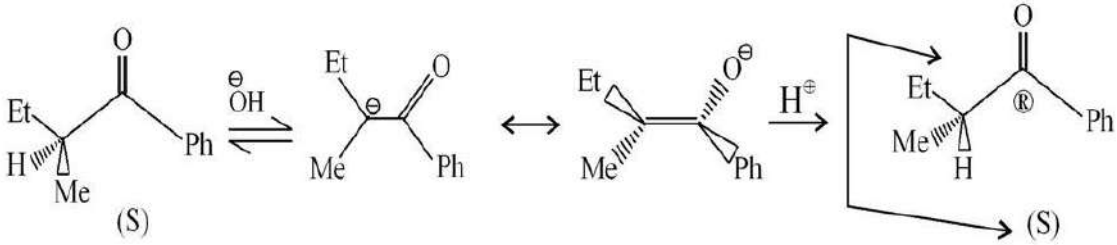
A carbocation formed by removal of an electron-withdrawing group is stabilised by resonance. Since a carboication is sp^2 hybridised, it is planar and can recombine with an anion from both faces leading to racemisation.

Example:



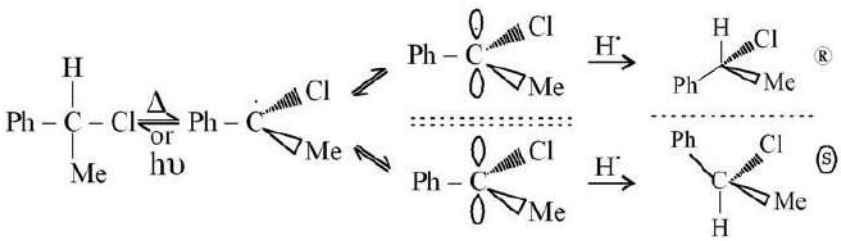
3.5.2.2 Through carbanion intermediate formation: A chiral molecule undergoing racemisation must have an acidic proton at the chiral centre. This proton is removed by a base to generate a carbanion intermediate which undergoes inversion through a plannar transition state. Recombination of $H^{\oplus}$ from both faces results in racemisation.

Example:

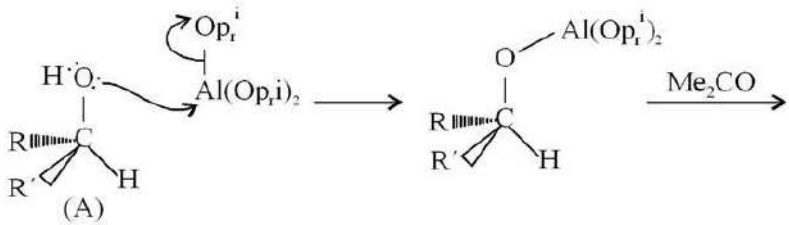


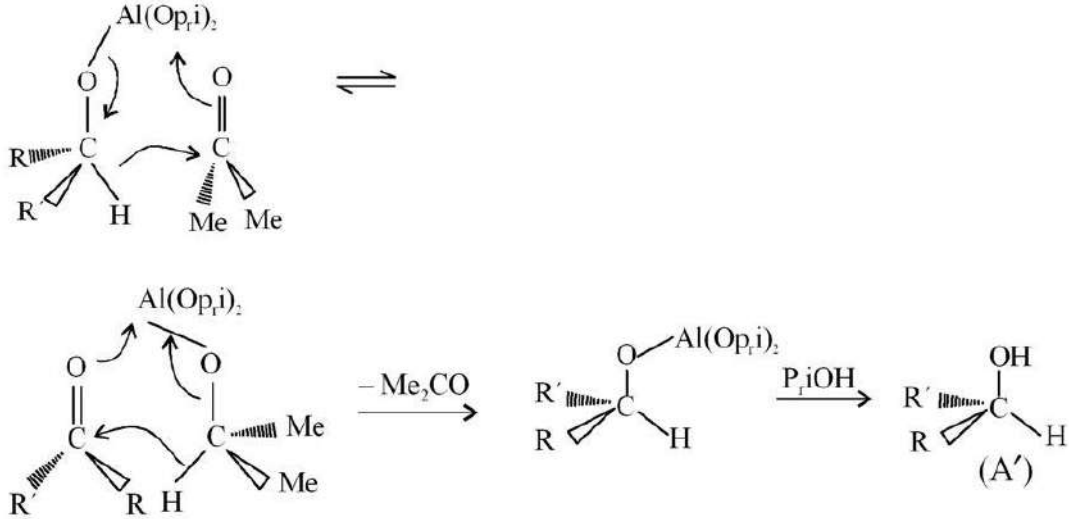
3.5.2.3 Through radical intermediate formation: A molecule containing a hydrogen atom at the chiral centre undergoes homolysis under the influence of heat or light to give a carbon radical. It has a planar structure. Recombination of the previously detached H˙ from both faces leads to racemisation.

Example:



3.5.2.4 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.

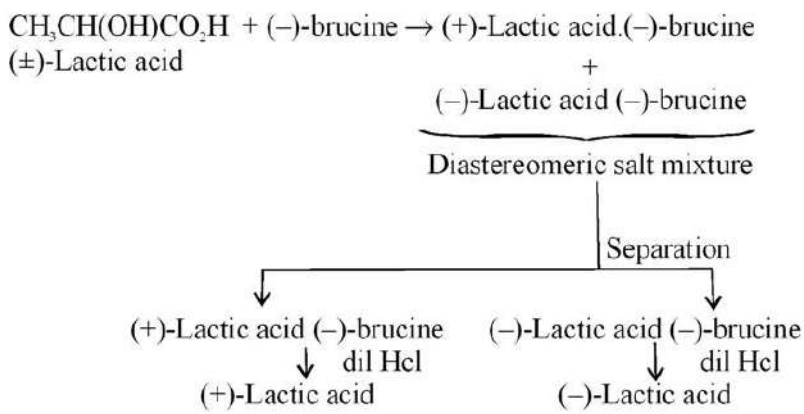
In this case, the ketone RR′CO formed as an achiral intermediate initiates reversible oxidation and reduction reactions and sets up an equilibrium between the enantiomeric products A and A′.

3.5.3 Resolution :

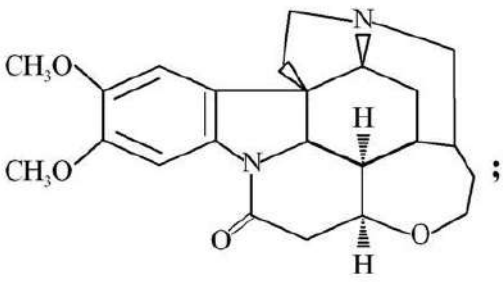
Resolution is the process of separating constituent enantiomers from a racemic compound.

Resolution of racemic compounds (racemates) via formation of diastereomeric salts.

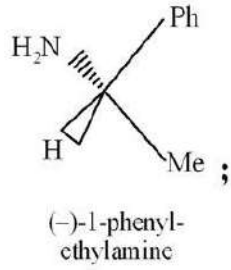
3.5.3.1 Resolution of racemic acid: The racemic acid e.g. (±)-lactic acid is treated with an optically active base e.g. (–)-brucine (resolving agent) to give a mixture of diastereomeric salts. They are separated by fractional crystallisation or chromatography. Subsequent decomposition of each of the diastereomeric salts with dilute mineral acid would give rise to enantiomerically pure acid. This is illustrated as follows:



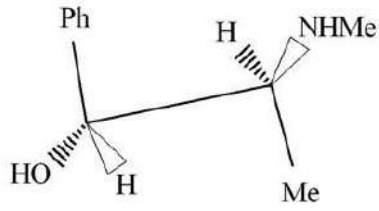
Some common 'resolving agent' for acid.



Brucine

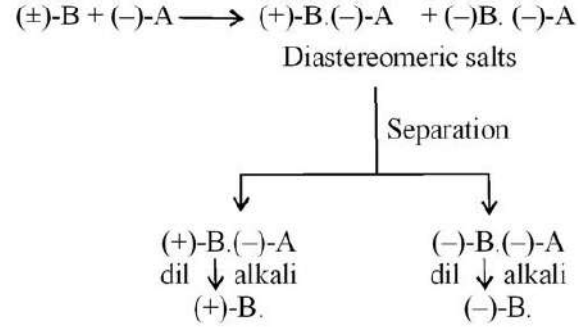


(–)-1-phenyl-ethylamine

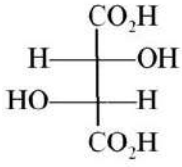


(–)-Ephedrine

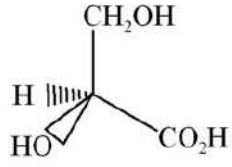
3.5.3.2 Resolution of racemic base: The racemic base is treated with an optically active acid to afford a mixture of two diastereomeric salts. They are separated by fractional crystallization. Subsequent decomposition of each of them with dilute alkali would furnish enantiomerically pure base. If (±)-B is a racemic base and (–)-A is an enantiomer of acid A, the overall strategy for resoloution is outlined below.



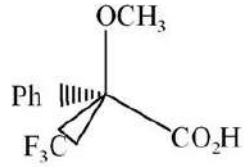
A few common resolving agent for bases



(+)-Tartaric acid



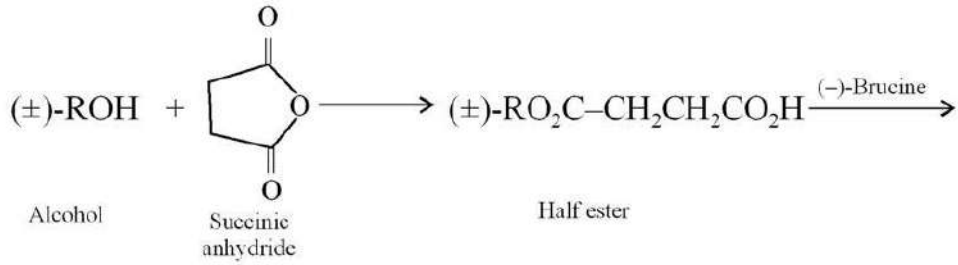
(–)-Malic acid

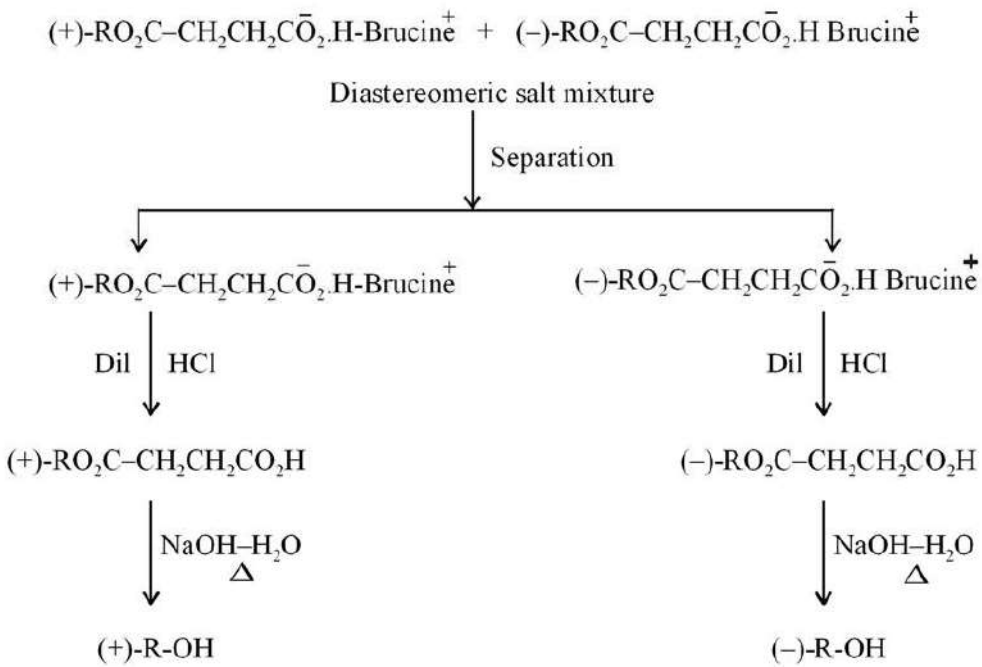


Mosher's acid

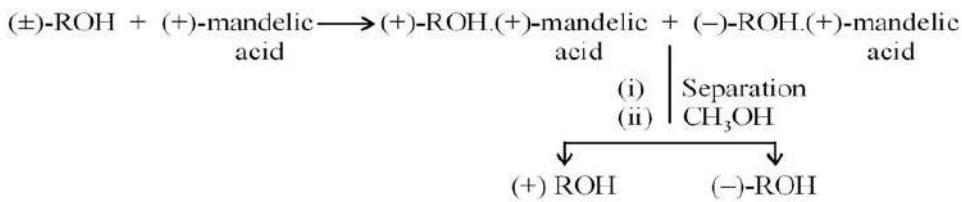
3.5.3.3 Rosolution of racemic alcohol: Racemic alcohol is converted into the half ester of succinic or phthalic acid by heating with succinic or phthalic anhydride in presence of pyridine. The half ester of the acid is then treated as racemic acid and resolved accordingly.

The following is an illustrative example. The pure diasteromeric salf 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.



3.5.4 Optical purity and enantiomeric excess :

Optical purity (OP):

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).

$$\text{So, } OP = \frac{[\alpha]_{obs}}{[\alpha]_{max}} \times 100$$

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, $ee + 100 = 2\ \%\ x_+$

$$\text{or, } \%\text{ of } x_+ = \frac{ee+100}{2}$$

$$\text{and, } \%\text{ of } x_- = 100-\left(\frac{ee+100}{2}\right)$$

$$= \frac{100-ee}{2}$$

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.

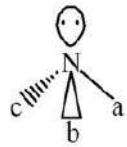
Illustration: A mixture composed of 90% R enantiomer and 10% S enantiomer has 90% – 10% = 80% ee.

If the specific rotation of a nonracemic sample is (+) ve, the (+)-enantiomer will be in excess in the sample.

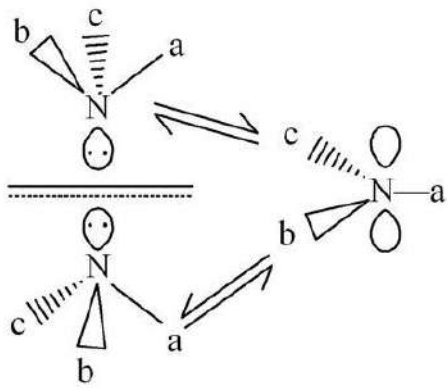
3.5.5 Invertomerism of chiral trialkylamines :

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 Sp^3 hybridised pyramidal tertiary amine of the type Xabc undergoes inversion through a Sp^2 planar transition state giving a pair of nonsuperposable 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.

3.5.6 Summary :

- 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.

3.5.7 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 –13.6°. What relative molar proportion of (S)-(+)-butanol and (R)-(–)-2-butanol would give a specific rotation of +6.8°?

5) $R^1 R^2 R^3 N$ can be obtained in optically pure form. Justify or criticise.

3.5.8 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

Unit 4 ❑ Stercochemisty-II

Structure

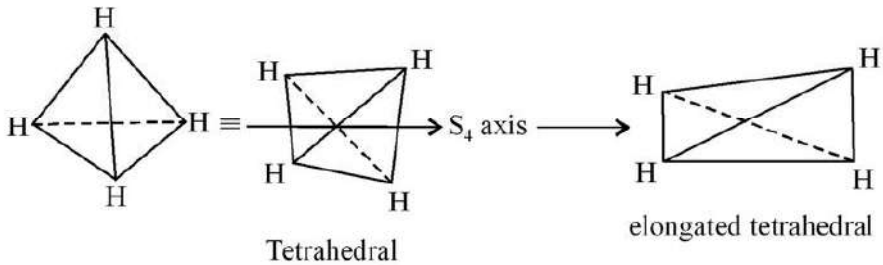
4.0 Objectives

In this unit learner will know about :

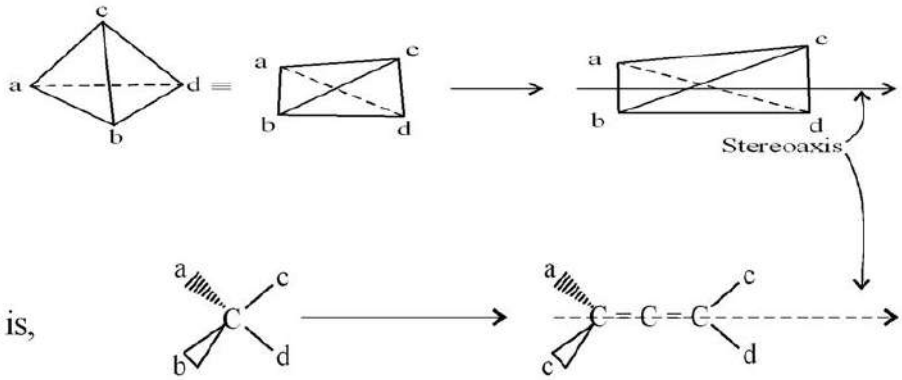
- The chirality arising out of stereoaxis.
- The concept of prostereoisomerism.
- Different types of comformations and this nomenclatures.
- Conformational analysis of some alkanes and substituted alkanes.

4.1 Introduction

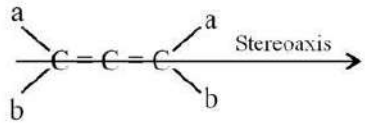
It has been found that there are several compounds which do not have any chiral centre but yet chiral and exist in enantiomeric forms. In such cases, chirality arises out of stereoaxis or chiral axis and is known as axial chirality. A tetrahedral framework of methane has an S_4 axis. If this framework is stretched along the S_4 axis, it is converted into an elongated tetrahedral framework as shown.



The elongated tetrahedral framework can accomodate the linear groupings C=C=C or C–C possessed by a large number of molecules such as allenes, alkylidenecycloalkanes, spiro compounds or biphenyls. A tetrahedral molecule of the type C*abcd having C_1 symmetry is thus converted into an elongated framework with C_1 symmetry as shown.



The framework also maintains chirality if a = c &/or b = d, but a ≠ b.

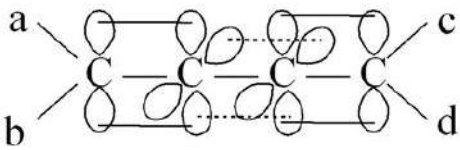


The nonplanar arrangement of two sets of substituents about an axis as above is called a stereoaxis. Some compounds possessing stereoaxis belong to the class of cumulated double bond system, attenes and the other class as biphenyls.

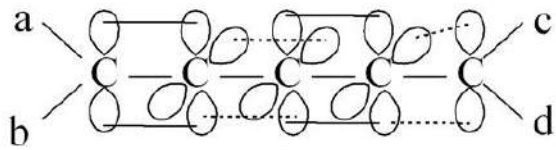
4.2 Stereoisomerism of substituted cumulenes, allenes, alkylidencycloalkanes, spiro compounds and biphenyls are discussed below

4.2.1 Stereoisomerism of substituted cumulenes with even and odd number of double bonds :

A cumulene [ab $(C=)_n$cd] is a hydrocarbon with three or more cumulative (consecutive) double bonds. The simplest member is butatriene ($H_2C=C=C=CH_2$) which is simply called cumulene. In cumulene, the end carbon atoms are sp^2 hybridised and the rest of the carbon atoms are sp hybridised as shown.

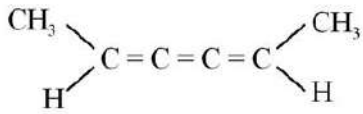


n = 3, odd number of double bonds



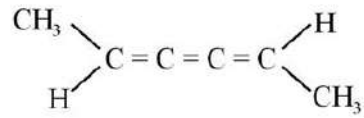
n = 4, even number of double bonds

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

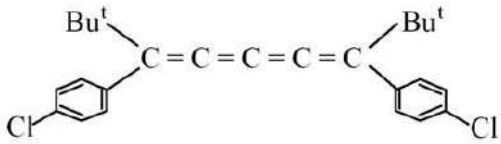


trans (E)

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.

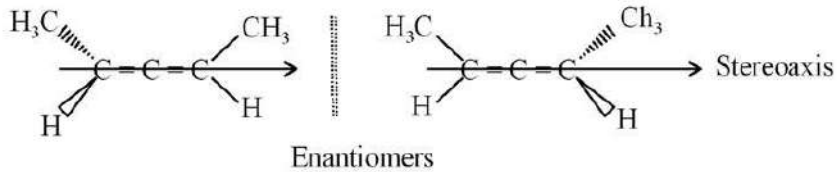
The following compound exhibits enantiomerism.



4.2.2 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.

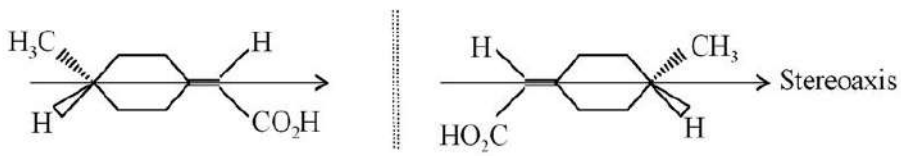
Example: Pentane-2,3-diene



Enantiomers

4.2.3 Appropriately substituted alkylidenecycloalkane

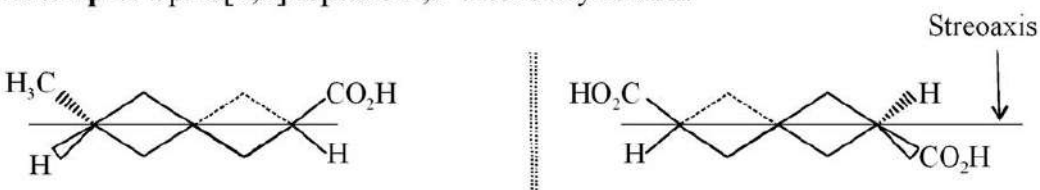
Example: 4-Methylcycloalkylideneacetic acid



Enantiomers

4.2.4 Properly substituted spiro compound

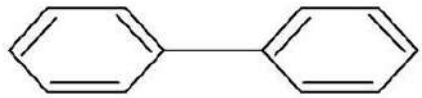
Example: Spiro[3,3]heptane-2,6-dicarboxylic acid



Enantiomers

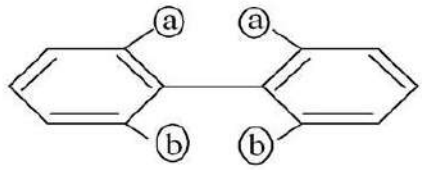
4.2.5 Biphenyls :

Biphenyl is a compound in which two phenyl rings are connected by a single bond called pivotal bond as shown below:

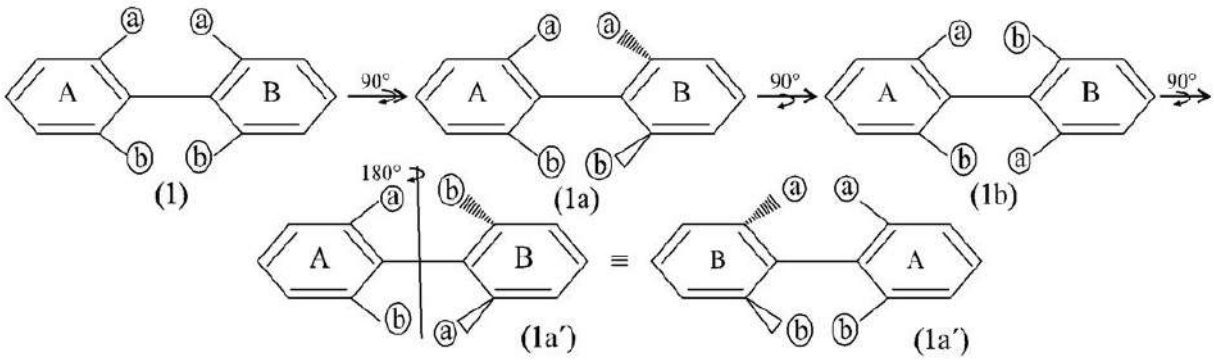


Biphenyl

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

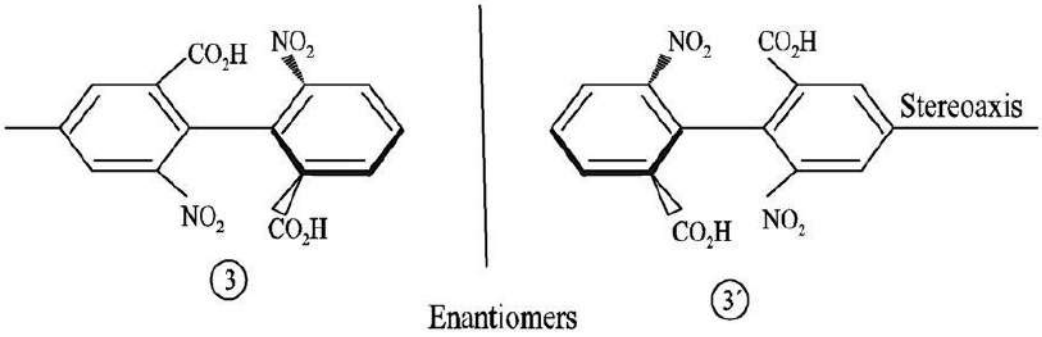


affects the stability of the molecule. In that case, to reduce the steric repulsion one ring rotates with respect to the other and ultimately the two rings become orthogonal to each other as shown below.



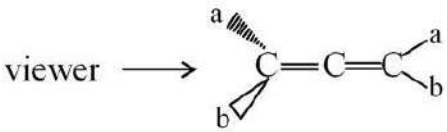
The ring B rotates with respect to the ring A giving rise to two conformational isomers 1a and 1a′ which are mirror images of each other and exist as a pair of enantiomers. Each of the conformational isomers is known as atropisomer (Greek, 'a' meaning 'not' and tropos meaning 'turn') Atropisomerism is 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′).

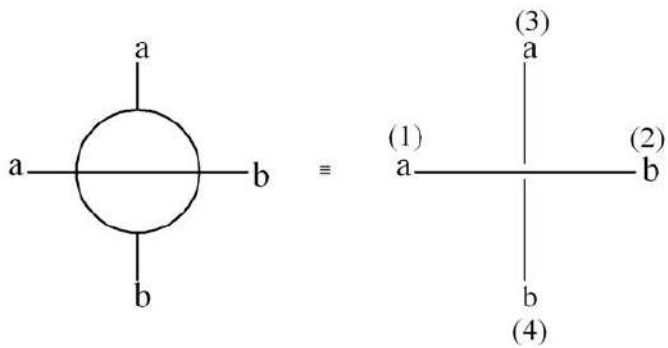


4.2.6 Configurational descriptors (Ra/Sa and P/M) :

In order to assign Ra / Sa configurational descriptor to an axially chiral molecule such as properly substituted allene,

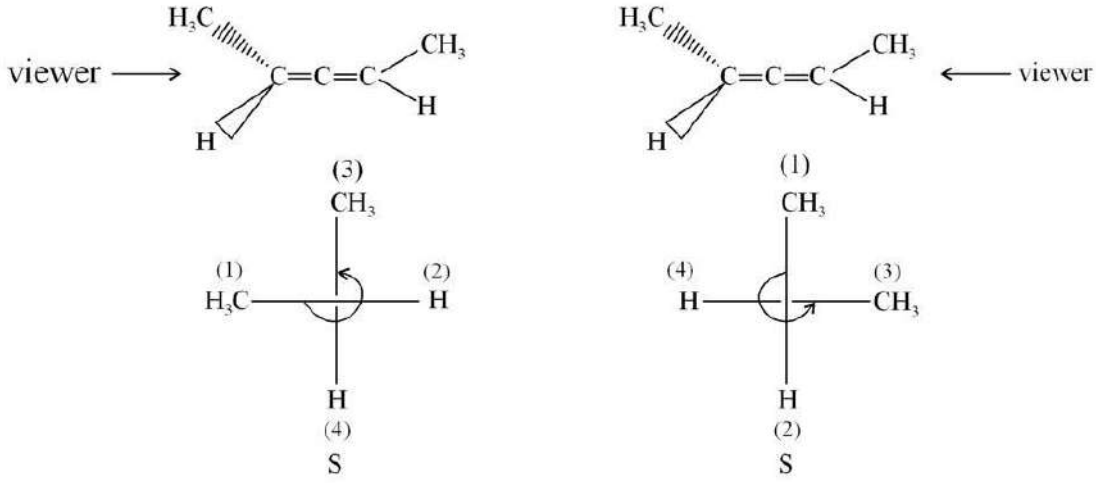


the molecule is viewed along the chiral axis from the near carbon with two ligands in a horizontal position to the far carbon with two ligands in a vertical position and projected to a Newman projection as shown below.



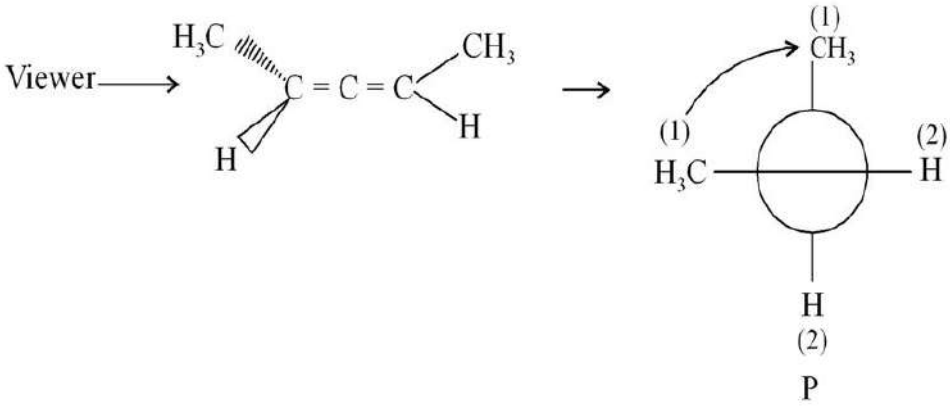
The near ligands a and b are numbered 1 and 2 and the far ligands a and b are numbered 3 and 4 following the priority sequence. The standard subrule (O) which says that near ligands precede far ligands is then applied to it. The sequence 1→2→3 describes an anticlockwise turn and so the configuration is S. It leads to the same configurational descriptor which is S in this case when viewed from the other end.

Example:



4.2.7 Helix nomenclature :

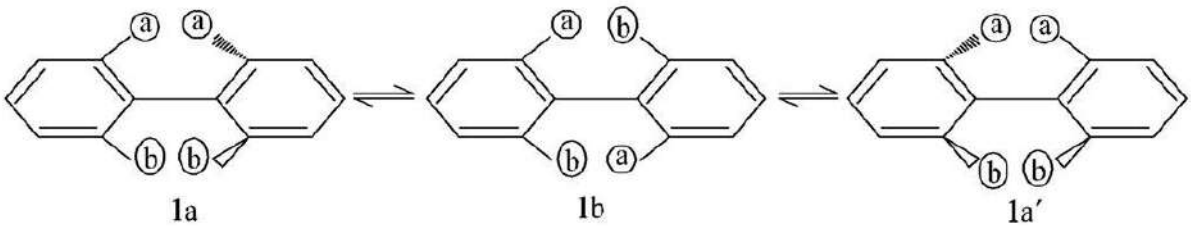
A restricted rotation about a stereoaxis due to steric congestion may lead to helicity. The stereoaxis may thus be looked at as a type of helicity. To designate a stereoaxis by helix nomenclature, the first priority ligand attached to the near carbon and that to the far carbon are considered. If the 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 chiralily. S denotes CIP nomenclature. P is the helix nomenclature.

4.2.8 Racemisation of chiral biphenyls :

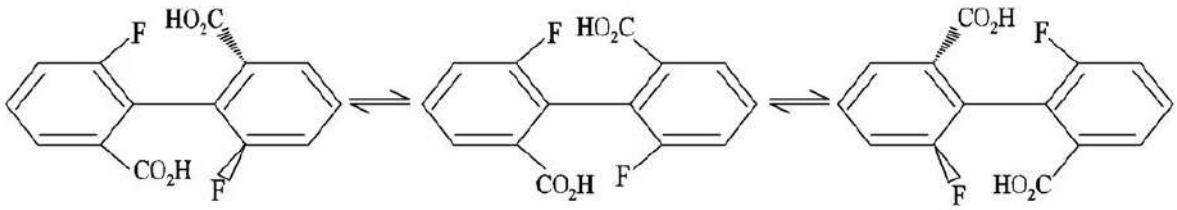
In biphenyls the atropisomers 1a and 1a′ are capable of interconversion by rotation about C–C bond joining the two aryl rings.



1a 1b 1a′

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, OCH_3 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.



4.2.9 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 $1 \rightarrow 2 \rightarrow 3$ 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.

4.2.10 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.

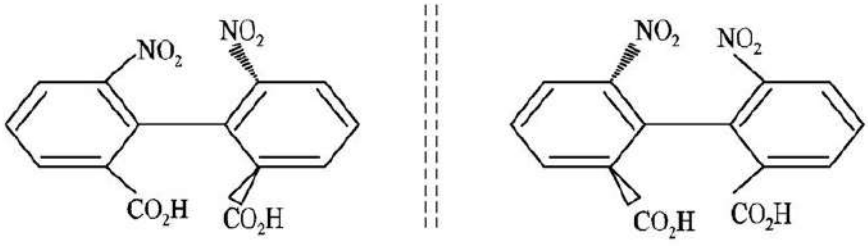
4.2.11 Answers :

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)



4.3 Topicity

4.3.1 Introduction :

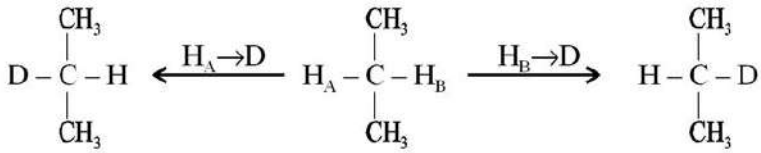
Topicity describes the geometric relationship between two or more ligands in a molecule. These ligands are called homomorphic (Greek homos meaning same and morphe meaning form) if they are identical in all respect when separated from the rest of the molecule. That means, the homomorphic ligands must 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.

4.3.2 Homotopic ligands and faces :

Two criteria viz. substitution addition and symmetry criteria are applied to determine the topic relationships of ligand and faces.

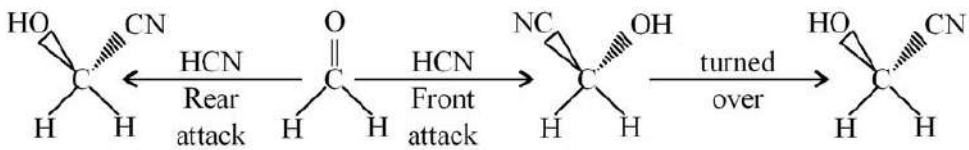
Substitution-addition criteria :

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 CH_3CHDCH_3.



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 H_A and H_B are homotopic ligands.

Two corresponding faces of a double bond (C=O /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 formaldehycle gives rise to the same cyanohydrin as shown below.

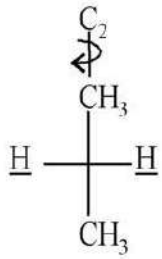


The two faces of the C = O double bond of formaldehyde are thus homotopic.

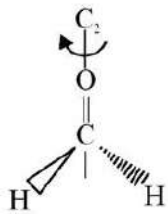
Symmetry criteria :

Homotopic ligands are connected by C_n and faces by C_2 axis.

Thus, two underlined hydrogens in propane are homotopic since they interchange their positions by the operation of a C_2 axis.

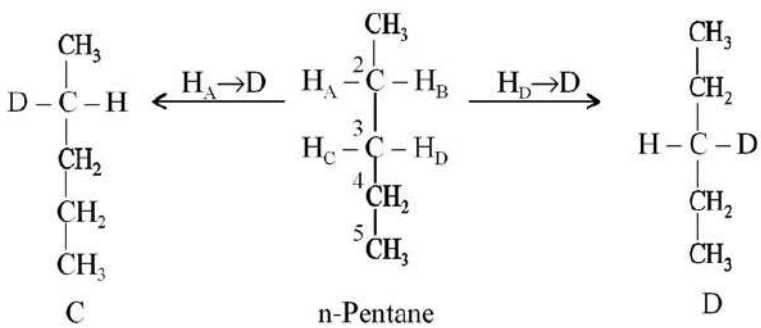


Homotopic faces are also interchangeable by the operation of a C_2 axis.

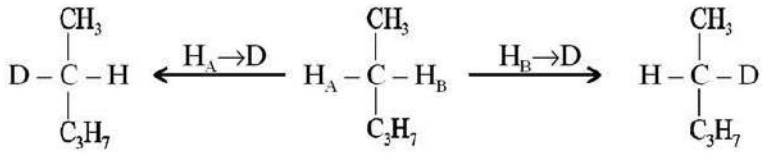


Thus two faces of the carbonyl group are homotopic.

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.

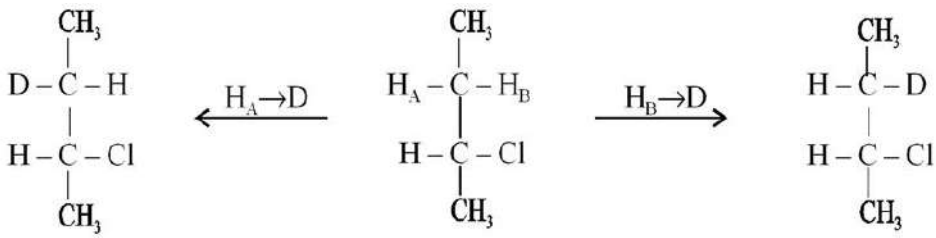


Here, H_A and H_D so also H_A and H_C are constitutionally heterotopic because they after substitution separately by another ligand lead to constitutional isomers. Here C and D are constitutional isomers. On the other hand, stereoheterotopic ligands after substitution generate different stereoisomers (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 H_A and H_B at C(2) in n-pentane above.



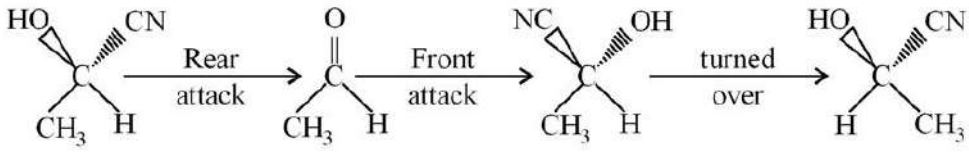
E n-Pentane F

E and F are enantiomers of each other. So H_A and H_B are enantiotopic ligands. If diastereomers are produced after substitution the ligands are called diastereotopic ligands. For example H_A and H_B in 2-chlorobutane.



G 2-Chlorobutane H

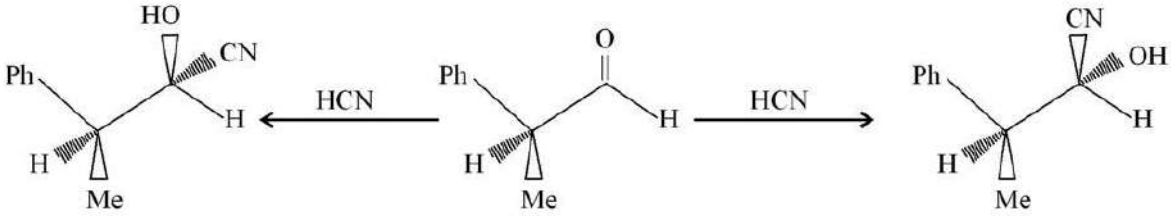
G and H are diastereomers of each other and hence H_A and H_B in 2-chlorobutane are diastereotopic ligands. The faces of a double bond (C = O / C = C) are heterotopic if addition of an achiral reagent to one or the other face will give stereoisomeric products (i.e. enantiomers, diastereomers etc.). Thus respective addition of HCN to the front and back faces of acetaldehyde produces a pair of enantiomeric lactonitriles as shown.



(S) Acetaldehyde (R)
I 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 σ, i or S_n. That means an improper elements of symmetry is present in the molecule.

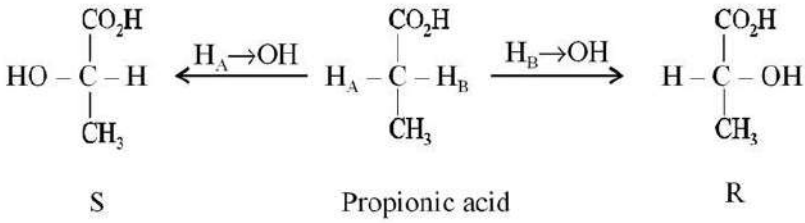
Thus H_A and H_B in n-pentane interchange their positions through σ plane indicating that they are enantiotopic. The two faces of C = O in acetaldehyde are interchangeable by σ operation. So the two faces in acetaldehyde are enantiotopic. Diastereotopic ligands and faces are not related by any symmetry element.

4.3.3 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.

Prochiral centre :

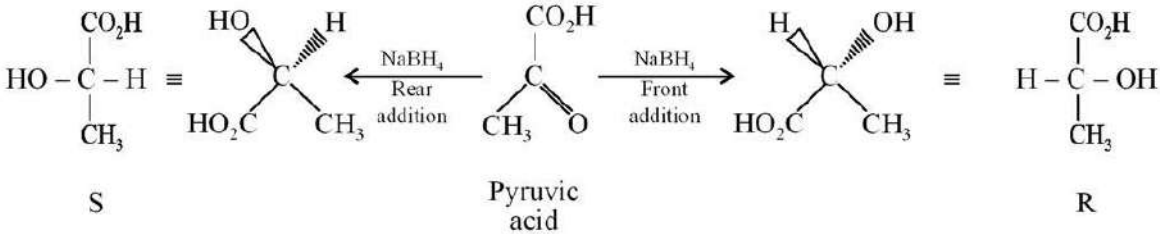
Respective replacement of stereoheterotopic ligands H_A and H_B in propionic acid by an achiral ligand OH produces a pair of enantiomeric lactic acids.



The C(2) centre in propionic acid is called prochiral centre.

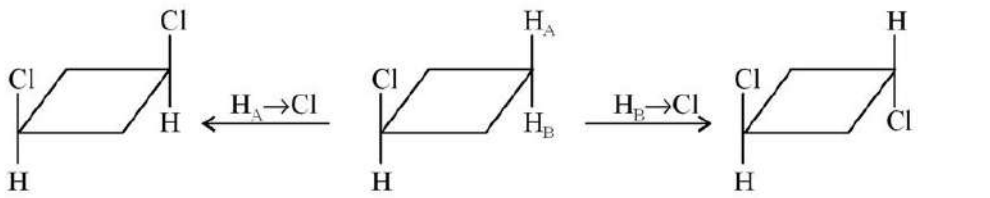
Prochiral faces :

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 H_A and H_B in chlorocyclobutane by an achiral ligand Cl leads to cis-and trans-1,3-dichlocyclobutane which are achiral diastereomers.

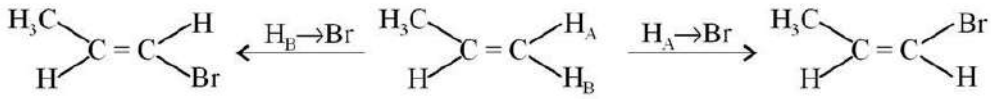


Cis-
1,3-dichlorocyclobutane

Chlorocyclobutane

trans-1,3-dichlorocyclobutane

2) Respective replacement of heterotopic ligands H_A and H_B in propene by an achiral ligand bromine produces (Z) and (E)-propenyl bromide which are also achiral diastereomers.



E-Propenylbromide propene Z-Propenyl bromide

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.

4.3.4 Configurational descriptors :

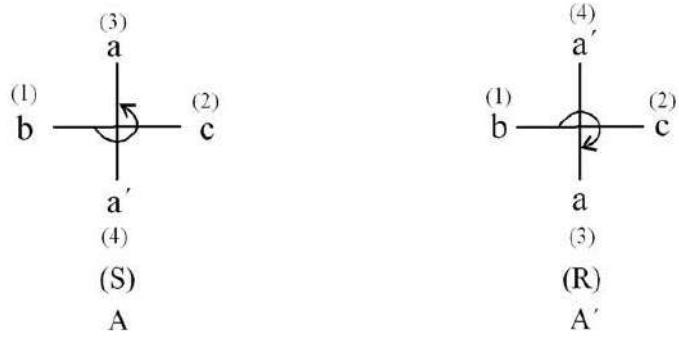
As the configurational descriptors R, S, E, Z etc are used to distinguish stereoisomers from one another, it is desirable to provide descriptors for stereoheterotopic ligands and faces.

Descriptors for stereoheterotopic ligands :

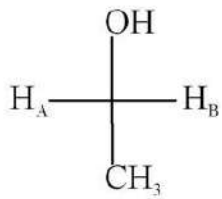
1. Molecules having a single prochiral centre: Molecules with a single prochiral centre such as Caabc can be represented by Fischer projection formula A as shown.

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.

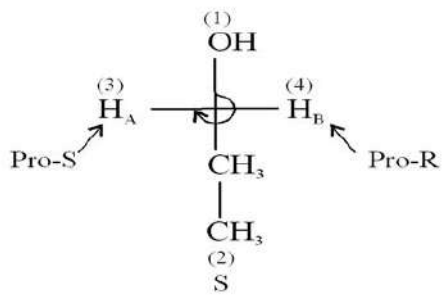
The priority order is thus b > c > a > a′ and A can exist as A and A′.



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.



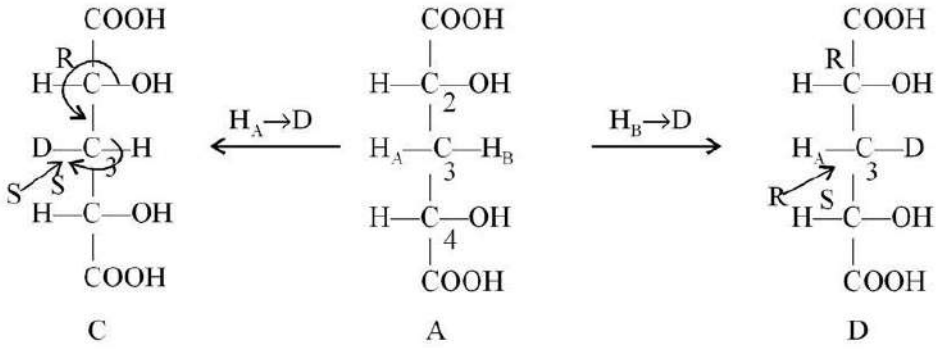
The hydrogen atoms H_A and H_B are enantiotopic. If hypothetical priority is given to H_A over H_B, the priority order is OH > CH_3 > H_A > H_B. The hypothetical configuration of the newly created chiral centre would thus be 'S' as shown.



Hence, H_A is pro-S, by default H_B is pro-R.

2. Molecules containing pseudoasymmetric centre :

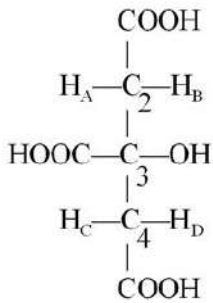
The two hydrogen atoms H_A and H_B at C(3) of 2,3-dihydroxyglutaric acid A are diastereotopic because their respective replacement by D gives rise to a pair of diastereomers C and D as shown below.



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. H_A is thus pro-S and H_B is pro-R.

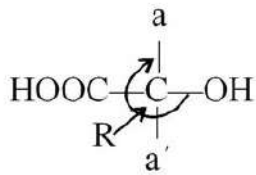
3. Molecules having more than one prochiral centre :

Citric acid has three prochiral centres C(2), C(3) and C(4)



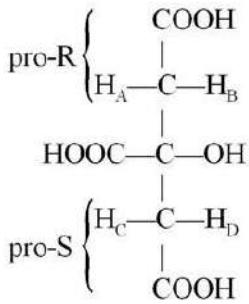
citric acid

and both enantiotopic and diastereotopic H's. C(3) is prochiral because it bears two homomorphic ligands —CH_2COOH, Citric acid can therefore, be represented as

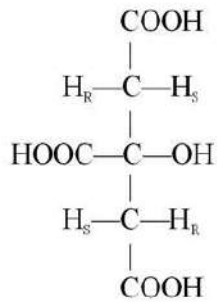


The priority order is OH > COOH > a > a′. So the ligand a i.e. $-CH_2OOH$ is pro-R and a′ is pro-S.

That is,

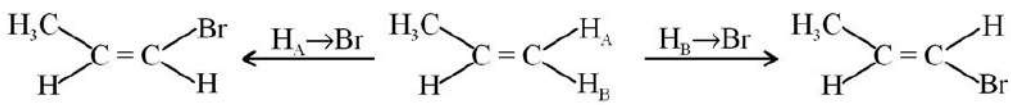


The topic descriptors to each of the H's can be assigned as H_A is pro-S, H_B (pro-R), H_C (pro-S) and H_D (pro-R). The subscripts of the group is now added to the individual subscripts of H's. The all four H's are thus labeled as



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

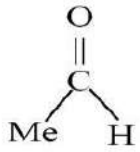
trans-(E)-propenyl-bromide

5. Descriptors for stereoheterotopic faces :

Enantiotopic faces of a molecule is two-dimensionally chiral. If one looks at the plane of a π 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).

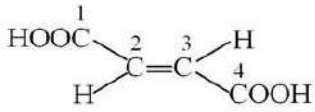
Example: i) C=O faces



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)

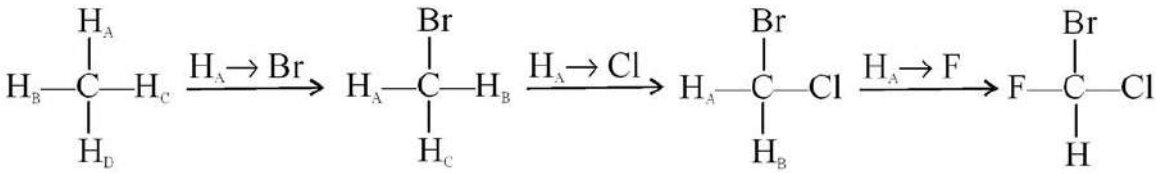
4.3.5 Summary :

• 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 faces.

• 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 pro-R 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.

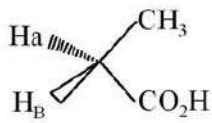
Example :



pro-pro-prochiral pro-prochiral prochiral chiral

4.3.6 Questions :

1) Classify the indicated pairs of atoms as homotopic, enantiotopic or diastereotopic:



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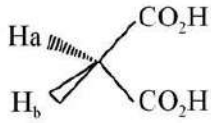

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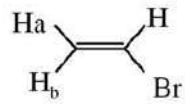


2) Give an example of a molecule the heterotopic ligands of which are prostereogenic but not prochiral.

4.3.7 Answers :

1) See text

2) See text

4.4 Conformations of Acyclic molecules

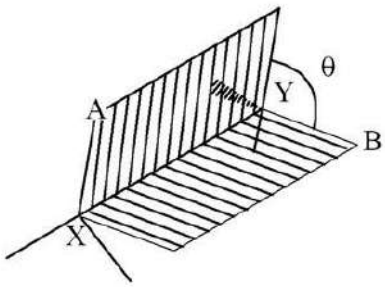
4.4.1 Introduction :

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.

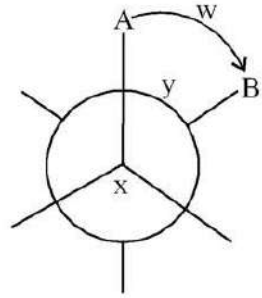
Since the energy a molecule (potential energy) depends on the geometry it possesses so one conformation differ in energy from the other. Thus, as we rotate carbon carbon single bond the energy of the system changes with the change of dihedral angle (θ) or torsion angle (ω). We have already mentioned dihedral angle in section 3.1.

Torsion angle (ω):

Although torsion angle (ω) is similar to dihedral angle (θ) but it has slightly different implecation. 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.

4.4.2 Conformations and related terms :

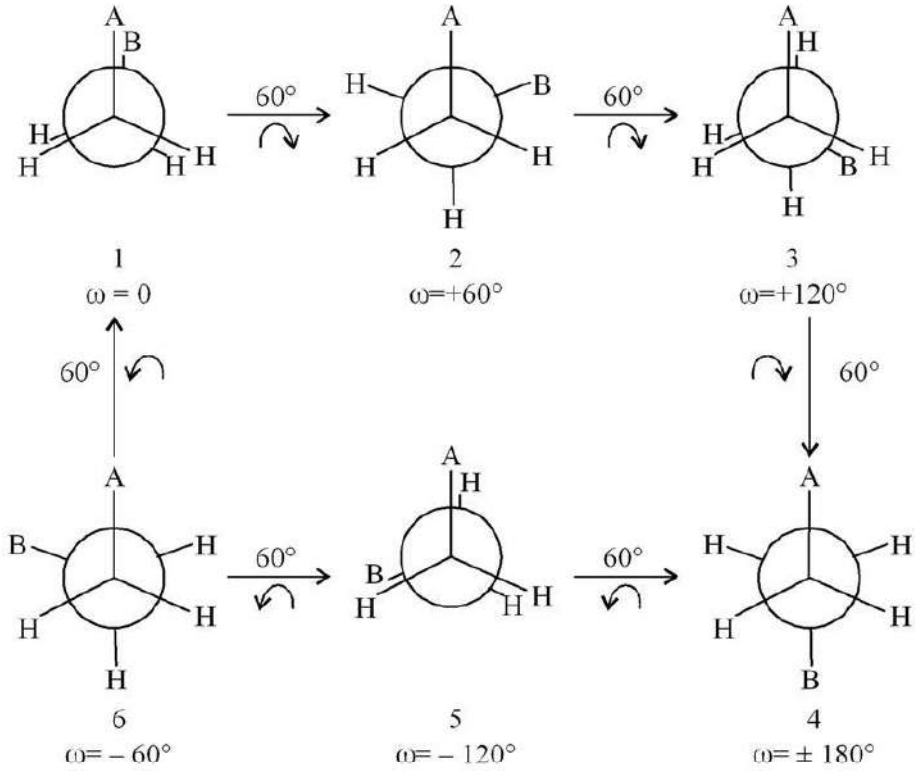
Conformers:

The conformations that correspond to energy minima are called conformers. That is, the conformations which lie in the minima in the energy profile diagram (c.f. section 4.5) are called conformers. In fact, staggered conformations with energy minima are called conformational isomers or conformers.

Conformational energy ($\Delta G°$): Difference in potgential energy between the most stable conformer and the designated less strable 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 (cf. 4.4.3) in liquid stabe is about 2.4 KJ mol^{-1}.

4.4.3 Conformational nomenclature :

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 (reference) 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 $\omega = 0°$ and anti or staggered with $\omega = \pm 180°$.

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 (ω) are listed in the following Table and Figure there of.

Table

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

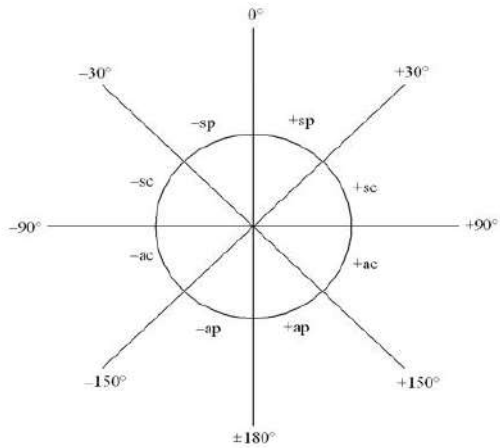
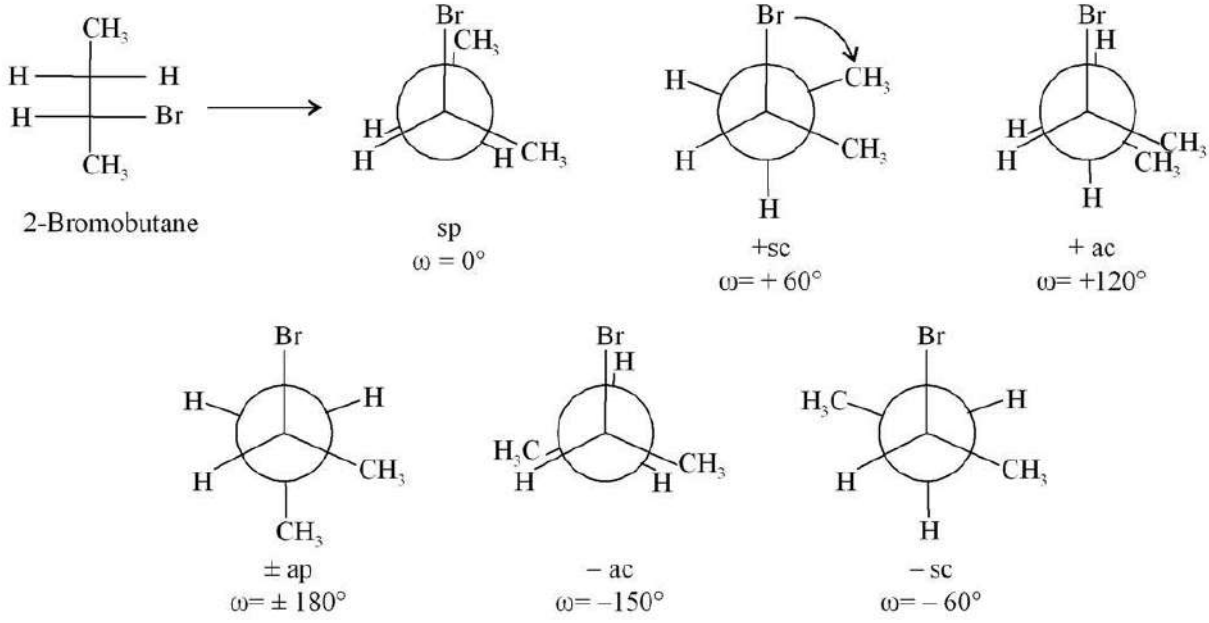


Figure: Specifying Torsion Angles

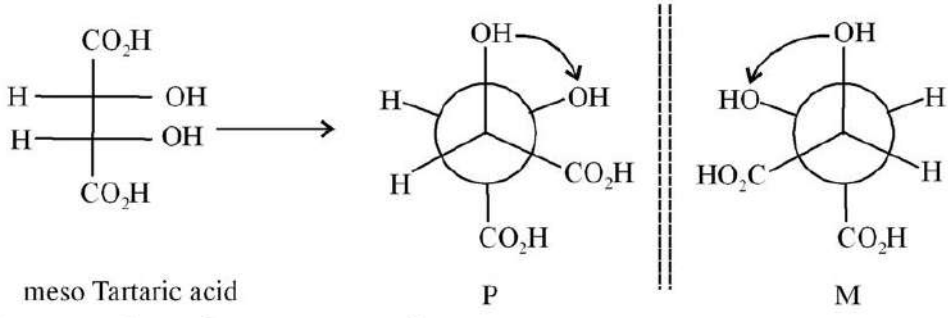
Example :

Designation of conformations of 2-bromobutane is given below.



P/M descriptors :

The P/M descriptors assigned to axially chiral molecules has already been discussed in section 4.1.4. Sometimes it is more convenient to describe the chirality of conformational isomers of acyclic molecules in terms of P/M descriptors. This is illustrated with two enantiomeric conformational isomers of meso tartaric acid.



4.4.4 Energy barrier to rotation :

The difference in the maximum energy of the transition state between the two inter-converting conformers and the minimum enertgy 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.

4.4.5 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 (E_S) of a conformer can thus be expressed as the sum of all these four energy functions as:

$$Es = E(l) + E(\alpha) + E(\omega) + E(r)$$

where, $E(l)$ = 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.

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.

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.

4.4.6 Relative stability of conformers on the basis of steric effect, dipole-dipole interaction and H-bonding :

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.

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.

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.

$$\overset{\delta-}{X}-\overset{\delta+}{H}\cdots:\overset{\delta-}{Y}$$

Hydrogen bond

Intramolecular H-bonding stabilises the gauche conformer.

4.5 Conformational Analysis

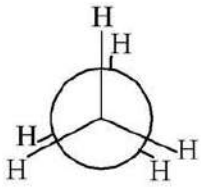
We have mentioned earlier that as we rotate carbon carbon single bond energy of the system changes with the change of dihedral angle (θ) or torsion angle (ω) in a conformer. Conformational analysis also deals with the reactivity of various conformations.

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.

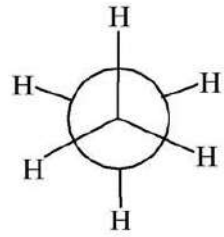
4.5.1 Conformational analysis of :

Ethane, CH_3CH_3

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.

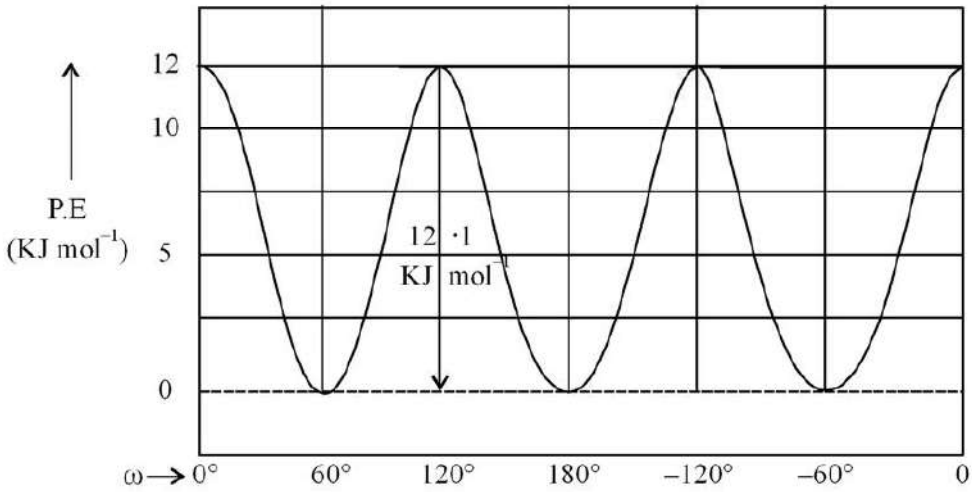


Figure: Energy profile diagram of ethane

The energy barrier of rotation in ethane is around 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,

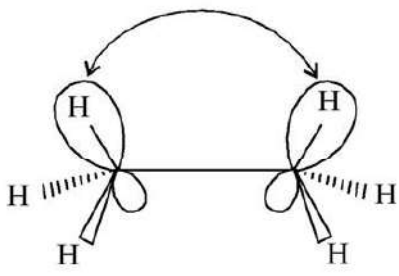
ii) bond opposition strain, and

ii) unfavourable overlap of bond orbitals.

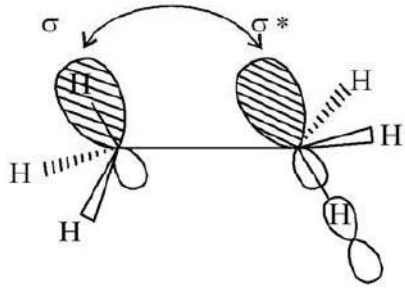
i) The distance between the nonbonded pairs of hydrogen atoms in eclipsed conformation is 230 pm which is just within the van der Waals radii of hydrogen atoms (240 pm). This accounts for only 10% of the total energy barrier.

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 σ_{C-H} bond orbitals in the eclipsed conformation and favourable interaction between filled σ_{C-H} bonding and empty σ^*_{C-H} antibonding orbitals in the staggered conformation.



Destabilising repulsive interaction between σ_{C-H} filled orbitals



Stabilising interaction between filled σ_{C-H} bonding and empty σ^*_{C-H} antibonding orbital.

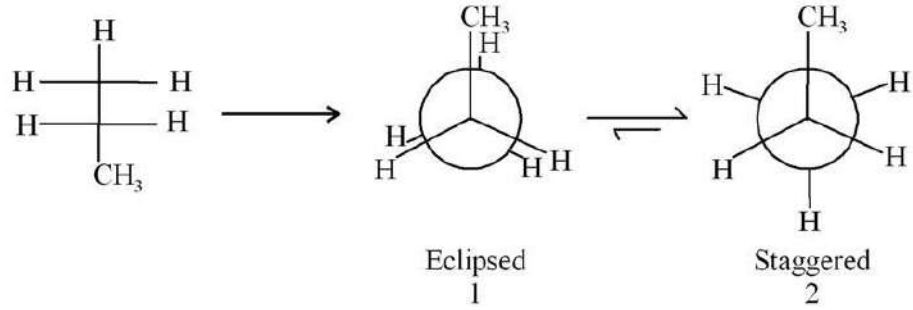
Figure: Orbital interactions

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.

4.5.2 Propane, $CH_3CH_2CH_3$ (Ref. grs. CH_3/H) :

The eclipsed and staggered conformations of propane that exist in equilibrium are shown as



Eclipsed
1

Staggered
2

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.

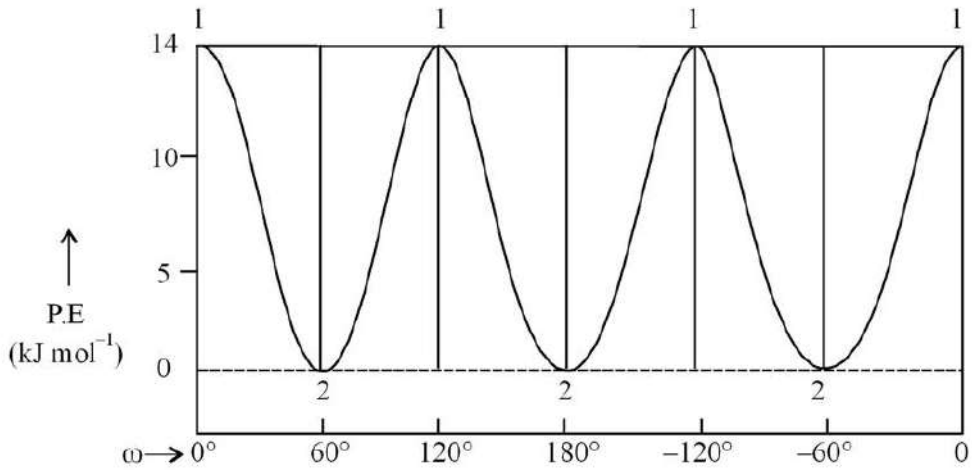


Figure: Energy profile diagram of propane

As the H/H gauche and CH_3/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 CH_3/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 CH_3/H eclipsing interaction in eclipsed propane.

4.5.3 n-Butane, $\overset{1}{CH_3} - \overset{2}{CH_2} - \overset{3}{CH_2} - \overset{4}{CH_3}$ (Ref. grs. CH_3 / CH_3)

Conformational analysis means first of all we have to identify 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.

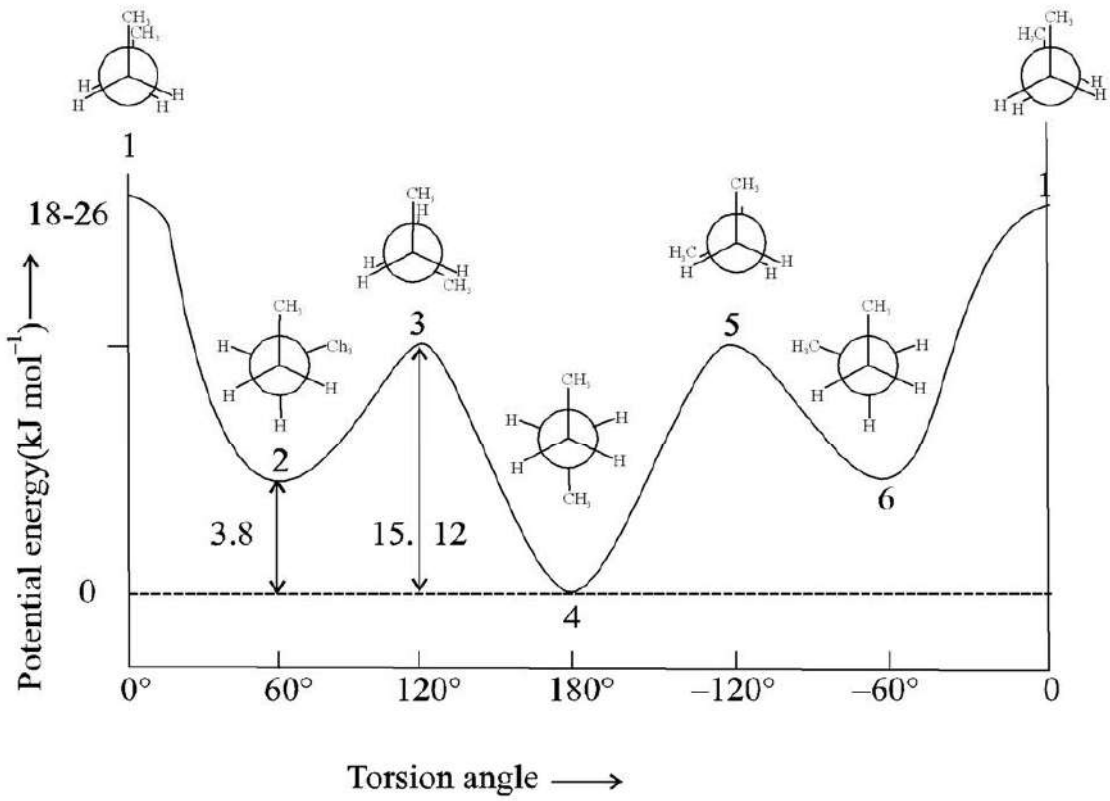


Figure: Potential energy diagram of n-butane (gas phase)

There are two different types of eclipsed forms, one corresponding to the fully eclipsed 1 in which two methyls 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 C_{2V} point group and is achiral. The partially eclipsed conformer (conformational isomer) 3 forms nonsuperposable 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 $\omega = 180°$, 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.

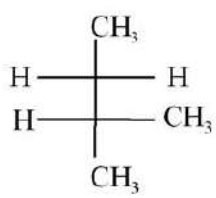
The anti form belongs to C_{2h} point group and is achiral. The gauche conformations with $+60°$ and $-60°$ have a C_2 axis each passing through the mid-point of C(2)–C(3) and bisecting the dihedral angle between two methyls and belong to C_2 point group. They are therefore, chiral and exist as a pair 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 CH_3/H eclipsing and one H/H eclipsing which raises the energy barrier to about 16 ($6\times2+4\times1$) kJ mol^{-1}. The experimental value is 15.12 kJ mol^{-1}. The conformer with $\omega = 180°$ has minimum energy because it is devoid of CH_3/CH_3 van der Waals repulsive interaction. Its potential energy is arbitrarily taken as zero and is the most stable conformer. The gauche conformers with $\omega = +60°$ 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.

4.5.4 2-Methylbutane, $\overset{1}{C}H_3-\overset{2}{C}H(CH_3)-\overset{3}{C}H_2-\overset{4}{C}H_3$ (Ref. grs. CH_3/H)



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.

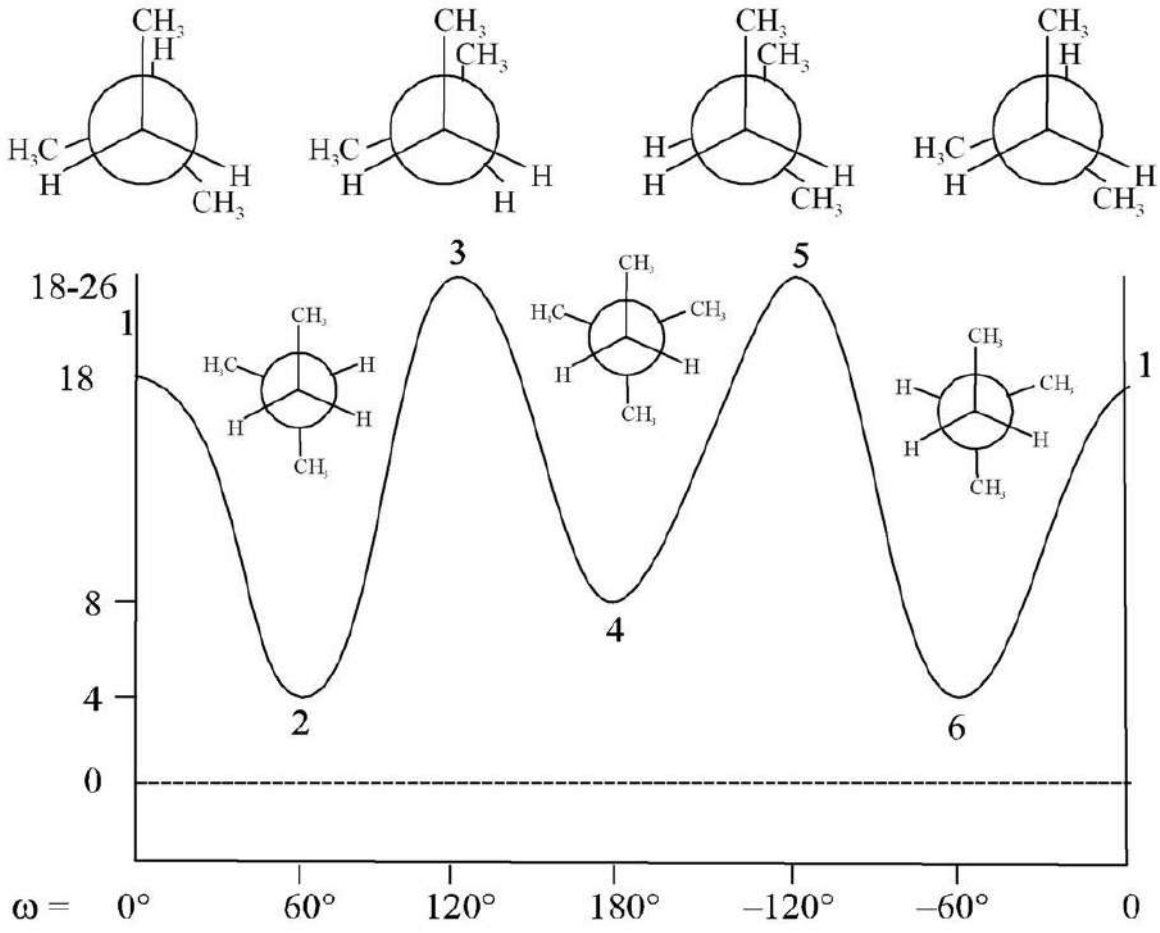


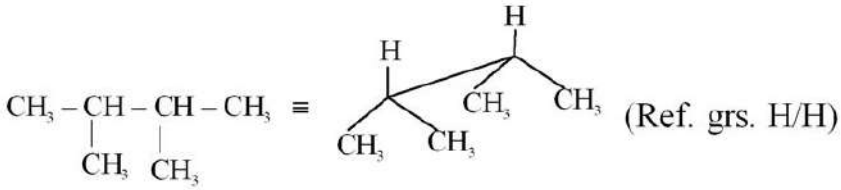
Figure: Energy profile diagram of 2-methylbutane

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 CH_3/CH_3 gauche butane interaction will be at lower energy than the anti form 4 involving two CH_3/CH_3 gauche butane interactions.

So considering steric factor P.E. of the conformations:

$3 = 5 > 1 > 4 > 2 = 6$

4.5.5 Conformation of 2, 3-dimethylbutane



The energy profile diagram can be predicted in the light of steric interaction. The conformations produced by rotation around C(2) – C(3) bond in 60° intervals in 2,3-dimethylbutane along with their calculated potential energy values are represented in the following energy profile diagram.

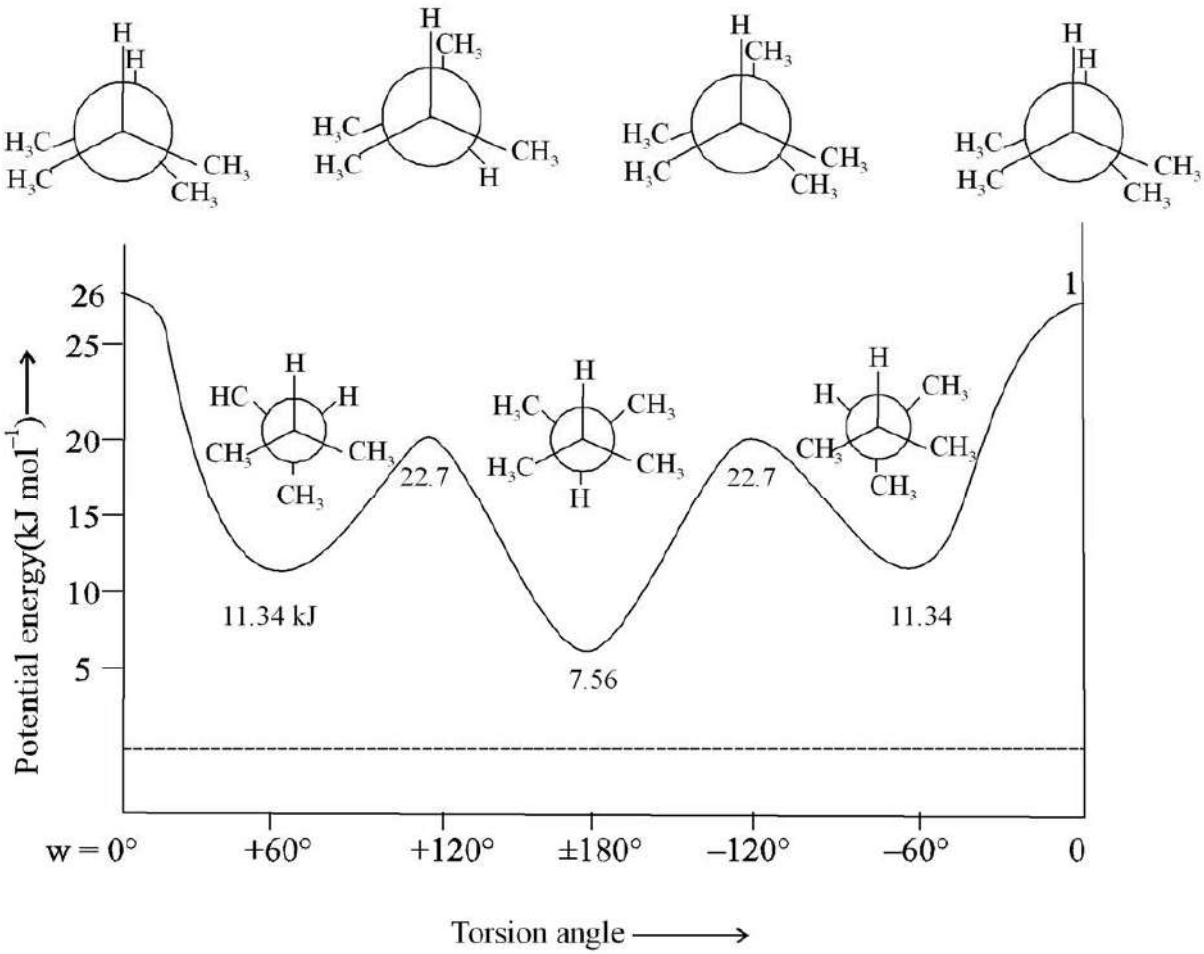
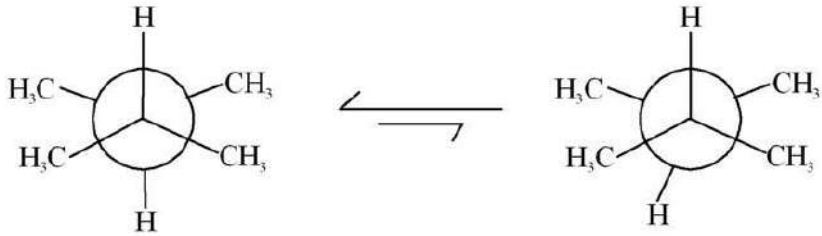


Figure: Energy profile of 2, 3-dimetylbutane

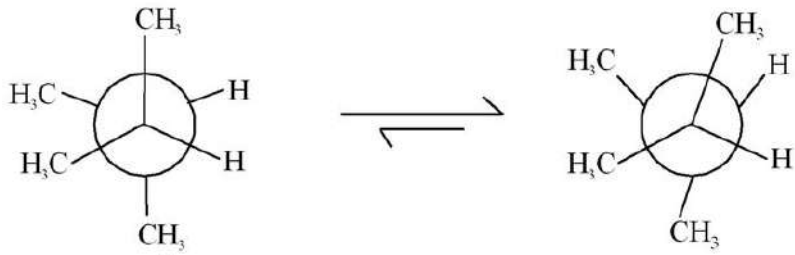
The anti and gauche conformers are equally populated as evidenced from IR and NMR spectra. The anti and gauche forms should therefore, have an equal energy so that the conformational energy (i.e. the difference in potential energies between the most stable conformer and the designated less stable conformation) becomes zero. The total population of the gauche forms is thus twice that of the anti. The higher stability of the gauche forms relative to the anti can be explained as follows.

In 2,3-dimethylbutane the CH_3–C–CH_3 bond angle widens to 114° due to van der Waals repulsive interaction between the methyl groups (Thorpe Ingold effect). As a result, the front CH_3 groups in the anti form tend toward eclipsed with the rear methyl groups. This increases the van der Waals repulsive interactions in the anti form which is thereby destabilised.



Anti

On the other hand, the methyl groups in gauche conformation tend toward a CH_3 / CH_3 perpendicular form. This causes reduction of van der Waals repulsive interactions between two methyl groups in the gauche form which is thereby stabilised.



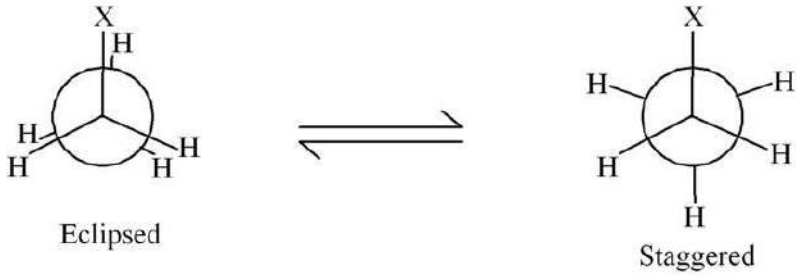
gauche

4.5.6 Conformations 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.

4.5.6.1 Conformations 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.

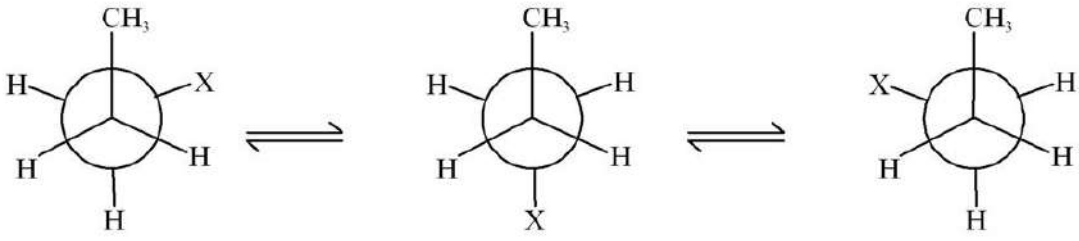


Eclipsed Staggered

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.

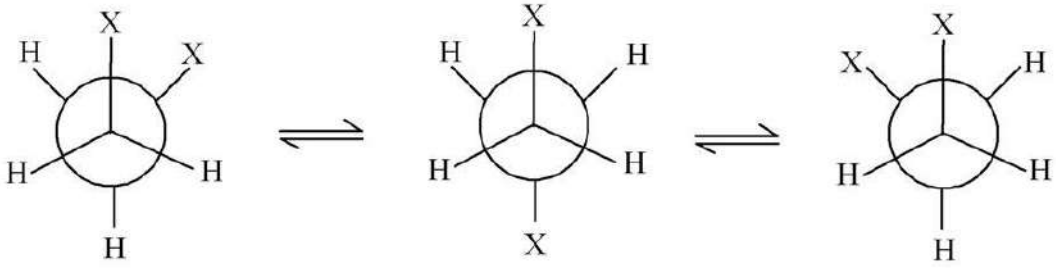
4.5.6.2 Conformation of 1-halopropane: An achiral anti and two enantiomeric gauche conformers of $CH_3CH_2CH_2X$ exist in equilibrium as shown below.



P-gauche anti M-gauche

The gauche form is preferred over the anti because of stabilising interaction between the partially negatively charged X and positive end of CH_3. This has been confirmed by electron diffraction studies. Such stabilisation is absent in the anti conformer because of larger distance between X and CH_3.

4.5.6.3 Conformations 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.

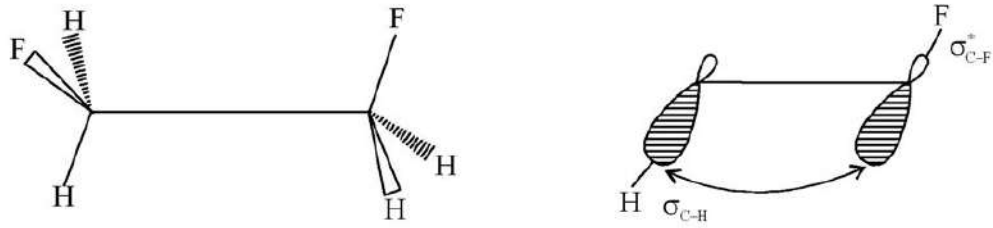


P-gaucha anti M-gaucha

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.

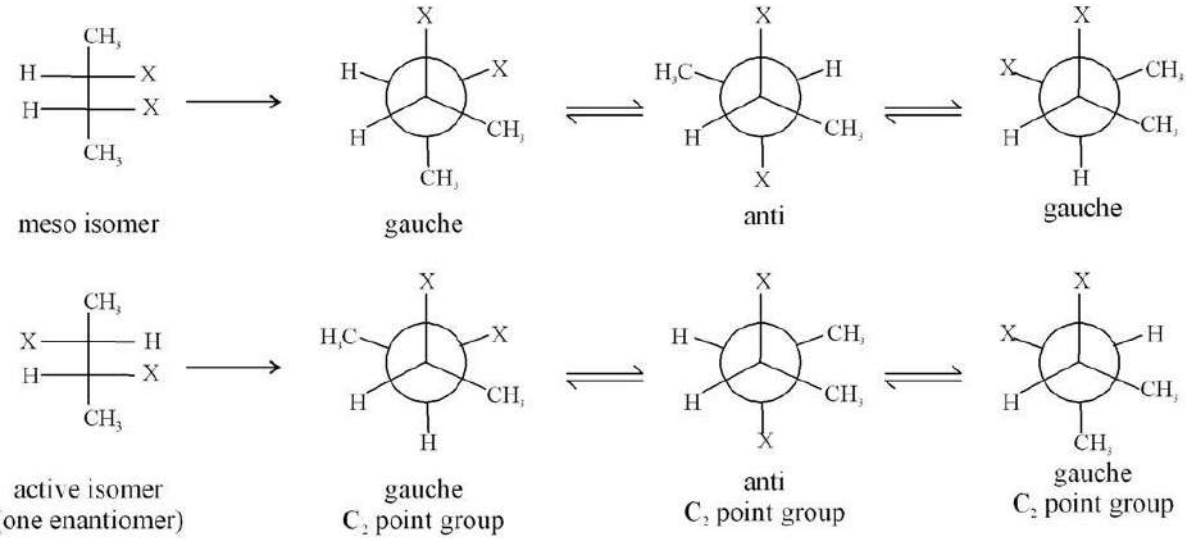
1,2-Dichloro and 1,2-dibromoethane exhibit a similar type of potential energy diagram as that of n-butane but the situation is different in 1,2-difluoroethane. In 1,2-difluoroethane the gauche conformer is more stable than the anti. This can be rationalised in terms of hyperconjugation. The destabilising 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 σ_{C-H} with σ^*_{C-F} (Gauche effect) as shown below:



4.5.6.4 Conformations of 2,3-dihalobutane, $CH_3 - \underset{X}{CH} - \underset{X}{CH} - CH_3$ **(X = Cl, Br)**

The diastereomeric meso and active isomers of 2,3-dihalobutane exist in several conformations as shown below.

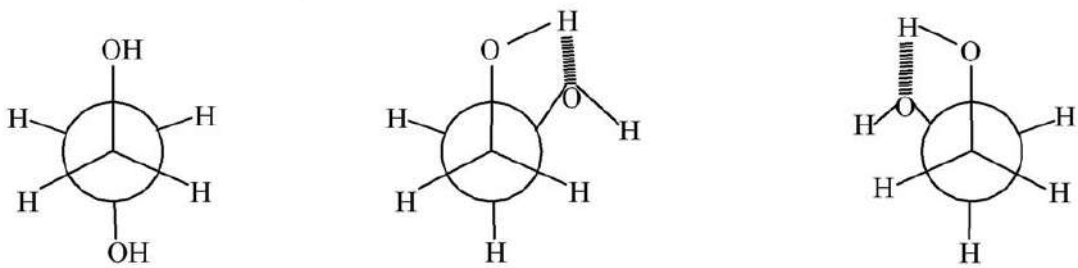


In this case, the most populated anti conformer of the meso isomer is stabilised by two CH_3/X van der Waals force of attraction. On the other hand, dipole-dipole repulsive force between two X atoms destabilises the most populated gauche forms of the active isomer. The meso isomer is therefore, more stable than the active isomer of 2,3-dihalobutane.

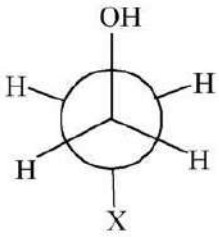
4.5.7 Conformations of 1,2-diol and 1,2-holohydrin :

Molecules of the type $HO–CH_2–CH_2–X$ 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.

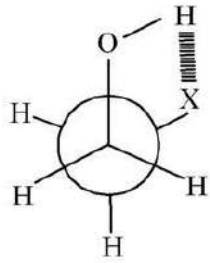
4.5.7.1 Ethylene glycol, $HOCH_2–CH_2–OH$



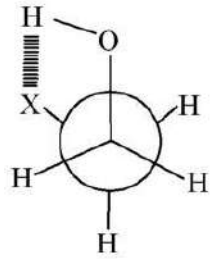
4.5.7.2 Halosubstituted ethanol, $HO - CH_2 - CH_2 - X$ (X = cl, Br, F)



Anti



P-gauche

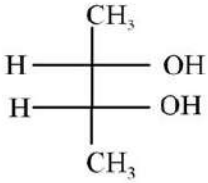


M-gauche

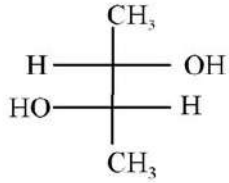
Ethylene glycol or halohydrin such as halogen substituted ethanol adopts gauche conformations because of strong intramolecular H-bonding.

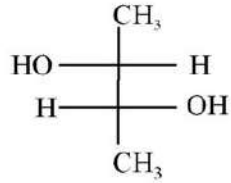
4.5.7.3 Butane-2,3-diol (CH_3–CH(OH)–CH(OH)–CH_3)

Butane-2,3-diol exists in two diastereomeric forms, the meso and the optically active isomers as shown below.



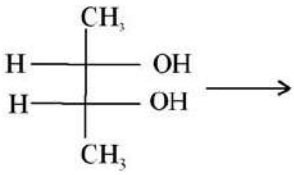
meso isomer



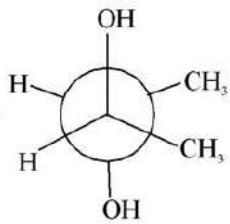


Optically active isomers

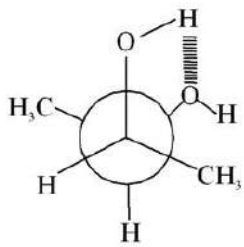
The meso isomer has three preferred conformations of which the enantiomeric gauche forms predominate over the anti due to the formation of intramolecular H-bond and are equally populated.



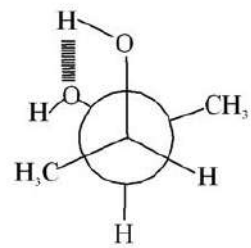
meso isomer



Anti



P-gauche

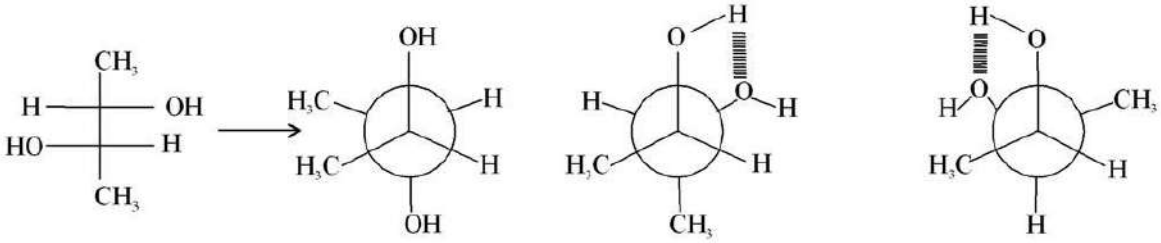


M-gauche

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.

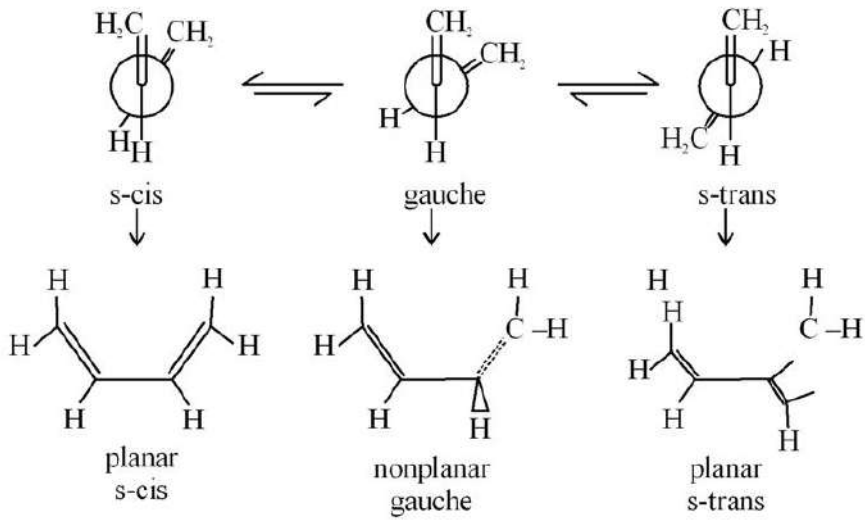
The intramolecularly H-bonded gauche form with two methyls anti is favoured over that with two methyls gauche.



The gauche conformer with two methyls anti of the active isomer is preferred over the gauche conformer of the meso isomer.

4.5.8 Conformations of conjugated systems (s-cis and s-trans) :

An example of conjugated system is 1,3-butadiene, $H_2\overset{1}{C}=\overset{2}{C}H-\overset{3}{C}H=\overset{4}{C}H_2$. Rotation around C(2) – C(3) single bond gives two planar conformations. s-cis and s-trans and a nonplanar gauche conformation as shown below.



The planar s-trans conformation ($\omega = 180°$) is the most stable because of maximum conjugation and minimum steric interaction in it. The hydrogen atoms at C(1) and C(4) in s-cis are in close proximity to each other. So it suffers from van der Waals steric repulsion although it has some overlap of π orbitals. The gauche form is not planar and thus has an

orbital overlap much less than optimal. The energy barrier for rotation about C(2) – C(3) is approximately 28 kJ mol^{-1} from s-trans side to s-cis and about 16 kJ mol^{-1} from s-cis side to s-trans as evidenced from IR and UV spectra under matrix isolation condition. The difference in energy of 12 kJ mol^{-1} between these two conformations is in favour of s-trans making the population of s-trans at room temperature to about 99% and s-cis 1% only. Acyclic unsaturated aldehydes, esters and amides also exist in s-cis and s-trans conformations.

4.5.9 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 $\omega = 0°$, 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.

4.5.10 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.

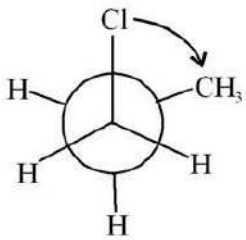
4) Explain why 2-chloroethanol exists exclusively in the gauche conformations in liquid state.

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.

4.5.11 Answer :

1) For the 1st part see text.

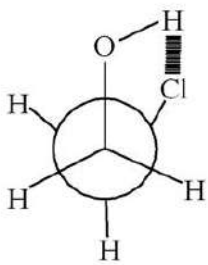


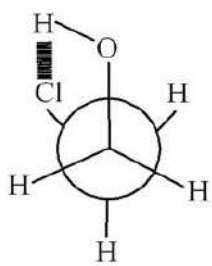
+ sc for $\omega = +30°$ to $+90°$

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}.

Unit 5 ❑ General Treatment of Reaction Mechanism-II

Structure

5.1 Objectives

In this chapter, the principles of chemical thermodynamics, the principles of reaction kinetics, relation between the structure of organic molecules and acidity/ basicity have been discussed. The knowledge on free energy change, enthalpy and entropy change will lead us to know 'how far a reaction will proceed'. The knowledge about the kinetic isotope effect makes the idea of the mechanism of a reaction.

5.2 Introduction

A mechanism is the actual process by which a reaction takes place-which bonds are broken, in what order, how many steps are involved, the relative rate of each step, etc. In order to state a mechanism completely, we should have to specify the positions of all atoms, including those in solvent molecules, and the energy of the system, at

every point in the process. When we consider the conversion of starting materials into products, which constitute an organic reaction, one of the things that we particularly want to know is 'how far will the reaction go over towards products?' Systems tend to move towards their most stable state, so we might expect that more stable the products are, compared with the starting materials, the equilibrium will lie more towards products.

5.3 Reaction thermodynamics

5.3.1 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 otherhand, 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:

$$\ln K = \Delta G^\circ/RT \quad \text{.....(1)}$$

The sign of ΔG° tells us whether products or reactants are favoured at equilibrium. If ΔG° is negative for a reaction, the products will be favoured at equilibrium. If ΔG° is positive, the reactants will be favoured at equilibrium. If ΔG° is zero, the equilibrium constant for the reaction will be 1.

5.3.2 Enthalpy and entropy factor

A small change in ΔG° makes a big difference in K. The relation between ΔG° (change in standard Gibbs free energy), ΔH° (standard enthalpy change of reaction) and ΔS° (standard entropy change of reaction) is given below-

The change in enthalpy (ΔH°) 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. ΔS° represents the entropy difference between the reactants and products. If ΔS° 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 ΔS° 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 ΔG. If stronger bonds are broken and weaker bonds are formed, then heat is consumed and the reaction is endothermic.

- **Standard free energy change (ΔG°):** It is the difference in free energy between the reactants and products (all are in their standard states).
- **Standard enthalpy change (ΔH°):** 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 (ΔS°):** 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.

5.3.3 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, ΔH°).

ΔH° (reaction) = sum of the bond energies of bonds being broken - sum of the bond energies of the bonds being formed.

ΔH° (reaction) = ΣH(reactant bonds broken) –ΣH(product bonds formed)

- Steps for calculating heat of reaction (enthalpy change of reaction), ΔH° 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):

   ΔH°(reaction) = ΣH(reactant bonds broken) -ΣH(product bonds formed)

3. Substitute bond energy values into the equation and solve for ΔH°(reaction)

For the general chemical reaction in which reactants form products:

chemical reaction:	reactants	→	products
bonds are	broken	→	made
energy is	absorbed	→	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 break bonds > H make bonds ΔH reaction 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 break bonds < H make bonds ΔH reaction 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:

$\Delta H°$(reaction) = sum of the bond energies of bonds being broken - sum of the bond energies of the bonds being formed.

$\Delta H°$ (reaction) = ΣH(reactant bonds broken) -ΣH(product bonds formed)

Example 1. For example, we could use the bond energies to calculate the heat of reaction (enthalpy change for the reaction), $\Delta H°$, 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 CCl_4 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 HC1 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):

$\Delta H°$(reaction) = ΣH(reactant bonds broken) -ΣH(product bonds formed)

3. Substitute bond energy values into the equation and solve for $\Delta H°$(reaction)

$CH_4(g) + 4Cl_2(g)$			$CCl_4(g) + 4HCl(g)$	
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
ΣH(reactant bonds broken) = 2624			ΣH(product bonds formed) = 3084	

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

5. Note that the reaction is exothermic, ΔH is negative (ΔH = -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

$\Delta H°$(reaction) = ΣH(reactant bonds broken) -ΣH(product bonds formed)

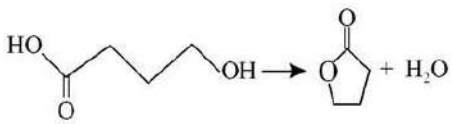
= – 276.9 + 248.2

= – 28.7 Kcal/mole

5.3.4 Intermolecular and intramolecular reactions

Intra-molecular esterification (i.e., lactone formation) is more favorable than intermolecular. Similarly intra-molecular hemiacetal formation is more favorable than

intermolecular. These facts can be explained on the basis of entropy factor.



$$CH_3COOH + MeOH \longrightarrow CH_3\text{–}COOCH_3 + H_2O$$

In each case, the bonds formed (C–O & O–H) corresponds to those broken. So AH 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 (ΔS_{vib}) is also likely to be negligible. Hence both ΔH and ΔS are not far from zero. So that ΔG 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 ΔG 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.

5.4 Concepts of organic acids and bases

5.4.1 Defination of 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, HC1, 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:

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

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.

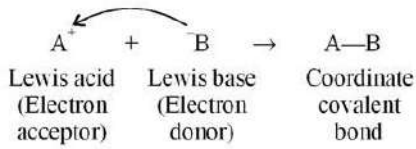


Figure 11: A Lewis Base (B) donates its electrons to a Lewis Acid (A) resulting in a coordinate covalently bonded compound, also known as an adduct.

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 ah 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 certfral 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.

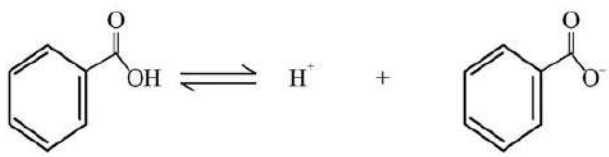
Lewis Bases donate an electron pair. Lewis Bases utilize the highest occupied molecular orbital or HOMO. An atom, ion, or molecule with a lone-pair of electrons can thus be a Lewis base. Each of the followings can "give up" their electrons to an acid, e.g., OH^-, CN^-, CH_3COO^-. H_2O:, :NH_3, CH_3–NH_2 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., HC1, 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.

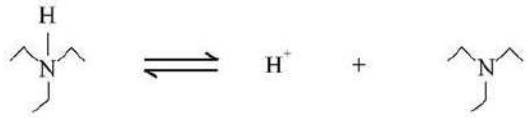


benzoic acid (neutral acid) — benzoate anion (anionic conjugate base)

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 add) triethylamine (neutral conjugate base)



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.

5.4.2 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.

1. **Hybridisation:** In organic chemistry, there are three types of hybridisation: sp^3 (for single bonds), sp^2 (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≡C–H
C Hybridisation	sp^3	sp^2	sp
pKa	~50	~43	~25
Conjugate Bases	$H_3C–CH_2^-$	$H_2C=CH^-$	$H–C≡C^-$
			stability increases →

An alkene is about 10^7 times more acidic than an alkane, and an alkyne is about 10^{15} times more acidic than alkane. Alkyne (sp hybridisation) have more s character than alkene (sp^2) and alkane (sp^3). Why does having more 5 character means more acidic? Recall from your general chemistry or physical chemistry lectures that the 5 orbital is spherical around the centre of the atom (nucleus). On the other hand, each of the p orbitals (p_x, p_y, and p_z) 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 attfact).

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 5 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:

Acidity increases →

Acids	$H_3C\text{-}NH_2$	$H_2C{=}NH$	$H\text{–}C{\equiv}\overset{+}{N}\text{-}H$
C Hybridisation	sp^3	sp^2	sp
PKa	~38	~ 31	~ 11
Conjugate Bases	$H_3C\text{–}NH^-$	$H_2C{=}N^-$	$H\text{–}C{\equiv}N$

← Basicity increases

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.

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

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 $CH_4 < NH_3 < H_2O < HF$.

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	HCI	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.

3. Inductive effect :

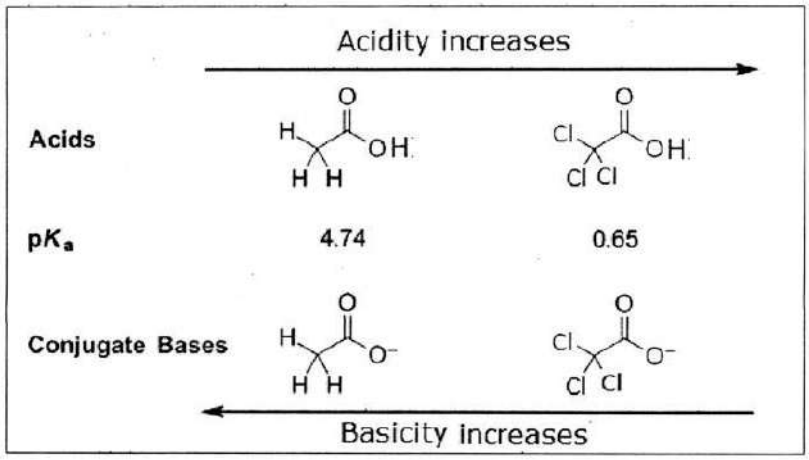
In the section above, it has been shown how electronegativity affects the acidity of the H^+ directly bonded to the electronegative atom. Here, we shall see that an electronegative functional group can also affect the acidity of H^+ that is several bonds away from itself. We shall also see a non-electronegative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

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 σ 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 o bonds' phenomenon is known as the electron-withdrawing inductive effect, also known as the '–I effect'.

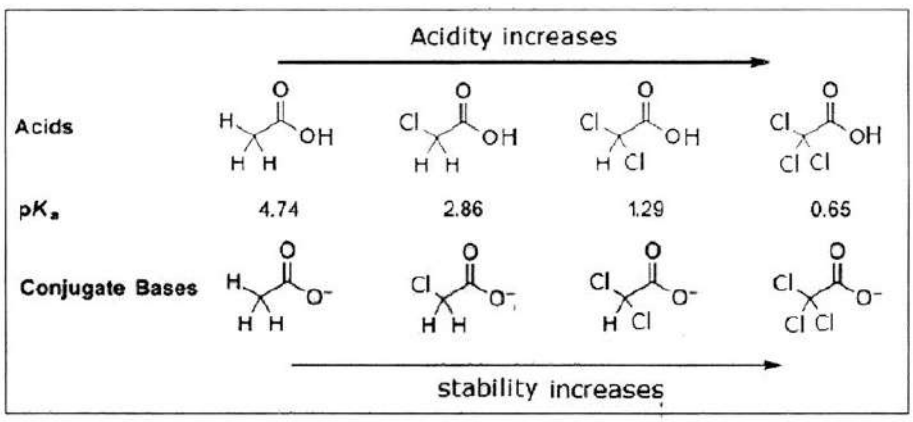
Have a look at the acetic acid derivatives below.



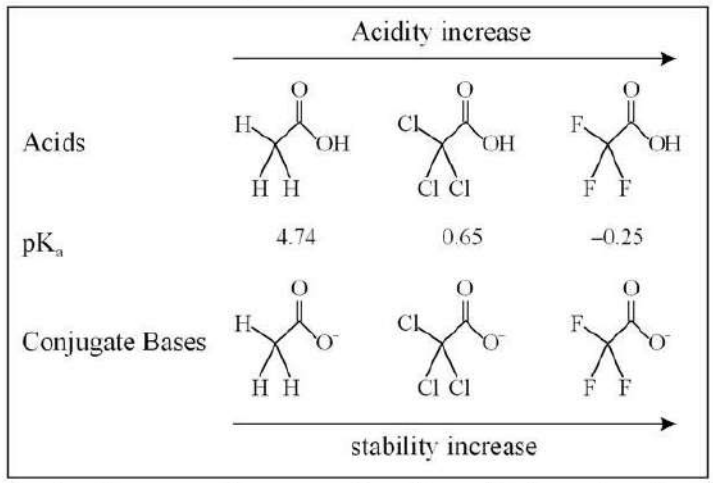
The electronegativity of the chlorine atom pulls electron density away from the acidic H towards itself, making chloroacetic acid about 4 orders of magnitude (10^4 times) more acidic than normal acetic acid! This shows the inductive effect that chlorine has.

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.



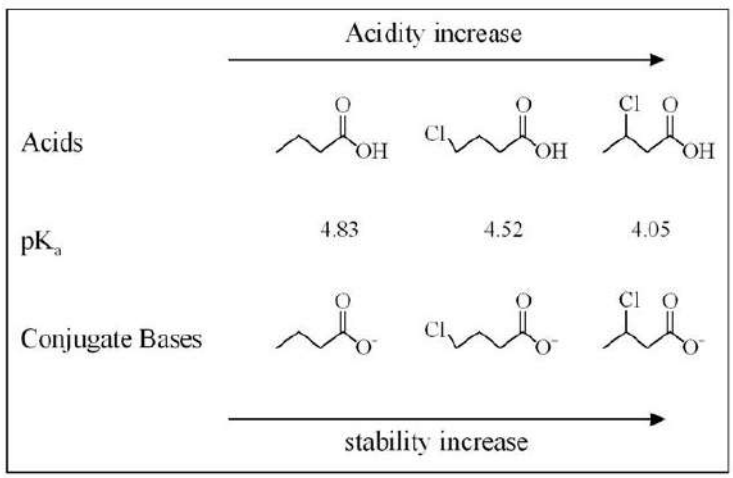
The addition of more electronegative EWGs means more stability of conjugate base and more acidity of the corresponding acid. The acidity of trichloroacetic acid (TCA) and trifluoroacetic acid (TFA) is compared below:



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.

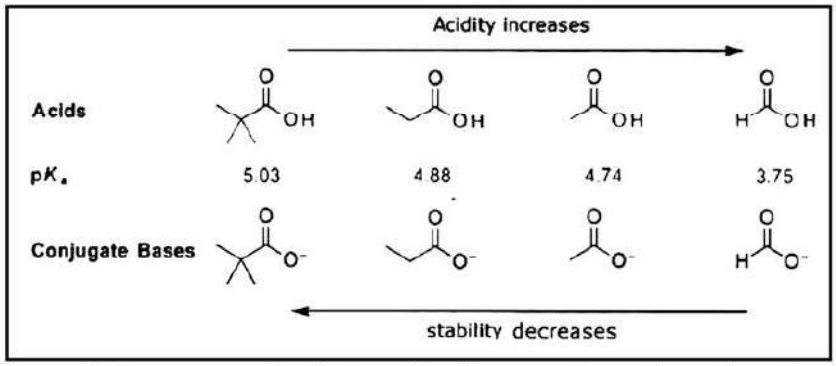


The chlorine atom in 2-chlorobutanoic acid is closer to the carboxylic group than that in 3-chlorobutanoic acid. Therefore, the stability of the corresponding conjugate bases increases from left to right resulting the mentioned order of acidity.

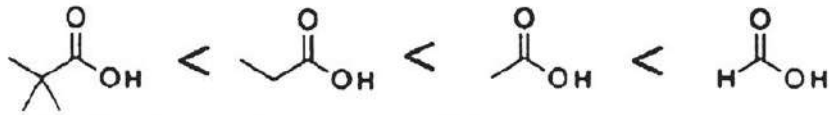
3.2. Electron-donating Inductive Effect :

Alkyl functional group affects the acidity of H^+ by inductively pushing the electron density away from it through the a 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 a bonds' phenomenon is known as the electron-donating inductive effect, sometimes written as '+I effect'.

Have a look at the acetic acid derivatives below.

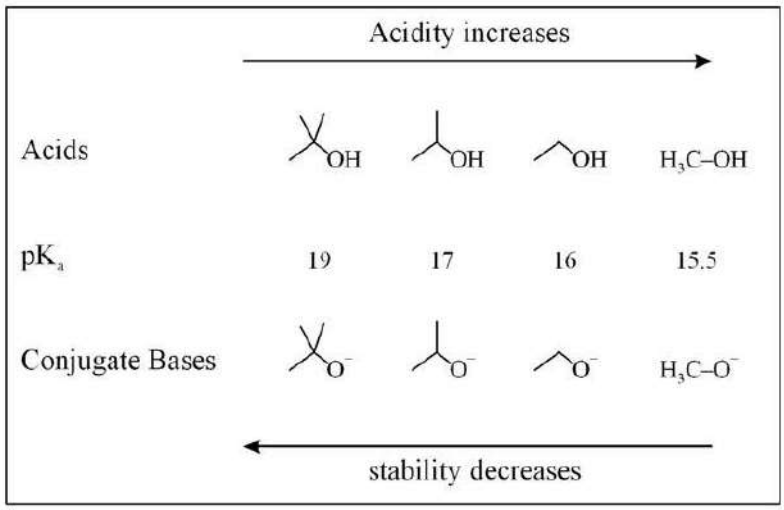


The methyl groups push electron density away from themselves towards the carboxylate group. It destabilises the anionic conjugate bases. With increasing the number of methyl groups (EDG) the electron density is increased more and the decrease in stability of conjugate base is more making the following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

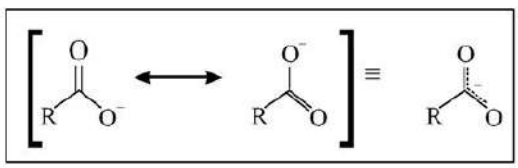


4. Resonance (Delocalisation) :

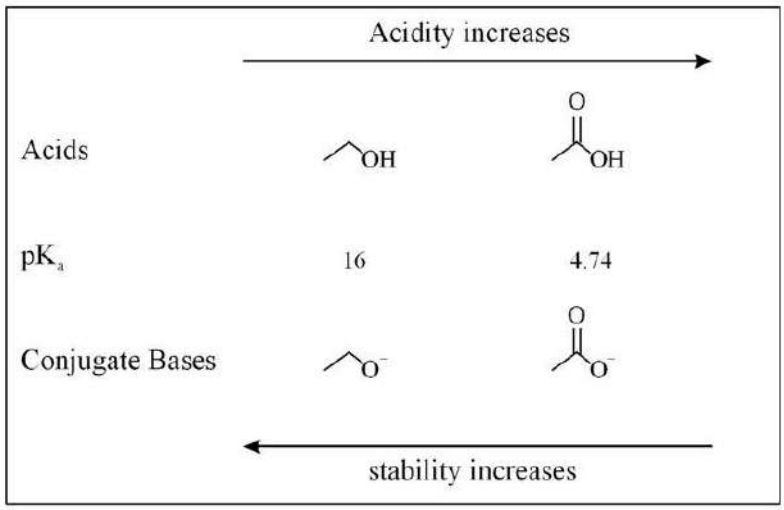
Resonance can greatly stabilise charged species through the delocalisation of charge. Since the acidity of organic compounds is influenced by the stability of conjugate bases (charged species), resonance plays an important role in determining the acidity of various compounds. Similar to the inductive 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.

4.1. Resonance in Carboxylic Acids :

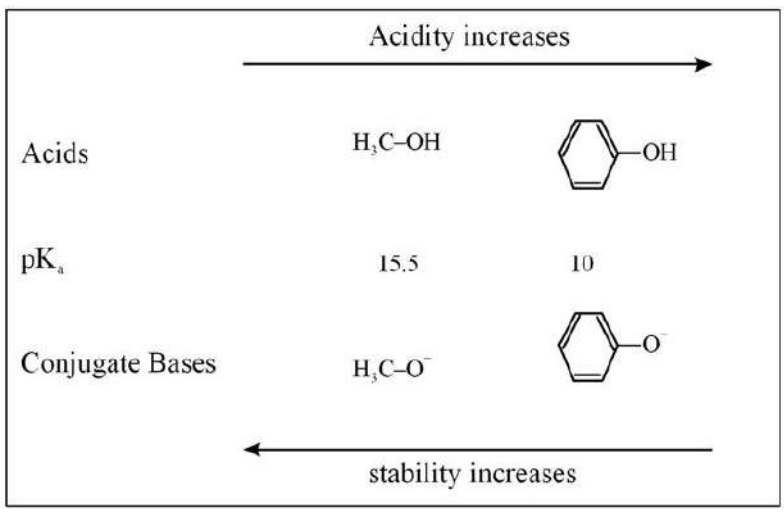
This resonance stabilises the carboxylate anion (conjugate base of carboxylic acid), making carboxylic acids as acidic. We can compare the pKa of ethanol and acetic acid to see how the resonance increases the acidity of carboxylic acids:



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

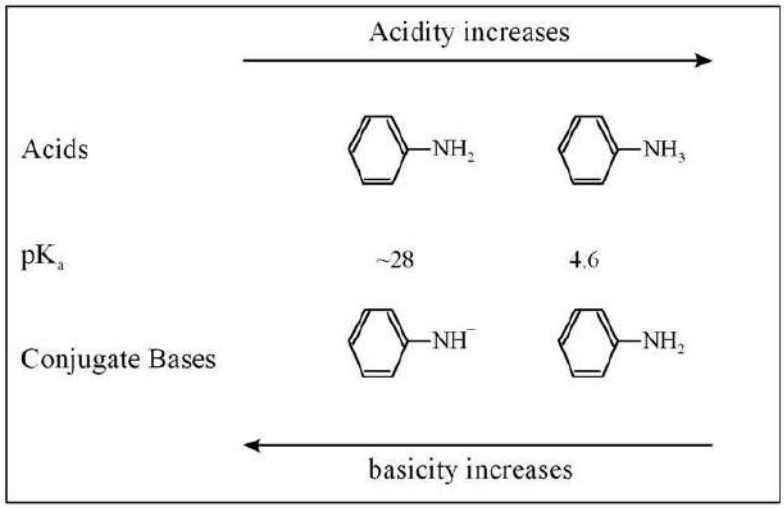


Now acidity is compared between a non-conjugated alcohol (methanol) and a conjugated alcohol (phenol):



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.

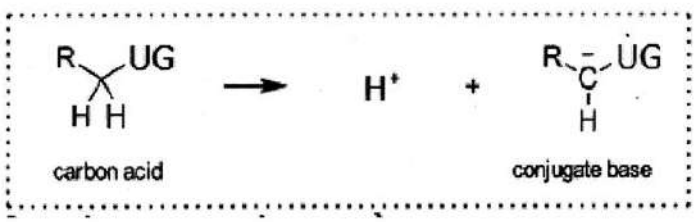
You can observe something interesting when comparing neutral and protonated aniline



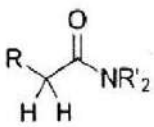
In neutral aniline, the free electron pair of the nitrogen delocalises to the benzene ring, giving stability. Protonation of the anilinet nitrogen takes away the conjugation, making the anilinium (which is a cationic acid) unstable. Instability of a cationic acid makes a strong acid. This, in conjunction 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.

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 a-carbon, whilst its hydrogen is known as the α-hydrogen. Deprotonation of α-hydrogens results in the formation of carbanion, called the α-carbanion. Overall, this type of acid is known as carbon acid.

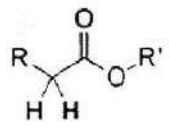


Examples of UG (unsaturated groups)



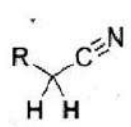
Amides

$pK_a = \sim 25$



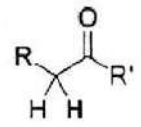
Esters/carboxylic acids

$pK_a = \sim 25$



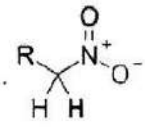
Nitriles

$pK_a = \sim 25$



Ketones/aldehydes

$pK_a = \sim 20$

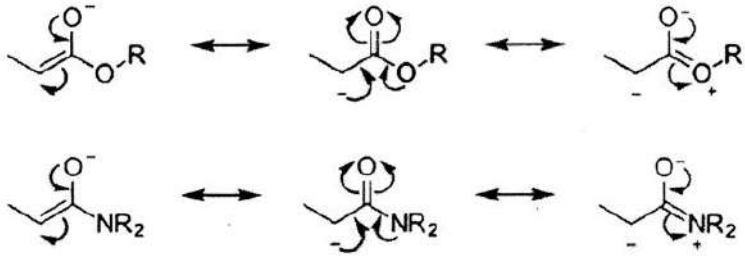


Nitro

$pK_a = \sim 9$

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 NR_2 groups in the carboxylic acid family is more involved in resonance with the carbonyl group. Because of this, the α-carbanion has to 'compete' and 'share' the resonance with the carbonyl group. This makes the α-hydrogen of the carboxylic acid family more acidic than the aldehydes/ketones.

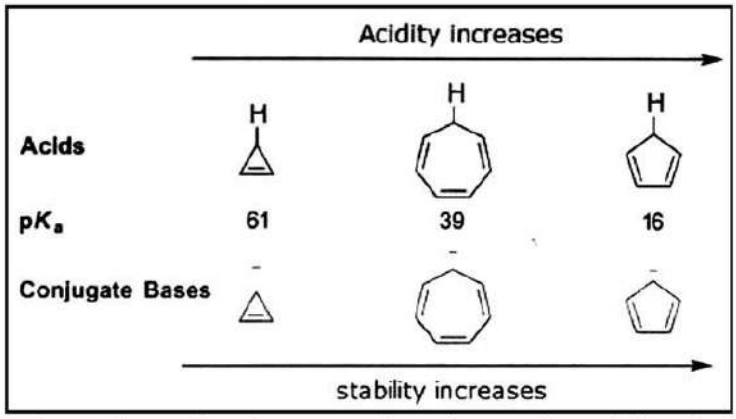


In aldehydes/ketones, the the α-carbanion has carbonyl group only for itself, making the resonance stabilision better. This makes their α-hydrogens more acidic.

5. Aromaticity :

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.



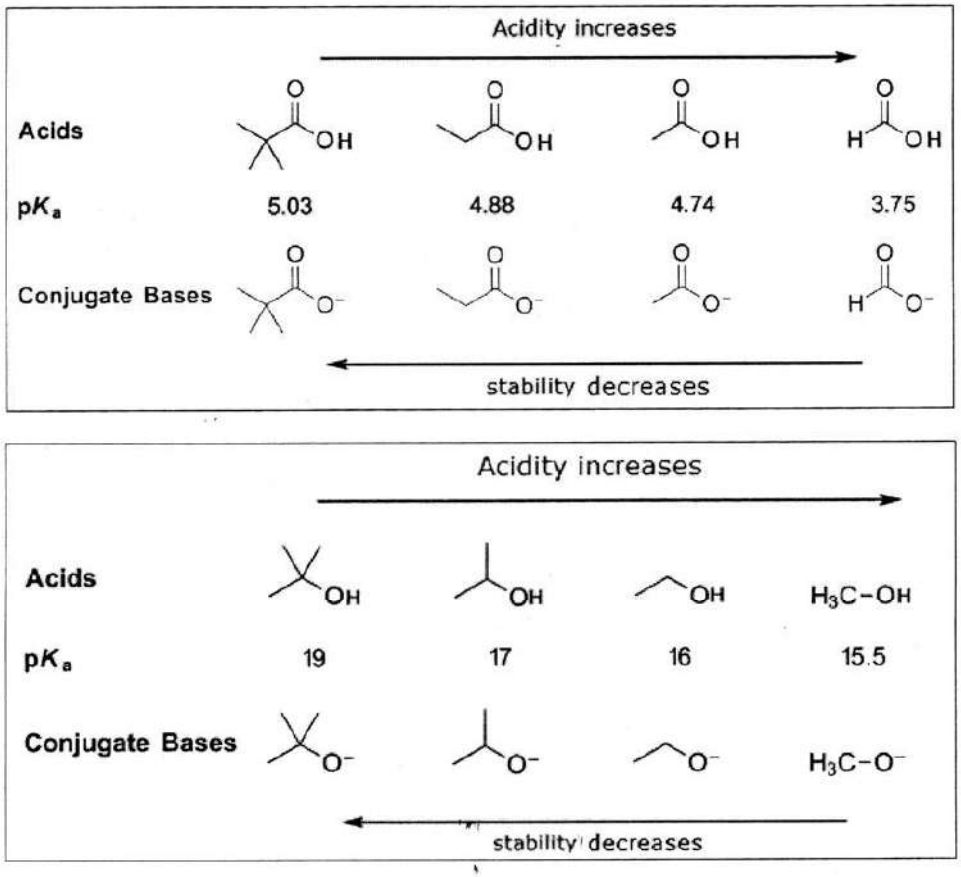
The conjugate base of cyclopropene is anti aromatic and therefore very much unstable. On the other hand, the conjugate base of cycloheptatriene is not planar; making it nonaromatic and therefore unstable than the conjugate base of cyclopentadiene which is aromatic. The acidity order is cyclopropene 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

6. 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.

5.4.3 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.

I. Basicity Increases with Increasing 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 (pKaH of 38) is stronger base than NH_3 (pKaH of 9.2). It can be used to deprotonate terminal alkynes (pKa = 25), for example, whereas ammonia will not.

1. The Effect of Charge

Basicity increases with increased negative charge

$:NH_3$ < $:\overset{\ominus}{N}H_2$ < $:\overset{2\ominus}{N}H$

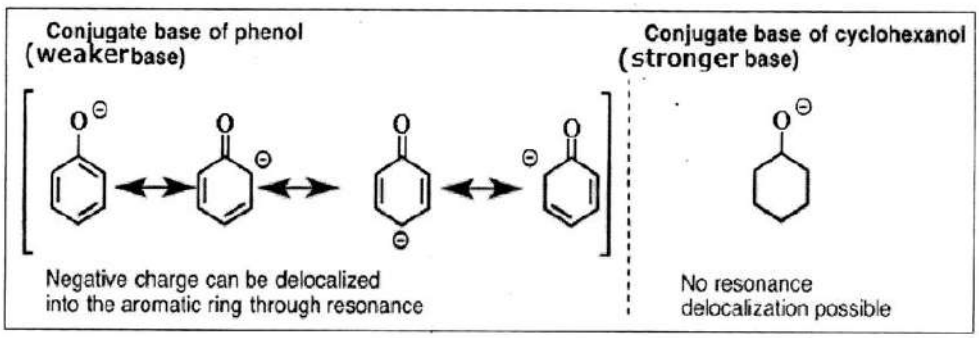
Least basic — Most basic

pKaH = 9.2 pKaH = 38

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.

II. 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.

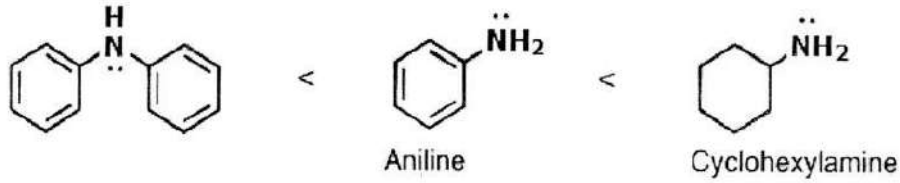


By analogy, we should also expect that aniline is a weaker base than cyclohexylamine. That is indeed the case! The the pKaH of aniline is 4.6, and pKaH of cyclohexylamine is 11.2. (The higher is the pKaH, the stronger is the base). The basicity is decreased even further when a second phenyl ring is attached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



Least basic **Most basic**

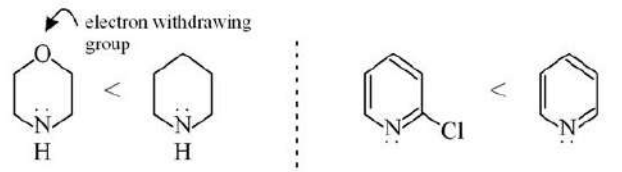
pKaH = 0.78 **pKaH = 4.6** **pKaH 11.2**

III. Inductive effect:

Lower charge density = moire stability = lower basicity.

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

3. Electron withdrawing groups decrease amine basicity



Morpholine	Piperidine	2-chloropyridine	pyridine
Less basic	More basic	Less basic	More basic
pKaH=8.36	pKaH=10.9	pKaH=0.49	pKaH=5.2

4. Pi-Acceptors and Pi-Donors :

We've seen that resonance tends to decrease basicity (Factor 2) and so do inductive effects (Factor 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?

The basicity of amides is much lower than that of amines. Why?

Less basic More basic

- Oxygen is more electronegative than nitrogen, so inductive effects play a role
- However, a more important factor is revealed when examining the key resonance forms...

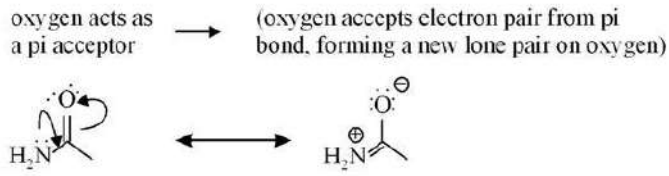
It seems worthwhile to devote a section to how the basicity of nitrogen is affected by its interactions with other functional groups in a pi-system. Specifically, the basicity of nitrogen is decreased when it acts as a pi-donor, and the basicity of nitrogen is increased when it acts as a pi-acceptor.

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"**).

The basicity of nitrogen is decreased when it Is attached to a Pi-Acceptor



nitrogen acts as
a pi donor

(nitrogen donates a lone pair
to form a new pi-bond)

Major resonance
contributor
Note that nitrogen can't act
as a base in this resonance form!
the oxygen of amides is more
basic than the nitrogen

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, **the 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.

familiar examples of pi-acceptors

—NO_2 —SO_3H —C≡N

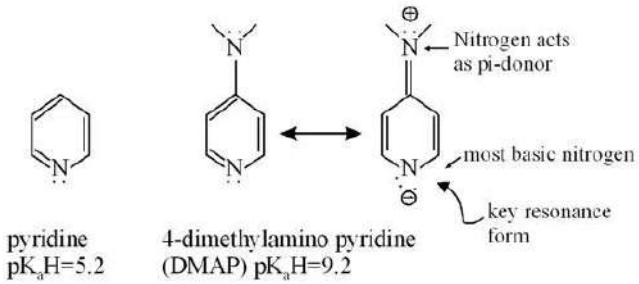
[CF_3 is an example of a functional group that is a meta director but not a pi acceptor, since it has no pi bonds]

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- donating NMe_2 group to the 4-position results in a 10^4 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 ($pK_aH = 9.2$)



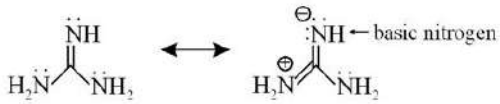
pyridine $pK_aH=5.2$ 4-dimethylamino pyridine (DMAP) $pK_aH=9.2$

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 NMe_2! The NMe_2 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.

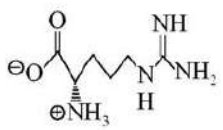
Another example of how basicity of nitrogen can be increased by attachment to pi-donors is found in guanidines. In guanidine there are two pi-donating NH_2 groups which can donate electron density to the (pi-accepting) C=NH.

Guanidines are strongly basic due to pi-donation from two NH_2 groups



"Guanidine" (pKaH=13.6)

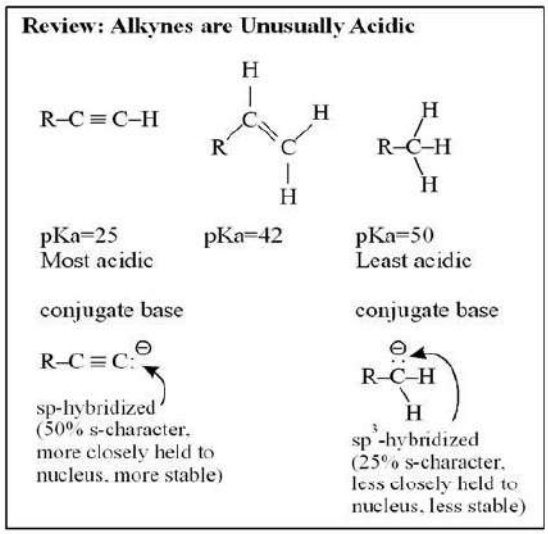
Arginine is the most basic amino acid due to its guanidine side chain



Arginine $pK_aH=12.5$

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 >50).



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 sp^3 hybridized orbital (25% s-clraracter). 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 th§ relative basicity of nitriles, pyridine, and piperidine?

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

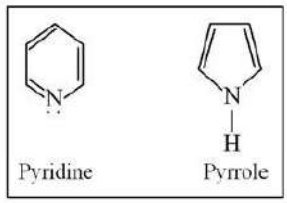
	Ph–C=N:	<		<	
Hybridization of nitrogen	sp		sp^2		sp^3
pKaH	–10		5.2		11
	least basic				**most basic**

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).

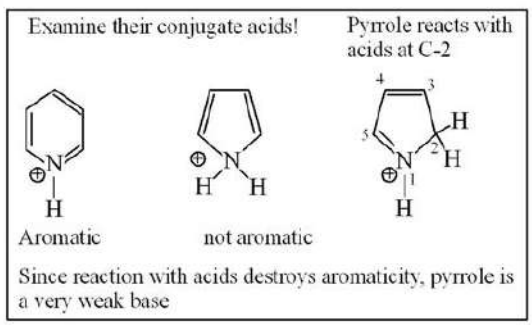
Bonus Factor: Aromaticity

What's more basic between pyridine and pyrrole?



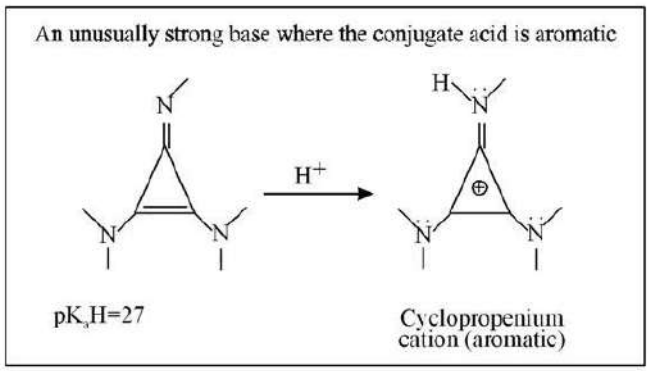
It turns out that the nitrogen in pyrrole is unusually non-basic. In fact, even when subjected to acid, pyrrole reacts at carbon (C-2), and not on the nitrogen. Pyridine [pKaH - 5.2] is far more basic than pyrrole [pKaH about -3.6]

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.

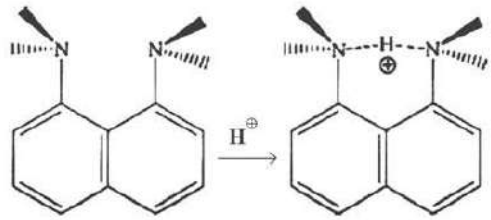
5.4.4 Proton Sponge :

1,8-Bis(dimethylamino) naphthalene is anorganic compound, classified as 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.



5.4.5 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.

5.4.5.1 Characteristics of hard, soft & borderline acids & bases:

Type of Acid/Base	CHARACTERISTICS	EXAMPLES
Hard acids	* Atomic centres of small ionic radii (<90 pm). * High positive charge. * Empty orbitals in their valence shells. * Low electronegativity (0.7-1.6) and low electron affinity. * Likely to be strongly solvated. * High energy LUMO.	H^+, Li^+, Na^+, K^+, Be^{2+}, Ca^{2+}, Sr^{2+}, Sn^{2+} Al^{3+}, Ga^{3+}, In^{3+}, Cr^{3+}, Co^{3+}, Fe^{3+}, Ir^{3+}, La^{3+}, Si^{4+}, Ti^{4+}, Zr^{4+}, Th^{4+}, U^{4+}, VO^{2+}, UO_2^{2+} $BeMe_2$, BF_3, BCl_3, $B(OR)_3$, $AlMe_3$
Soft acids	* Large radii (>90 pm). * Low or partial positive charge. * Completely filled orbitals in their valence shells. * Intermediate electronegativities (1.9-2.5) * Low energy LUMO's with large magnitude of LUMO	Cu^+, Ag^+, Au^+, Hg^+, Cs^+, Ti^+, Hg^{2+}, Pd^{2+}, Cd^{2+}, Pt^{2+} Metal atoms in zero oxidation states BH_3
Border line 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 . * electronegative atomic centres (3.0- 4.0). * Weakly polarizable. * Difficult to be oxidized. * 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). * High polarizability * Easily undergo oxidation. * Low energy HOMO'S but large magnitude HOMO coefficients.	S^{2-}, RSH, RS^- R_2S, I^-, CN^-, SCN^-, $S_2O_3^-$, R_3P, R_3AS, $(RO)_3P$, RNC, CO, C_2H_4, C_6H_6, R^-, H^-
Border line bases		Aniline, pyridine, N_3^-, Br, NO_2^-, SO_3^{2-}, N_2

5.4.5.2 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.

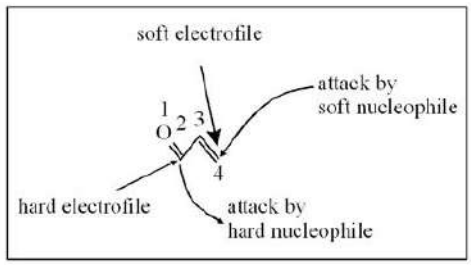
$$CH_3X + SCN^- \xrightarrow{-X^-} CH_3SCN$$

Nucleophilic addition of α,β-unsaturated carbonyl compounds:

The α,β-unsaturated carbonyl compounds have two type of carbon electrophilic centers.

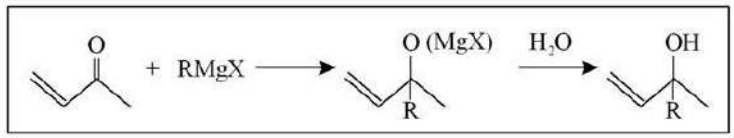
1) Carbonyl carbon - Hard electrophilic center.

2) P-carbon - Soft electrophilic center.

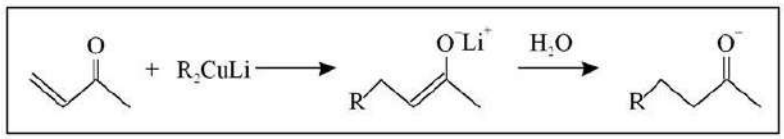


Therefore, the hard nucleophiles like Grignard reagents attack the carbonyl

carbon (hard electrophile) resulting in 1,2-nucleophilic addition to C=0 group.



Whereas, the soft nucleophiles like Lithium organocuprates, thiols etc., attack the β-carbon (soft nucleophile) resulting in 1,4-conjugate addition.



5.4.6 Nucleophilicity Vs Basicity :

First of all, remember that basicity is a subset oi 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: nucleophile attacks 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.

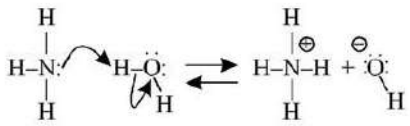
So how do reactions of nucleophiles at hydrogen differ from reactions of nucleophiles at carbon? Well, they're more easily reversible, for one thing. We can measure acidity (and, by extension, basicity) through the measure known as pKa, which is a reflection of the position of the equilibrium between 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 remerftber 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

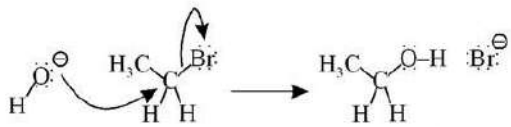
electrophiles are significantly more sensitive to steric effects, because empty orbitals on carbon are not as accessible. Steric hindrance is like a fat goalie.

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

"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)
"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

5.5 Tautomerism

The phenomenon in which two structural isomers undergo rapid interconversion and exist in dynamic equilibrium in the liquid state or in solqtion under normal laboratory condition is known as tautomerism.

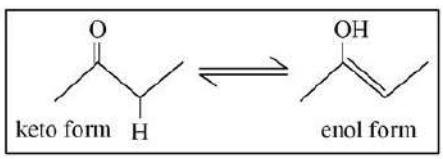
The two forms are known as tautomers. The tautomers differ from each other in electron distribution and in position of relatively mobile atom or group.

The tautomerism is classified into cationotropy and anionotropy depending upon whether atom or group of atoms shifts as cation or anion.

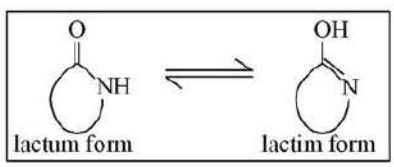
5.5.1 Prototropy :

The cationotropy in which the migrating cation is proton is known as prototropy. Some examples of prptotropy are given below:

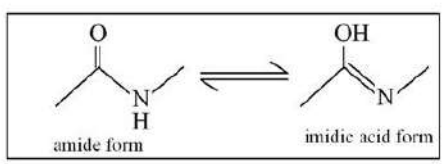
1. Keto-enol tautomerism:



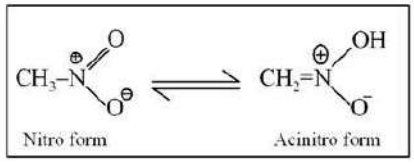
2. Lactum-lactim tautomerism:



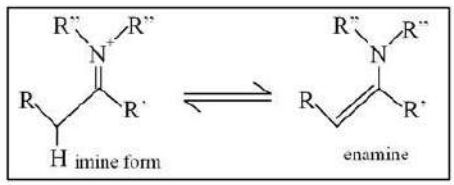
3. Amide-imidic acid tautomerism:



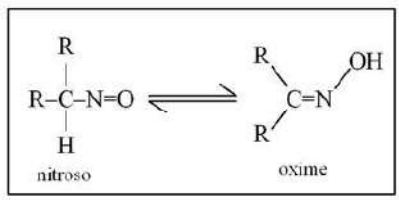
4. Nitro-acenitro tautomerism:



5. Imine-enamine tautomerism:

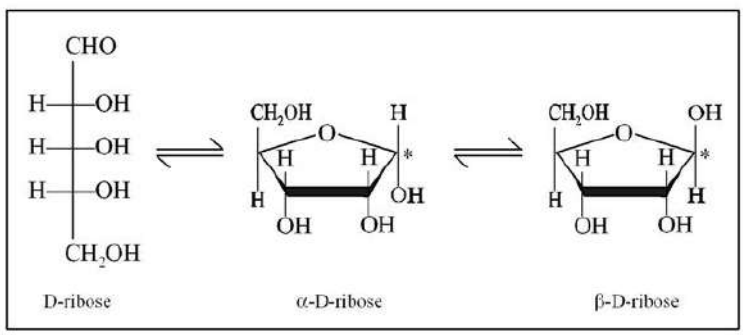


6. Nitroso-oximino tautomerism:



5.5.2 Ring chain tautomerism :

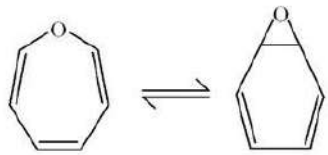
The type of tautomerism where ane tautomer is cyclic and the other is acyclic, is known as ring chain tautumerism.



5.5.3 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.



5.5.4 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 n-n 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=C(OH)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 pairson 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.

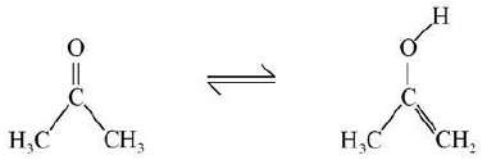
v) Steric factor also plays a part.

5.5.5 Composition of equilibrium in different systems :

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=0 double bond, C-C single bond, C-H bond

enol: C=C double bond, C-0 single bond, O-H bond

If we look up the bond energies for these bonds we find

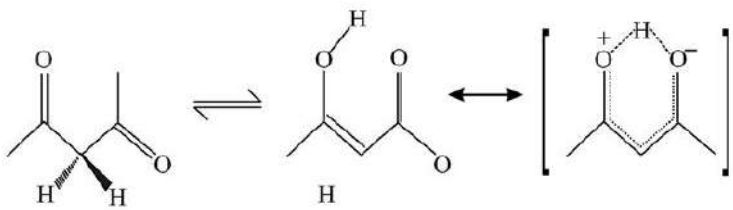
keto: 745 + 347 + 413 = 1505 kJ/mol

enol: 614 + 358 + 467 = 1439 kJ/mol

This rough calculation tells us that, generally, the keto form will predominate. How'ever 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.

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.



Pentan-2,4-dione (Acetylacetone)

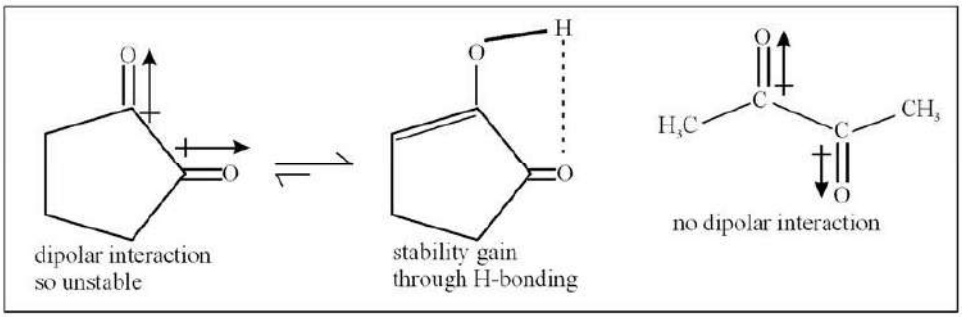
4-Hydroxy-3-penten-2-one (Enol form)

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.

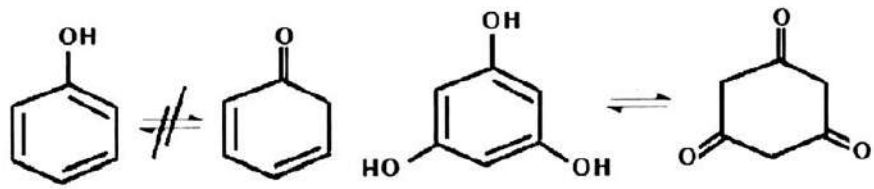
3. 1,2-dicarbonyl system:

1,2 cyclopentadione exist exclusively in enol form, whereas biacetyl exist almost exclusively in keto form. In biacetyl the C=O group rotates aroupd the single bond to avoid dipolar repulsion and gain stability. Therefore instead of forfning an Intramolecular H-bonded enol, the biacetyl take anti conformation and remain almost exclusively in keto form.



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%

5.6 Reaction Kinetics

5.6.1 Rate of reaction :

Rate of reaction i.e., velocity of reaction is the amount of chemical change per unit time. The rate is generally expressed as the decrease in concentration of a reactant or as the increase in concentration of a product per unit time. If 'C' be the concentration of a reactant at time't' then rate is -dc/dt. If 'x' be the concentration of product at time't' then the rate would be dx/dt.

5.6.2 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.

5.6.3 Order of a reaction :

It is the number of concentration terms on which reaction rate depends. It is the sum of power of each concentration term. In the above reaction order is (a + b).

5.6.4 Molecularity :

The number of species involved in rate determining step is called molecularity.

5.6.5 Rate determining step (r.d.s.) :

If a reaction takes place in a number of steps then the slowest step is called rate determining step. The rate of overall reaction depends only on the rate of rate determining step.

5.6.6 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

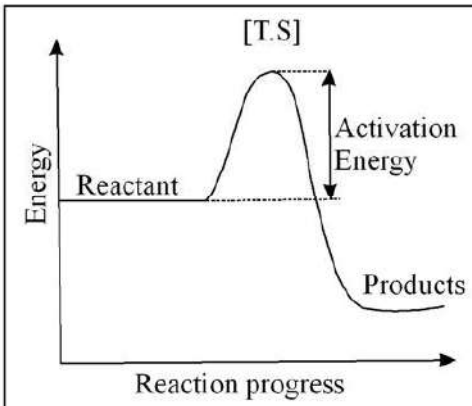
bond rules. It can't be isolated because it is an energy maximum. A transition state is often shown by putting it in square brakets with a double dagger superscript.

5.6.7 Activation energy :

Activation energy is the energy difference between reactant and transition state. The rate of reaction depends on the value of activation energy of rate determining step. With low activation energy the rate becomes faster.

5.6.8 Reaction energy diagram :

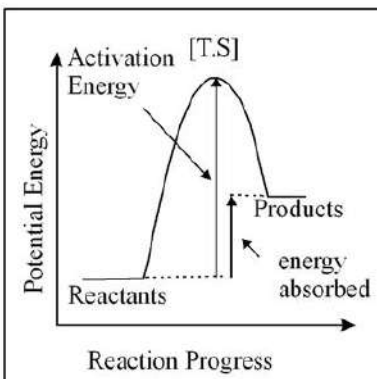
To depict graphically the energy changes during transformation from starting material to product. For exothermic reaction, the energy profile diagram is given below-



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

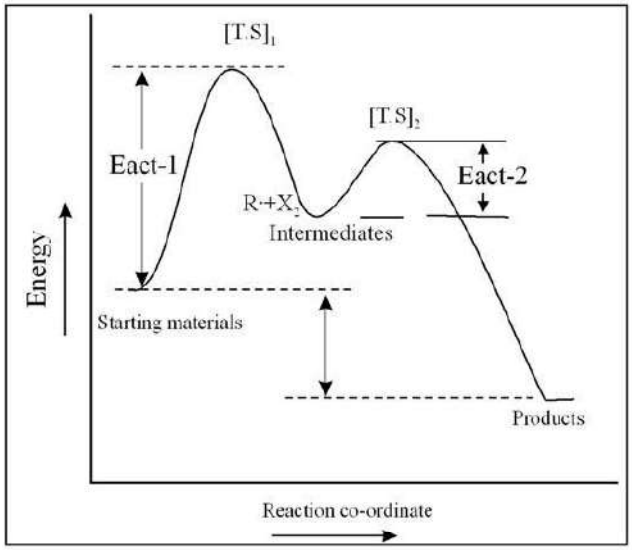
In case of endothermic reaction-



In an endothermic reaction the products have more energy than the reactants, so energy is taken in

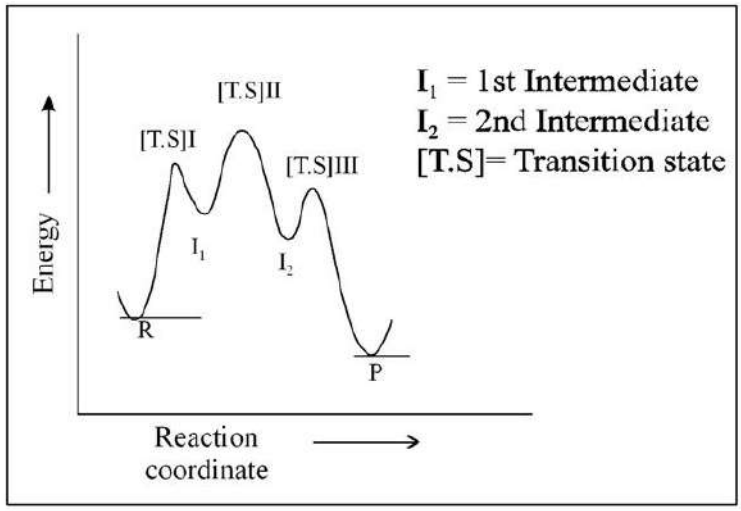
Also in an endothermic reaction stronger bonds are broken and weaker bonds are made, so overall energy is taken in

The energy profile diagram considering the following condition is given below ΔH= -Ve, $[T.S]_2$ is more stable than $[T.S]_1$

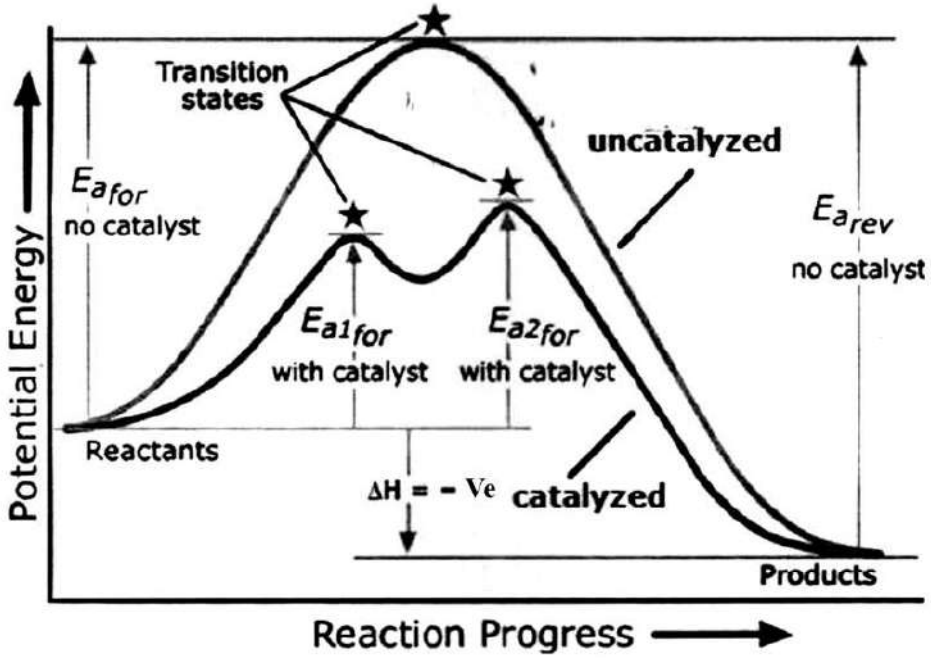


Problem : Draw a energy profile diagram of a three step exothermic process in which the 2nd step is rate determining step and 2nd intermediate is more stable than the first intermediate.

Solution:



Energy profile diagram of a catalyzed reaction compared to uncatalyzed reaction-



Ea for = activation energy for forward reaction

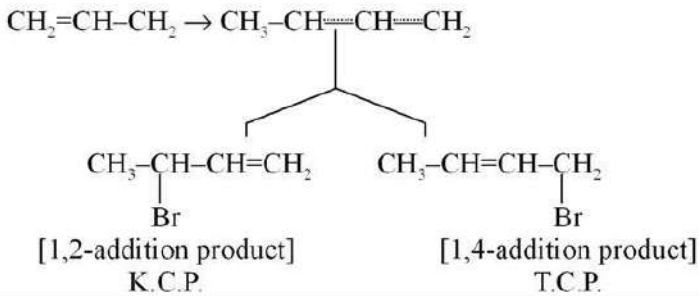
Ea rev = activation energy for reverse reaction

5.6.9 Thermodynamically controlled and kinetically controlled reactions :

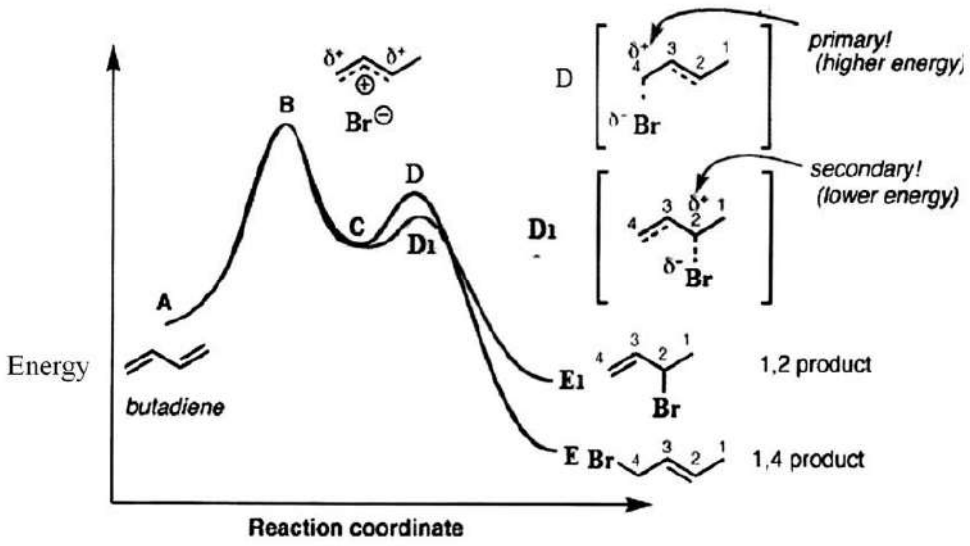
Thermodynamically controlled reactions are those where the products are interconvertible and remain in equilibrium under the reaction condition and the degree of formation of product i.e., concentration of product depends on the relative thermodynamic stability of the product.

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.

5.6.10 Primary and secondary kinetic isotope effect :

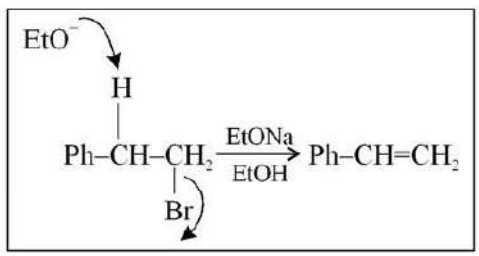
A large difference in the rate of a reaction is observed when one of the atoms

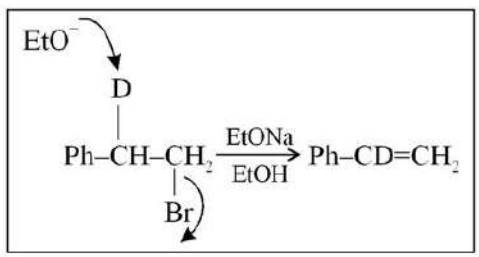
of a bond that breaks in the r.d.s. is replaced by its isotope. This is called primary kinetic isotope effect.

If a C-H bond breaks in r.d.s. of a reaction, substitution of H by D results in decrease in reaction ra:e ir.i 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 Such effect is known as **secondary isotope** effect.

5.6.10.1 Example of primary kinetic isotope effect: In case of E-2 reaction of 2-phenyl- 1-bromo ethane with NaOEt/EtOH, K_H/K_D is 7.1. If 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.





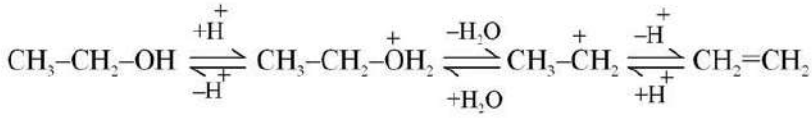
5.6.10.2 Example of secondary kinetic isotope effect: The solvolysis of t-butylchloride -D_9 is found to be slower than that in the corresponding t-butylchloride. The K_H/K_D is 2.32. The difference in the rate has been attributed to an electronic effect. There is a decrease of hyperconjugative electron 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.

5.6.11 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.



5.6.12 Hammond postulate :

One usually knows more about the precise structure of an intermediate rather than the [T.S]. One uses his knowledge of the structure of intermediates to draw conclusion about the structure of [T.S] by Hammond postulate.

It states that "For any single reaction step, the geometry of [T.S] resembles the side to which it is closure in free energy."

In the case of exothermic reaction the [T.S] resembles the reactant more compared to the product and for endothermic reaction the [T.S] resembles the product more compared to reactant.

5.7 Summary

I. A very large equilibrium constant (in the millions or billions) means the reaction goes "to completion", and a tiny equilibrium (very close to zero) constant means the reaction hardly moves forward at all.

II. Intra-molecular reaction is more favorable than intermolecular, when ring is not very small and large.

III. 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.

IV. Acidity is influenced by hybridization, electronegativity, bond strength, inductive effect, resonance, aromaticity, solvent etc.

V. The more unstable an electron pair is, the more basic it is.

VI. Proton Sponge is a special class of organic compound which exhibits exceptional basicity.

VII. Base is that species which attacks hydrogen and nucleophile attacks any atom other than hydrogen

VIII. According to HSAB principle, 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.

IX. 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.

X. Stability of keto-enol tautomerism are affected by conjugation, H-bonding, solvent, aromaticity, temperature, steric crowding etc.

XI. The rate of a reaction depends on the value of activation energy of rate determining step. With low activation energy the rate becomes faster.

XII. The principle of microscopic reversibility state that the forward and backward reaction must follow the same mechanism (run under the same condition)

XIII. Hammond postulate states that "For any single reaction step, the geometry of [T.S] resembles the side to which it is closure in free energy."

5.8 Keywords

Free energy, Entropy, Enthalpy, Acid, Base, Proton sponge, HSAB principle, Ring-Chain Tautomerism, Valence tautomerism, Keto-enol Equilibrium, Transition State, Rate Determining Step, Activation Energy, Energy Profile Diagram, Kinetically and Thermodynamically Controlled Product, Isotope Effect, Microscopic reversibility, Hammond Postulate.

5.9 References

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5.10 Model questions

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
5. CH_3—CH_2—CH_2—COOH, CH_3—CH_2—CH(Cl)-COOH, CH_3—CH(Cl)—CH_2—COOH, CH_2(C1)—CH_2—CH_2—COOH
6. Which is more acidic between p-chloro phenol and p-fluoro phenol?
7. 2,6-dihydroxy benzoic acid is a much stronger acid than 2-hydroxy benzoic acid. Explain.
8. Why is N,N-dimethyl aniline a weak base than N,N,2,6-tetramethyl aniline?
9. The enol content of Ph-CO-CPh-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. The enol content of acetylacetone in equilibrium is very high (80%). Explain
12. Write down the principle differences in tautomerism and resonance.
13. 2,3-dimethyl 2-cyclobutenone exists exclusively in the keto form. Explain
14. 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.
15. What is primary kinetic isotope effect? Explain with an example.
16. 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.
17. State the Hammond postulate. Explain with an example.
18. What do you mean by kinetically and thermodynamically controlled product?

Unit 6 ❑ Nitrogen Compounds

Structure

6.0 Objectives

In this unit, we shall discuss on the preparation and several important reactions of primary, secondary, tertiary alkyl amines, alkyl nitrites, nitro alkanes, alkyl nitriles, isonitriles, and diazonium salts. We shall also learn separation and identification of primary, secondary, tertiary alkyl amine, chemical differentiation between alkyl nitrite and nitro alkane as well as alkyl nitrile and isonitrile.

6.1 Introduction

Nitrogen, in conjunction with carbon, phosphorus, oxygen, and hydrogen, is one of the most important elements of living matter, present in proteins, nucleic acids, and other nitrogen-containing organic compounds. All living organisms contribute organic nitrogen compounds to the water. A major input of dissolved organic nitrogen occurs when organisms die and cell substances are released to the ambient water. The characteristic functional groups formed by nitrogen are typically active and therefore display a wide range of biological, environmental and industrial functions. Some important classes of organic molecules containing nitrogen are the alkyl amines, alkyl nitrites, nitro alkanes, alkyl nitriles, isonitriles, diazonium salts etc.

6.2 Amines (Aliphatic ajid Aromatic)

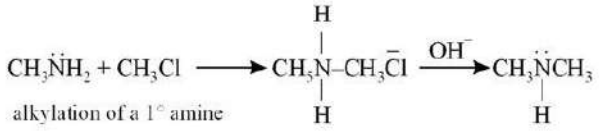
6.2.1 Preparation :

The alkylation of ammonia, Gabriel synthesis, reduction of nitriles, reduction of amides reduction of nitrocompounds, and reductive amination of aldehydes and ketones are the methods which are commonly used to prepare amines.

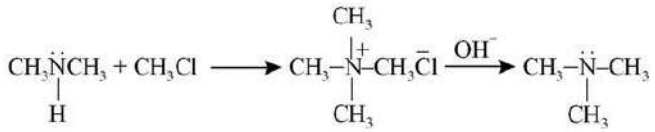
6.2.1.1 Alkylation of ammonia (Hoffmann's method): The reaction of ethanolic solution of ammonia with an alkyl halide leads to the formation of a primary amine. The primary amine, formed can also react with the alkyl halide to form a disubstituted amine (i.e., 2° amine) that can further react to form a tri-substituted amine (i.e., 3°

amine). Therefore a mixture of three classes of amines is obtained, together with some quaternary ammonium compound. The order of reactivity of halides is RI > RBr > RCl and the mechanism of reaction is SN^2.

alkylation of ammonia



alkylation of a 1° amine

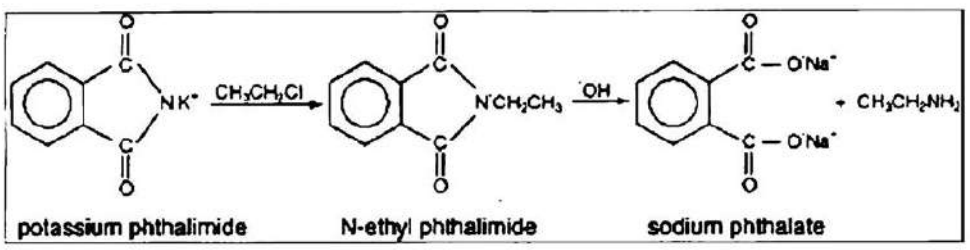


alkylation of a 2° amine

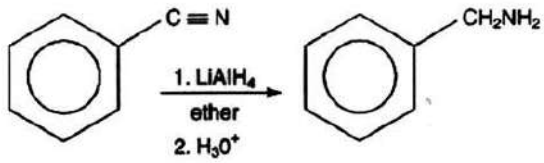
6.2.1.2 Reduction of alkylazides: A primary amine can be best prepared from alkylazide by reduction with Na/alcohol or Zn/CH_3COOH.

Ethyl Azide

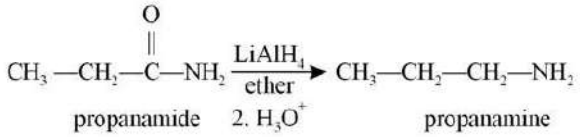
6.2.1.3 Gabriel synthesis: In this method phthalimide is converted, by means of ethanolic KOH into its salt potassium phthalimide which, on heating with an alkyl halide produces N-alkyl phthalimide. This can be hydrolyzed by aqueous acids or bases into the primary amine and phthalic acid.

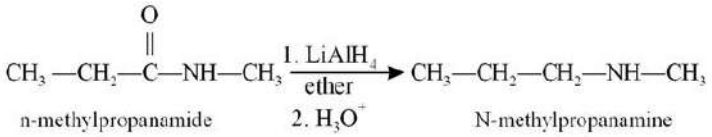


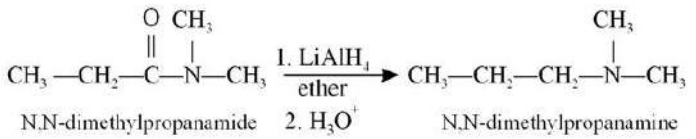
6.2.1.4 Reduction of nitriles: Nitriles can be reduced by lithium aluminum hydride ($LiAlH_4$) or Na/ethanol to primary amines.



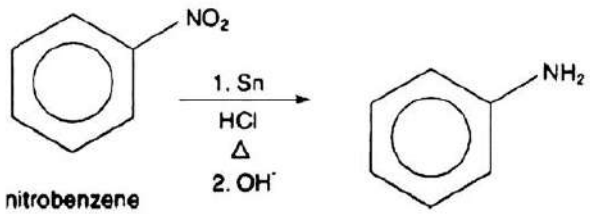
6.2.1.5 Reduction of amides: Primary amines can be prepared from amides by reduction with lithium aluminum hydride, while N-substituted and N, N-disubstituted amides give secondary and tertiary amines, respectively.



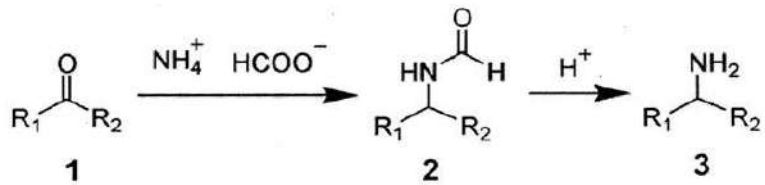




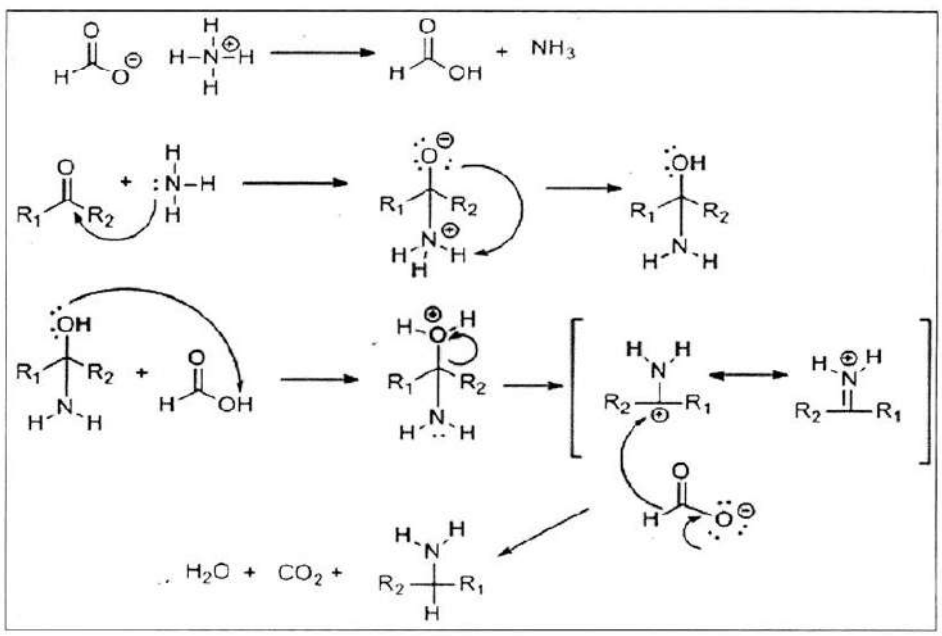
6.2.1.6 Reduction of nitrocompounds: Aromatic amines are normally prepared by reduction of the corresponding aromatic nitrocompounds with metal/acid or Ni/H_2 or LAH.



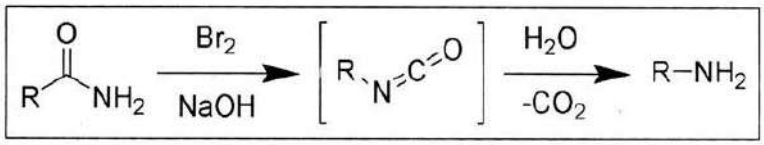
6.2.1.7 Reductive amination of aldehydes and ketones (Leuckart reaction): The Leukart reaction is the chemical reaction that converts aldehydes or ketones to amines by reductive amination in the presence of heat. The reaction proceeds via two mechanisms: one using ammonium formate and the other using formamide as the reducing agent. It requires high temperatures, usually between 120 and 130°C, although under the presence of formamide, the temperature can be greater than 165 °C



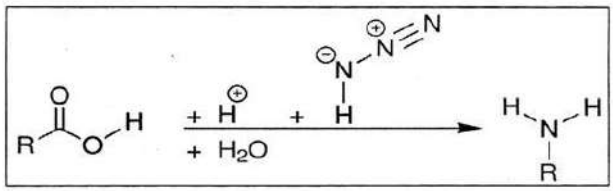
Mechanism:



6.2.1.8 Hofmann rearrangement: The Hofmann rearrangement is the organic reaction of a primary amide to primary amine with one fewer carbonatom



6.2.1.9 Schmidt rearrangement: Carboxylic acid reacts with hydrazoic acid in presence of acid to give amine.

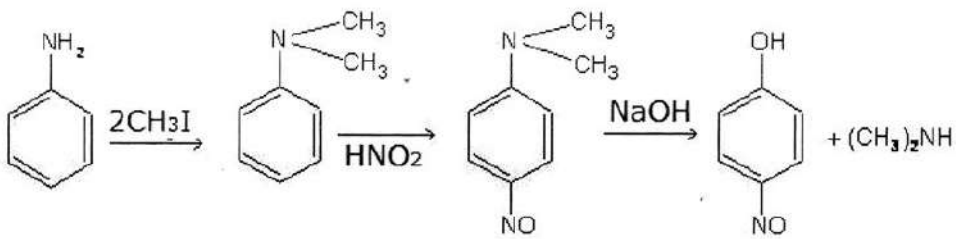


6.2.1.10 Secondary amine from cyanamide: A convenient method for the preparation of secondary amines which are not contaminated with primary or tertiary amines is the reaction of cyanamide with alkyl halides to N,N- dialkylcyanamides which can easily be hydrolyzed by acid or alkali to dialkylamines.

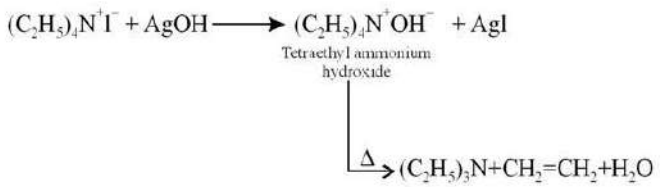
6.2.1.11 Reduction of alkyl isocyanides with Na/C_2H_5OH gives 2° amines:

$$CH_3NC \xrightarrow{Na,C_2H_5OH} CH_3CHCH_3$$

6.2.1.12 Hydrolysis of p - nitroso dialkyl aniline with boiling alkali gives secondary amine:

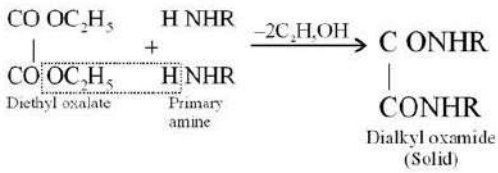


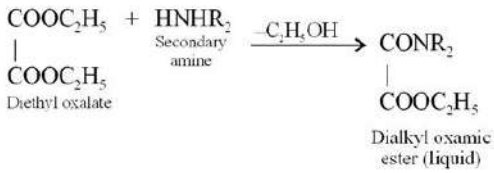
6.2.1.13 Decomposition of tetra - alkyl ammonium hydroxide leads to 3° amine:



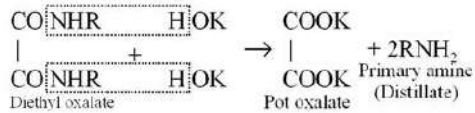
6.2.2 Separation of primary, secondary and tertiary amines by Hoffmann's method :

The mixture of three amines is treated with diethyl oxalate. The primary amine forms a solid oxamide, a secondary amine gives a liquid oxamic ester while tertiary amine does not react.



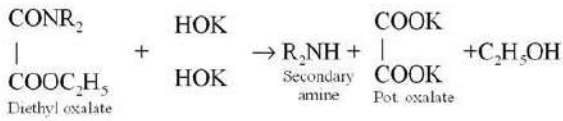


Primary amine is recovered when solid oxamide is heated with caustic potash solution and collected as distillate on distilling the reaction mixture.



The liquid (mixture of oxamic ester + tertiary amine) is subjected to fractional distillation when tertiary amine distils over.

The remaining liquid is distilled with KOH to recover secondary amine.



6.2.3 Seperation and identification between primary, secondary and tertiary amine using Hinsberg reagent: (Hinsberg's method) :

It involves the treatment of the mixture with benzene sulphonyl chloride, i.e., Hinsberg's reagent ($C_6H_5SO_2Cl$). The solution is then made alkaline with aqueous alkali to form sodium or potassium salt of monoalkyl benzene sulphonamide (soluble in water).

$$C_6H_5SO_2Cl + HNR_2 \rightarrow C_6H_5SO_2NHR \xrightarrow{NaOH} C_6H_5SO_2N(Na)R \text{ [Soluble Salt]}$$

Primary amine

The secondary amine forms N,N-dialkyl benzene sulphonamide which does not form any salt with NaOH and remains as insoluble in alkali solution.

$$C_6H_5SO_2Cl + HNR_2 \rightarrow C_6H_5SO_2NR_2 \xrightarrow{NaOH} \text{No reaction}$$

Sec. amine (Insoluble in water, soluble in ether)

Tertiary amine does not react.

$$C_6H_5SO_2Cl + R_3N \rightarrow \text{No reaction}$$

The above alkaline mixture of the amines is extracted with ether.

Two distinct layers are formed. Lower layer, the aqueous layer consists of sodium salt of N-alkyl benzene sulphonamide (primary amine) and upper layer, the ether layer consists of N,N-dialkyl benzene sulphonamide (secondary amine) and tertiary amine.

Two layers are separated. The upper layer is fractionally distilled. One fraction obtained is tertiary amine and the other fraction is treated with concentrated HCl to recover secondary amine hydrochloride which gives free secondary amine on distillation with NaOH.

$$C_6H_5\ SO_2\ NR_2 + HCl + H_2O \rightarrow C_6\ H_5\ SO_2.\ OH + R_2\ NH.\ HCl$$

$$R_2\ NH.\ HCl + NaOH \rightarrow R_2\ NH + NaCl + H_2O$$

The aqueous layer is acidified and hydrolysed with dilute HC1. The hydrochloride formed is then distilled with NaOH when primary amine distils over.

$$C_6H_5SO_2N\ (Na)\ R + HC1 \rightarrow \underset{\text{Sulphonamide of primary amine}}{C_6H_5SO_2NHR} + NaCl$$

$$C_6H_5SO_2NHR + HCl + H_2O \rightarrow C_6H_5SO_3H + RNH_2.\ HCl$$

$$RNH_2.\ HCl + NaOH \rightarrow RNH_2 + NaCl + H_2O$$

6.2.4 Reaction :

6.2.4.1 Reaction with Nitrous Acid: Nitrous acid (HNO_2) reacts with aliphatic amines in a fashion that provides a useful test for distinguishing primary, secondary and tertiary amines.

1"-Amines + HONO (cold acidic solution)	Nitrogen Gas Evolution from a Clear Solution
2°-Amines + HONO (cold acidic solution)	An Insoluble Oil (N-Nitrosamine)
3°-Amines + HONO (cold acidic solution)	A Clear Solution (Ammonium Salt Formation)

Nitrous acid is a Bronsted acid of moderate strength (pK_a = 3.3). Due to its unstability, it is prepared immediately before use in the following manner

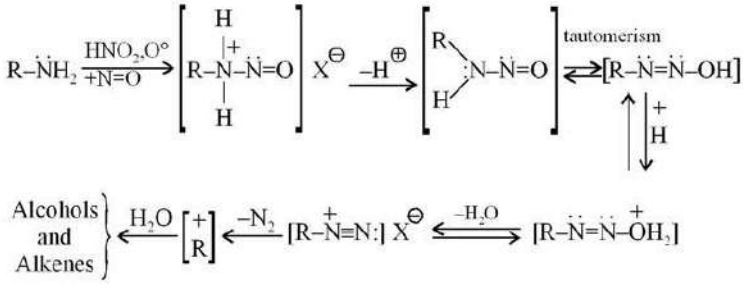
$$NaNO_2 + H_2SO_4 \xrightarrow{H_2O,0^\circ} H\text{–}\ddot{O}\text{–}\ddot{N}\text{=}\ddot{O} + NaHSO_4$$

Under the acidic conditions of this reaction, all amines undergo reversible salt formation:

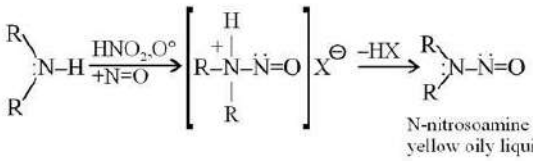
$$R^2\text{–}\underset{\displaystyle R^3}{\overset{\displaystyle R^1}{\underset{|}{\overset{|}{N}}}}\text{:} + HX \rightleftharpoons R^2\text{–}\underset{\displaystyle R^3}{\overset{\displaystyle R^1}{\underset{|}{\overset{|}{N^{\oplus}}}}}\text{–H}\ X^{\ominus} \quad \{X = HSO_4 \text{ or } NO_2\}$$

This happens with 3°-amines, and the salts are usually soluble in water. The reactions of nitrous acid with 1°- and 2°- aliphatic amines may be explained by considering their behavior with the nitrosonium cation, $NO^{(+)}$, an electrophile, produced from nitrous acid solutions.

Primary Amines



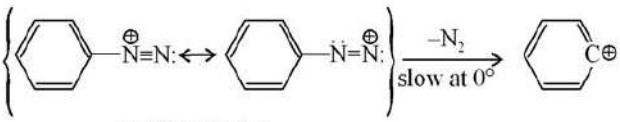
Secondary Amines



The distinct behavior of 1°, 2° & 3°-aliphatic amines is an instructive challenge to our understanding of their chemistry, but is of little importance as a synthetic tool. The S_N1 product mixtures from primary amines are difficult to control, and rearrangement is common when branched primary alkyl groups are involved. The N-nitrosamines formed from 2°-amines are carcinogenic, and are not generally useful as intermediates for subsequent reactions.

Aryl Amines :

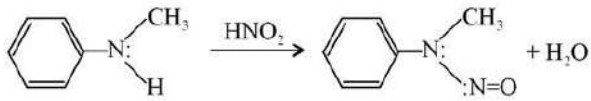
1°-aryl amine reacts with nitrous acid to generate relatively stable diazonium cation that serve as intermediate for a variety of aromatic substitution reactions. Diazonium cations may be described by resonance contributors, as in the bracketed formulas shown below. The left-hand contributor is dominant due to its greater bonding. Loss of nitrogen from it is slower 1° aliphatic amines because the C-N bond is stronger due attaining double bond character. Aqueous solutions of these diazonium ions have sufficient stability at 0° to 10 °C that they may be used as intermediates in a variety of nucleophilic substitution reactions.



aryl diazonium ion

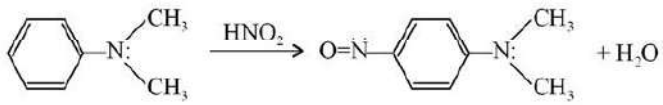
2°-Aryl Amines:

2°-Aryl amines give N-nitrosamine derivatives on reaction with nitrous acid, and thus behave identically to their aliphatic counterparts.

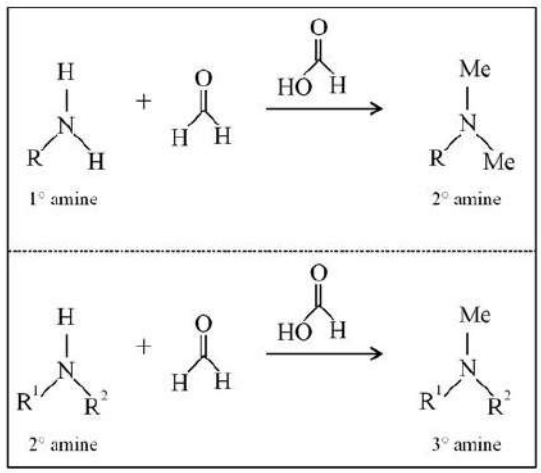


3°-Aryl Amines:

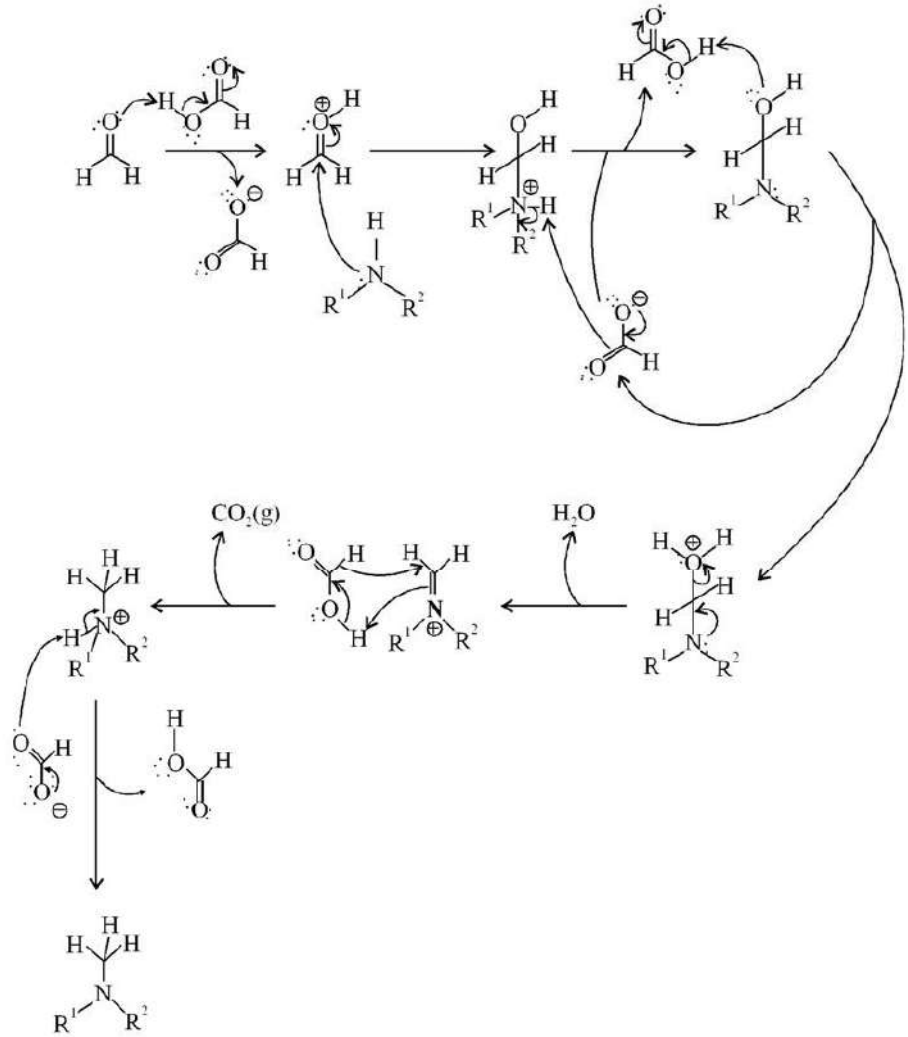
Depending on ring substitution, 3°-aryl amines may undergo aromatic ring nitrosation at sites ortho or para with respect to $-NH_2$ group. The nitrosonium cation $[NO^+]$ is not sufficiently electrophilic to react with benzene itself, or even toluene, but highly activated aromatic rings such as amines and phenols are capable of substitution. Of course, the rate of reaction of $[NO^+]$ at nitrogen is greater than that of ring substitution, as shown in the previous example.



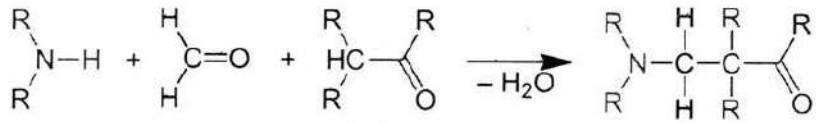
6.2.4.2 Eschweiler-Clarke methylation: The Eschweiler-Clarke methylation is used to convert a primary or secondary amine to a tertiary amine using formaldehyde and formic acid. The reaction proceeds through iminium ion intermediate.



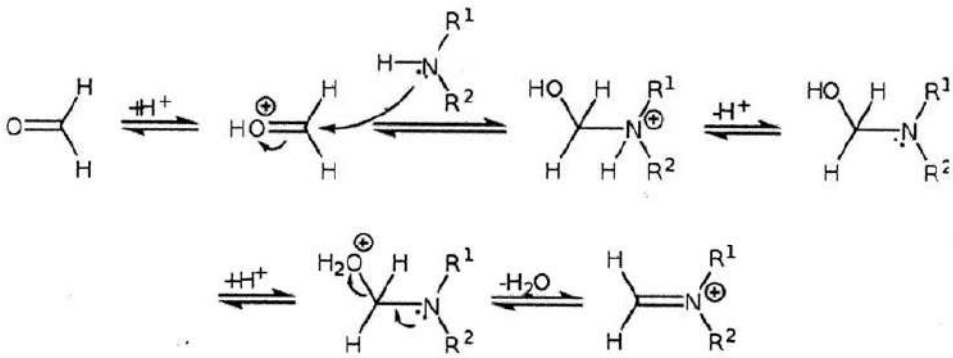
Mechanism:



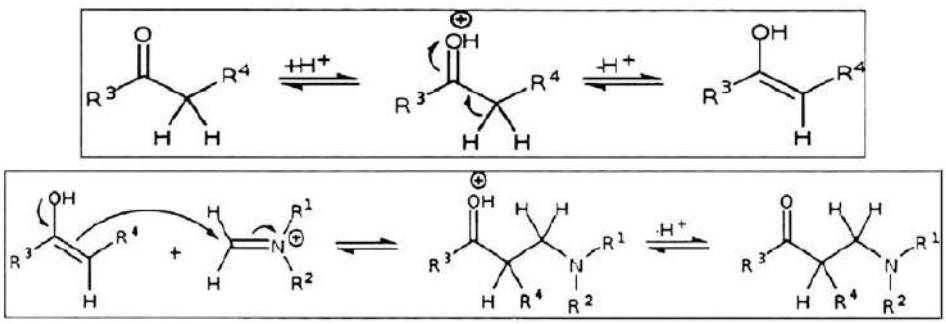
6.2.4.3 Mannich Reaction: This reaction is the multi-component condensation of a nonenolizable aldehyde, a primary or secondary amine and an enolizable carbonyl compound to lead (β-amino carbonyl compound also known as a Mannich base, using an acid or base catalyst. The involvement of the Mannich reaction has been proposed in many biosynthetic pathways, especially for alkaloids.



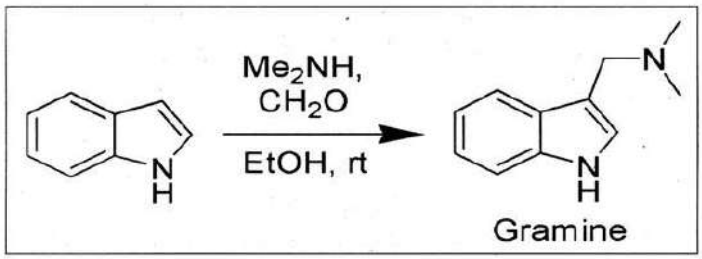
Mechanism: The mechanism of this reaction starts with the formation of an iminium ion from the amine and the formaldehyde.



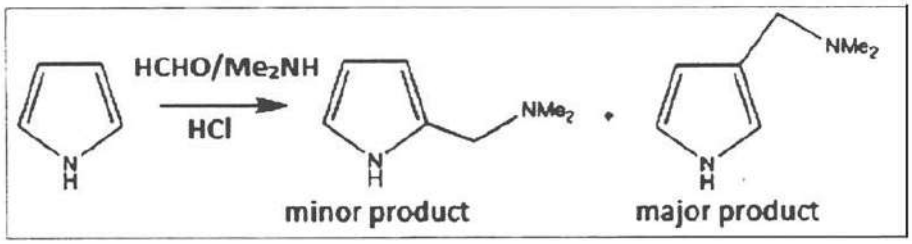
The compound with the carbonyl functional group can tautomerize to the enol form, after which it can attack the iminium ion.

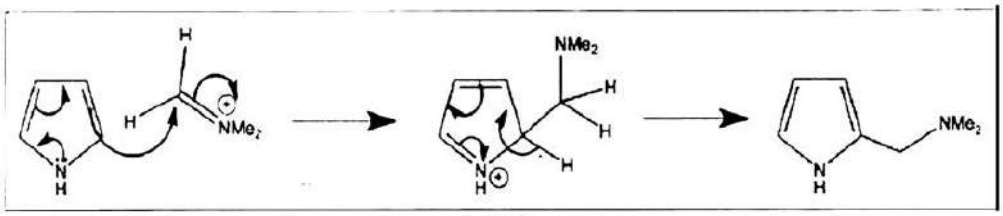


Mannich reaction of Indole:

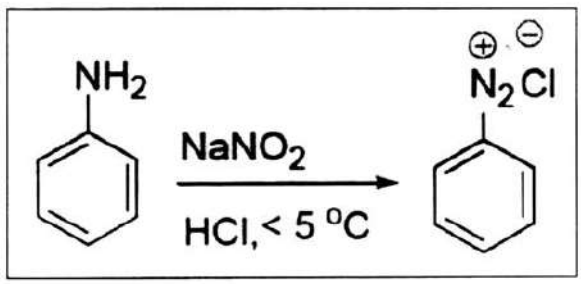


Mannich reaction of Pyrrole:

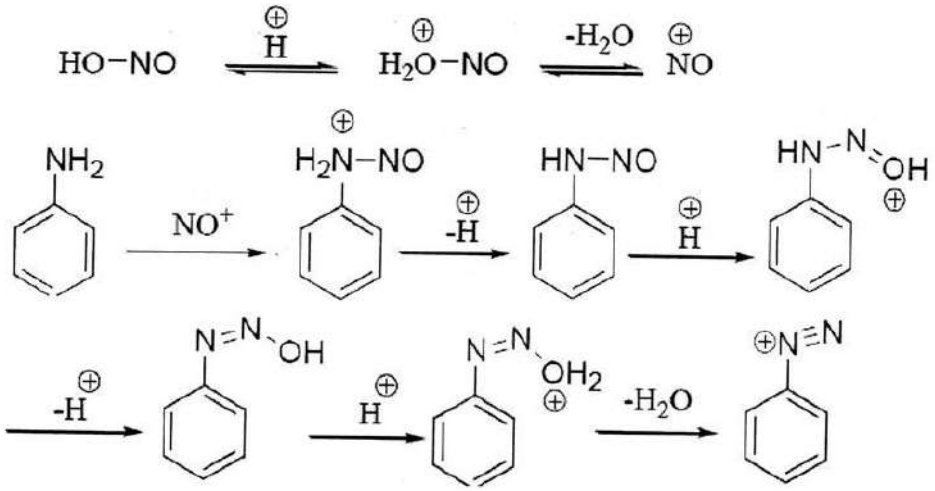




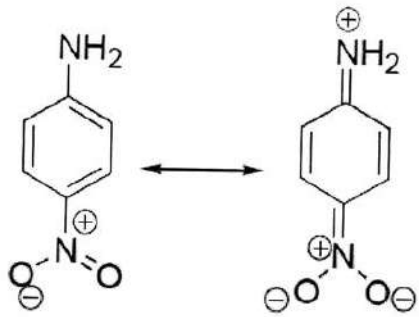
6.2.4.4 Diazo-coupling reaction: Addition of aqueous solution of $NaNO_2$ to a solution of amine hydrochloride in presence of excess of HC1 which is cooled by an ice-bath such that the temperature of the reaction remains below 5°C leads to diazotization of primary aromatic amine.



Mechanism:



If aromatic nucleus contain electron withdrawing groups then the aromatic amines are difficult to diazotize because the nucleophilicity of the amino-nitrogen is reduced by the conjugation of unshared electron pair with pi electrons of aromatic nucleus.



6.2.5 Phenylenediamine :

6.2.5.1 Preparation of ortho phenylenediamine: To prepare o-phenylenediamine, 2-nitrochlorobenzene is treated with ammonia and the resulting 2-aminonitrobenzene is then hydrogenated in presence of metal catalyst (like Ni, Pd etc). It is best prepared by reducing o-nitroaniline by Zn powder and aqueous ethanolic NaOH (74-85%).

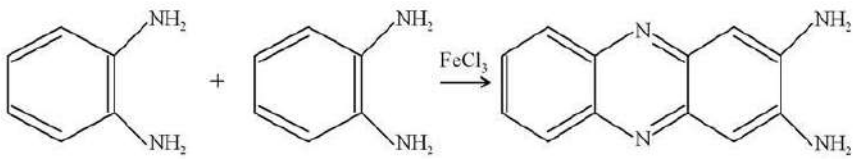
$$ClC_6H_4NO_2 + 2NH_3 \rightarrow H_2NC_6H_4NO_2 + NH_4Cl$$

$$H_2NC_6H_4NO_2 + 3H_2 \rightarrow H_2NC_6H_4NH_2 + 2H_2O$$

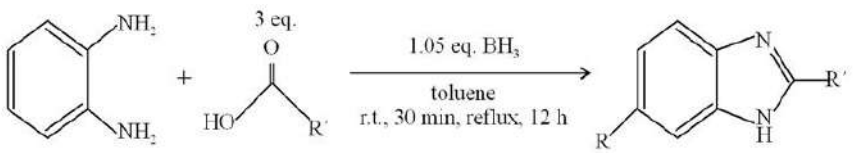
The reduction of 2-nitroaniline by Sn/HCl or Zn/HCl also give o-phenylenediamine.

6.2.5.2 Reaction:

1. When o-phenylenediamine is treated with $FeCl_3$ solution, a dark red colour is produced due to the formation of 2,3-diaminophenazine.

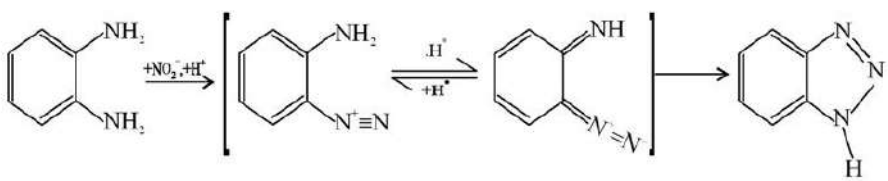


2. When o-phenylenediamine is heated with organic acids, then benzimidazoles are produced.

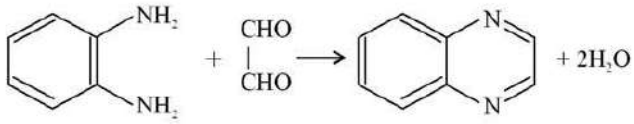


R'=Ar, alkyl, benzyl, vinyl

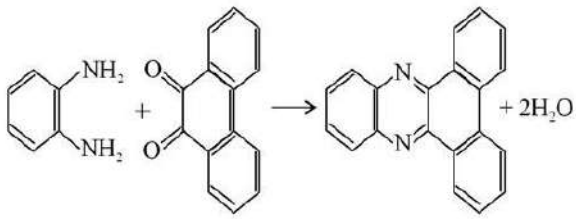
3. The reaction of o-phenylenediamine with nitrous acid (a solution of the diamino compound in acetic acid is treated with aqueous sodium nitrite) leads to the formation of benztriazole. This conversion proceeds via diazotization of one of the amine group. The synthesis can be improved when the reaction is carried out at low temperatures (5-10 °C).



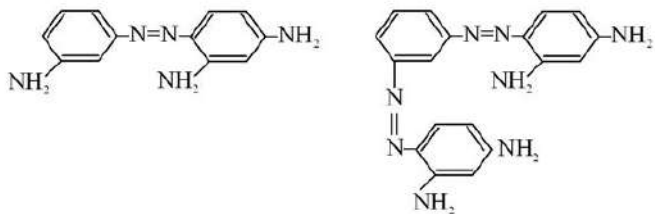
4. O-phenylenediamine condenses with a-dicarbonyl compound e.g., glyoxal to form quinixaline.



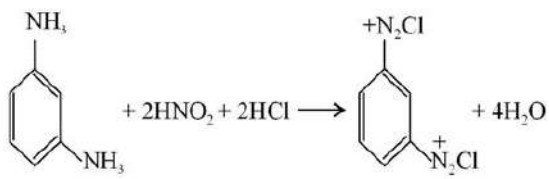
This reaction is used to identify o-diamines; the α-dicarbonyl compound employed for this purpose is phenanthraquinone, resulting in the formation of a sparingly soluble phenazine derivative:



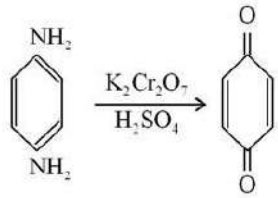
6.2.5.3 Meta-phenylenediamine (benzene-1,3-diamine, 1,3-diaminobenzene) : It is best prepared by the reduction of m-dinitrobenzene with Fe/HCl. Its most characteristic reaction is the formation brown dyes-Bismark Brown -when it reacts with nitrous acid; a monazo and a bisazo compound are formed.



On the other hand, by dissolving m-phenylenediamine in concentrated HC1, and by keeping HNO_2 always in excess, both amino groups get diazotization to give the tetrazo compound.



6.2.5.4 Para phenylenediamine: p-Phenylenediamine *(benzene-I : 4-diamine, I: 4-diaminobenzene)* may be prepared by the reduction of p-nitroaniline or aminoazobenzene. It is a white crystalline solid, m.p. 147°. On vigorous oxidation it forms p-benzoquinone:



p-Phenylenediamme can be diazotised in the ordinary way, and is used in the preparation of dyes.

6.2.6 Diazomethane :

6.2.6.1 Preparation: It may be prepared in various ways;

1. **Method of Von Pechmann:** Methylamine is treated with ethylchlorofomate to give N- methylurethan, which on treatment with HNO_2 in ethereal solution, forms N-methyl-N-nitroso-urethan. It decomposes to diazomethane on warming with methanolic KOH.

$$CH_3{\cdot}NH_2 + Cl{\cdot}CO_2C_2H_5 \rightarrow CH_3{\cdot}NH{\cdot}CO_2C_2H_5 \xrightarrow{HNO_2}$$

$$CH_3{\cdot}N(NO){\cdot}CO_2C_2H_5 \xrightarrow{HNO_2} CH_2N_2 + CO_2 + C_2H_5OH$$

An improved method starts with methylurea

$$MeNHCONH_2 \xrightarrow{HNO_2} MeN(NO)CONH_2 \xrightarrow{KOH} CH_2N_2 + KNCO + 2H_2O$$

2. Method of McKay: Methylamine hydrochloride and nitroguanidine are allowed to react in KOH solution, the product N-methyl-N-nitroguanidine is treated with nitrous acid to produce the N-methyl-N-nitroso-N-nitroguanidine, which is then warmed with KOH to obtain diazomethane.

$$CH_3{\cdot}NH_2{\cdot}HCl + NH_2{\cdot}\overset{\overset{NH}{\|}}{C}{\cdot}NH{\cdot}NO_2 + KOH \rightarrow$$

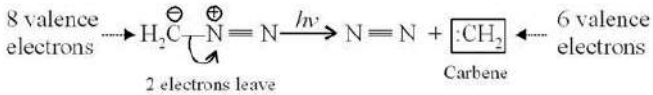
$$NH_3 + KCl + CH_3{\cdot}NH{\cdot}\overset{\overset{NH}{\|}}{C}{\cdot}NH{\cdot}NO_2 \xrightarrow{HNO_2} CH_3{\cdot}N(NO){\cdot}\overset{\overset{NH}{\|}}{C}{\cdot}NH{\cdot}NO_2 \xrightarrow{KOH} CH_2N_2$$

3. *Method of Backer et al.* (1951). The nitroso-derivative of P-toluene-N-methylsulphonamide is distilled with ethanolic potassium hydroxide:

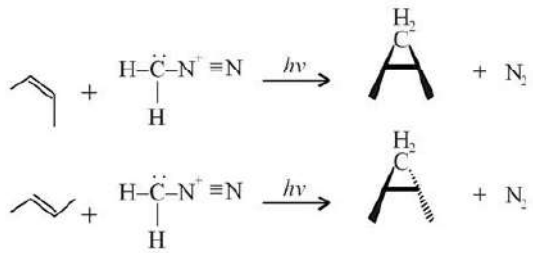
$$CH_3{\cdot}C_6H_4{\cdot}SO_2N(CH_3){\cdot}NO + KOH \rightarrow CH_2N_2$$
$$+ CH_3{\cdot}C_6H_4{\cdot}SO_3K + H_2O \quad (80\text{-}90\%)$$

6.2.6.2 Reaction:

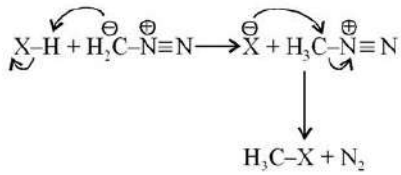
A. Photolysis diazomethane produces carbene



Diazomethane reacts with alkene through the formation of carbene such as and produces cyclopropane. Cis-2-butene is converted to cis- 1, 2 dimethylcyclopropane and trans configuration is maintained during the reaction.

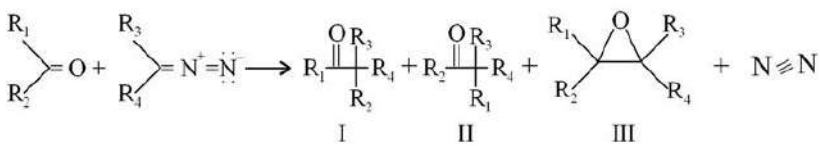


B. It reacts with halogen acids to form methyl halide



C. The Buchner-Curtius-Schlotterbeck (reaction with ketone and aldehyde):

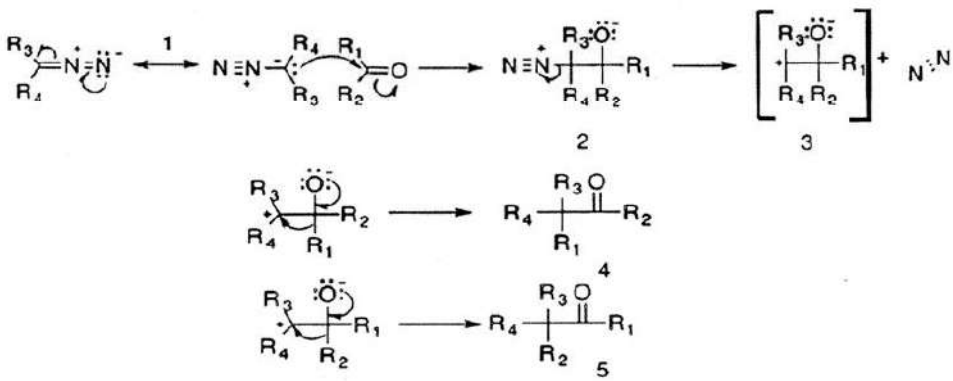
The reaction of aldehydes/ ketones with aliphatic diazoalkanes leads to produce homologated



The reaction yields two possible carbonyl compounds (I and II) along with an epoxide (III). The ratio of the products is determined by the reactant used and the reaction conditions.

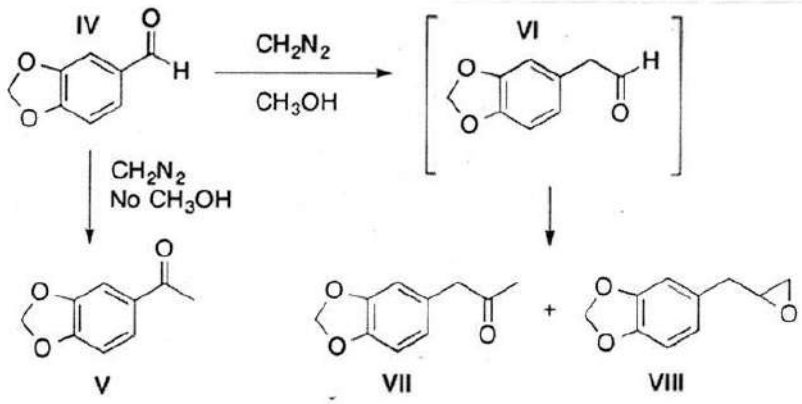
Mechanism:

The general mechanism is shown below. The diazo compound does a nucleophilic attack on the carbonyl-containing compound (nucleophilic addition), producing a tetrahedral intermediate (2). This intermediate decomposes by the evolution of nitrogen gas forming the tertiary carbocation intermediate (3). The reaction is then completed either by the reformation of the carbonyl through an 1,2-rearrangement or by the formation of the epoxide. There are two possible carbonyl products: one formed by migration of R_1 (4) and the other by migration of R_2 (5). The relative yield of each possible carbonyl is determined by the migratory preferences of the R-groups.

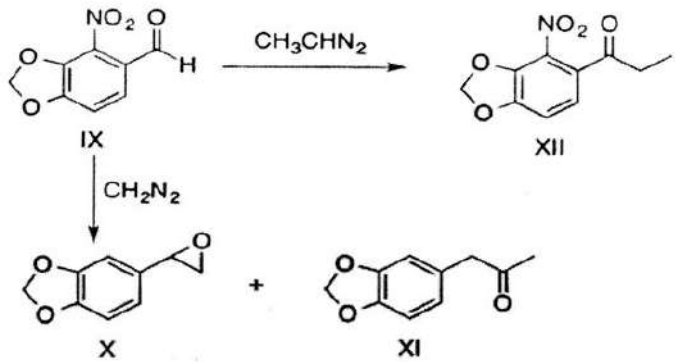


The epoxide is formed by an intramolecular addition reaction in which a lone pair from the oxygen attacks the carbocation (6).

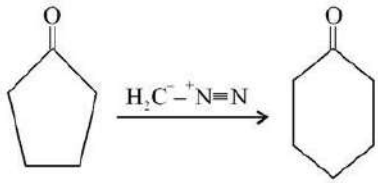
Example:



The diazoalkane employed can also determine relative yields of products by influencing migratory preferences, as conveyed by the reactions of o-nitropiperonal with diazomethane and diazoethane. In the reaction between o-nitropiperonal (IX) and diazomethane, an aryl shift leads to production of the epoxide (X) & (XI). When diazoethane is substituted for diazomethane, a hydride shift produces the ketone (XII), the only isolable product.

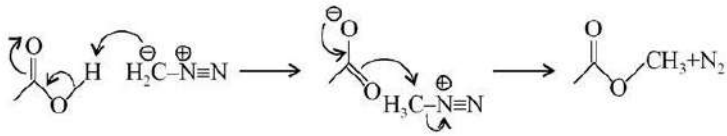


The Buchner-Curtius-Schlotterbeck reaction can be used to facilitate one carbon ring expansions when the substrate ketone is cyclic. For instance, the reaction of cyclopentanone with diazomethane forms cyclohexanone (shown below). The Buchner ring expansion reactions utilizing diazoalkanes have proven to be synthetically useful as they can not only be used to form 5- and 6-membered rings, but also more unstable 7- and 8-membered rings.



D. Reaction with carboxylic acid:

Diazomethane abstracts proton from carboxylic acid to form carboxylate anion which further attacks CH_3N_2 through SN^2 pathway and form ester with the production of N_2.

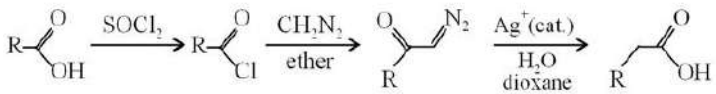


Diazomethane is protonated by the carboxylic acid, forming a carboxylate

The carboxylate then attacks the methyl group, displacing N_2

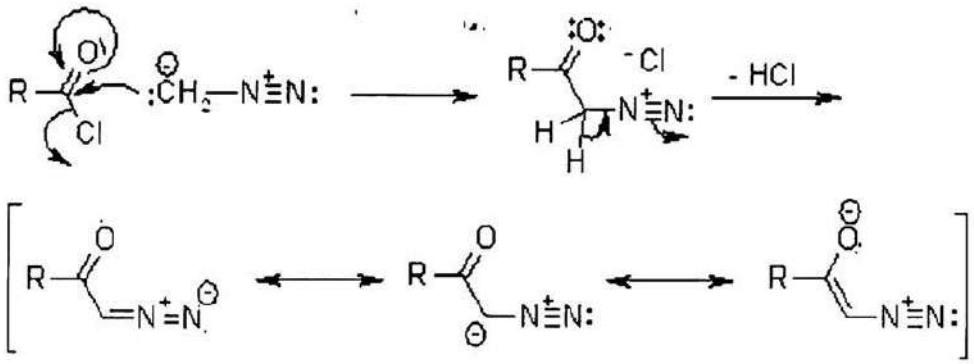
E. Arndt-Eistert Synthesis:

The Arndt-Eistert Synthesis allows the formation of homologated carboxylic acids or their derivatives by reaction of the activated carboxylic acids with diazomethane and subsequent Wolff-Rearrangement of the intermediate diazoketones in the presence of nucleophiles such as water, alcohols, or amine.

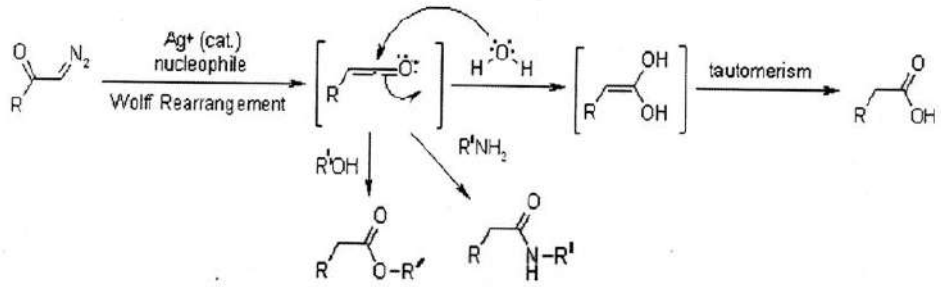


Mechanism:

In the first step, the diazomethane carbon is acylated by an acid chloride or mixed anhydride, to give a-diazoketone. The excess diazomethane can be destroyed by addition of small amounts of acetic acid or vigorous stirring.

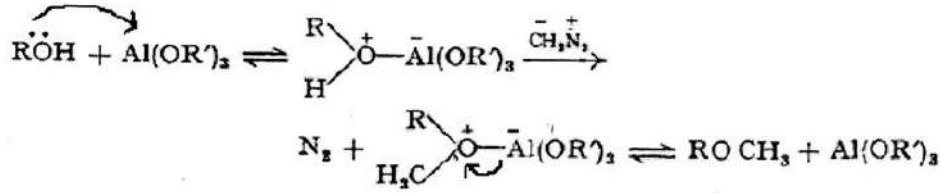


The key step of the Arndt-Eistert Homologation is the Wolff-Rearrangement of the diazoketone to ketenes, which can be accomplished thermally, photochemically or by silver (I) catalysis. The reaction is conducted in the presence of nucleophiles such as water (to yield carboxylic acids), alcohols (to give esters) or amines (to give amides), to capture the ketene intermediate and avoid the competing formation of diketenes.



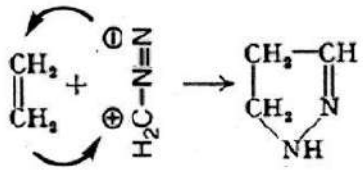
F. Reaction with alcohol:

Alcohols can also be methylated by diazomethane in the presence ol a suitable catalyst, e.g., an aluminium alkoxide.

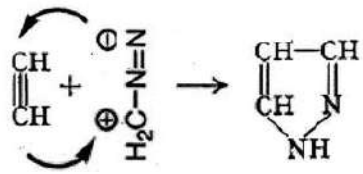


G. Reaction with alkyne and alkyne:

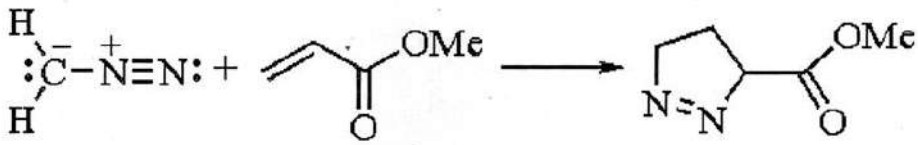
Diazomethane adds on ethylenic compounds to form pyrazoline derivatives; pyrazoline is formed with ethylene.

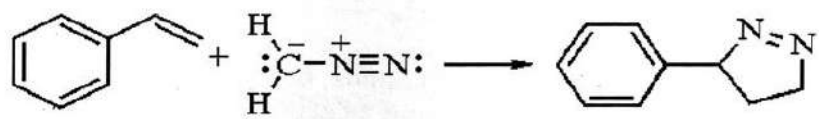


Diazomethane also adds on acetylenic compounds to form pyrazole derivatives; with acetylene pyrazole is formed.



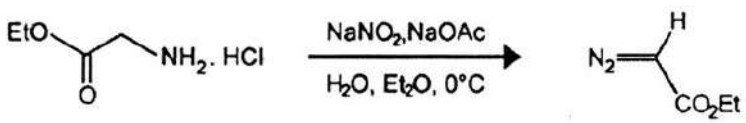
Example:





6.2.7 Diazoacetic ester

6.2.7.1 Preparation: This compound can be prepared by reaction of the ethyl ester of glycine with sodium nitriteand sodium acetate in water.



6.2.7.2 Reaction:

The reactions of diazoacetic ester are similar to those of diazomethane.

1. It is reduced by zinc dust and acetic acid to ammonia and glycine

$$N_2CHCO_2Et \xrightarrow[CH_3COOH]{Zn\text{-}dust} H_2N—CH_2—COOH + NH_3$$

2. When it is boiled with dilute halogen acid, it eliminates nitrogen to form glycollic ester

$$CHN_2 \cdot CO_2C_2H_5 + H_2O \rightarrow CH_2OH \cdot CO_2C_2H_5 + N_2$$

3. When, however, diazoacetic ester is wanned with concentrated halogen acid, ethyl halogeno-acetate is formed, e.g.,

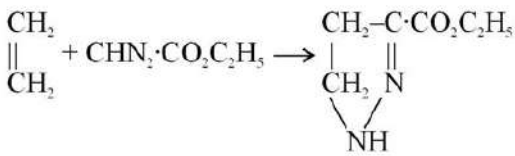
$$CHN_2 \cdot CO_2C_2H_5 + HC1 \rightarrow CH_2C1 \cdot CO_2C_2H_5 + N_2$$

4. Diazoacetic ester reacts with compounds containing an active hydrogen atom, e.g., it forms acetylglycollic ester with acetic add, and the ethyl ether of glycollic ester with ethanol

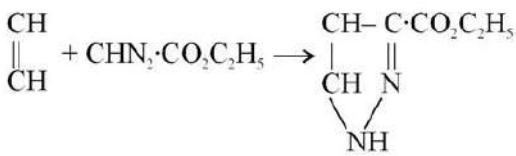
$$CH_3 \cdot CO_2H + CHN_2 \cdot CO_2C_2H_5 \rightarrow CH_3 \cdot CO \cdot O \cdot CH_2 \cdot CO_2C_2H_5 + N_2$$

$$C_2H_5OH + CHN_2 \cdot CO_2C_2H_5 \rightarrow CH_2(OC_2H_5) \cdot CO_2C_2H_5 + N_2$$

5. It reacts with ethylenic compounds to form pyrazoline derivatives, e.g., with ethylene it forms pyrazoline-3-carboxylic ester



6. With acetylenic compounds it forms pyrazole derivatives, e.g., with acetylene, it gives pyrazole-3-carboxylic ester



6.3 Nitro compounds

Nitro compounds are characterized by the presence of nitro group ($-NO_2$) in their molecules.

They may be aliphatic or aromatic compounds according to whether the nitro group is attached to alkyl or aryl groups.

1. Aliphatic nitro compounds $R - NO_2$
2. Aromatic nitro compound $Ar - NO_2$

The aliphatic nitro compounds may be further classified into primary, secondary or tertiary nitro compounds according as the nitro group is attached to primary, secondary or tertiary carbon atom respectively.

6.3.1 Preparation :

6.3.1.1. Preparation of aliphatic nitro compounds

A. Vapour phase nitration of alkanes:

Hydrocarbons when heated with forming nitric acid at 693 - 793 K, are converted to nitro alkenes. Nitration of methane end lower members can be carried out by this nitration technique.

$$CH_3 - CH_3 + HNO_3 \xrightarrow{\Delta} CH_3 - CH_2 - NO_2 + H_2O$$

(Fuming) (Low yield)

This direct nitration of alkanes is relatively more difficult in comparison to the nitration of arenes. Hence this method has no significance as a laboratory method but may be of commercial importance in the bulk production of small nitro alkanes

Since the process occurs at high temperature therefore, C - C bond of alkanes also undergo cleavage at this temperature and a mixture of nitro alkanes are formed.

For e.g.,

$$CH_3 - CH_3 + HNO_3 \xrightarrow{675K} \underset{\text{Nitroethane}}{CH_3\ CH_2\ NO_2} + \underset{\text{Nitro methane}}{CH_3\ NO_2}$$

B. Treatment of alkyl halides with alcoholic silver nitrate:

Alkanes (iodo) on treatment with alcoholic $AgNO_2$ give 80% of nitroalkanes and 20% alkyl nitrites.

$$CH_3 - CH_2 - I + AgNO_2 \longrightarrow \underset{\text{nitro ethane}}{CH_3 - CH_2 - NO_2} + \underset{\text{ethyl nitrate}}{C_2H_5 - O - N = O}$$

alcoholic

This method is primarily used to prepare primary nitro compounds. Secondary and tertiary halides give major proportion of alkenes due to β-elimination reaction.

Hence 2° and 3° nitro alkenes are not prepared by this method.

When alkyl bromides or iodides are treated with potasium nitrites, the major product is alkyl nitrite with nitro alkanes as the minor product

$$RI + KNO_2 \rightarrow \underset{\substack{\text{Alkyl nitrite}\\\text{(major product)}}}{R - O - N = O} + \underset{\substack{\text{Nitro nitrite}\\\text{(minor product)}}}{R - N\begin{matrix}=O\\ \searrow O\end{matrix}}$$

Even $NaNO_2$ or KNO_2 give a fairly good yield (60%) of nitro compound if the reaction is carried out in solvents like dimethyl formamide (DMF) or dimethyl sulphoxide (DMSO).

C. Oxidation of t-alkyl amines with $KMnO_4$:

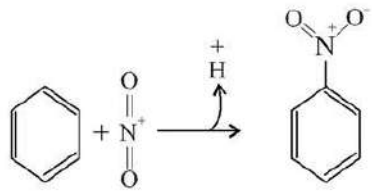
In this reaction, the amine must be primary and $-NH_2$ group should be attached to a tertiary carbon.

$$\begin{matrix}CH_3\\|\\CH_3 - C - NH_2\\|\\CH_3\end{matrix} \xrightarrow{KMnO_4} \begin{matrix}CH_3\\|\\H_3C - C - NO_2\\|\\CH_3\end{matrix}$$

6.3.1.2 Preparation of Aromatic nitro compounds:

A. Aromatic nitro compounds are typically synthesized by nitration. Nitration is

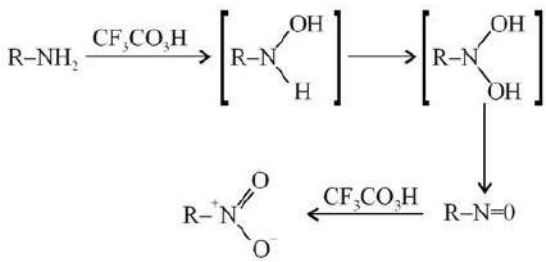
achieved using a mixture of nitric acid and sulfuric acid, which produce the nitronium (NO_2^+), which act as a electrophile



B. Displacement of the diazonium group by $CuNO_2$ leads to nitroarenes (the **Sandmeyer reaction**):

$$ArNH_2 \xrightarrow[NaNO_2/HCl]{HNO_2} ArN_2Cl \xrightarrow{CuNO_2} Ar\text{-}NO_2$$

C. Nitro compounds can be produced by oxidised of amine by peracids



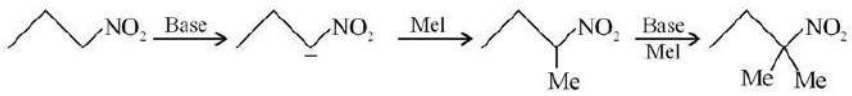
As the nitro group is strongly electron withdrawing and shows affinity with the C=O group. An anion is easily formed with base and stabilised by resonance as nitronate anion.

Nitro methane, $MeNO_2$, have a pKa of 10.2. So in order to remove the proton of nitro alkane an appropriate base is required.

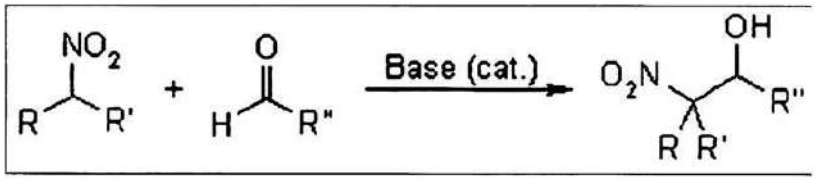
As the nitronate ion is delocalized, it is a soft nucleophile and reacts as stabilized, soft, carbanion.

6.3.2 Reaction :

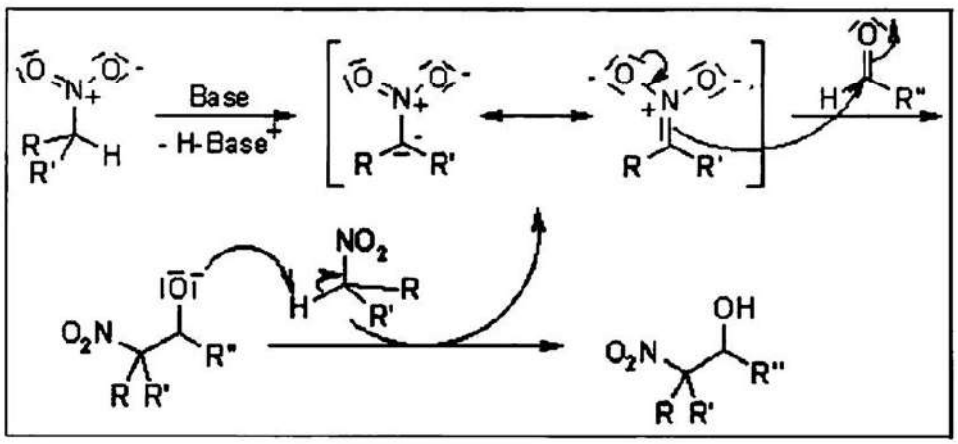
A. Alkylation:



B. Henry Reaction: This reaction is analogousfo the Aldol reaction;

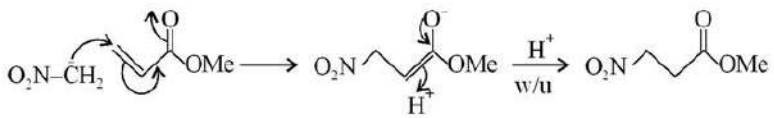


Mechanism:



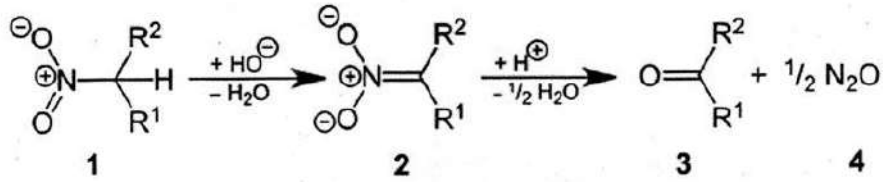
C. Michael Additions :

The Michael addition is a conjugate addition of nitronate ion to the double bond of α,β-unsaturated carbonyl compound as double bonded C atom is the soft centre and the carbonyl carbon being the hard centre. It proceeds by the following mechanism;

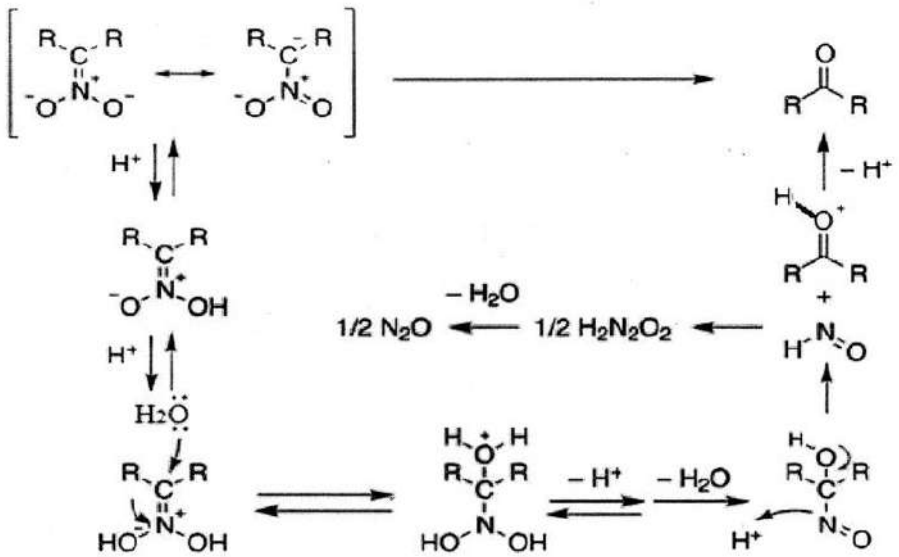


D. Nef reaction :

The Nef reaction is an organic reaction describing the acid hydrolysis of a salt of a primary or secondary nitroalkane (1) to an aldehyde or a ketone (3) and nitrous oxide (4). The ambident behaviour can be seen in the Nef reaction.

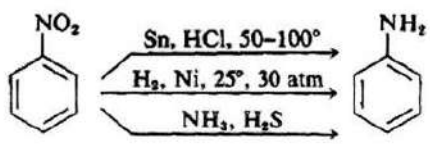


Mechanism:

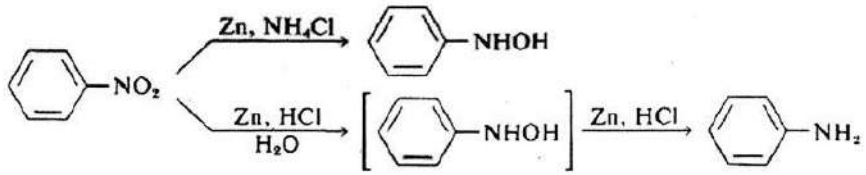


E. Reduction:

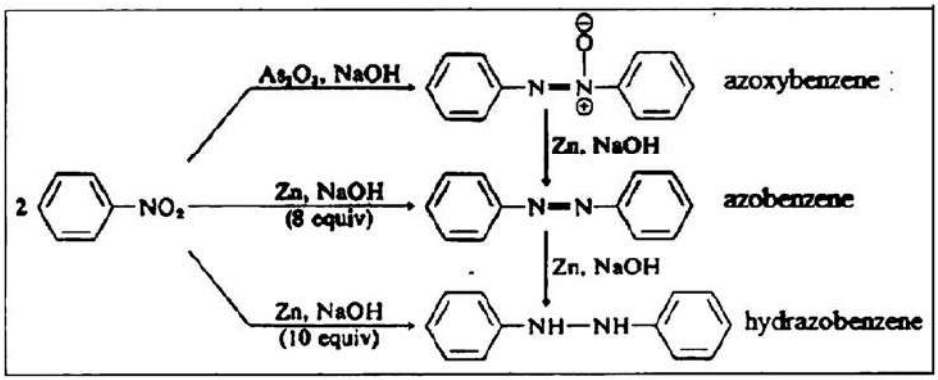
Reduction of nitro compounds occurs readily with a variety of reducing agents and such reductions afford a particularly useful synthesis of aromatic amines



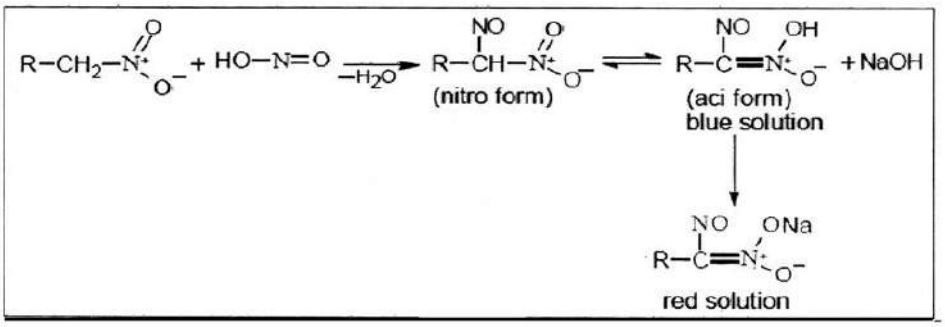
Thus N-aryl-substituted azanols can be obtained directly from the corresponding nitro compounds with zinc and ammonium chloride solution. However, zinc and hydrochloric acid gives the amine.



Reduction of aryl nitro compounds with less-powerful reducing agents, especially in alkaline media, gives what may appear to be a mysterious conglomerate of bimolecular reduction products. For example with nitrobenzene,



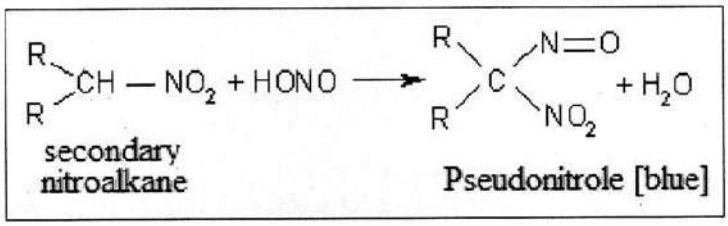
F. Reaction with nitrous acid:



Primary, secondary & tertiary nitroalkanes react in different way with nitrous acid.

a) Primary nitroalkanes react with nitrous acid to give blue solution of nitroso-nitroalkane (aci form) & dissolve in sodium hydroxide to give red solution.

b) Secondary nitroalkanes react with nitrous acid to give blue solution of nitroso-nitroalkane (pseudo aci form) & not dissolve in sodium hydroxide due to absence of α-hydrogen atom.



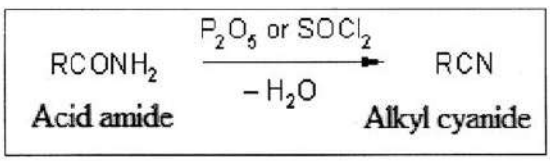
c) Tertiary nitroalkanes does not react with nitrous acid due to absence of α-hydrogen atom.

6.4 Alkyl nitrile and Alkyl isonitrile

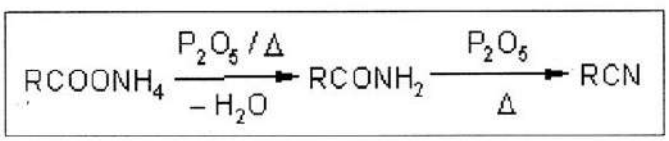
6.4.1 Preparation:

1. From acid amides:

Alkyl or aryl cyanides may be prepared by dehydration of acid amide using phosphorus pentoxide (P_2O_5) or thionylchloride ($SOCl_2$)

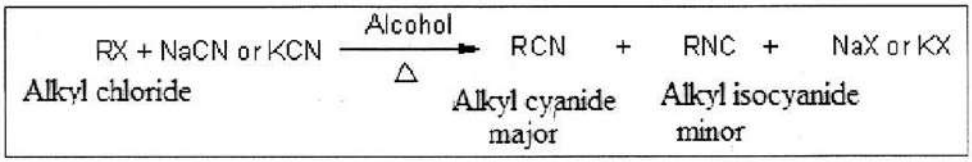


In the above reaction, you may also use ammonium salts of carboxylic acids $RCOONH_4$ in place of amides.



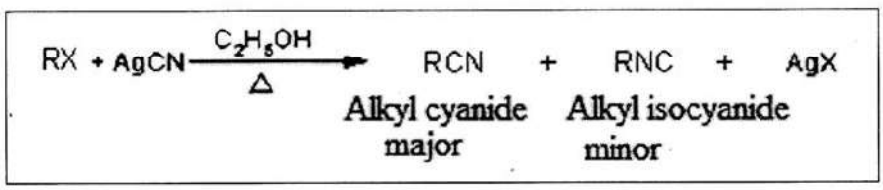
The major advantage of this method is that pure cyanide is obtained without any contamination with isocyanide.

2. From alkyl halides:



The cyanide ion (–C ≡ N :) is ambident in natlire; has an unshared pair of electrons on both carbon as well as nitrogen. Hence the alkyl group may attach either through carbon or through nitrogen giving cyanides or isocyanides respectively. When [illegible] pathway and gives alkyl cyanide as major product.

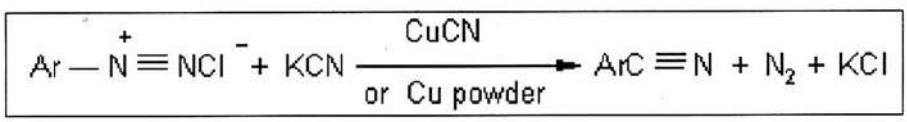
But alkyl isocyanides are the major product when silver cyanide is used in place of NaCN or KCN. In practice, this reaction takes place through SN_2 pathway and gives alkyl isocyanide (major).



The above method cannot be used for aryl cyanides or aryl isocyanides as aryl halides do not easily undergo nucleophilic substitution reactions.

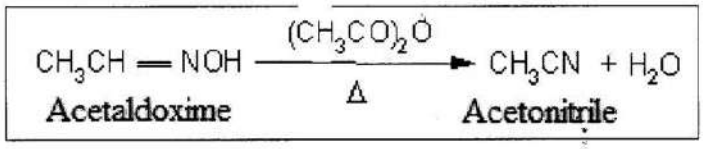
3. From aromatic diazonium salts:

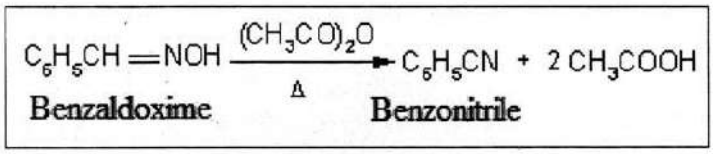
Aryl diazonium salts react with a mixture of copper (I) cyanide or coppe powder and sodium or potassium cyanide to give aryl cyanides with loss of nitrogen. The above reaction is a special case of Sandmeyer or Gattermann reaction. Alkane diazonium salts being very unstable even at low temperature, this method cannot be used for the preparation of alkyl cyanides.



4. From aldoximes:

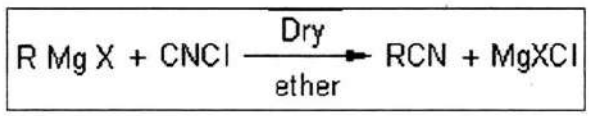
Dehydration of aldoximes with phosphorus pentoxide (P_2O_5) or acetic anhydride gives alkyl or aryl cyanide.

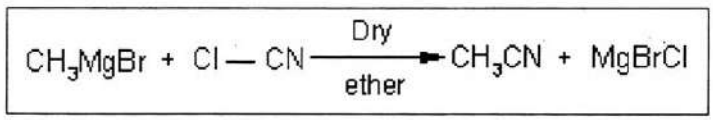




5. Using Grignard reagents:

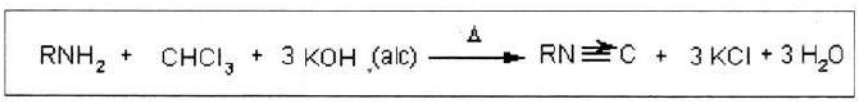
Cyanogen chloide can be treated with Grignard reagent to give alkyl cyanides. Tertiary alkyl cyanides can be prepared easily by this method.

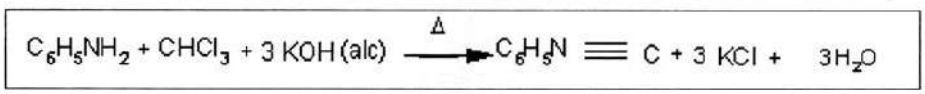




6. From primary amines:

The carbylamine reaction can be used to prepare alkyl and aryl isocyanides. A mixture of primary amine can be heated with chloroform and alcoholic potassium hydroxide solution.





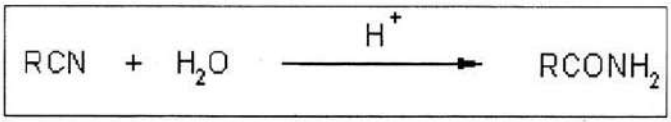
A major disadvantage of this method is that it cannot be used to prepare alkyl cyanides.

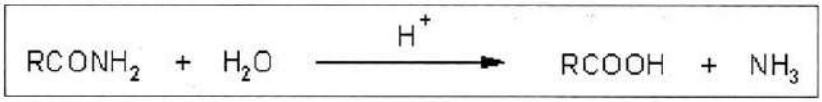
6.4.2 Reaction :

A. Hydrolysis of cyanide:

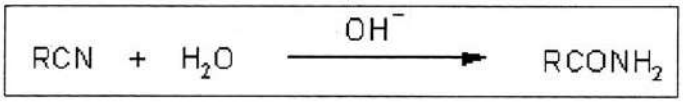
Cyanides are easily hydrolyzed under acidic as well as basic conditions to give acid amides. Acid amides undergo further hydrolysis to carboxylic acids and ammonia. Using mild conditions, the reaction can be stopped at the amide stage.

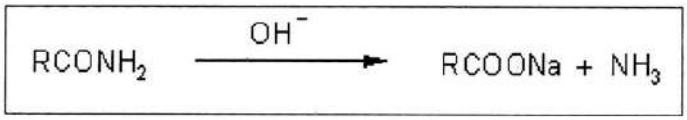
Under acidic condition:





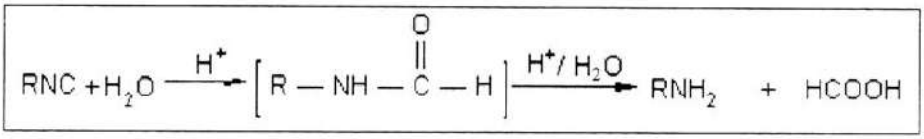
Under basic condition:



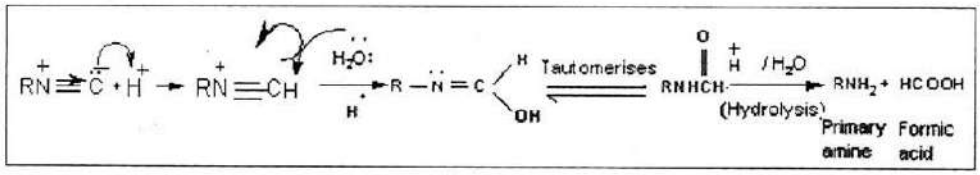


B. Hydrolysis of isocyanide:

Isocyanides are hydrolyzed by dilute mineral acids to give primary amine and formic acid. Isocyanides are not hydrolyzed by base. Because the negative charge present on carbon atom in isocyanides initially attracts electrophiles (H^+) but repels nucleophiles (OH^-). When a proton gets attracted to negatively charged carbon atom, the tendency of this carbon atom to attract a nucleophile increases due to presence of positive charge on the N atom and hydrolysis is facilitated as shown below.



Mechanism:



C. Reduction (Complete reduction and Partial reduction)

Complete Reduction of cyanide:

Alkyl cyanides can be completely reduced either catalytically by hydrogen or chemically by lithium aluminium hydride to give the corresponding primary amine.

$$RCN + 2H_2 \xrightarrow{\text{Pt or Ni}} RCH_2NH_2$$

Complete Reduction of isocyanide:

Isocyanides on reduction give N- methyl amines i.e. secondary amine.

$$RNC + 2H_2 \xrightarrow[\text{or } Na/C_2H_5OH]{\text{Pt or Ni}} RNHCH_3$$

Partial reduction:

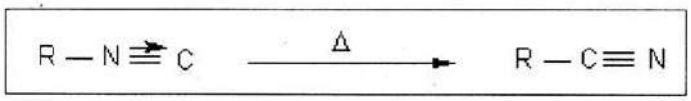
On reducing the solution of a nitrile in ether with hydrogen chloride gas and stannous chloride at room temperature, a precipitate of amine hydrochloride is formed which on hydrolysis with boiling water gives aldehydes.

$$SnCl_2 + 2HCl \longrightarrow SnCl_4 + 2[H]$$

$$RCN + 2[H] + HCl \xrightarrow[290\text{-}295\ K]{\text{Ether}} RCH \equiv NH.HCl \xrightarrow{\text{Boiling water}} RCHO + NH_4Cl$$

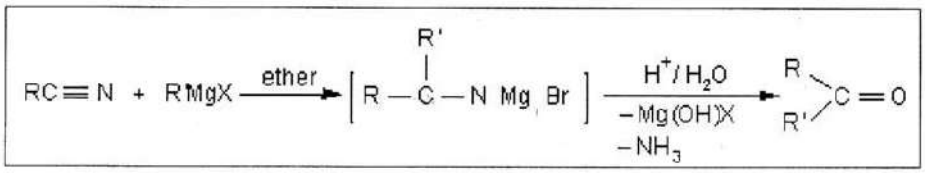
D. Isomerisation:

Cyanides are formed by rearrangement of isocyanides by heating them for a long time.



E. Reaction with Grignard reagent:

Grignard reagent reacts with nitriles to give ketones



F. Addition reactions:

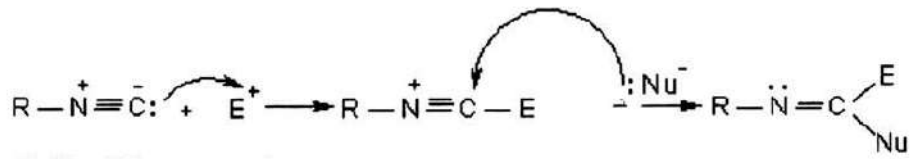
Addition products are formally reaction of isocyanides with sulphur, halogens, ozone, etc. cyanides do not undergo these reaction

$CH_3 — N^+ \equiv C^- + S \longrightarrow CH_3 — N = C = S$
Methyl isocyanide — Methyl isothiocyanate

$CH_3NC + Cl_2 \longrightarrow CH_3 — N = CCl_2$
Methyl isocyanide — Methyl iminocarbonyl chloride

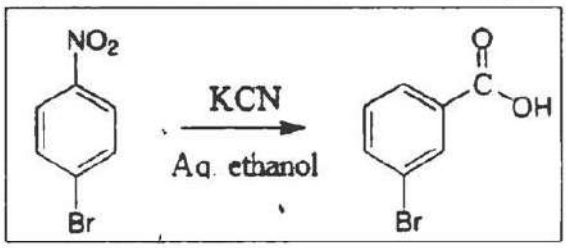
$C_2H_5NC + O_3 \longrightarrow C_2H_5N = C = O + O_3$
Ethyl isocyanide — Ethyl isocyanate

In usual addition reactions, the electronhile and nucleophile add to two different atoms of the unsaturated system but in isocyanides, the mechanism of addition reactions is different as electrophile and nucleophile add to the same carbon atom. The negative charge on carbon atom accepts an electrophile to form species in which the positive charge on nitrogen atom - gets neutralised by the addition of the nucleophile to the carbon atom.

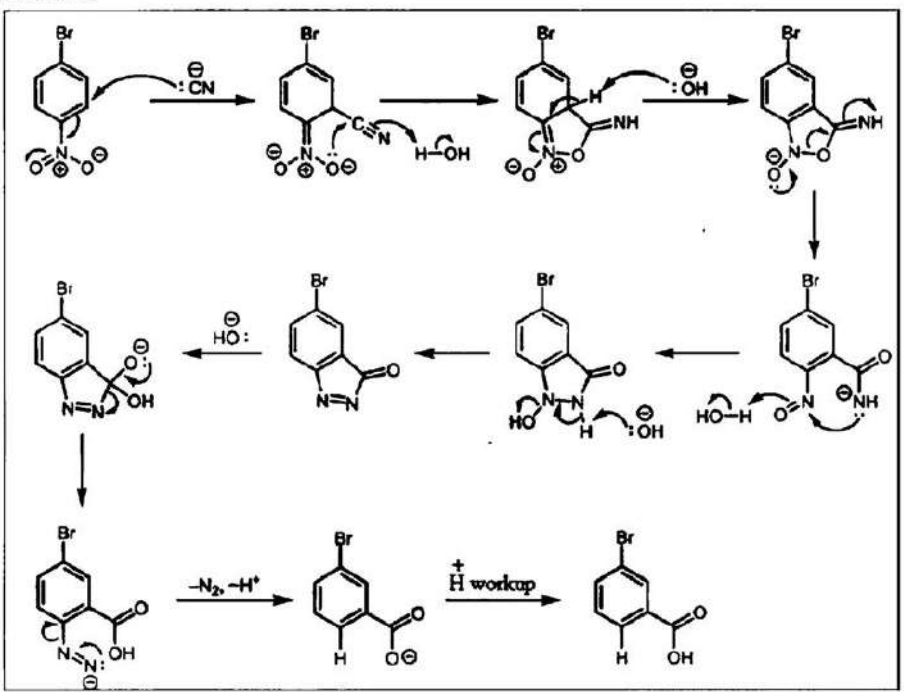


G. Von Ricter reaction:

The von Richter reaction is the reaction of aromatic nitro compounds with potassium cyanide in aqueous ethanol to give the product of *cine* substitution (ring substitution resulting in the entering group positioned adjacent to the previous location of the leaving group) by a carboxyl group. It is not generally synthetically useful due to the low chemical yield and formation of numerous side products.

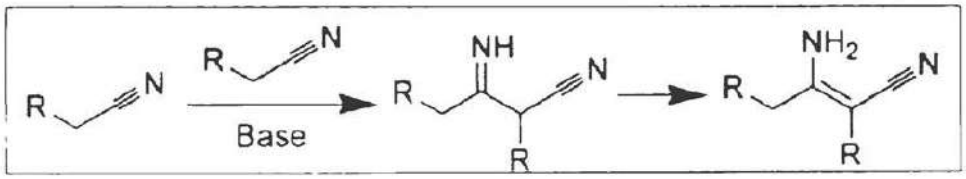


Mechanism:



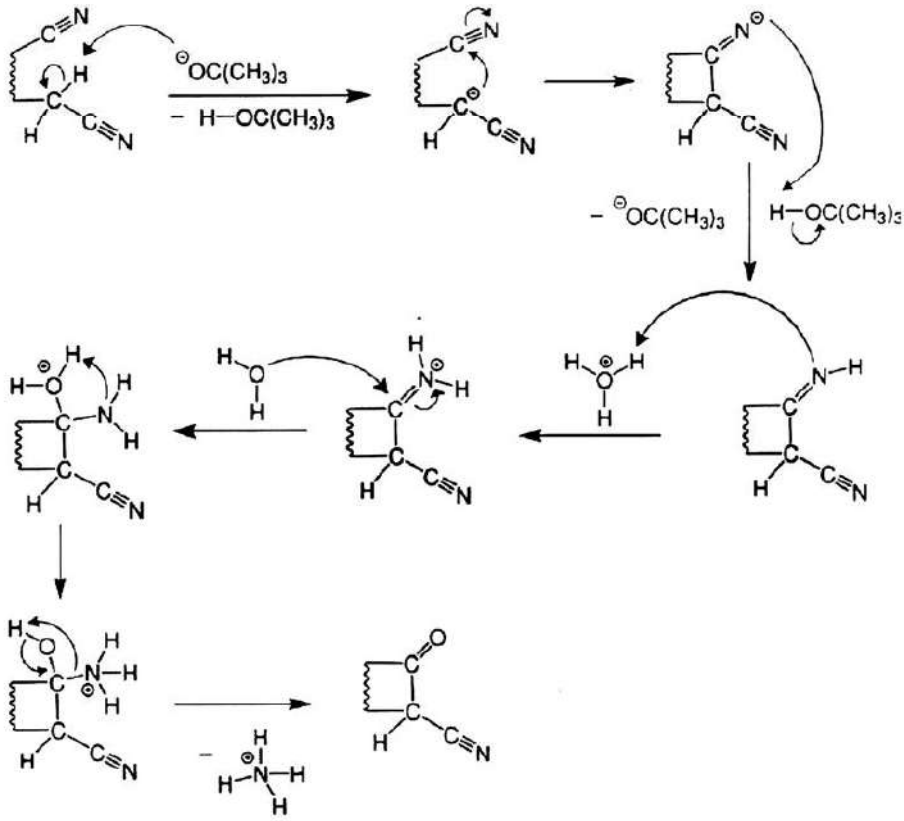
H. Thorp condensation:

The Thorpe reaction is a chemical reaction described as a self-condensation of aliphatic nitriles catalyzed by base to form enamines.



Mechanism:

The Thorpe-Ziegler reaction or Ziegler method is the intramolecular modification with a dinitrile as a reactant and a cyclic ketone as the final reaction product after acidic hydrolysis. The reaction is conceptually related to the Dieckmann condensation.

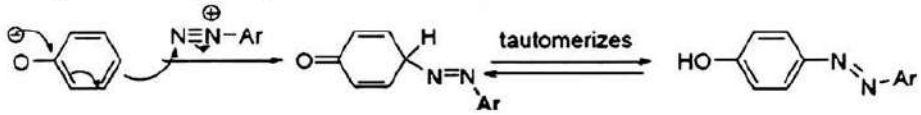


6.5 Diazonium salts

6.5.1 Reaction :

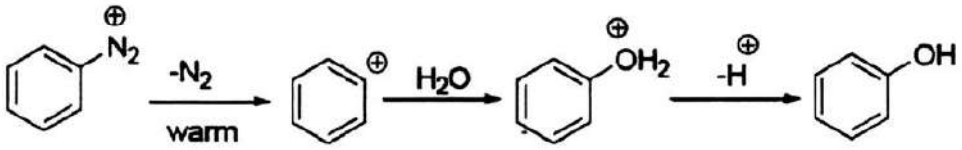
A. Reactions of nucleophiles at nitrogen:

Nucleophiles react with diazonium ions to give covalent diazo-compounds. For example, phenol via phenoxide ion couples with diazonium salt at pH 9-10 to afford paraazophenols in good yield.



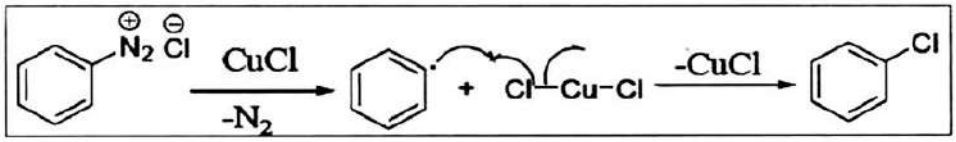
B. SN1 Reaction:

Diazonium salts decompose on warming into nitrogen and aryl cation which is highly reactive and could be attacked by any nucleophile in its vicinity.



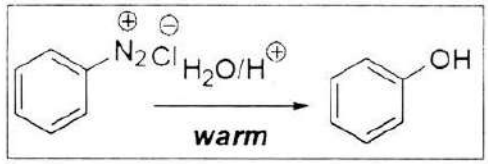
C. One Electron Reduction:

Diazonium ions could be reduced by single electron transfer to give an aryl radical and - nitrogen. Copper (I) is frequently used for this purpose and the aryl radical is highly reactive capable of abstracting a ligand from the transition metal ion or a hydrogen atom from a covalent bond.



D. Replacement by Hydroxyl:

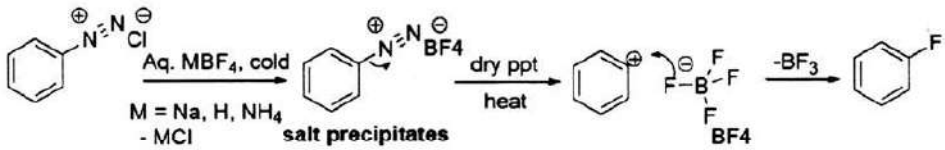
Diazonium salt on warming in water gives phenol via SN^1 mechanism. The reaction is generally performed in acidic solution to preserve phenol in its unionized form.



E. Replacement by Halogen:

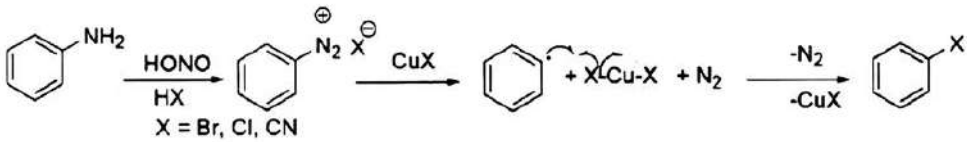
1] Schiemann Reaction:

Treatment of an aqueous solution of diazonium salt with fluoroboric acid under cold conditions gives diazonium fluoroborate as precipitate, which could be dried and gently heated to afford the flurobenzene by decomposition. The reaction involves SN^1 mechanism.



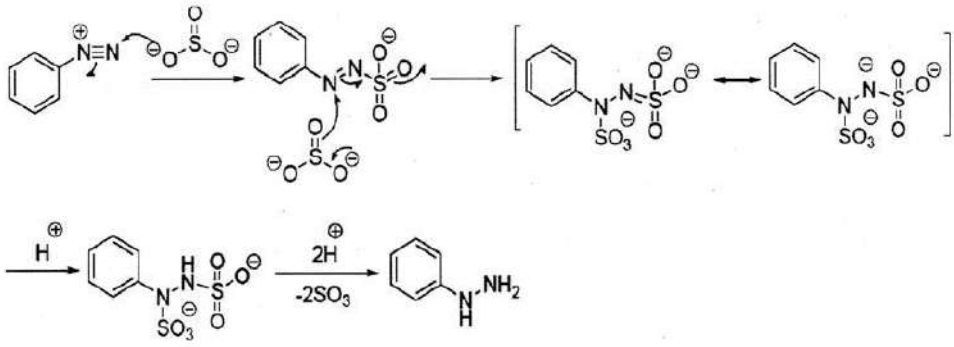
2] Sandmeyer Reaction:

This method provides an effective route for the preparation of aromatic bromides and chlorides. Addition of cold aqueous solution of diazonium chloride to a solution of CuCl in HCl medium gives a sparingly soluble complex which is separated and heated to give aryl chloride or bromide by decomposition.



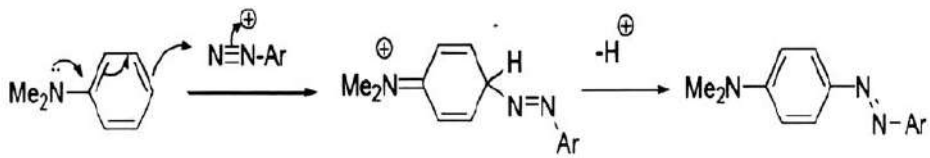
G. Reduction to Arylhyrazone:

The reduction of aromatic diazonium salts can be accomplished with sodium sulfite or $SnCl_2$ or electrolysis to provide arylhydrazines. In case of sodium sulfite based reduction, the diazonium ion with a sulfite anion may give a covalent azo-sulfite that, having a double bond conjugated to an electron-accepting group, may add to a second nucleophilic sulfite ion which on hydrolysis provides the hydrazine.

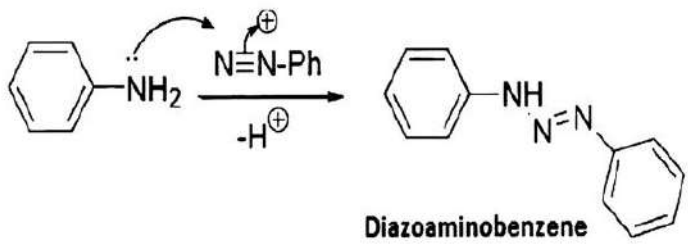


H. Coupling Reaction:

Diazonium ions are weak electrophiles, however, they undergo coupling with activated aromatic nuclei such as aryl amines, phenols and aromatic heterocyclic compounds. For example, N,N-dimethylaniline reacts with diazonium ion almost at the para-position. However, the careful control of the pH of the reaction medium is necessary for the success of the process.

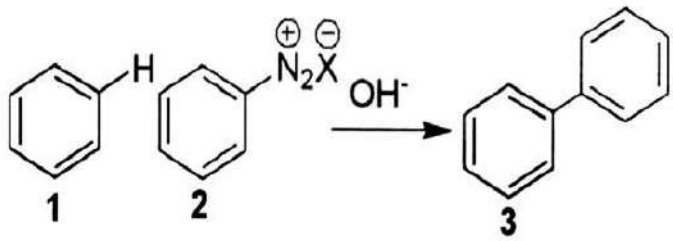


In case of primary and secondary aromatic amines, the reaction preferentially takes place at the nitrogen atoms of the diazonium ions. For example, aniline adds to the aromatic diazonium salt to give diazoaminobenzene.

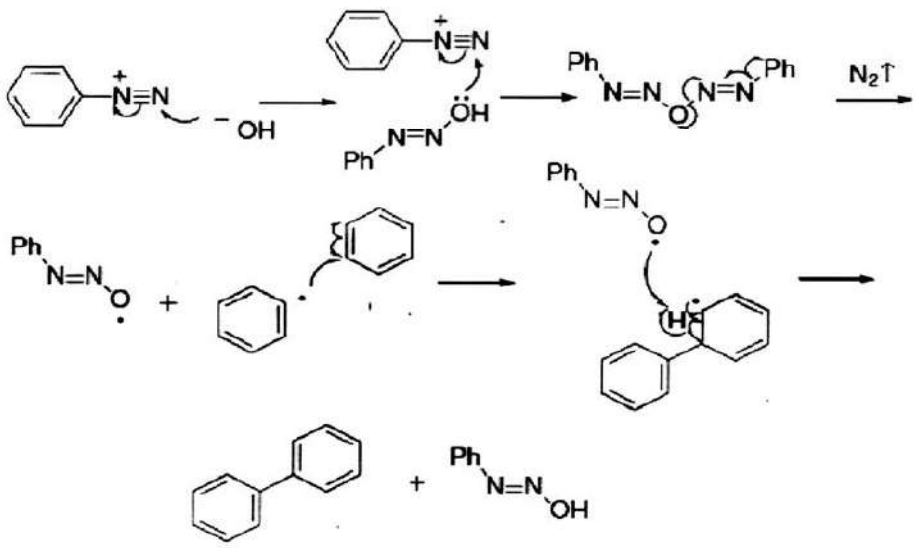


Diazoaminobenzene

I. Gomberg reaction:

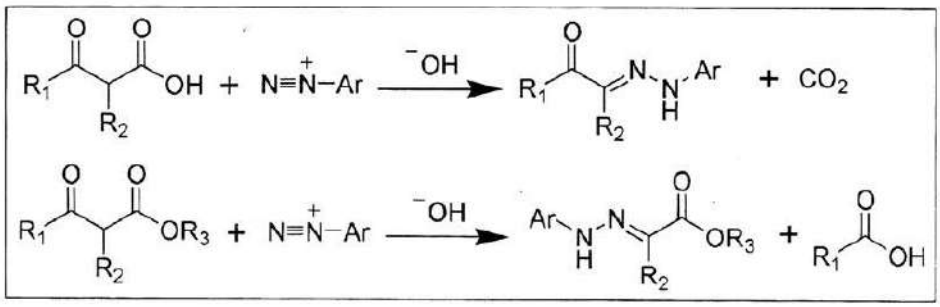


Mechanism:



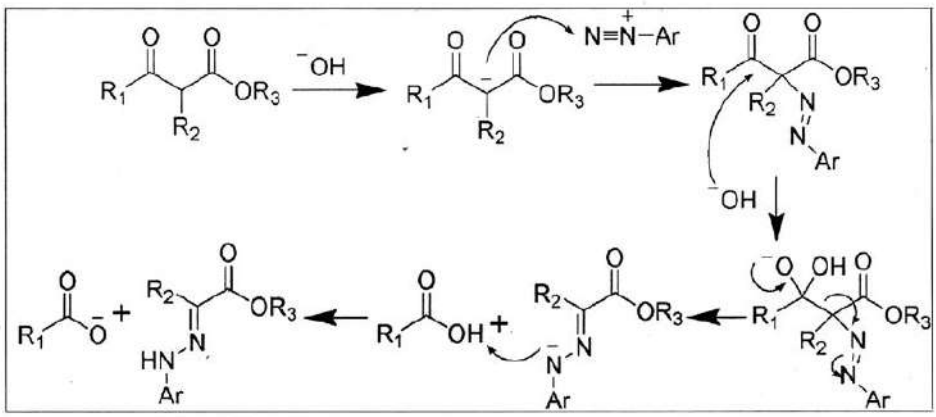
J. Japp-Klingemann reaction:

The Japp-Klingemann reaction is a chemical reaction used to synthesize hydrazones from β-keto-acids (or β-keto-esters) and aryl diazonium salts.



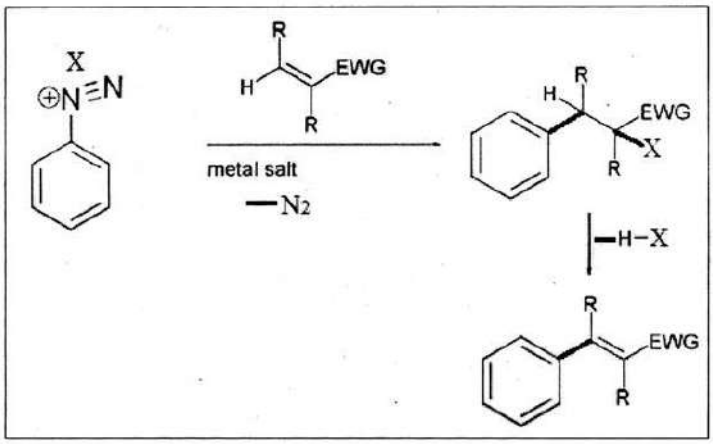
Mechanism:

Firstly the β-keto-ester is deprotonated to form enolate anion which attacks the diazonium salt to produce the azo compound. However, in most cases, the hydrolysis of azo compound produces a tetrahedral intermediate, which quickly decomposes to release the carboxylic acid. After hydrogen exchange, the final hydrazone is produced.



K. Meerwein Reaction:

The Meerwein arylation is an organic reaction involving the addition of an aryl diazonium salt (ArN_2X) to an electron-poor alkene usually supported by a metal salt. The reaction product is an alkylated arene compound.



An electron-withdrawing group (EWG) on the alkene makes it electron deficient and although the reaction mechanism is unclear, involvement of an aryl radical produced after loss of nitrogen in the diazonium salt followed by a free radical addition. In the primary reaction product the intermediate alkyl radical is then captured by the diazonium counterion X which is usually a halogen or a tetrafluoroborate. In a subsequent step an elimination reaction liberates HX (for instance hydrochloric acid) and an aryl vinyl compound is formed. The reaction mechanism from the arene's view ranks as a radical-nucleophilic aromatic substitution.

6.6 Summary

I] Amines are generally obtained though alkylation of ammonia, Gabriel synthesis, reduction of nitriles, reduction of amides, reduction of nitrocompounds, and reductive amination of aldehydes and ketones.

II] The mixture of three amines, primary, secondary and tertiary are separated by several methods like Hofmann's method, Hinsberg's method etc.

III] The Eschweiler-Clarke methylation is used to convert a primary or secondary amine to a tertiary amine.

IV] Mannich reaction is the condensation of a nonenolizable aldehyde, a primary or secondary amine and an enolizable carbonyl compound to lead β-amino carbonyl compound.

V] The Arndt-Eistert Synthesis is the reaction of the activated carboxylic acids

with diazomethane and subsequent Wolff-Rearrangement of the intermediate diazoketones in the presence of nucleophiles such as water, alcohols, or amine to produce acid, ester or amide (one carbon more in each case) respectively.

VI] The Nef reaction is the acid hydrolysis of a salt of a primary or secondary nitroalkane to an aldehyde or a ketone and nitrous oxide.

VII] Primary, secondary & tertiary nitroalkanes react in different way with nitrous acid. They can be identified by this reaction.

VIII] Alkyl nitriles and isonitriles are prepared from acid amides, alkyl halides, aldoximes. Grignard reagents, primary amine, aromatic diazonium salts etc.

IX] The Von Richter reaction is the reaction of aromatic nitro compounds with potassium cyanide in aqueous ethanol to give the product of cine substitution (ring substitution resulting in the entering group positioned adjacent to the previous location of the leaving group) by a carboxyl group.

X] The Thorpe reaction is the self-condensation of aliphatic nitriles catalyzed by base to form enamines.

XI] Gomberg reaction involves the reaction of aromatic diazonium salt and aromatic compound in presence of base to form biaryl compound.

XII] The Japp-Klingemann reaction is used to synthesize hydrazones from β-keto-acids (or β- keto-esters) and aryl diazonium salts.

XIV] The Meerwein reaction involves the addition of an aryl diazonium salt (ArN_2X) to an electron-poor alkene usually supported by a metal saltto produce an alkylated arene compound.

6.7 Keywords

Amine, preparation and reaction, Hinsberg's method, Eschweiler-Clarke methylation, Mannich reaction, Arndt-Eistert Synthesis, Nef reaction, nitroalkanes, alkyl nitrite, Alkyl nitriles and isonitriles, Von Richter, Thorpe reaction, Gomberg, Japp-Klingemann, Meerwein.

6.8 References and further readings

1] Finar, I. L. Organic Chemistry (volume I), Dorling Kindersley (India) Pvt. Ltd.

2] Clayden J., Greeves, N., Warren, S. Organic Chemistry, Second edition. Oxford University Press 2012.

3] March, J. Advanced Organic Chemistry, Fourth edition, wiley.

4] Normann, R.O.C., Coxon, J.M. Principles of Organic Synthesis.

6.9 Model questions

1. Diazomethane easily methylates phenols or carboxylic acids but not alcohols. Explain
2. How can you distinguish chemically between N-methyl aniline and N,N-dimethyl aniline?
3. Synthesize $Me_3C—NH_2$ and $Me_3C—CH_2—NH_2$
4. Alkaline hydrolysis of benzonitrile affords the salt pf an acid but in presence of H_2O_2 an amide is formed. Explain.
5. Chemically distinguish between Et-CN and Et-NC
6. How do you prepare nitromethane and methyl nitrite?
7. Carry out the following conversion

$$Cl—CH_2—COOH \rightarrow CH_3—NO_2$$

8. Write down the mechanism of Nef reaction.
9. What happens when primary and secondary nitroalkane is separately boiled with 85% H_2SO_4? Explain the fact.
10. Transform from benzene diazonium chloride to benzoic acid.
11. What happens when meta-phenylene diamine is treated with nitrous acid? Explain the formation products.
12. Write down the reaction of benzene and benzene diazonium chloride in presence of NaOH and give the mechanism.
13. Write down the reaction mechanism between ethyl acetoacetate and benzene diazonium chloride in presence of alkali..
14. Complete the following conversion-

$$Me—COOH \rightarrow Me—CH_2—COOH$$

Notes

Notes