1. Isomerism

The existence of different compounds having same molecular formula but different physical and chemical properties is called isomerism. If the difference in properties is due to difference in their structural formulae, it is called structural isomerism. And if the difference in properties is due to the arrangement of groups in space, it is called stereo isomerism. The different compounds are named as isomers.

Isomerism is broadly divided into two types

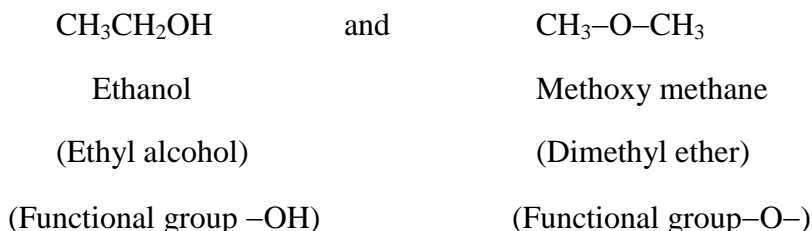   (i) Structural isomerism and   (ii) Stereoisomerism

2. Structural Isomerism

Two or more compounds with the same molecular formula, which differ in the bonding arrangement of atoms within the molecules, are called structural isomers and the phenomenon is called structural isomerism. There are different types of structural isomerism.

2.1 Functional Group Isomerism

The isomers having same molecular formula but different functional groups in the molecule are called functional isomers. The following classes of organic compounds show functional isomerism among themselves.

(a) Alcohols and ethers are functional isomers.

     CH_3CH_2OH and CH_3-O-CH_3

       Ethanol   Methoxy methane

   (Ethyl alcohol)   (Dimethyl ether)

(Functional group −OH)   (Functional group−O−)

(b) Aldehydes and ketones are functional isomers.

$$CH_3CH_2-\underset{\underset{H}{|}}{C}=O$$
Propanal
(Propionaldehyde)
(Functional group−CHO)

$$CH_3-\overset{\overset{O}{\|}}{C}-CH_3$$
Propanone
(acetone)
(Functional group $>$C=O)

(c) Carboxylic acids and esters are functional isomers.

$$CH_3-\overset{\overset{O}{\|}}{C}-OH$$
ethanoic acid

$$H-\overset{\overset{O}{\|}}{C}-OCH_3$$
Methyl methanoate

(d) Dienes, allenes and alkynes are functional isomers.

$CH_2=CH-CH=CH_2$ $CH_2=C=CH-CH_3$ $CH_3CH_2C\equiv CH$
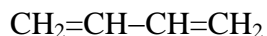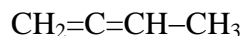
Buta−1, 3−diene   Buta−1, 2−diene (An allene)   But−1−yne

(e) Nitro alkanes and alkyl nitrites are functional isomers.

$CH_3CH_2-NO_2$ CH_3CH_2-ONO
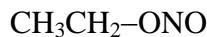
Nitroethane   Ethyl nitrite

(f) 1°, 2° and 3° amines share functional isomers.

$CH_3CH_2CH_2NH_2$ $CH_3CH_2-NH-CH_3$ $\underset{\overset{|}{CH_3}}{CH_3-N-CH_3}$
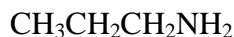
Propan−1−amine   N−methyl ethanamine   N, N−Dimethyl methanamine
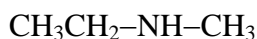
(1° amine)   (2° amine)   (3° amine)
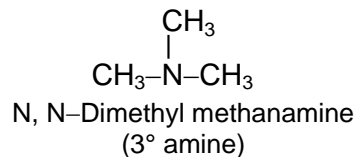
(g) Cyanides and isocyanides are functional isomers.

$CH_3C\equiv N$ $CH_3-N \gtreqless C$
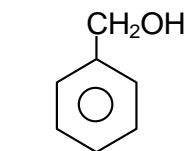
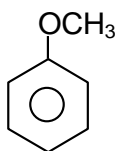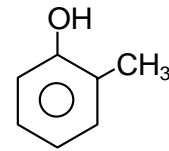Ethane nitrile   Methyl isocyanide

(h) Aromatic alcohols, phenols and ethers are also functional isomers.

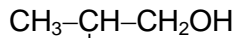Benzyl alcohol   Anisole   o−Cresol

2.2   Chain Isomerism

The isomers having same molecular formula, same functional groups (if any) but differing in the length of carbon chain (straight or branched) are called chain isomers.

(a) C_4H_9OH has two chain isomers.

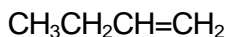$CH_3CH_2CH_2CH_2OH$ $\underset{\overset{|}{CH_3}}{CH_3-CH-CH_2OH}$

Butan−1−ol   2−Methyl propan−1−ol
(n−Butyl alcohol)   (Iso−butyl alcohol)

(b) C_4H_8 has two chain isomers.

ISOMERISM

$CH_3CH_2CH=CH_2$

But–1–ene
(Butylene)

$CH_3-CH=CH_2$
CH_3
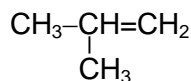
2–Methyl propene
(Iso–butylene)

2.3 Position Isomerism

The isomers having same molecular formula, same functional group (if any), same length of principal chain or side chain or size of ring but differ in the position of either substituent or functional group are called position isomers. The IUPAC names of position isomers must differ **only and only** in the numbers used to denote positions. For example,

(a) The molecular formula C_4H_8 has two position isomers.

$CH_3CH_2CH=CH_2$
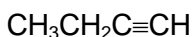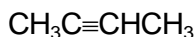
But–1–ene
(Butylene)

$CH_3CH=CHCH_3$
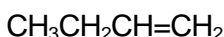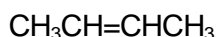
But–2–ene
(Dimethyl ethylene)

(b) The molecular formula C_4H_6 has two position isomers.

$CH_3CH_2C\equiv CH$

But–1–yne
(Crotonylene)

$CH_3C\equiv CHCH_3$
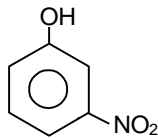
But–2–yne
(Dimethyl acetylene)
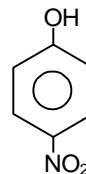
(c) The molecular formula $C_6H_6O_3N$ has three position isomers.
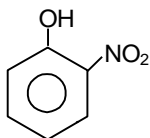
ortho–nitrophenol
(1, 2–substitution)

meta–nitrophenol
(1, 3–substitution)

para–nitrophenol
(1, 4–substitution)

DEGREE OF UNSATURATION

Deficiency of two hydrogen atoms in a molecule is a result of either a pi–bond or a ring in the structure of that molecule. The sum of pi–bonds and rings in the structure of a compound collectively is called **degree of unsaturation or double bond equivalents** in that compound.

The most general type of formula for any organic species is $(C_aH_bN_cO_d)$. If the compound contains other atoms also, the tetravalent atoms are replaced by carbon, monovalent atoms are replaced by hydrogen, divalent atoms are deleted and trivalent atoms are deleted with one H each. One Hydrogen is added for intermediate carbocation, carbanion and carbon free radical while two hydrogen are added for intermediate carbene and nitrene. As a result of all these operations, we will get a hydrocarbon. Now this concluded hydrocarbon is compared with saturated alkane to determine the degree of unsaturation or double bond equivalents.

Example 1: $C_{12}H_{16}N_2OCl_2$

$C_{12}H_{16}N_2OCl_2$ will give $C_{12}H_{18}N_2O$ after replacing Cl atoms by H atoms and $C_{12}H_{16}$ after removing O and N. Corresponding saturated alkane should be $C_{12}H_{26}$.
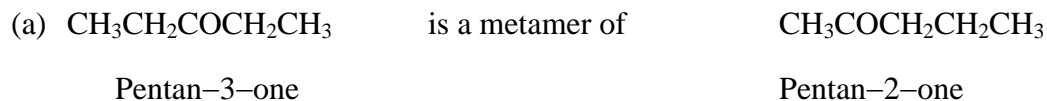
$$\text{Double bond equivalents} = \frac{26-16}{2} = 5$$

Example 2: $C_{13}H_{10}BrNO$

$C_{13}H_{10}BrNS$ will give $C_{13}H_{11}NO$ after replacing Br by H atom. Removal of O and N gives us $C_{13}H_{10}$. The corresponding saturated alkane will be $C_{13}H_{28}$.
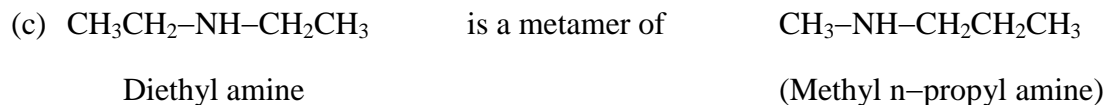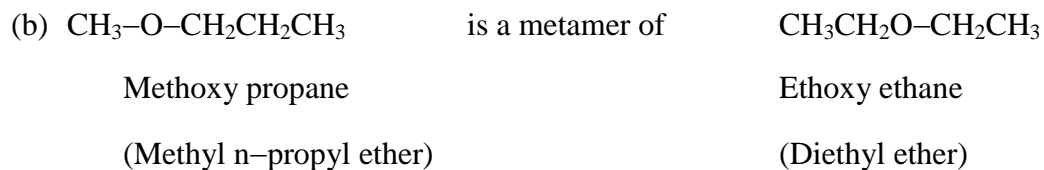
$$\text{Double bond equivalents} = \frac{28-10}{2} = 9.$$

2.4 Metamerism

It is a special type of either chain or position isomerism where the isomers have different number of carbon atoms (or alkyl groups) on either side of the multivalent functional group having at least one hetero-atom (i.e. $-O-, -S-, -NH-, -CO-$ etc.). Metamerism occurs among the members of the same family. For example,

(a) $CH_3CH_2COCH_2CH_3$ is a metamer of $CH_3COCH_2CH_2CH_3$

     Pentan−3−one   Pentan−2−one

These two are also related as position isomers as the position of $>\!C\!=\!O$ in the two isomers is different.

(b) $CH_3-O-CH_2CH_2CH_3$ is a metamer of $CH_3CH_2O-CH_2CH_3$

     Methoxy propane   Ethoxy ethane

     (Methyl n−propyl ether)   (Diethyl ether)

(c) $CH_3CH_2-NH-CH_2CH_3$ is a metamer of $CH_3-NH-CH_2CH_2CH_3$

     Diethyl amine   (Methyl n−propyl amine)

2.5 Tautomerism

It is a special type of functional isomerism in which the functional isomers are spontaneously interconverted to each other and exist as equilibrium mixture. Tautomerism mainly involves intramolecular transfer of a hydrogen atom between two atoms (at least one of them must be highly electronegative like O, N etc.) along with delocalization of electrons. This hydrogen transfer must lead to change in functional group and should be spontaneous. The driving force of this spontaneity is generally either resonance or hyperconjugation but can be any intramolecular reversible reaction also.

Most common example of tautomerism is Keto-enol tautomerism, in which hydrogen from α–carbon atom of aldehyde or ketone is shifted to oxygen that results into formation of enols.
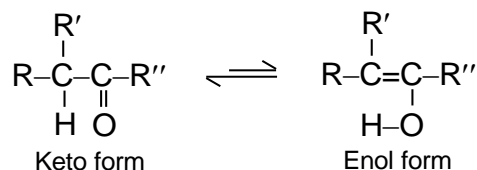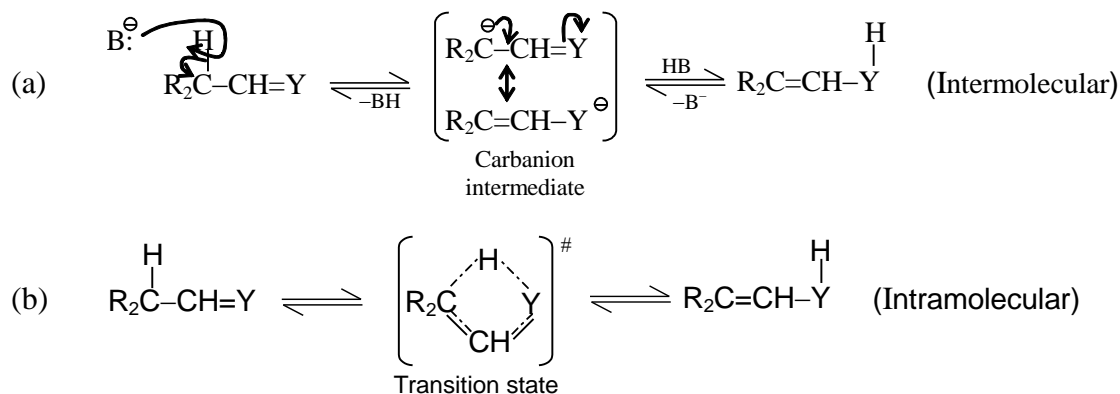

Keto form   Enol form

$$\Delta H = (\varepsilon_{C-H} + \varepsilon_{C-C} + \varepsilon_{C=O}) - (\varepsilon_{C=C} + \varepsilon_{C-O} + \varepsilon_{O-H}) = 359 - 347 = 12 \text{ kcal/mol.}$$

In most cases, the equilibrium lies towards the left. Thus, the keto form is thermodynamically more stable than enol form by about 12 kcal/mol.

The term tautomerism is used for isomers that are fairly readily interconvertible and that differ from each other only (a) in electron distribution and (b) in the position of a relatively mobile atom or group, The mobile atom is generally hydrogen and the phenomenon is then called as **prototropy**.

Both acids and bases catalyse such interconversions. Possible limiting mechanisms are those (a) in which proton removal and proton acceptance (from the solvent) are separate operations and a carbanion intermediate is involved. i.e. an intermolecular pathway and (b) in which one and the same proton is transferred intramolecularly.

(a)

Carbanion intermediate

(b)

Transition state

**In cases where aldehyde / ketone is α,β-unsaturated, transfer of hydrogen occurs from γ-position and so on.**

Mostly the keto form is more stable than enol form but in certain cases, enol form can become the predominant form. The enol form is predominant in following cases:

1. Molecules in which the enol form is stabilized by intramolecular hydrogen bonding and conjugation.

(Cross–conjugation and intramolecular
hydrogen bonding)

(Conjugation and intramolecular
hydrogen bonding)
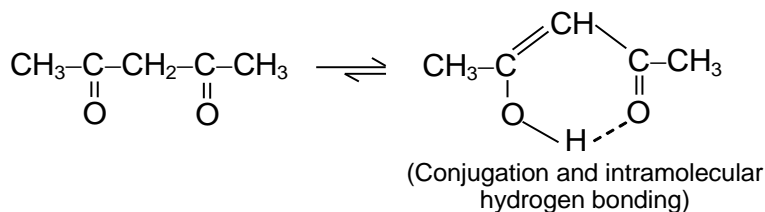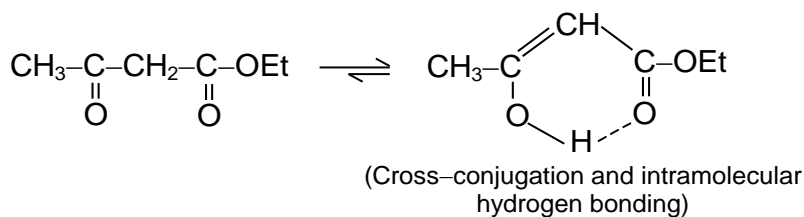
2. When the keto form is not aromatic but the enol form is aromatic.

Cyclohexadienone   Phenol
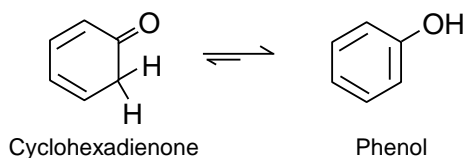
3. When enol is stabilized by large extent of conjugation.

Keto form

Enol form (hoghly conjugated)
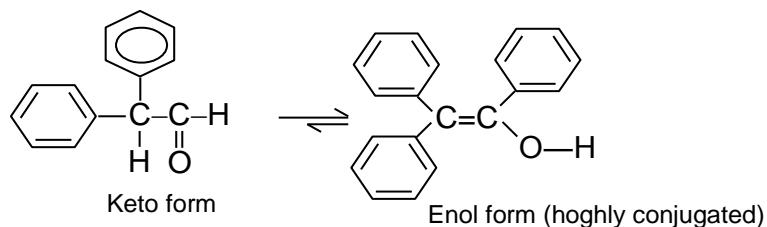
4. Molecules, which contain two bulky aryl groups at α carbon .

Keto form (5%)   Enol form (95%)
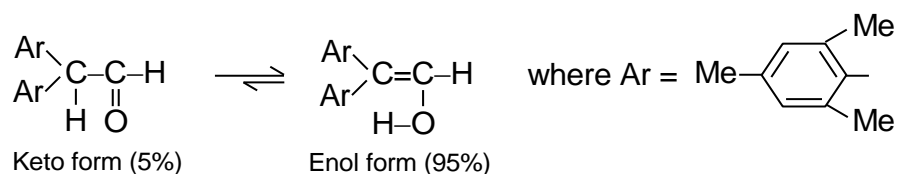
In the keto form of 2,2–dimesitylethanal, the Ar–C–Ar bond angle is 109°, whereby the bulky aryl groups experience greater steric repulsion. This steric repulsion eases off when the keto form transforms to enol form, where the Ar–C–Ar bond angle widens to 120°.

5. Highly fluorinated enols.
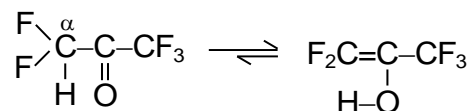
Because of the greater acidity of α–hydrogen atom (due to the presence of strongly electron withdrawing fluorine groups), the conversion to its enol form is high.

The extent of enolization is also affected by the solvent, concentration and temperature. Thus, acetoacetic ester has an enol content of 0.4% in water and 19.8% in toluene. This is because water reduces the enol content by hydrogen bonding with the carbonyl group, making this group less available for intramolecular hydrogen bonding. The effectiveness of intramolecular hydrogen–bonding in stabilizing the enol, with respect to the keto form is seen on varying the solvent and particularly on transfer to a hydroxylic solvent with $MeCOCH_2COMe$.

Solvent	% Enol
Gas phase	92
Hexane	92
Liquid	76
MeCN	58
H_2O	15

Thus, the proportion of enol in the non–polar solvent (hexane) is the same as in the gas phase and higher than in the liquid itself, the latter acting as a polar auto–solvent. The proportion drops again in the more polar MeCN and more dramatically in water. What is happening is the increasing relative stabilization of the keto form by solvation, this being particularly marked in water where intermolecular hydrogen bonding of the keto form's C=O groups can now take place as an alternative to its enolization.

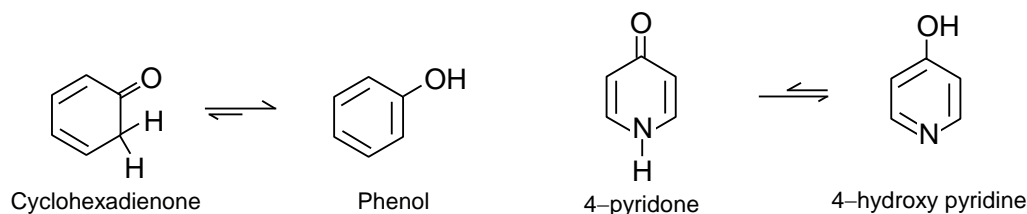Also, the enol content of pentan–2,4–dione ($CH_3COCH_2COCH_3$) is found to be 95% and 45% at 27.5° and 275°C respectively.

When a strong base is added to a solution of a ketone with α–hydrogen atom, both the enol and keto form can lose a proton. The resulting anion is same in both the cases as they differ only in the placement of electrons. They are not tautomers but canonical forms.
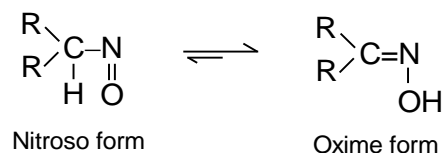
(Carbanion)   (Enolate ion)
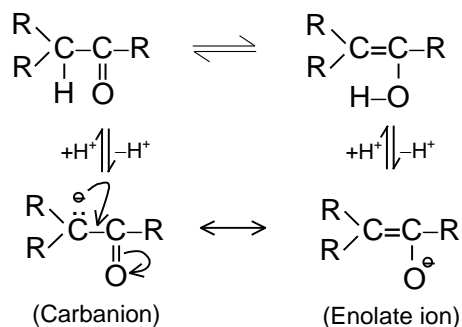
Other Types of Tautomerism

(i)   Phenol−Keto tautomerism:

Cyclohexadienone   Phenol   4−pyridone   4−hydroxy pyridine

In these cases, enol form is more stable than keto form because of the aromatic stabilization.
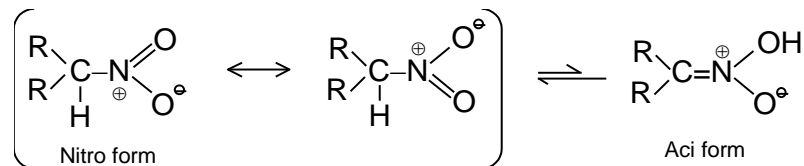
(ii)   Nitroso−Oxime tautomerism:

Nitroso form   Oxime form

This equilibrium, surprisingly, lies far to the right and as a rule nitroso compounds are stable only when there is no tautomerizable hydrogen atom.

(iii)   Nitro−Aci tautomerism:

Aliphatic nitro compounds are in equilibrium with the aci forms.

Nitro form   Aci form

The nitro form is much more stable than the aci form because nitro group has resonance. Aci form of nitro compounds is also called **nitronic acids**.

(iv)   Imine−Enamine tautomerism: Imine form predominates generally. Enamines are stable only when there is no hydrogen atom attached to nitrogen.

Imine form   Enamine form
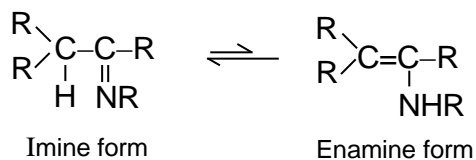
(v)   Aldehydes and Ketones having hydroxy group, 1° amino group, 2° amino group can undergo tautomerism due to intramolecular reversible nucleophilic addition reaction leading to cyclization. The cyclic tautomer is less stable (minor) if ring size is 3 or 4 membered as these rings have lot of strain. However, cyclic isomer dominates if the ring is unstrained or of very less strained (5, 6, 7… membered rings).

2.6   Ring-Chain Isomerism

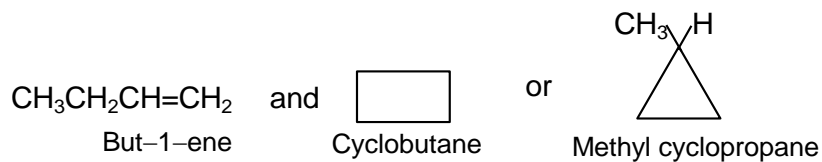Compounds having same molecular formula but possessing open chain and cyclic structures are called ring-chain isomers and the phenomenon is called ring-chain isomerism.

For example,

(a) C_3H_6 represents

$CH_3CH=CH_2$ and

Propene   Cyclopropane

(b) C_4H_8 represents

$CH_3CH_2CH=CH_2$ and   or

But−1−ene   Cyclobutane   Methyl cyclopropane
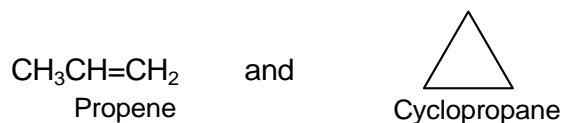
2.   Stereo Isomerism

Isomers having the same structure but differ in relative arrangement of atoms or group of atoms in space are called stereoisomers. Stereoisomerism is of three kinds.

(a) Conformational isomerism (b) Geometrical isomerism (c) Optical isomerism

## 2.1   Conformational Isomerism (Rotational Isomerism)

A bond between two carbon atoms is formed by the overlap of sp^3 hybrid orbitals of carbon atom along their internuclear axis as a result of which the electron distribution within the molecular orbital thus formed is cylindrically symmetrical along the internuclear axis. Due to this symmetry, rotation about carbon–carbon single bond is almost free, as a result number of momentary arrangements of atoms called **conformations or rotational isomers or rotomers** can result.

(a)   Conformations of ethane

In ethane, the two carbon atoms are connected by a σ–bond. If one of the methyl group in ethane molecule is kept fixed and the other is rotated about the C–C bond, infinite number of possible conformations of ethane result. The two extreme ones are termed as staggered & eclipsed and all the conformations lying between them are termed as gauche or skew conformations. The conformations can be represented by Newman and Sawhorse projections.

(i) Newman projection

These projection formulae are obtained by viewing the molecule along the bond joining the two carbon atoms. The bonds of the front carbon are shown from the center of the circle while the bonds of the rear carbon are shown from the periphery of the circle.

Eclipsed   Staggered
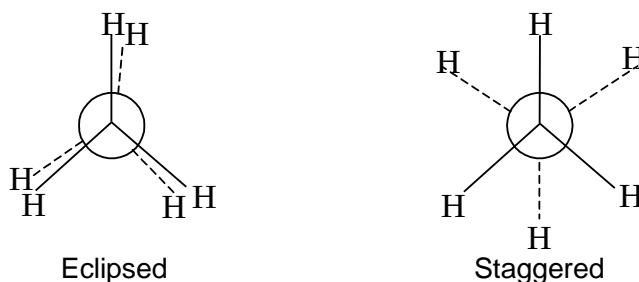
(ii) Sawhorse projection

In this projection, the molecule is viewed along the axis of the model from above and right. The central C–C bond is drawn as a straight line, slightly tilted to right for the sake of clarity. The line is drawn somewhat longer. The front carbon is shown as the lower left hand carbon whereas the rear carbon is shown as the upper right hand carbon. Each carbon has three lines corresponding to three atoms/groups (H atoms in the case of ethane).
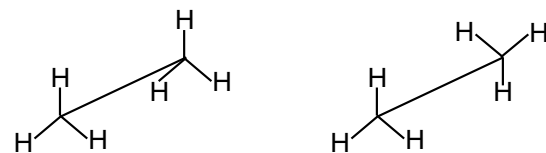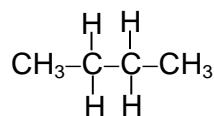
Sawhorse projections of ethane

(b)   Conformations of n–butane

In order to examine the conformations of n–butane, it is considered as a derivative of ethane in which one hydrogen atom of each carbon is replaced by a methyl group. Thus, butane is considered as dimethyl ethane as shown below,

Thus, each of the two central carbon atoms (C_2 and C_3) in n–butane is linked to one methyl group and two hydrogen atoms. If now one of these carbon atoms is fixed and the other is rotated around the central bond through an angle of $360°$, an infinite number of conformations are possible. Out of them, six important ones are as follows,
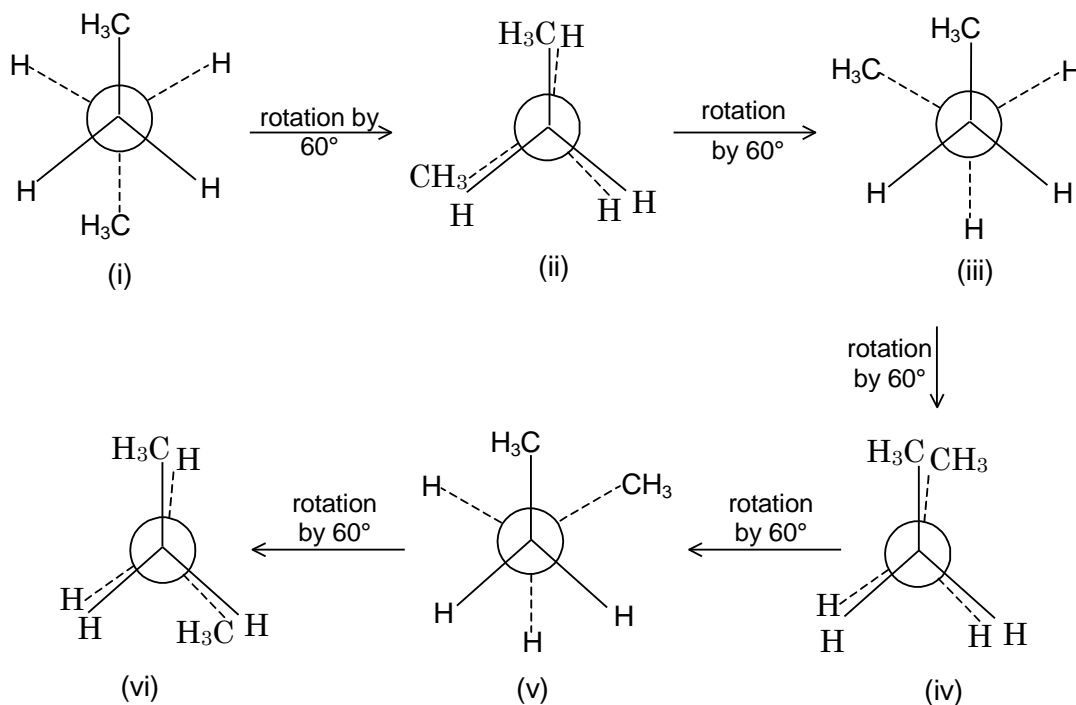
Relative stabilities of conformations

Out of the four conformations listed above, anti-conformation (I) is the most stable since in this conformations the two non-bonded methyl groups (dihedral angle $180°$) and the four non–bonded hydrogen atoms are as far apart as possible. The next in order of higher energy

come the two gauche conformations (III and V) in which the two non-bonded methyl groups are only 60° apart and hence causing crowding or steric strain. As a result of this steric strain, the two gauche conformations (III and V) are slightly less stable than the anti-conformation (I). However, the two gauche conformations are themselves of equal energy. Experimentally, it has been found that the gauche conformations are about 3.35 kJ mol^{-1} less stable than the anti conformations.

Next in order of higher energy fall the two partially eclipsed conformations (II and VI). In these conformations, there are two methyl−hydrogen eclipsing interactions and one hydrogen−hydrogen eclipsing interaction. Since each methyl−hydrogen eclipsing interaction introduces energy of 5.35 kJ mol^{-1}, therefore, partially eclipsed conformations of n−butane are less stable than anti and gauche conformations. However, the two partially eclipsed conformations are themselves of equal energy. Experimentally, it has found that partially eclipsed conformation (II and VI) is less stable than gauche conformation (III or V) by about 10.85 kJ mol^{-1} and than anti conformation (I) by about 14.2 kJ mol^{-1}.

The fully eclipsed conformation (IV) is however, the least stable. This is due to the reason that in this conformation, there is one methyl−methyl eclipsing interaction and two weak hydrogen−hydrogen eclipsing interactions. Experimentally, it has been found that fully eclipsed conformation is about 18.4 − 25.5 kJ mol^{-1} less stable than the most stable anti conformation. Thus, the relative energies of the four distinct conformations of n−butane follow the order,

Anti > Partially Staggered or Gauche > Partially eclipsed or Skew > Fully eclipsed.

However, in some cases the groups present on adjacent atoms attract each other by intramolecular hydrogen bond or by ionic bond. In such cases, the most stable conformer will be Gauche conformer as there will be dihedral repulsions in Syn conformer.

Ethylene glycol   Flurohydrin   Chlorohydrin
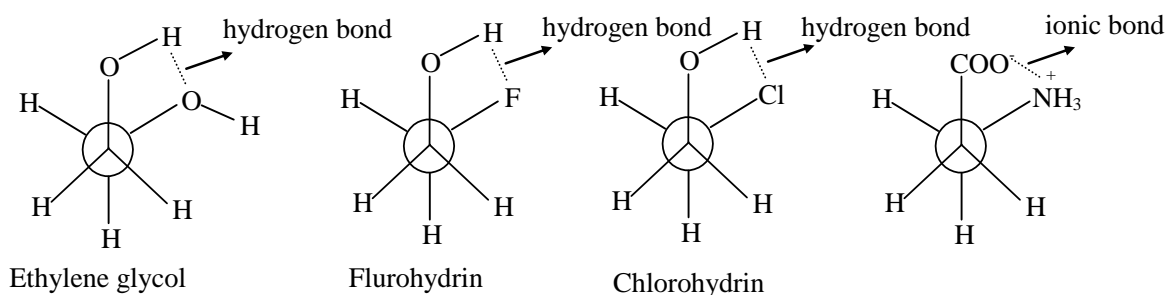
(c)   Cyclohexane

Cyclohexane is a non planar ring of six carbon atoms which mainly exists in chair conformer and boat conformer. Chair conformer is staggered and more stable while boat conformer is eclipsed and less stable. They cannot be separated as they are rapidly converted to each other by ring flipping. The energy required for ring flipping is low (though much more than free rotation of sigma bond of ethane) and can be provided by molecular collisions at low temperatures also.

Staggered Conformer
(Chair conformer)

Eclipsed Conformer
(Boat conformer)
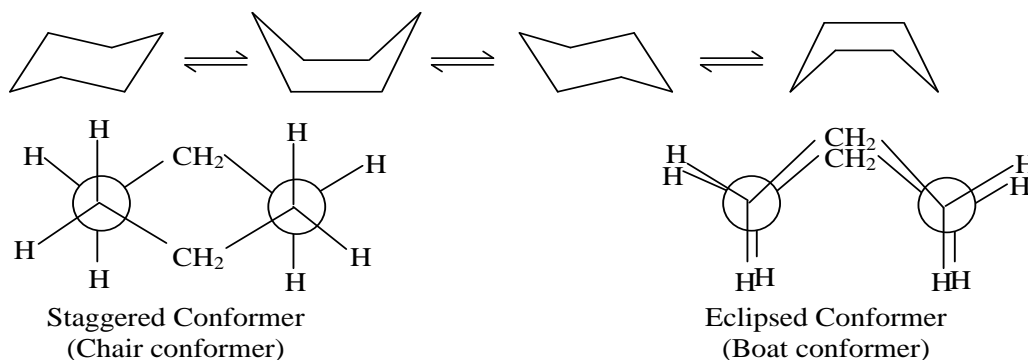
Besides chair and boat conformers, two more conformers of cyclohexane are half chair and twist boat. Half chair can be considered as the transition state for chair and boat interconversion. This is the state when carbon undergoing the flip has just reached in the plane of other four carbon atoms. This half cahir conformer has higher energy than the chair as well as boat conformers because of the strain in the ring when fifth carbon of the cyclohexane comes in the plane. The twist boat conformer is formed from the normal boat conformer so as to minimize the dihedral repulsion in the normal boat conformer. This twisting occurs till the decrease in dihedral repulsion dominates the increase in the angle strain of the ring.

half chair

lesser dihedral repulsion in
twist boat conformer

twist boat
(side view)
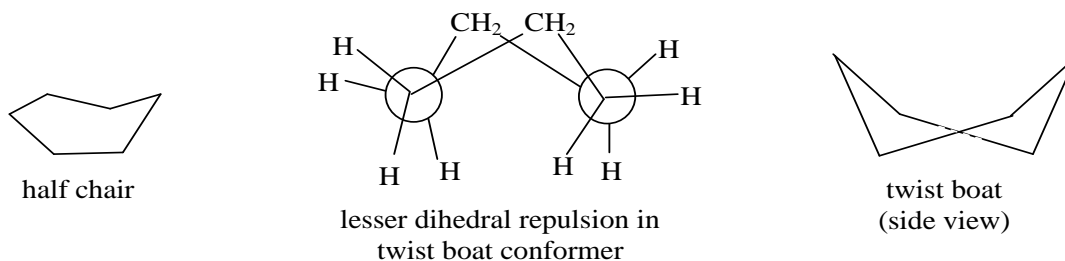
Overall energy order of all the four conformers is Chair < twist boat < normal boat < half chair. The stability order is, therefore, Chair < twist boat < normal boat < half chair. We can assume that the cyclohexane mainly exist in either the chair conformer or the twist boat conformer.

One more important observation is that in cyclohexane, the hydrogen atoms are either axial or equitorial. However, we can not distinguish between axial and equitorial hydrogen because they are rapidly changed to each other. Any ring flipping involves slight rotation along carbon carbon bonds of three carbon atoms, as a result of this slight rotation, axial and equitorial hydrogen atoms of these three carbon atoms are changed to each other.
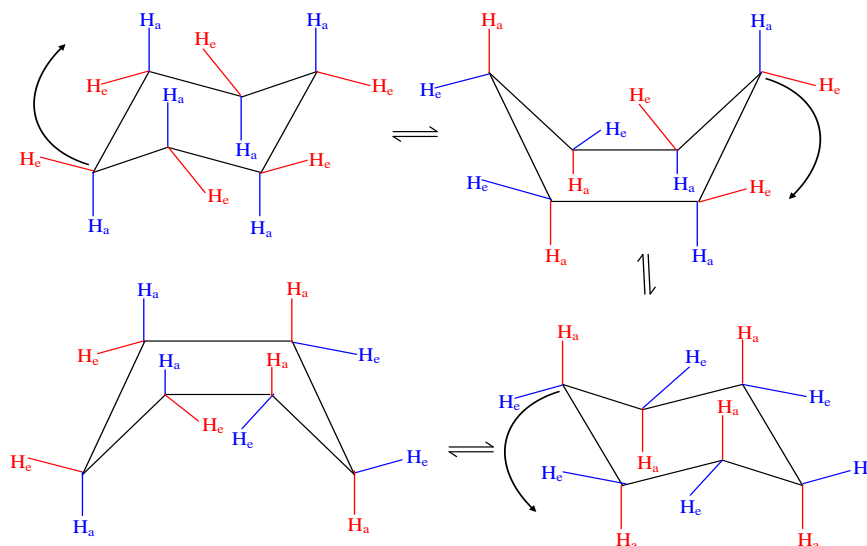
The Difference between the reactivity of axial and equatorial hydrogen or any other group can be observed easily in the cyclohexane systems where ring flipping is either prohibited or very difficult.

We must further remember that when any group is attached to cyclohexane ring, more steric repulsion is experienced by that group when it occupies axial position rather than equatorial position. If such group is very bulky (like tertiary butyl) it is more stable at equatorial position of boat conformer than at axial position of chair conformer. A smaller group like methyl, ethyl etc., is more stable at the axial position of chair conformer than at the equatorial position of boat conformer. The stability of various conformers of disubstituted cyclohexane also depends on these steric repulsions between the groups or the attraction (if any, like intramolecular hydrogen bond, ionic attraction).
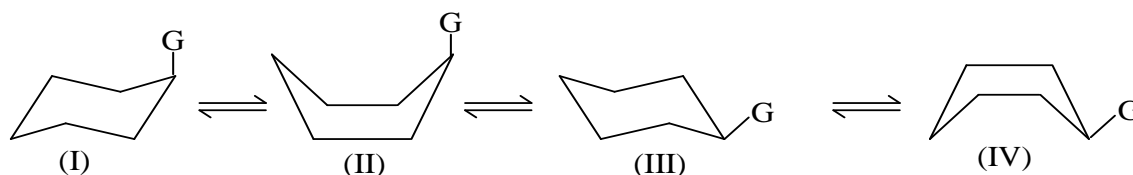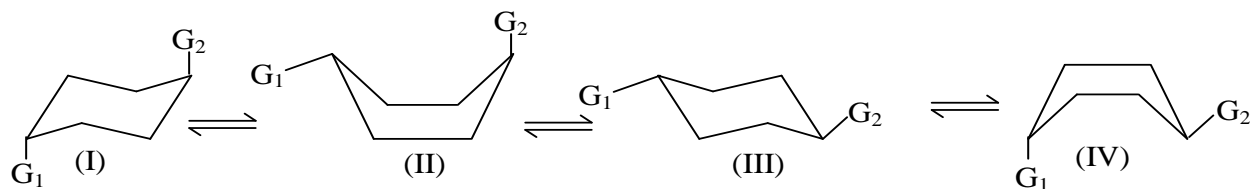

Stability order if group G is small (CH_3, C_2H_5, Cl, OH etc):
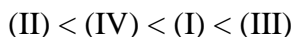
(II) < (IV) < (I) < (III)

Stability order if group G is very bulky (t-Butyl etc):
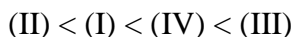
(II) < (I) < (IV) < (III)

Stability order of 1,4-Disubstituted cyclohexane (trans isomer) for different G_1 and G_2 groups is given by:

$G_1 = CH_3$ (small group)	$G_2 = CH_3$ (Small group)	(II) = (IV) < (I) < (III)
$G_1 = CH_3$ (smaller group)	$G_2 = C_2H_5$ (larger group)	(II) < (IV) < (I) < (III)
$G_1 = CH_3$ (smaller group)	$G_2 = t$-Bu (very bulky group)	(I) < (II) < (IV) < (III)
$G_1 = t$-Bu (very bulky group)	$G_2 = t$-Bu (very bulky group)	(I) < (II) = (IV) < (III)

In trans isomer as given above, intramolecular hydrogen bonding & ionic bond is not possible in any conformer.
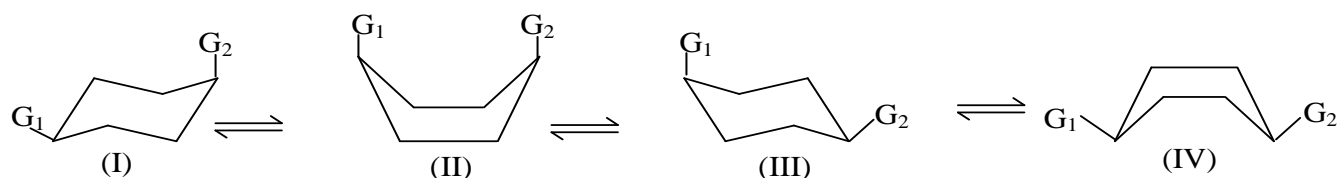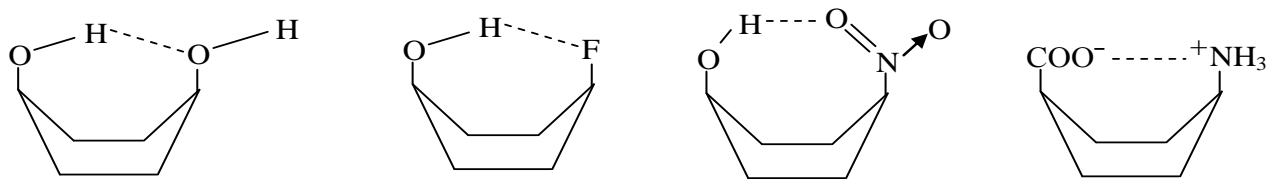

Stability order of 1,4-Disubstituted cyclohexane (cis isomer) for different G_1 and G_2 groups is given by:

$G_1 = CH_3$ (small group)	$G_2 = CH_3$ (Small group)	(II) < (IV) < (I) = (III)
$G_1 = CH_3$ (small group)	$G_2 = C_2H_5$ (Smaller group)	(II) < (I) < (III) < (IV)
$G_1 = t$-Bu (very bulky group)	$G_2 = t$-Bu (very bulky group)	(II) < (I) = (III) < (IV)
$G_1 = OH$ (small group)	$G_2 = OH$ (Small group)	(IV) < (I) = (III) < (II)

In cis isomer as given above, intramolecular hydrogen bonding & ionic bond is also possible in (II) conformer. Some other examples where hydrogen bonding or ionic bond is possible when two groups are at 1,4-position in cis isomers are:

Similarly Hydrogen bonding in 1,3-Disubstituted cyclohexane is possible only when both the groups are at axial positions of chair conformer.

$$G_1 \rightleftharpoons G_2 \rightleftharpoons G_2 \rightleftharpoons$$
(I) (II) (III) (IV)

Stability order of 1,3-Disubstituted cyclohexane (trans isomer) for different G_1 and G_2 groups is given by:

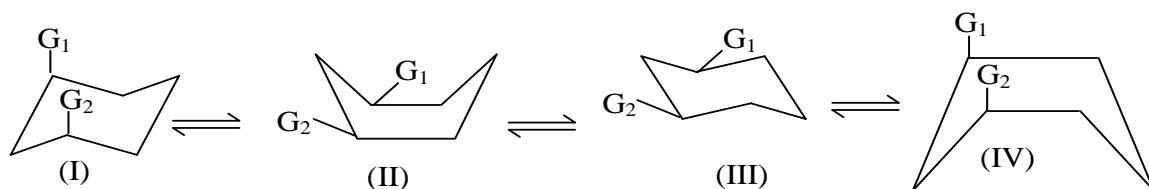| G_1 = CH$_3$ (small group)	G_2 = CH$_3$ (Smaller group)	(II) < (IV) < (I) = (III)
G_1 = CH$_3$ (small group)	G_2 = C$_2$H$_5$ (Smaller group)	(II) < (IV) < (I) < (III)
G_1 = t-Bu (very bulky group)	G_2 = t-Bu (very bulky group)	(II) < (I) = (III) < (IV)

In trans isomer as given above, intramolecular hydrogen bonding & ionic bond is not possible in any conformer.

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

Stability order of 1,3-Disubstituted cyclohexane (cis isomer) for different G_1 and G_2 groups is given by:

G_1 = CH$_3$ (small group)	G_2 = CH$_3$ (Small group)	(IV) < (II) < (I) < (III)
G_1 = CH$_3$ (small group)	G_2 = C$_2$H$_5$ (Smaller group)	(IV) < (II) < (I) < (III)
G_1 = t-Bu (very bulky group)	G_2 = t-Bu (very bulky group)	(IV) < (I) < (II) < (III)
G_1 = OH (small group)	G_2 = OH (Small group)	(II) < (III) < (IV) < (I)

In cis isomer as given above, intramolecular hydrogen bonding & ionic bond is also possible in (I) as well as (IV) conformer.

Similarly Hydrogen bonding in 1,2-Disubstituted cyclohexane is possible only when both the groups are at equitorial (trans isomer) or one at axial and other at equitorial position (cis isomer).
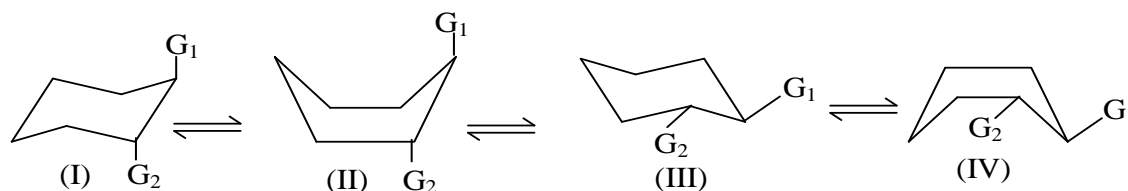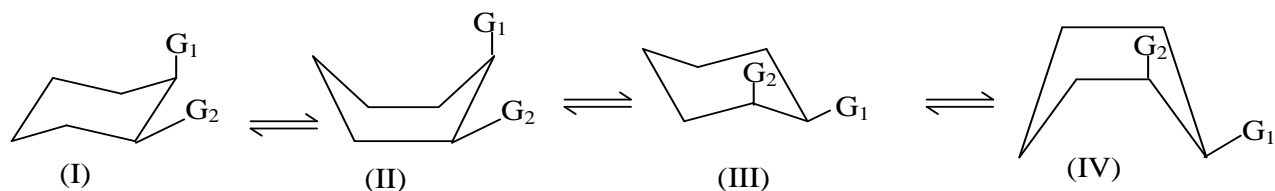

(I) G_2 (II) G_2 (III) (IV)

Stability order of 1,3-Disubstituted cyclohexane (trans isomer) for different G_1 and G_2 groups is given by:

$G_1 = CH_3$ (small group)	$G_2 = CH_3$ (Smaller group)	(II) < (IV) < (I) < (III)
$G_1 = CH_3$ (small group)	$G_2 = C_2H_5$ (Smaller group)	(II) < (IV) < (I) < (III)
$G_1 = $ t-Bu (very bulky group)	$G_2 = $ t-Bu (very bulky group)	(II) < (I) < (IV) < (III)
$G_1 = OH$ (small group)	$G_2 = OH$ (Small group)	(II) < (I) < (IV) < (III)

In trans isomer as given above, intramolecular hydrogen bonding & ionic bond is possible in conformer (III) as well as conformer (IV).

Stability order of 1,2-Disubstituted cyclohexane (cis isomer) for different G_1 and G_2 groups is given by:

$G_1 = CH_3$ (small group)	$G_2 = CH_3$ (Small group)	(IV) = (II) < (I) = (III)
$G_1 = CH_3$ (small group)	$G_2 = C_2H_5$ (Smaller group)	(IV) < (II) < (III) < (I)
$G_1 = $ t-Bu (very bulky group)	$G_2 = $ t-Bu (very bulky group)	(IV) = (II) < (I) = (III)
$G_1 = OH$ (small group)	$G_2 = OH$ (Small group)	(IV) = (II) < (I) = (III)

In cis isomer as given above, intramolecular hydrogen bonding & ionic bond is possible in all conformers.

ISOMERISM

2.2 Geometrical Isomerism

(a) Hindered rotation about carbon−carbon bond

A double bond consists of a σ−bond and a π−bond. The π−bond is formed by the sideways overlapping of unhybridized p−orbitals of two carbon atoms above and below the plane of carbon atoms. If one of the carbon atoms of the double bond is rotated with respect to the other, the p−orbitals will no longer overlap and the π−bond should break, but the breakage of this bond requires 251 kJ mol^{-1} of energy which is not provided by the collisions of the molecules at room temperature. Consequently, the rotation about a carbon−carbon double bond is not free but is strongly hindered or restricted. In other words, a π−bond prevents free rotation of the carbon atoms of the double bond with respect to each other. Due to this hindered rotation, the relative positions of atoms or groups attached to the carbon atoms of the double bond get fixed. For example, H_a and H_b cannot exchange their positions by rotations of C_1 with respect to C_2 without breaking the π−bond.
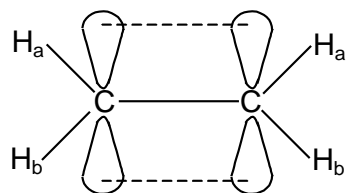
(b) Naming of Configuration of Geometrical Isomers

(i) Cis−trans nomenclature (Common System)

Alkenes can exist in two distinct isomers, which differ from each other only in the relative positions of atoms or groups in space around the double bond. For example, but−2−ene can exist in the following two forms (I and II).

cis−But−2−ene (I)   trans−But−2−ene (II)
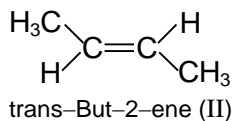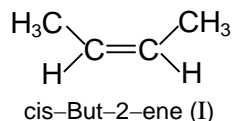
Both these isomers have the same structural formulae but differ in the relative spatial arrangement of hydrogen atoms and methyl groups around the double bond. The isomer I, in which the similar atoms or groups lie on the same side of the double bond is called the **cis−isomer** whereas the isomer II, in which the similar atoms or groups lie on the opposite sides of the double bond is called the **trans−isomer**. It is because of this reason that geometrical isomerism is also called **cis−trans isomerism**.

#### (ii) E & Z nomenclature (IUPAC System)

In the case, two atoms or groups attached to individual C−atoms are assigned priorities. According to this nomenclature, if the atoms or groups of same priority are on the same side of the double bond (or ring), the isomer is designated as **Z** (zusammen, in German means together) and if the two atoms or groups of same priority are on the opposite sides, the isomer is

designated as E (Entegegan, in German means opposite). The priority of a group or atom is based on the rules given below.

Rule 1: The atom of higher atomic number gets higher priority. If the two atoms attached to the double bond are isotopes, the isotope of higher mass number gets the higher priority.


Where * represents C-14 isotope
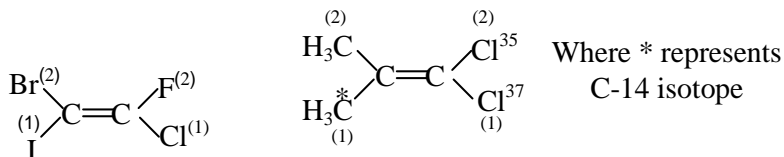
Rule 2: If two atoms directly attached to the concerned atom are identical, then the relative priority of the group is determined by the atomic numbers of the immediate next element of highest atomic number in the group (and so on, if necessary, work outwards till the first point of difference is reached). For example, in the following compound,
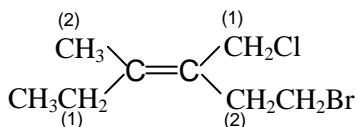
One of the carbon atoms (right side) of the double bond carries CH_2Cl and CH_2CH_2Br groups, since the first atom (i.e. C) attached to the carbon atom of the double bond is the same in CH_2Cl and CH_2CH_2Br groups, compare the atomic number of the immediate next atoms attached to each of these first atoms. Immediate atom in CH_2Cl is Cl and in CH_2CH_2Br is C. Therefore, CH_2Cl gets 1st priority while CH_2CH_2Br gets 2nd priority.

Rule 3: If immediate next atom of highest atomic number is also same, then the number of bonds with such atoms of highest atomic number is considered. The group having more number of bonds with immediate next atom of highest atomic number is given 1st priority. For example,
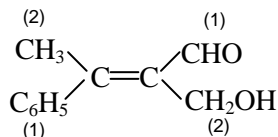
One of the atoms of the double bond carries CH_3 and C_6H_5 group. Since, in C_6H_5 group, the first carbon has more bonds with other carbons it is given 1st priority. Similarly, CHO has two bonds with oxygen while CH_2OH has only one bond with oxygen, CHO group gets higher priority than CH_2OH. Thus, the given isomer is 'E'.

## Necessary and sufficient conditions for geometrical isomerism

All compounds containing double bond necessarily do not show geometrical isomerism.

The necessary conditions for a molecule to exhibit geometrical isomerism are

(i)   The molecule must have restricted rotation either due to the presence of a double bond as C=C, C=N, N=N or due to cyclic structure.
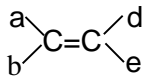
(ii) Each of the above two atoms (having restricted rotation) must have different substituents attached to them individually, which may be same or different. Thus, alkenes of the type abC=Cab and abC=Cde show geometrical isomerism.
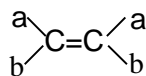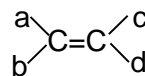

cis–isomer
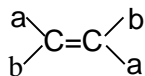
trans–isomer

Z–isomer

E–isomer

(If groups 'a' and 'd' have higher priority)

(If groups 'a' and 'd' have higher priority)

However, geometrical isomerism is not possible, if one or both the doubly bonded carbon atoms carry two similar substituents. This is because in such cases, the two possible configurations are, identical as shown below.

It is because of this reason that terminal alkenes such as propene, but−1−ene, 2−methyl prop−1−ene and alkenes carrying identical substituents on one of the doubly bonded carbon atoms such as 2−methyl but−2−ene and 2, 3−dimethyl but−2−ene etc. do not show geometrical isomerism.

Geometrical isomerism is also shown by compounds which contains $>C=N-OH$, $-N=N-$ structural units because lone pair is also considered as a group. Cyclic compounds also exhibit geometrical isomerism.

Compounds containing $>C=N-OH$ units are commonly called oximes. Oxime of formaldehyde is incapable of showing geometrical isomerism $\overset{H}{\underset{H}{>}}C=N-OH$ while oxime of any other aldehyde (other than formaldehyde) will exhibit geometrical isomerism.
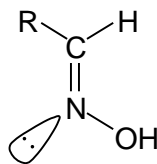
(syn isomer)
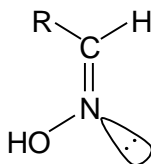
(anti isomer)

The nomenclature for aldoximes is syn (when H and OH are present on same side of the double bond) and anti (when H and OH are present on opposite sides of the double bond).

Oximes of symmetrical ketones $\left[\overset{R}{\underset{R}{>}}C=N-OH\right]$ do not show geometrical isomerism but oximes of unsymmetrical ketones $\left[\overset{R}{\underset{R}{>}}C=N-OH\right]$ are capable of showing geometrical isomerism.
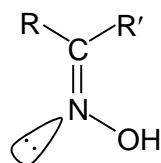
Syn (R′)
or anti (R)
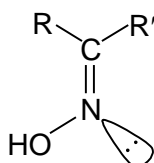
Syn (R)
or anti (R′)

Diazobenzene also exhibit geometrical isomerism.
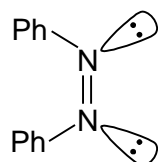
(Syn or cis)
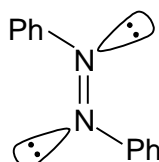
(Anti or trans)

Cyclic compounds too have restricted rotation because of the impossibility of free rotation around C–C single bond as the conformation of cyclic compound would twist on rotation. Appropriately placed substituents on cycloalkanes would be capable of showing geometrical isomerism.
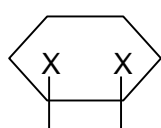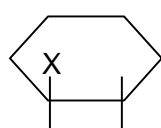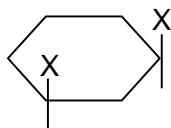
1,2–cis   1,2–trans   1,3–cis   1,3–trans   1,4–cis   1,4–trans

2.3 Optical Isomerism

Ordinary light has vibrations in all possible planes. In plane polarized light, the vibrations are only in one plane. The optical isomers differ in the action on plane polarized light. One of the isomer turn the plane of the polarized light to the right (**dextro rotatory**), the other turn it to the left (**laevo rotatory**). Optical activity is due to molecular asymmetry. Molecular asymmetry implies that the compound should not contain any plane of symmetry or centre of symmetry. A compound containing a single chiral atom (attached to four different atom or group of atoms) would always be optically active but compounds with more than one chiral carbon may not be optically active.

The observed rotation of the plane of polarized light (determined with the help of polarimeter) produced by a solution depends on: (a) the amount of the substance in tube; (b) on the length of the solution examined; (c) the temperature of the experiment; and (d) the wavelength of the light used.

For the measurement of optical rotations, a term **Specific Rotation** is introduced. This is a physical constant characteristic of a substance as much as the melting point, boiling point, density or its refractive index. It is defined as *the number of degrees of rotation 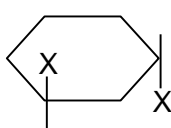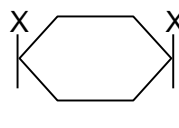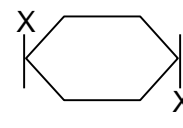observed when light is passed through 1 decimeter (10 centimeters) of its solution having concentration 1 gram per milliliter.* The specific rotation of a given substance can be calculated by using the following expression.

$$[\alpha]_D^{t^o} = \frac{a_{obs}}{l \times c}$$

where $[\alpha]_D^{t^o}$ stands for specific rotation determined at t^oC and using D-line of sodium light; α_{obs} is the observed angle of rotation ; l is the length of the solution is decimeters ; and C is the concentration of the active compound in grams per milliliter. For example, the specific rotation of amyl alcohol (2-methyl-1-butanol) at 25°C for D-line of sodium light is given by

$$[\alpha]_D^{25^o} = -5.756^\circ$$

The sign attached with the angle of rotation signifies the direction of rotation. Negative sign (–) indicates that the rotation is toward the left, while positive (+) sign means that the direction of rotation is toward right.

The rotation may be different in different solvents and this needs to be mentioned while reporting the specific rotation. Thus,

$$[\alpha]_D^{25^o} = +24.7^o (in\ chloroform)$$

The presence of optical activity always proves that a given compound is chiral, but its absence does not prove that the compound is achiral. A compound that is optically inactive may be achiral or it may be a racemic mixture. Organic compounds having atleast one chiral carbon atom or asymmetric carbon atom (a carbon atom attached to 4 different monovalent atom or groups) are always optically active. For example, lactic acid (2–hydroxy propanoic acid) $CH_3CH(OH)COOH$

contains a chiral carbon atom and exhibits optical activity. Lactic acid exists in two forms, one is the mirror image of the other and the two forms are non−super imposable.
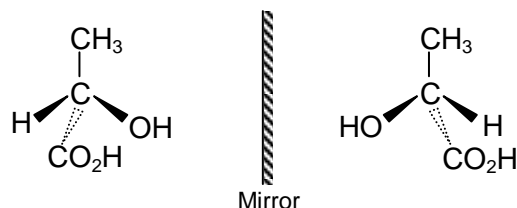
These 3−dimensional projections of lactic acid can be represented on 2−dimension by Fischer projection formula's. In drawing Fischer projection formula from a 3−dimensional projection, the group at the back of the plane (COOH) is pulled to bring in the same vertical plane as that of the CH_3 and the groups projecting in the front (H and OH) will be pushed to bring them on the same horizontal line. Thus, Fischer projection of lactic acid would be drawn as
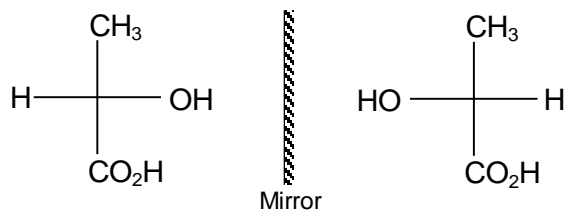
(Note: Fischer projections are drawn only for those molecules, which have chiral carbon atom).

These two isomers are called enantiomers. The stereoisomers, which are related as non superimposable mirror image−object are called enantiomers. One isomer and its enantiomer are mirror images of each other and they are not super imposable. Which of the two forms drawn is dextro or laevo, cannot be known by looking at their structures, it can only be determined experimentally using polarimeter. An equimolar mixture of two enantiomers of lactic acid shows no rotation of plane polarized light, thus it is optically inactive. It is called racemic form or racemic mixture and is designated as (±). The optical rotation of one enantiomer exactly cancels the optical rotation of other so that the net rotation is zero. The enantiomers can be separated from a racemic mixture and the process of separation is called resolution.

Criteria to display optical activity

Although the ultimate criterion to know whether a compound will exhibit optical activity or not is the non−superimposability of the mirror image (chirality) but other tests may also be used that are simpler to apply. One such test is the presence of any element of symmetry like plane of symmetry, centre of symmetry and an alternating axis of symmetry. The last element of symmetry as it is out of syllabi, so only first two symmetry elements are discussed below.

(i) **Plane of symmetry:** A plane of symmetry (also called a mirror plane) is a plane passing through the molecule such that the molecule is divided into 2 equals parts, one part being the mirror image of other (the plane acting as a mirror). For example,
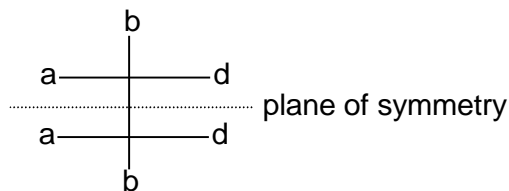
Such an isomer is called meso isomer, which is optically inactive due to the presence of plane of symmetry.

(ii) Centre of symmetry: A center of symmetry is an imaginary point within the molecule such that a straight line drawn from any part or element of the molecule to the center and extended an equal distance on the other side encounters an equal part or element. For example, 2, 4–dimethyl cyclobutane–1, 3–dicarboxylic acid possess a centre of symmetry, which is the centre of the ring. Centre of symmetry can be at the centre of molecule or over an atom or midway between a bond.
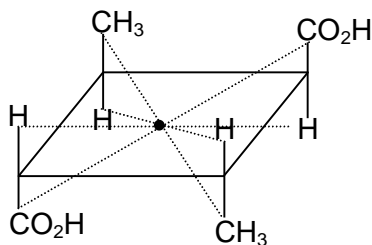
Another important example of the compound having a centre of symmetry is the trans form of dimethyl keto piperazine. The compound exists in two forms–cis and trans. The cis form of the compound exists in two enantiomeric forms but the trans form has a centre of symmetry and therefore, it is optically inactive.

cis–dimethyl ketopiperazine   trans–dimethyl ketopiperazine
(centre of symmetry)
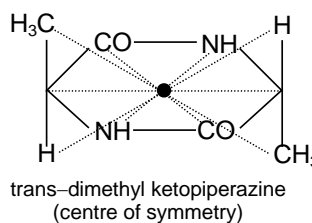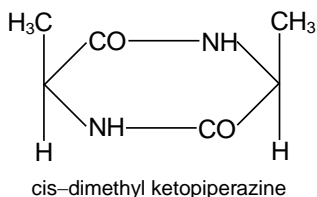
Similarly, α–truxillic acid is optically inactive because of the presence of a centre of symmetry.

α–truxillic acid
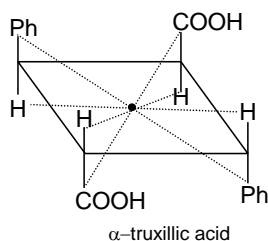
It must be noted that only even–membered rings can possess a centre of symmetry. It is not found in odd–membered rings.

Let us see the optical activity of 2–butanol.
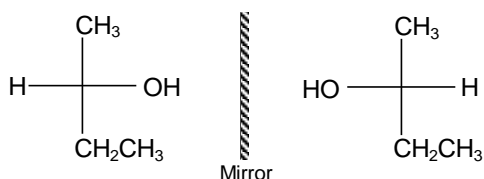
Structures I and II are mirror images of each other and are not super imposable. They are enantiomers of 2–butanol. A pair of enantiomers is always possible for molecules that contain one tetrahedral carbon atom with four different groups attached to it. The carbon atom C^2 is called a stereocentre.

Let us now see the optical activity in 2,3–dibromopentane. 2,3–dibromopentane has two asymmetric carbon atoms. The total number of stereoisomers is 2^n where n is the number of dissimilar asymmetric C atoms. The stereoisomers are
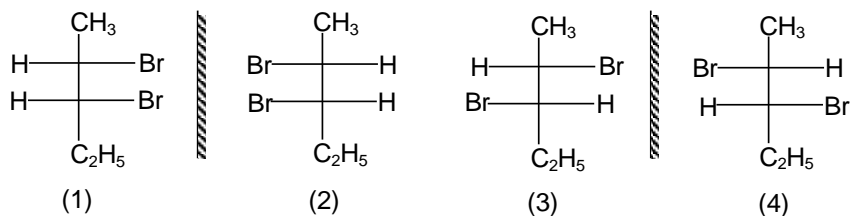
Structures (1) and (2) are mirror images of each other and so are enantiomers. Structures (3) and (4) are also mirror images of each other and they form another set of enantiomers, all stereoisomers 1 to 4 are optically active. Structures (1) and (3) are stereoisomers but they are not mirror images of each other. They are called diastereomers and they have different physical properties like melting point, boiling point and solubilities.

Physical and chemical properties of enantiomers are as follows

1. Enantiomers have identical physical properties like boiling point, melting point, solubility etc.

2. They rotate the plane of polarized light in opposite directions, though in equal amounts. The isomer that rotates the plane to the left (counterclockwise) is called the laevo isomer and is designated as (–), while the one that rotates the plane to the right (clockwise) is called the dextro isomer and is designated as (+). Because they differ in this property they are often called **optical antipodes**.

3. The chemical properties of enantiomers are the same towards achiral reagents, solvents, catalysts and conditions. Towards chiral reagents, solvents, catalysts and conditions enantiomers react at different rates. The transition states produced from the chiral reactant and the individual enantiomers are not mirror images. They are diastereomeric and hence have different enthalpies. The $\Delta H^{\neq}$ values are different for the two and hence the rates of reaction and the amounts of product formed. Their rates may be so far apart that one enantiomer undergoes the reaction at a convenient rate while the other does not react at all.

Resolution of Racemic Mixture

Although pure compounds are always optically active, if they are composed of chiral molecules, mixtures of equimolar amounts of enantiomers are optically inactive since the equal and opposite rotations cancel. Such mixtures are called **racemic mixtures or racemates**. Their properties are not always the same as those of the individual enantiomers. The properties in the gaseous or liquid state or in solution usually are the same, since such a mixture is nearly ideal, but properties involving the solid state, such as melting points, solubilities and heats of fusion, are often different. Thus, racemic tartaric acid has a melting point of 204−206°C and a solubility in water at 20°C of 206 g/litre, while for the (+) or the (−) enantiomers, the corresponding data are 170°C and 1390 g/litre. The separation of a racemic mixture into its two optically active components is called **resolution**. The methods used for the resolution of a racemic mixture are

(i) Mechanical Separation: In rare cases, the crystals of (+) enantiomer can be hand separated from those of the (−) enantiomer of the racemate.

(ii) Chemical Separation: Pasteur was the first investigator to resolve a racemate chemically and his method is used even today. For example, an optically pure compound, a (+) base, is reacted with a racemic acid, resulting in two salts: a (+) (+) salt and a (−) (+) salt. Since these are diastereomers, they have different solubilities and are separable by fractional crystallization, after which the enantiomers are recovered. If the diastereomers are liquids, they may be separable by fractional distillation, or chromatography.

(iii)Biochemical Separation: A third method, also used successfully by Pasteur, takes advantage of the fact that microorganisms usually can metabolize only one enantiomer of a racemate, while leaving behind a pure solution of the unused one. Now a days, the same result is obtained by using the enzyme that catalyzes the cell reaction rather than the whole microbe.

(iv) Separation Using Chromatography: Another technique is to pass a solution of a racemate through a chromatography column containing a chiral adsorbent. One of the enantiomer is preferentially adsorbed or may be preferentially eluted. A variant of this method is to elute with a chiral solvent.

Those stereoisomers, which are not mirror images are called diastereomers. Diastereomers have different physical properties. e.g. melting and boiling points, refractive indices, solubilities in different solvents, crystalline structures and specific rotations. Because of their differences in solubility, they often can be separated from each other by fractional crystallization. Because of slight differences in molecular shape and polarity, they can also be separated from each other by chromatography. Diastereomers have different chemical properties towards both chiral and achiral reagents. Neither any two diastereomers nor their transition states are mirror images of each other and so will not necessarily have the same energies. The $\Delta H^{\neq}$ values will be somewhat different and thus the rates of reaction will differ. However, since the diastereomers have the same functional groups, their chemical properties are not too dissimilar.

ISOMERISM

Number of optical isomers

As it has been discussed above, a compound containing two dissimilar carbon atoms can exist in four optically active forms. Reasoning in the same fashion, we will find that a compound containing three such asymmetric carbon atoms can exist in eight different configurations which represent optical isomers. Thus in general, the number of stereoisomers for a compound with n distinct (different) asymmetric carbon atoms is 2^n.

When an organic compound contains two similar asymmetric carbon atoms in its molecule, abdC−Cabd, the number of optically active isomers would be less than 2^n. Thus, tartaric acid [$HO_2CCH(OH)CH(OH)CO_2H$] has two similar asymmetric carbon atoms and exists in only three forms, of which two are optically active and one is optically inactive (meso form). Thus, the general guidelines for predicting the number of optical isomers are given as under.

1. **When the molecule is unsymmetrical:**

   Number of d and l isomers (a) = 2^n.

   Number of meso forms (m) = 0.

   $\therefore$ Total number of optical isomers (a + m) = 2^n.

   where n is the number of chiral carbon atom(s).

   Common example is $CH_3CH(Br)CH(Br)COOH$.

2. **When the molecule is symmetrical and has even number of chiral carbon atoms:**

   Number of d and l isomers (a) = 2^{n-1}.

   Number of meso forms (m) = $2^{\frac{n}{2}-1}$.

   $\therefore$ Total number of optical isomers = (a + m).

Common example is tartaric acid, $HOOCCH(OH)CH(OH)COOH$.

3. **When the molecule is symmetrical and has an odd number of chiral carbon atoms:**

   Number of d and l forms (a) = $2^{n-1} - 2^{\frac{n}{2} - \frac{1}{2}}$.

   Number of meso forms (m) = $2^{\frac{n}{2} - \frac{1}{2}}$.

   $\therefore$ Total number of optical isomers = (a + m) = $2^{(n-1)}$.

   Common example is $CH_3CH(OH)CH(OH)CH(OH)CH_3$.

Chirality in absence of chiral atom

You will be astonished to see that the compounds even if they do not have the chiral atom can still show optical activity. Allenes, cumulenes, biphenyls, spirane derivatives are some examples. Here are few cases where the molecule is chiral and shows optical activity and optical isomerism even though no chiral atom is present.
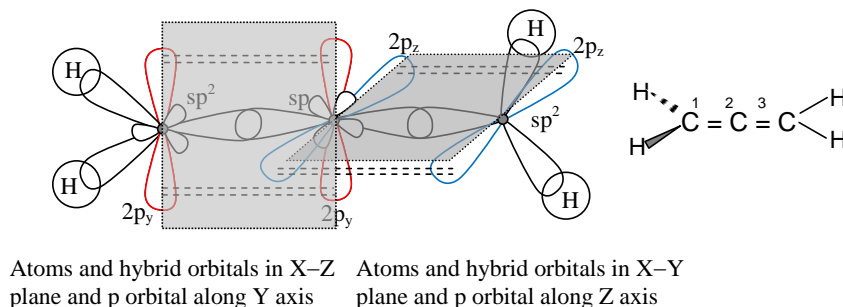
(i) Trans Cycloalkene

Trans form of double bond of a ring is chiral and optically active.
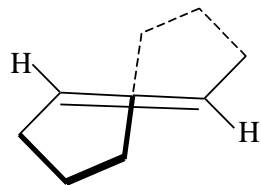
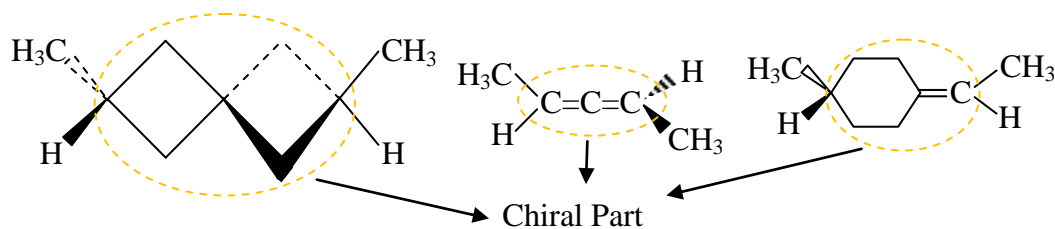### (ii) Allenes, cumulenes, spirane and their derivatives

If two terminal carbon connected through even number of continuous double bonds or rings (or double bonds plus rings), then two groups attached to one such carbon and the two groups attached to other such carbon will exist in different plane.

If we see the structure, C^1, C^3 are sp^2 hybridised but C^2 is sp hybridised. The participation of orbitals for C^1 clearly are $(s + p_x + p_z)$, for C^2 $(s + p_x)$ and for C^3 $(s + p_x + p_y)$ considering C–C–C–bond is along X–axis. Therefore, the orbital picture can be shown as

Atoms and hybrid orbitals in X–Z   Atoms and hybrid orbitals in X–Y
plane and p orbital along Y axis   plane and p orbital along Z axis

Therefore, within the molecule two distinct planes arise and any one or all of them may be plane of symmetry or may be none. Very clearly, if $R^1 = R^2$, $R^3 \neq R^4$ then X–Z plane within the compound will bisect it into two equal halves. So, X–Z plane will be the plane of symmetry. However, none is the plane of symmetry if both terminal carbon atoms are attached individually with two different groups (as shown ahead).
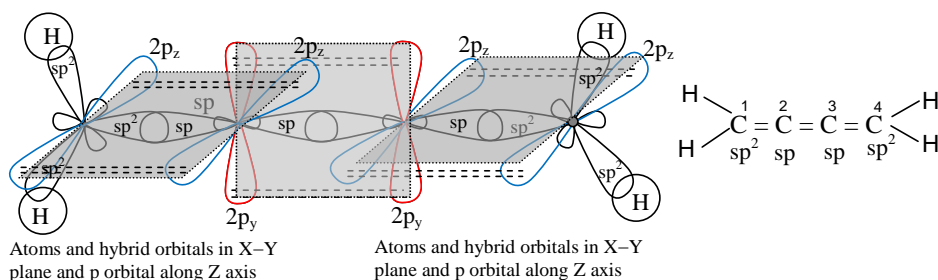
Chiral Part

Such chiral parts will show optical activity and optical isomerism but will not show geometrical isomerism.

However, if two terminal carbon connected through odd number of continuous double bonds or rings (or double bonds plus rings), then two groups attached to one such carbon and the two groups attached to other such carbon will exist in same plane.

If we see the structure, C^1, C^4 are sp^2 hybridised but C^2, C^3 is sp hybridised. The participation of orbitals for C^1 is ($s + p_x + p_y$), for C^2 is ($s + p_x$), for C^3 is ($s + p_x$) and for C^4 ($s + p_x + p_y$) considering C−C−C−bond is along X−axis. Therefore, the orbital picture can be shown as

Atoms and hybrid orbitals in X−Y plane and p orbital along Z axis

Atoms and hybrid orbitals in X−Y plane and p orbital along Z axis

Therefore, within such molecules all atoms or groups are in one plane (having plane of symmetry). Such parts will not show optical isomerism due to plane of symmetry. However, they will show geometrical isomerism if both terminal atoms are individually attached to two different groups.

cis isomer

trans isomer
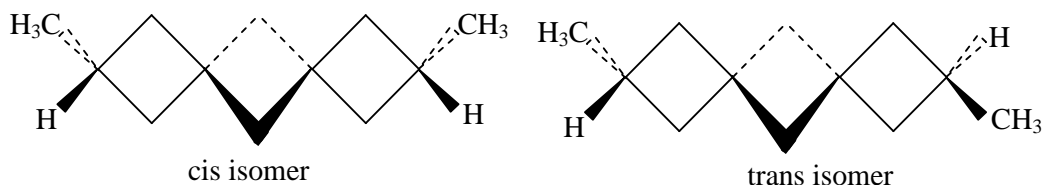
(iii) Biphenyl System

For the biphenyl compounds having all sp^2 hybridized carbon atoms if the o, o′−substituents are very bulky then to release steric strain, the rotation around C−C bond axis takes place causing permanent loss of planarity of the compound.

Here as the o, o′ groups are very bulky biphenyl rings change their planarity as shown. Now the bulky groups are situated at 90° angle apart. Hence, none of the planes X−Y or X−Z are the planes of symmetry. So, compound is optically active.

X–Y plane   X–Z plane
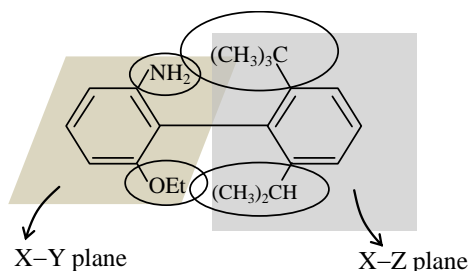
Such compounds having individually unsymmetrical biphenyl in perpendicular plane with restricted rotation will be chiral and optically active because there is no plane or centre of symmetry.
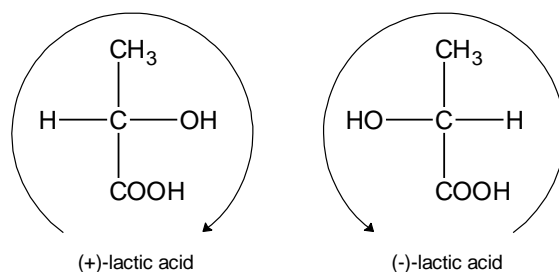
## Absolute and Relative Configuration

While discussing optical isomerism, we must distinguish between *relative* and *absolute* configuration (arrangement of atoms or groups) about the asymmetric carbon atom. Let us consider a pair of enantiomers, say (+)⁻ and (–)⁻ lactic acid.

(+)-lactic acid   (-)-lactic acid

We know that they differ from one another in the direction in which they rotate the plane of polarised light. In other words, we know their relative configuration in the sense that one is of opposite configuration to the other. But we have no knowledge of the absolute configuration of the either isomer. That is, we cannot tell as to which of the two possible configuration corresponds to (+) - acid and which to the (–) - acid.

D and L system

The sign of rotation of plane-polarized light by an enantiomer cannot be easily related to either its absolute or relative configuration. Compounds with similar configuration at the asymmetric carbon atom may have opposite sign of rotations and compounds with different configuration may have same sign of rotation. Thus *d*-lactic acid with a specific rotation + 3.82° gives *l*-methyl lactate with a specific rotation -8.25°, although the configuration (or arrangement) about the asymmetric carbon atom remains the same during the change.

+3.82   -8.25°
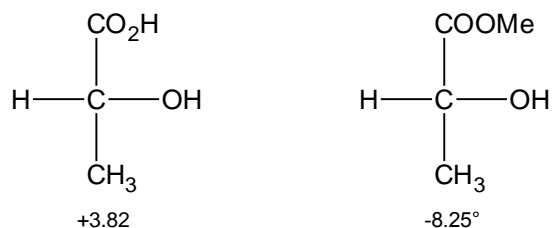
Obviously there appears to be no relation between configuration and sign of rotation. Thus D/L-system has been used to specify the configuration at the asymmetric carbon atom. In this system, the configuration of an enantiomer is related to a standard, glyceraldehyde. The two forms of glyceraldehyde were arbitrarily assigned the absolute configurations as shown below.

(+)-glyceraldehyde   (-)-glyceraldehyde
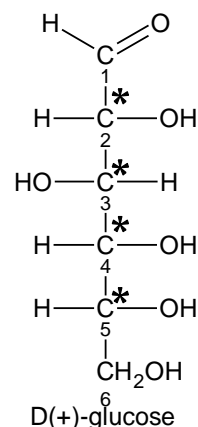
D configuration   L configuration
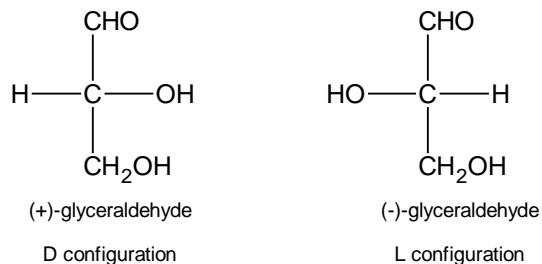
If the configuration at the asymmetric carbon atom of a compound can be related to D (+)-glyceraldehyde, it belongs to D-series; and if it can be related to L(−)-glyceraldehyde, the compound belongs to L-series. Thus many of the naturally occurring α-amino acids have been correlated with glyceraldehyde by chemical transformations. For example, natural alanine (2-aminopropanoic acid) has been related to L(+)-lactic acid which is related to L(−)-glyceraldehyde. Alanine, therefore, belongs to the L-series.

In general, the absolute configuration of a substituent (X) at the asymmetric centre is specified by writing the projection formula with the carbon chain vertical and the lowest number carbon at the top. The D configuration is then the one that has the substituent 'X' on the 'right' of the asymmetric carbon, whereas the L configuration has the substituent 'X' on the 'left'. Thus,

D configuration   L configuration
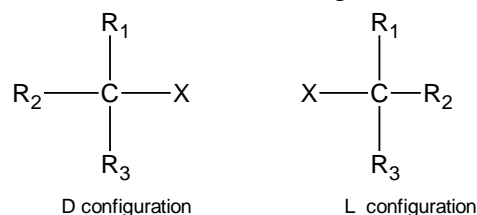
When there are several asymmetric carbon atoms in a molecule, the configuration at one centre is usually related directly or indirectly to glyceraldehyde, and the configurations at the natural (+)-glucose there are four asymmetric centres (marked by asterisk). By convention for sugars, the configuration of the highest numbered asymmetric carbon is referred to glyceraldehyde to determine the overall configuration of the molecule. For glucose, this atom is C–5 and, therefore, OH on it is to the right. Hence the naturally occurring glucose belongs to the D-series and is named as D-glucose.

D(+)-glucose

*However, it must be clearly understood that lower case d and l (or + and -) refer to the direction of rotation of plane polarised light, which is a measured physical constant. It is not necessarily related to configuration around asymmetric carbon. Capital **D** and **L** are now used to refer to the absolute configuration around the asymmetric carbon.*

R and S System

This is a newer and more systematic method of specifying absolute configuration to optically active compounds. Since it has been proposed by R.S. Cahn, C.K. Ingold and V. Prelog, this system is also known as **Cahn-Ingold-Prelog system.** This system of designating configuration has been used increasingly since the early 1960's and may eventually replace the DL-system.

Cahn-Ingold-Prelog system is based on the actual three-dimensional or tetrahedral structure of the compound. In order to specify configuration about an asymmetric carbon *C *abde*, the groups *a, b, d* and *e* are first assigned and order of priority determined by the 'sequence rules'. These rules will be given later. For the present, let us assign priorities 1, 2, 3, 4 to the groups *a, b, d, e*. Thus the order of priorities may be stated as

$$a > b > d > e$$
$$(1) \quad (2) \quad (3) \quad (4)$$

Now the tetrahedral model of the molecule is viewed from the direction opposite to the group *'e'* of lowest priority (4). The **'conversion rule'** says that :

(i) If the eye while moving from $a \to b \to d$ travels in a clockwise or right-hand direction, the configuration is designated **R** (Latin, *Rectus* = right).

(ii) If the eye while moving from $a \to b \to d$ travels in counterclockwise or left-hand direction, the configuration is designated S (Latin, *Sinister* = left).
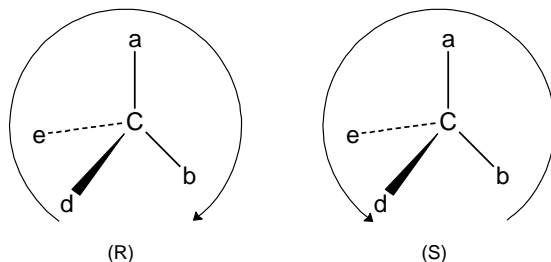
The **sequence rules** to determine the order of priorities of groups are

Rule 1: The atom of higher atomic number gets higher priority. If the two atoms attached to the double bond are isotopes, the isotope of higher mass number gets the higher priority.

Rule 2: If two atoms directly attached to the concerned atom are identical, then the relative priority of the group is determined by the atomic numbers of the immediate next element of highest atomic number in the group (and so on, if necessary, work outwards till the first point of difference is reached). For example, in the following compound,

Rule 3: If immediate next atom of highest atomic number is also same, then the number of bonds with such atoms of highest atomic number is considered. The group having more number of bonds with immediate next atom of highest atomic number is given 1st priority.

ISOMERISM

If more than one asymmetric centre is present in a molecule, the configuration at each centre is specified by the symbol **R** or **S** together with the number of the asymmetric carbon. Thus L-lactic acid has the configurations (2R, 3R).

Optical Isomerism in Compounds with more than One Chiral Carbon

In the above discussion we have seen that an asymmetric carbon atom can produce molecular asymmetry. Thus the molecules containing an asymmetric carbon exist in two optically active forms, (+)-isomer and (−)-isomer, and an equimolar mixture of the two, (±)-mixture, which is optically inactive. When there are two or more asymmetric carbon atoms in a molecule, the problem is complicated considerably.

An organic compound which contains **two dissimilar asymmetric carbons,** can give four possible stereoisomeric forms. Thus 2-bromo-3-chlorobutane may be written as
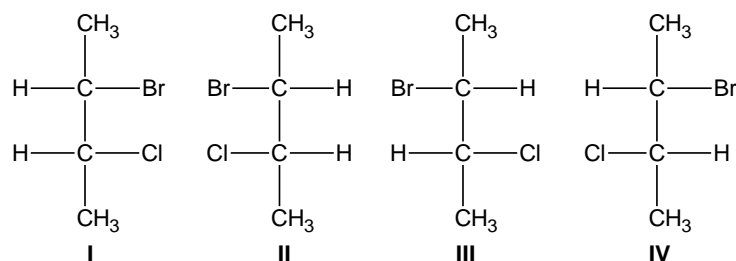
$$H_3C \overset{*}{\underset{\underset{Br}{|}}{CH}} \overset{*}{\underset{\underset{Cl}{|}}{CH}} CH_3$$
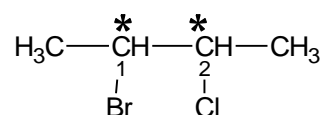
The two asymmetric carbons in its molecular are dissimilar in the sense that the groups attached to each of these are different.

$$C_2 \text{ has } CH_3, H, Br, CHClCH_3$$

$$C_3 \text{ has } CH_3, H, Cl, CHBrCH_3$$

Such a substance can be represented in four configurational forms.

The forms I and II are optical enantiomers (related as object and mirror image) and so are forms III and IV. These two pairs of enantiomers will give rise to two possible racemic modifications.

It may be noted that forms **I (2 S, 3S)** and **III (2 S, 3 R)** are not mirror images or enantiomers, and yet they are optically active isomers. Similarly, the other two forms *i.e.,* **II (2 R, 3 R)** and **IV (2 R, 3 S)** are also not enantiomers but optically active isomers.