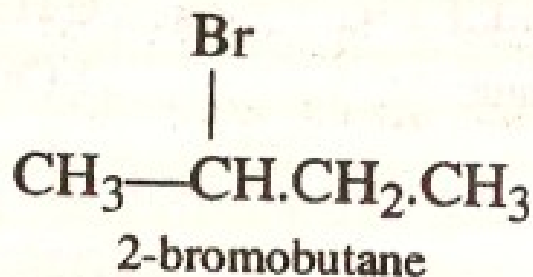# Stereochemistry

INTRODUCTION : The part of the science with deals with structure in the three dimensions is called Stereo-chemistry.

Different compounds which have the same molecular formula are known as isomer ; and the phenomenon is known as 'isomerism' .

The existence of two isomeric forms of 2-bromobutane and 1, 2-dibromoethylene can only be explained with the help of their three-dimensional structures.

$$\underset{\text{2-bromobutane}}{CH_3 - \overset{\overset{\displaystyle Br}{\displaystyle |}}{C}H.CH_2.CH_3} \qquad\qquad \underset{\text{1, 2-dibromoethylene}}{Br.CH = CHBr}$$
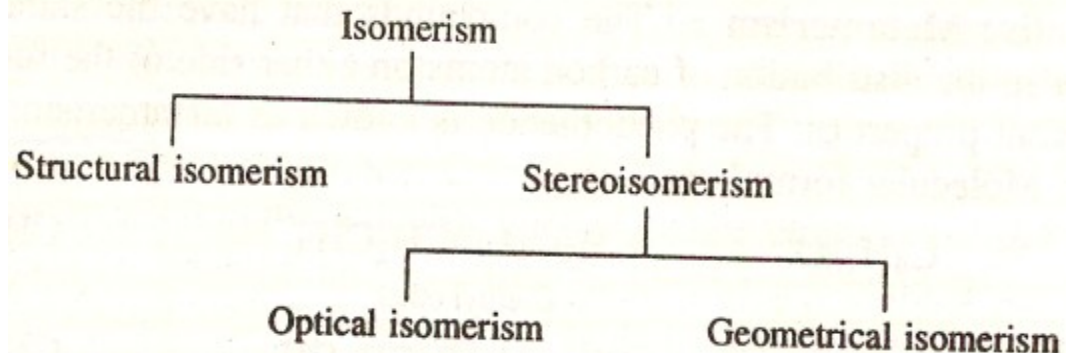
Stereochemistry

The isomers which have the same structural formula but differ in the spatial arrangement of various substituent atoms or groups are called stereoisomers and phenomenon is known as stereoisomerism.

TYPES OF ISOMERISM : On the basis of the different arrangement of atoms or groups in the molecule as well as in space, the isomerism may be classified into two catagories, viz.,

(i)   Structural isomerism
(ii) Stereoisomerism

Stereochemistry

(i) **Structural Isomerism:** Structural isomerism is due to the difference in structure and is exhibited in following different ways :

(a) Chain or nuclear isomerism

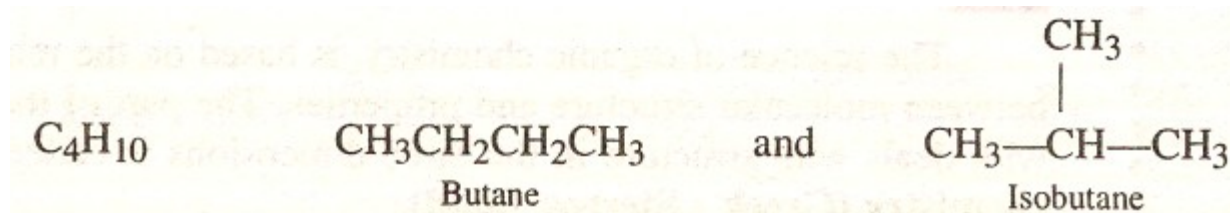(b) Positional isomerism

(c) Functional isomerism

(d) Metamerism

(e) Tautomerism   .

(a) Chain isomerism-: The compounds that have the same molecular formula but differ in the arrangement of the carbon skeleton in the molecule and hence different properties. The phenomenon is known as chain isomerism.
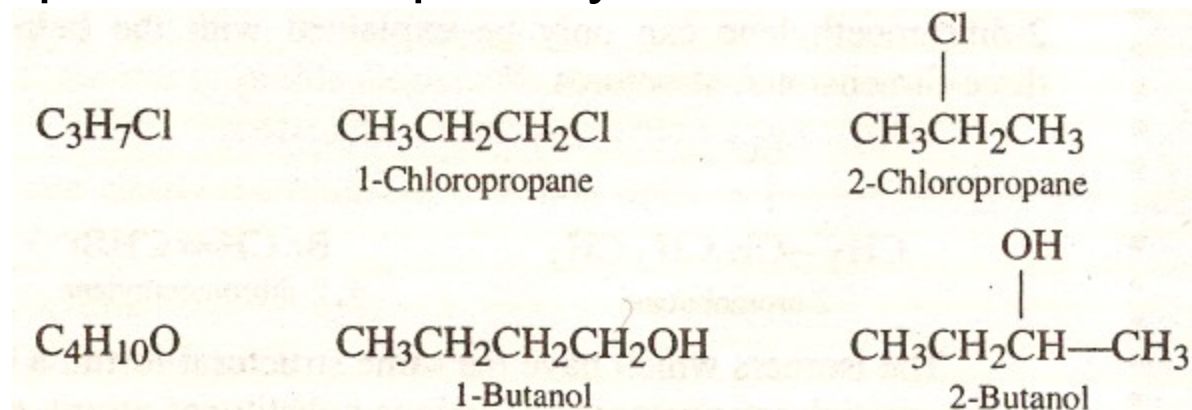
Stereochemistry

Example :

Molecular formula :

$$C_4H_{10} \qquad CH_3CH_2CH_2CH_3 \qquad \text{and} \qquad \underset{\text{Isobutane}}{CH_3—\overset{\displaystyle CH_3}{\overset{|}{C}H}—CH_3}$$

Butane

(b) Positional isomerism: Positional isomerism is exhibited by compounds having same carbon skeleton but differing in the position occupied by the substituent group.

Example :

Molecular formula :

$$C_3H_7Cl \qquad \underset{\text{1-Chloropropane}}{CH_3CH_2CH_2Cl} \qquad \underset{\text{2-Chloropropane}}{CH_3CH_2\overset{\displaystyle Cl}{\overset{|}{C}}H_3}$$

$$C_4H_{10}O \qquad \underset{\text{1-Butanol}}{CH_3CH_2CH_2CH_2OH} \qquad \underset{\text{2-Butanol}}{CH_3CH_2\overset{\displaystyle OH}{\overset{|}{C}}H—CH_3}$$
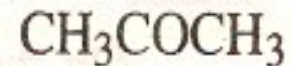
Stereochemistry

(c) Functional isomerism: Functional isomerism is exhibited by compounds having different functional groups, *i.e.,* compounds with the same molecular formula but belonging to different homologous series. **Example :**
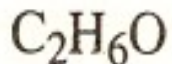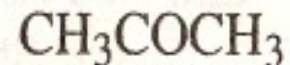
Molecular formula :
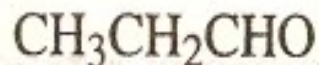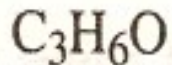
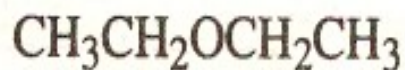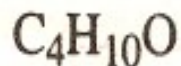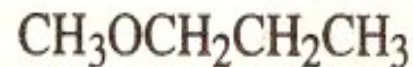| C_3H_6O	CH_3CH_2CHO	CH_3COCH_3
	Propionaldehyde (aldehyde)	Propanone (ketone)
C_2H_6O	CH_3CH_2OH	CH_3COCH_3
	Ethanol (alcohol)	Dimethyl ether (ether)

Stereochemistry

(d) Metamerism: The compounds that have the same molecular formula but differ in the distribution of carbon atoms on either side of the functional group and hence different properties. The phenomenon is known as metamerism.

Example :
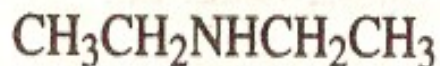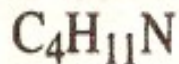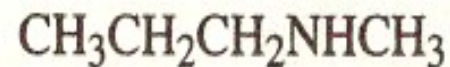
Molecular formula :

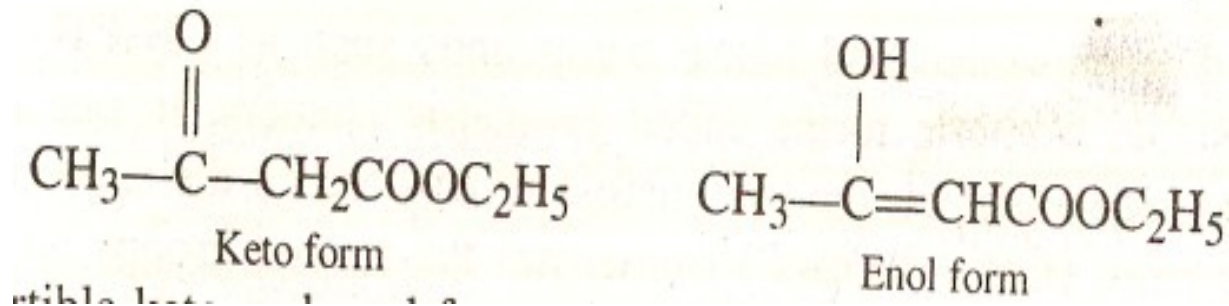| $C_4H_{10}O$	$CH_3CH_2OCH_2CH_3$	$CH_3OCH_2CH_2CH_3$
	Diethyl ether	Methyl propylether
$C_4H_{11}N$	$CH_3CH_2NHCH_2CH_3$	$CH_3CH_2CH_2NHCH_3$
	Diethyl amine	Methyl propylamine

Stereochemistry

(e) **Tautomerism:** It is a special type of structural isomerism in which the isomers are in dynamic equilibrium with each other, *e.g.,* ethyl acetoacetate is an equilibrium mixture of the following keto-enol form :

$$CH_3—\overset{\overset{\displaystyle O}{\|}}{C}—CH_2COOC_2H_5 \qquad CH_3—\overset{\overset{\displaystyle OH}{|}}{C}=CHCOOC_2H_5$$

Keto form   Enol form

Interconvertible keto and enol form of a compound are known as 'tautomers' and their interconversion is called tautomerization.

Stereochemistry

Other examples of tautomerism :

(a) Phenol ⇌ Cyclohexadienone

(b) $CH_3-\overset{\overset{O}{\|}}{C}-H$ (Acetaldehyde) (Keto) ⇌ $CH_2=\overset{\overset{OH}{|}}{C}-H$ (Vinyl alcohol) (Enol)
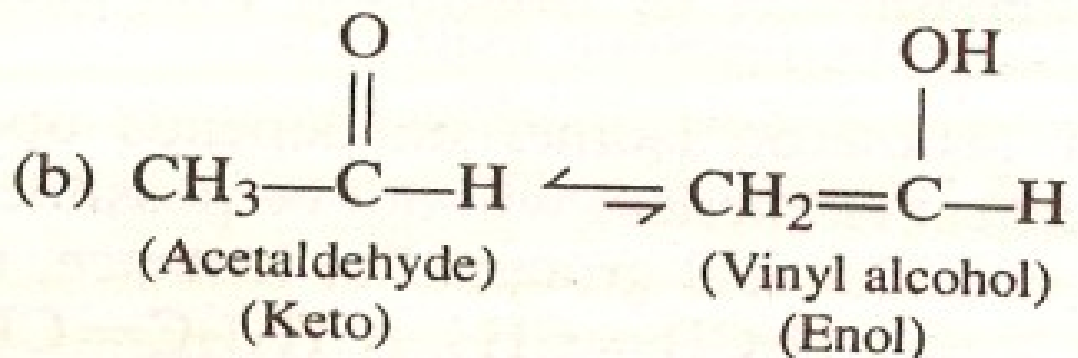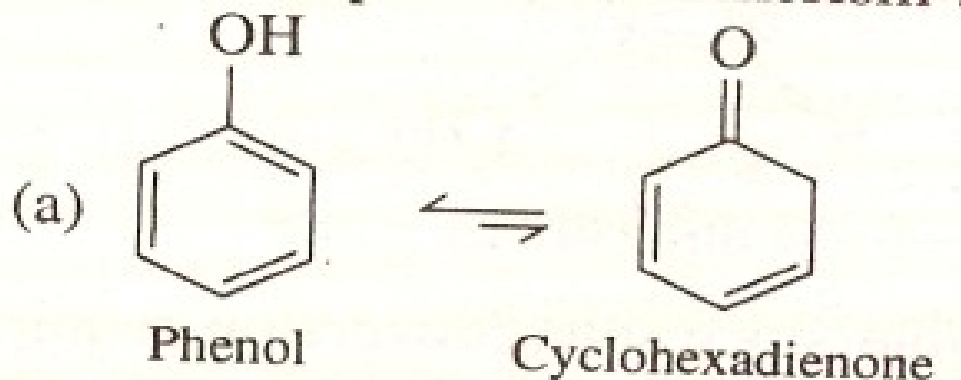
Stereochemistry

(ii) Stereoisomerism : Stereoisomerism is defined as isomerism in compounds of identical structures but differing in spatial arrangement of atoms. Stereoisomers thus have the same structural formula but differ in the spatial arrangement of the various substituent atoms or groups.

Stereoisomers are roughly divided into two classes :

(a) Conformational isomerism   (b) Configurational isomerism

(a) Conformational isomerism: The stereoisomers which are non superimposable but easily interconvertible by rotation about single bonds are known as conformational isomers or conformer or conformational enantiomers or conformational diastereomers. This type of isomerism is found in alkanes and cycloalkanes.

Stereochemistry

(b) Configurational stereoisomers: The stereoisomers which are non-superimposable and non-interconvertible by rotation around single bonds are known as 'configurational isomers' and the phenomenon is known as configurational isomerism.

These isomers may further be divided into two parts :

(i) Geometrical isomers (Diastereomers)   (ii) Optical isomers (Enantiomers)

(i) Geometrical Isomerism :

Geometrical isomerism (also known as cis-trans isomerism) is a consequence of the spatial geometry associated with double bond which restricts rotation about it.

Stereochemistry

This process, which is really a transfer of electrons from the π molecular orbital to the p-atomicorbital is associated with high energy requiring about 60 kcal/mole energy. Thus at ordinary temperatures, rotation about a double bond is prevented and hence compounds such as $CH_3CH=CHCH_3$ exist is isolable and stable isomeric forms called geometric isomers. In one isomer, called cis isomer, the two methyl groups are on the same side of the double and while the trans isomer has the methyl groups on opposite sides of the double bond.

cis-2-Butene   trans-2-Butene
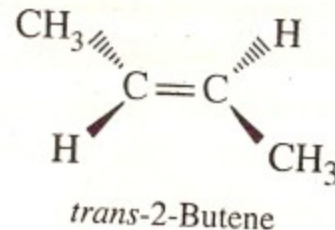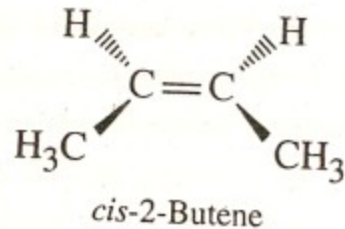
Stereochemistry

The two compounds are normally quite stable since interconversion requires high energy and can only be achieved at high temperatures or by irradiation with ultraviolet light.

E and Z system of nomenclature of geometrical isomers :

When, there are three or four different atoms or groups attached to the carbon atoms of a double bond, it is difficult to assign cis or trans designation to the geometric isomers.

Example :
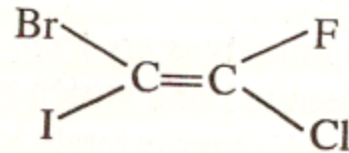
Stereochemistry

It is difficult to name the such substance either the *cis* or the *trans* isomer. To eliminate this confusion, a more general system for designating configuration about a double bond has been adopted. This method, which is called the *E* **and** Z system, is based on a priority system originally developed by Cahn, Ingold and Prelog for use with optically active substances. The following simple steps need to be followed fdr specifying the configuration.

(i)   Assign a priority number 1 or 2 to groups on each carbon atoms of the double

bond.

(ii) Compare the priority of groups (or atom) at one carbon relative to the other.

Stereochemistry

(iii) The configuration is represented as Z (German; Zusammen-together) if both the first priority groups are on the same side of the double bond. If the first priority groups are on opposite sides of the diouble bond, the configuration is *E* (enteggen-across).

Atoms or groups are assigned priority by the following rules :

(a) Substituents are listed in order of decreasing atomic number of the atom directly joined to the carbon. Higher priority is assigned to atoms (directly attached to the carbon atom) of higher atomic number.

(b) Where two or more of the atoms connected to the asymmetric carbon are the same, the atomic number of the second atom determines the order.

If isotopes of the same element are attached, the

Stereochemistry

isotope with higher mass number will have a higher priority. If the priority cannot be decided by rule, it is then determined by comparing the next atoms in the group and so on.

(c) A doubly or triply bonded atom is considered equivalent to two or three such atoms. Thus a carbonyl group is considered as if, carbon had two single bonds to oxygen, i.e.,

$$\mathrm{>C=O} \quad \text{equal to} \quad \mathrm{>C-O} \atop \mathrm{\underset{O}{|}}$$
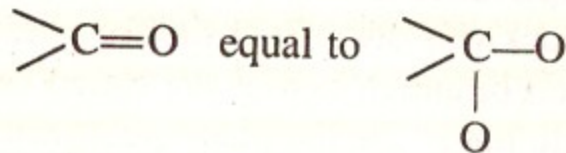
Stereochemistry

Example : Let us consider an' example of an alkene in which one of the doubly bonded carbon atom has Br and I and the other has F and Cl Since I has a higher atomic number than Br, it is assigned higher priority; Similarly Cl is of higher priority than F in the second olefinic carbon atom.
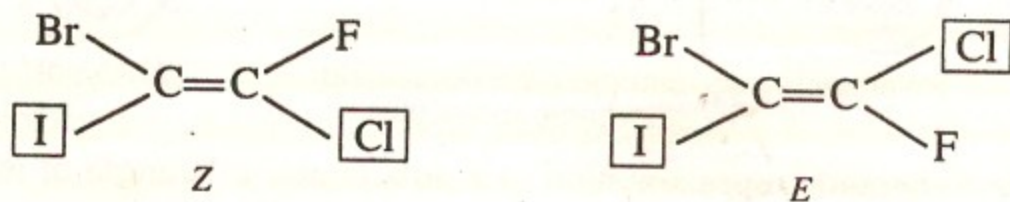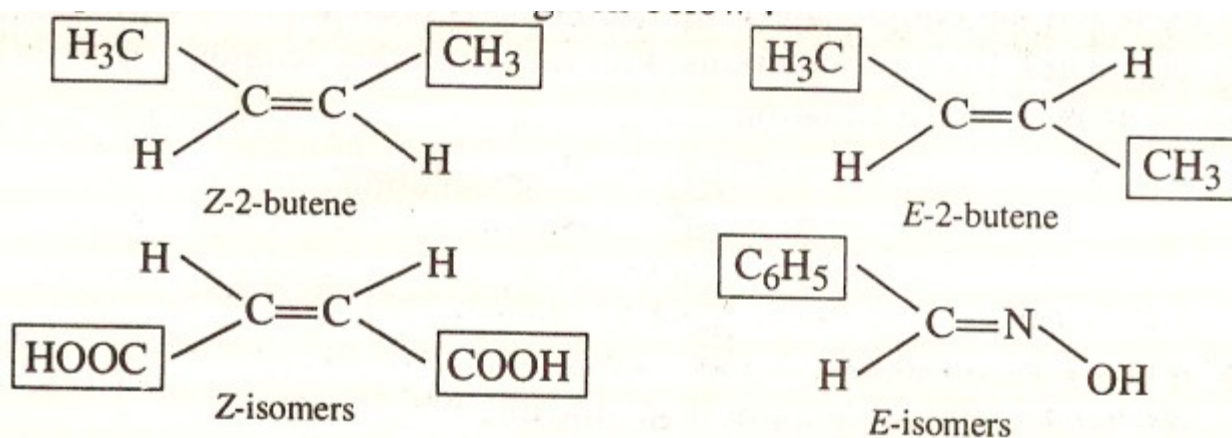

Thus it is the E and Z configurations of the two isomers of I-bromo-2-chloro-2-fluoro-I-iodo-ethene.

The ▢ breaketed group, indicates group of higher priority on the respective olefinic carbon atom.

Stereochemistry

Some examples of E-Z isomers are given below:

H_3C CH_3 $C=C$ H H
Z-2-butene

H_3C H $C=C$ H CH_3
E-2-butene

H H $C=C$ $HOOC$ $COOH$
Z-isomers

C_6H_5 $C=N$ H OH
E-isomers

(ii) Optical Isomerism :

Certain compounds can exist in two stereoisomeric forms whose molecular struc-tures cannot be superimposed on one another. Such a pair of compounds is known as optical isomers and phenomenon as optical isomerism. Inspite of this difference in the molecular arrangement,

Stereochemistry

the physical properties of such isomers are identical, e.g., they have the same melting points, boiling points, etc. Solutions of certain organic compound when placed in the path of plane polarised light, rotate the plane of polarisation to a certain fixed angle. This property of rotating plane of polarisation is known as optical activity

and such compound are said to be optical active. The substances which rotate the plane-polarized light to the right or clockwise are called dextro rotatory and those which rotate to the left or anticlockwise are called laevo rotatory. The substances which do not rotate the plane-polarized light either way are said to be optically inactive.
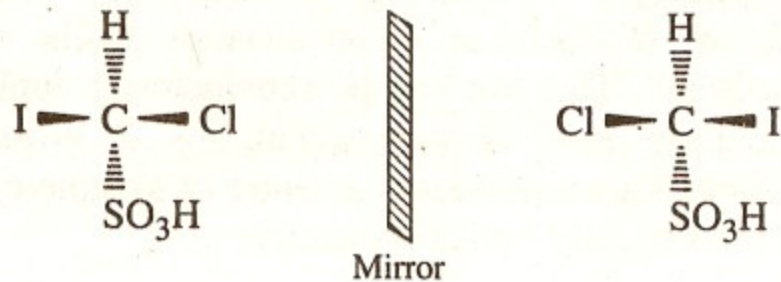
Stereochemistry

Enantiomerism: Isomers whose structures differ only in being mirror-images of each other and they have identical physical properties except the direction of rotation of plane-polarized light. Such isomers are called enantiomers and the phenomenon is known as enantiomerism. The enantiomers react at different rates and form products in different amounts in asymmetric. environment. They have different solubilities in same chiral solvent. They act at different rates, if anyone of the reagent solvent or catalyst is chiral. A substance composed of equimolecular amounts of a pair of enantiomers is a racemic modification.
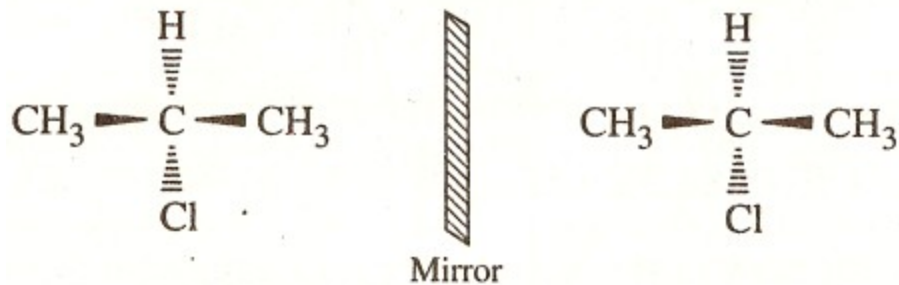
Stereochemistry

CHIRALITY: Molecules that are not superimposable on their mirror images are chiral (Greek, Cheir, 'handedness'). A hand and a glove are chiral objects whereas a ball and a cube are achiral objects. Achiral objects can be superimposed on their mirror images. There is close relationship between chirality and optical activity and quite often the scriptions optically active and chiral are interchangeably. Chirality in molecules is usuaily due to the presence of an sp3 carbon atom with 'our different groups attached to it. Such a molecule has no plane of symmetry (a plane f symmetry divides a molecule in such a way that one half is the mirror image of the ther halt) and exists as a pair of enantiomers. A chiral carbon is the one" in which all the four substituents are different. Such 3 carbon atom is sometimes also referred to as asymmetric carbon atom.

Stereochemistry

Chloroiodomethanesulfonic acid
Not superimposable : enantiomers

Isopropyl chloride
Superimposable : not enantiomers

Stereochemistry

The chiral center: A carbon atom to which four different groups are attached is a chiral center. Many but not all molecules that contain a chiral center are chiral. Many but not all chiral molecules contain a chiral center. There are molecules that contain chiral centers and yet are achiral. (Such achiral molecules always contain more than one chiral center), if there is only one chiral center in a molecule. we can be certain that the molecule is chiral. There are chiral molecules that contain no chiral centers.
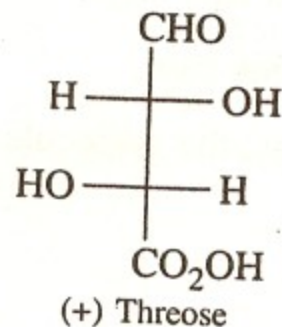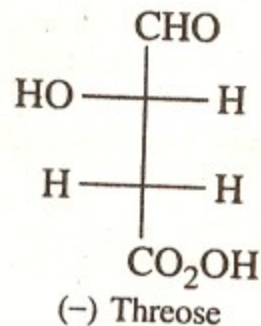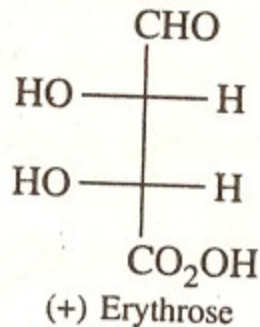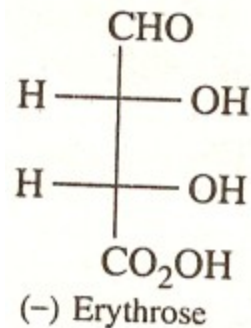
Stereochemistry

DIASTEREOMERS: Stereoisomers that are not mirror images of each other are called diastereomers. Compounds such as 2-chloro-3-hydroxybutanedioic acid have two dissimilar chiral carbon atoms and hence exists in four stereoisomeric forms. Stereoisomer **I** or **II** is a diastereomer of **III** and **IV**. Diastereomers are stereoisomers that are not enantiomers and they have the same configuration at one chiral centre but different configuration at the other.
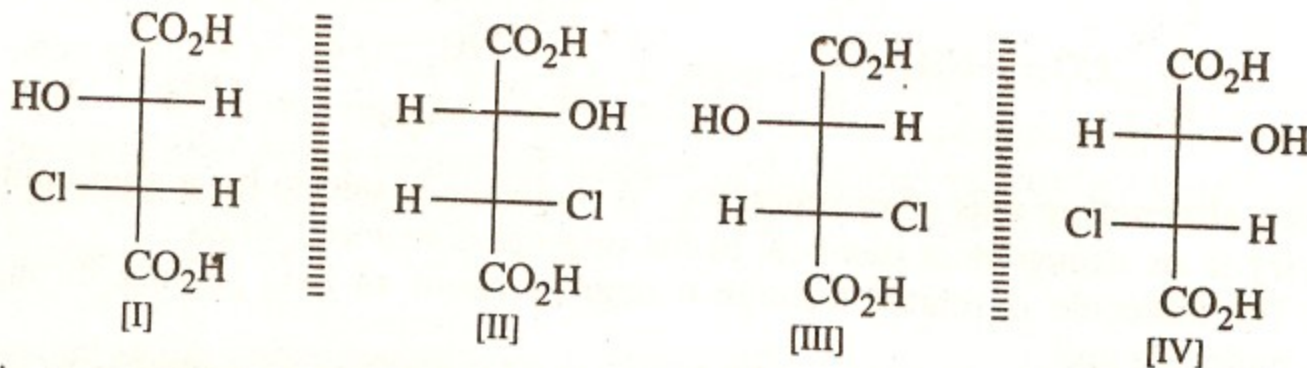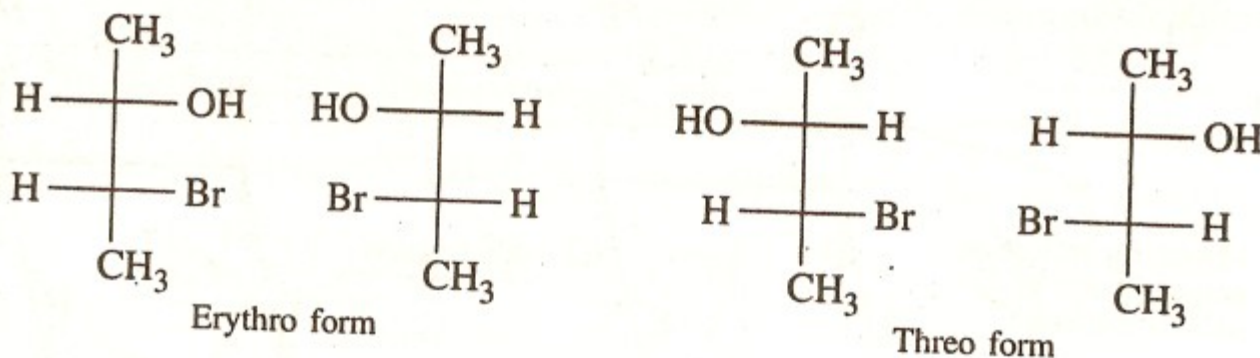
Stereochemistry

Diastereomers have different physical properties and similar but not identical chemical properties. Having different boiling points, melting points, refractive indices, solubilities, densities, molecular shape and polarity, they can be separated from each other by fractional distillation, fractional crystallization, chromatography, etc.

Another example of compounds with two dissimilar chiral carbon atoms are the four carbon sugars, erythrose and threose.

(−) Erythrose   (+) Erythrose   (−) Threose   (+) Threose

Stereochemistry

By analogy, diastereomers of compounds possessing two dissimilarly constituted chiral carbon atoms are commonly distinguished from each other by using prefix threo or erythro. The erythro diastereomer is one in which two like groups on the chiral carbon atoms are on the same side is the Fischer projection' formula as in erythrose. In contrast the threo diastereomer resembles threose as the two like groups are on opposite sides. For example 3-bromo-2-butanol.

Erythro form

Threo form

Stereochemistry

OPTICAL ISOMERISM WITHOUT CHIRAL CENTRES :

Generally the compounds containing an asymmetric carbon shows the optical activity. However, compounds which do not have asymmetric carbon can also shows optical activity if the molecule is dissymmetric.

Example: Allenes: Compounds in which a single carbon atom is connected to two other carbon atoms by a double bond are called allenes. Allene ($CH_2=C=CH_2$) is the simplest member of the series. In allenes the two terminal carbon atoms are sp^2 hybridized and utilize these three hybrid orbitals for forming σ bonds with two hydrogens and a carbon, while the central carbon atom is sp-hybridized and is attached to two carbons through these orbitals forming σ bonds. The central carbon atom still has two p-orbitals available for π-bonding. One of these can overlap to form a π-bond with the p-orbital of one of the methylene groups and the other will overlap in a perpendicular plane with the p-orbital of the other

Stereochemistry

methylene group.

As a consequence of this special geometry of allenes, any allene with the substitution pattern abc = c = cab will exist in two enantiomeric forms.

Example: 1, 3-diphenyl-propadiene exist in two enantiomeric form which are not superimposable to its mirror images and are optically active.


Mirror

1,3-Diphenyl propadiene .
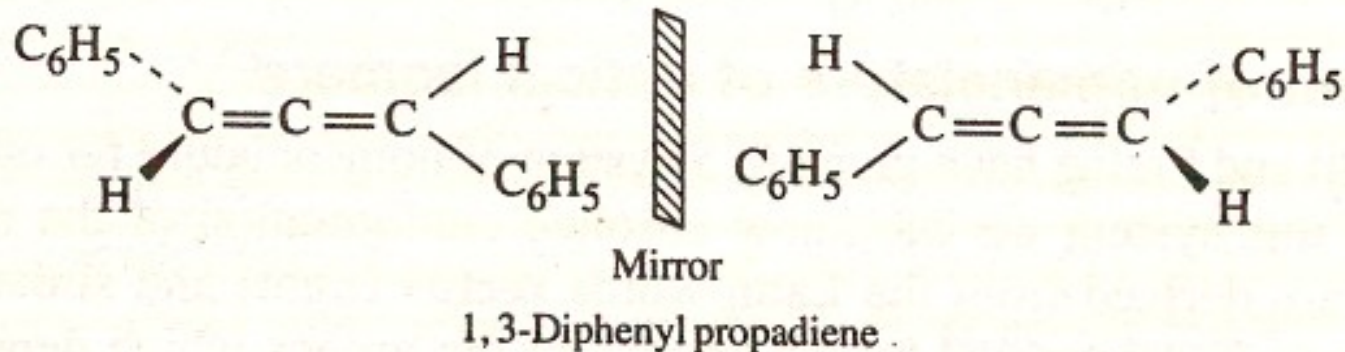
Stereochemistry

Rand S system of nomenclature of optical isomers:

With the help of this system we can know absolute configuration of the molecule. The symbol *R and* S are derived from the Latin words **rectus** (right) and **sinister** (left). The nature of the groups is determined by the priority of the groups which depends upon the following rules :

Rule 1: If the four atoms attached to the chiral center are all different, priority depends on atomic number, with the atom of higher atomic number getting higher priority.
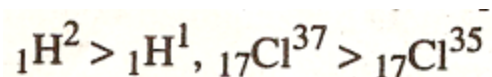
Thus, in bromochloro iodo methane

$$\begin{bmatrix} Cl \\ | \\ F—C—I \\ | \\ Br \end{bmatrix}$$
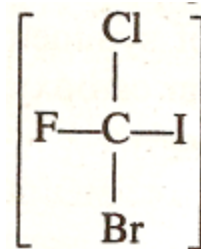
Stereochemistry

The priority sequence of four atoms are I (Z = 53) > Br (Z = 35) > Cl (Z = 17) > F (Z = 9). If two atoms are isotopes of the same element, the atom of higher mass number has the higher priority.

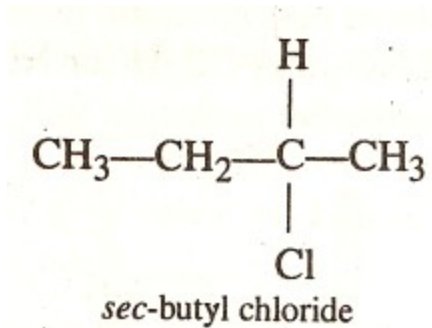**Example:** $_1H^2 > {_1}H^1, \ _{17}Cl^{37} > {_{17}}Cl^{35}$

Rule 2: If two atoms attached to the chiral centre are the same, we compare the atoms attach to each of these first atoms.

Example, in see-butyl chloride, in which two of the atoms attached to the chiral center are themselves carbon. In CH_3 the second atoms are H, H, H; in C_2H_5 they are C, H, H.

Stereochemistry

$$CH_3-CH_2-\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle Cl}{|}}{C}}-CH_3$$

sec-butyl chloride

Since. carbon has a higher atomic number than hydrogen, C_2H_5 has the higher priority. A complete sequence of priority for see-butyl chloride is therefore CI, C_2H_5, CH_3,H.

Rule 3: If there is a double or triple bond, both atoms are considered to be duplicated or triplicated. Thus,

Stereochemistry

$$-C{=}A \quad \text{equals} \quad -\overset{\displaystyle |}{\underset{\displaystyle A}{C}}{-}\overset{\displaystyle |}{\underset{\displaystyle C}{A}}$$

$$-C{\equiv}A \quad \text{equals} \quad -\overset{\displaystyle |}{\underset{\displaystyle A}{C}}{-}\overset{\displaystyle |}{\underset{\displaystyle C}{A}}$$

Example : In glyceraldehyde the OH group has the highest priority of all,

$$\begin{array}{c} H \\ | \\ C{=}O \\ | \\ H{-}C{-}OH \\ | \\ CH_2OH \end{array}$$

Glyceraldehyde

$$-\overset{\displaystyle H}{\underset{}{C}}{=}O \quad \text{equals} \quad -\overset{\displaystyle |}{\underset{\displaystyle O}{C}}{-}\overset{\displaystyle |}{\underset{\displaystyle C}{O}}$$

Stereochemistry

the O, O, H of -CHO takes priority over the O, H, H
of $-CH_2OH$. The complete sequence is then -OH, -CHO,-CH_2OH, -H

After giving priorities to four atoms or groups attached to an asymmetric centre, the molecule is now rotated so that the atom or group of lowest priority is directed away from the viewer. Now, the arrangement of remaining three atoms or groups is viewed in the decreasing order of their priorities. If the eye moves in a clockwise direction, the configuration is assigned as R (Rectus meaning 'right'). While if the eye moves in anti-clockwise direction, the configuration is assigned as S (Sinister, meaning 'left').

Stereochemistry
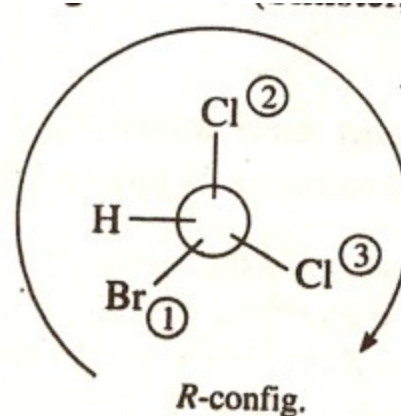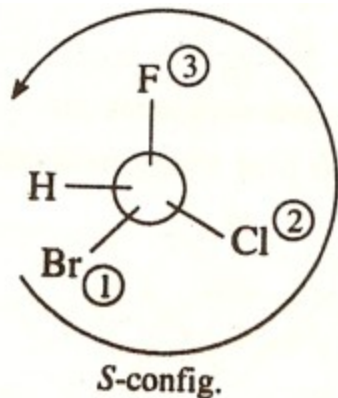
S-config. R-config.

Example : (1) *R and* S configuration of lactic acid, $CH_3CHOHCOOH$. In this case order of priority of different groups is as follows : -OH> -COOH> -CH3> -H Therefore, Rand S configuration are as follows :


R-config. S-config.
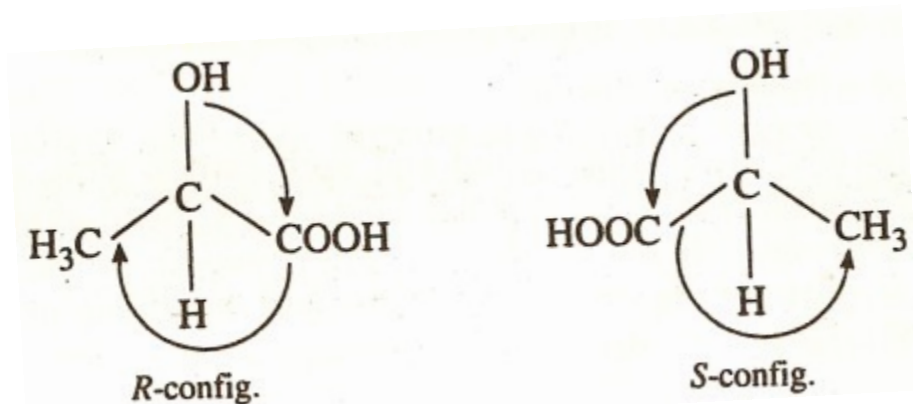
Stereochemistry

CONFORMATIONAL ISOMERISM : Different arrangements of atoms that can be converted jnto one another by rotation about single bonds are called conformations. Evidently, such compounds are capable of existing in large number of isomeric structures which are called rotational or conformational isomers or conformers. Arrangement I is called the eclipsed conformation; arrangement II is called the staggered configuration. To represent such conformations, we shall often use two kinds of three dimensional formulas: andiron formulas and newmann projections .

Stereochemistry
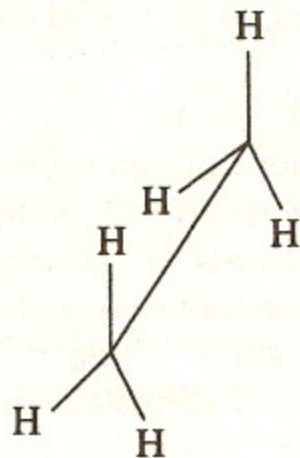
[I]
Elipsed conformations
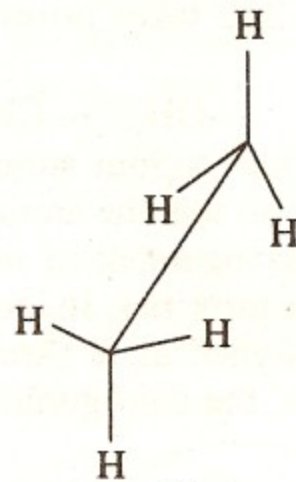
[II]
Staggered conformations
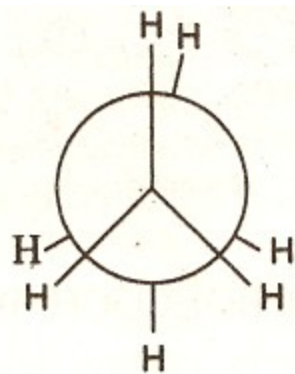
[I]
Eclipsed form
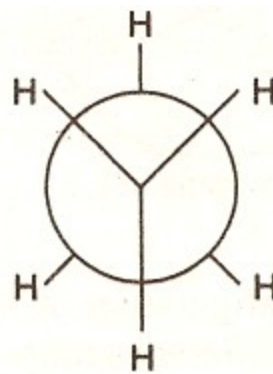
[II]
Staggered form

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Conformations of butane :

n-Butane is a four carbon alkene derived from ethane in which one hydrogen on each carbon is substituted by methyl group. In n-butane, we have to consider several kinds of conformations, one in which the two methyl groups are as far apart as possible in a fully staggered (anti) structure of lowest energy and the two equivalent conformations obtained by a rotation of 120^0 about the central C-C bond in either direction. In the latter

two conformations the methyl groups are closer to each other than allowed by the ordinary vander Waals radii. Therefore, these two conformations, called gauche or skew, are of somewhat higher energy than the *trans* (anti) form and this energy difference has been computed at about 0.8 kcal/mole and is commonly known as n-butane skew interaction. In performing a 360^0 rotation, we come across two different eclipsed forms in which the H and CH_3 are opposed and the third
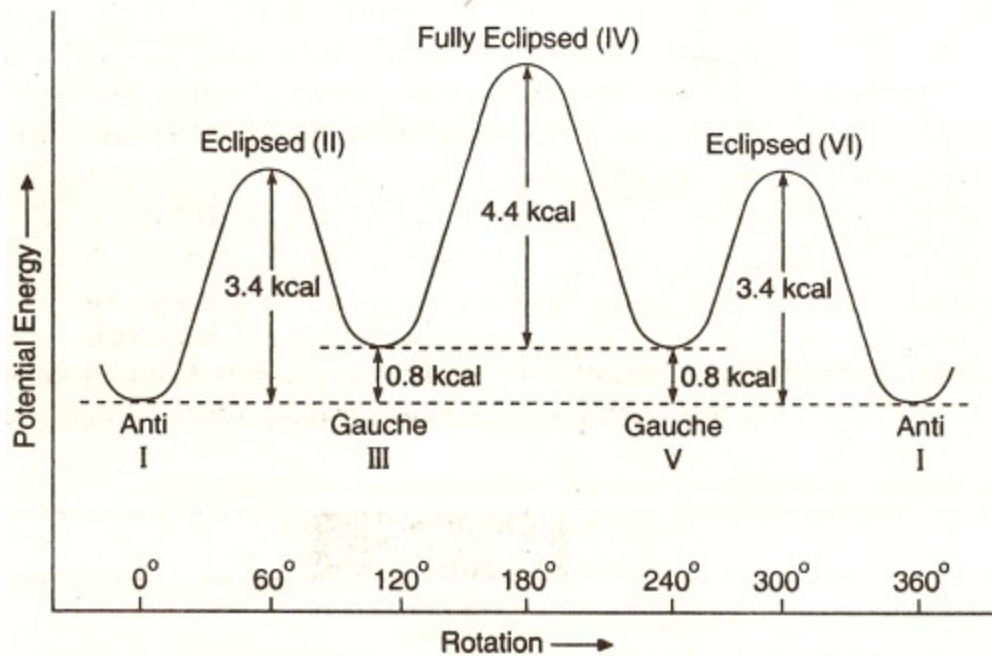
Stereochemistry

in which the two CH_3 groups are opposed. The corresponding energy barriers are 3.4 kcal/mole and 4.4-6.1 kcal/mole, respectively. Thus at ordinary temperatures and in most reactions the molecule can be expected to exist predominantly in the anti-staggered form. Here again the conformational isomers have never been isolated since the energy barriers are too smal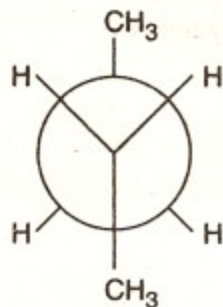l for their long-lived existence in such a non rigid system. **Relative stabilities of the conformations of n-butane:** The energy changes during rotation about C2-C3 bond in n-butane. The difference in energy **I** and **IV** is 5.2 kcal mole^{-1}, between **I** and **III** (or **V**) is about 0.8 kcal mole^{-1}. Therefore **IV** and I would be most stable conformations of n-butane. Conformations **III** and **V** would be slightly less than **I** and **II**; would be slightly more stable than **IV**.
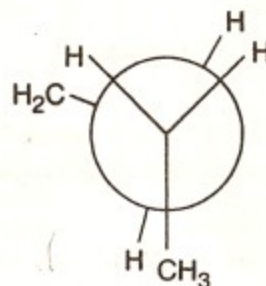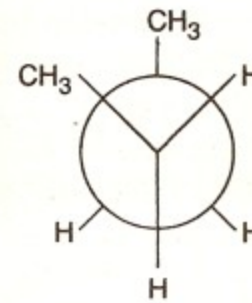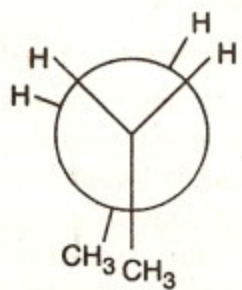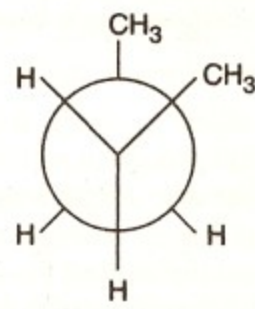
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