

3.2.Principles of Stereochemistry

3.2.1. Stereochemistry

- It is the branch of chemistry which deals with three dimensional arrangements of atoms in a molecule.

3.2.2. Configurational Isomerism

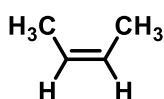
- Different configurations at one or more stereocentres.
- These isomers are non-superimposable and non-interconvertible by simple rotation around single bonds.
- These can be interconverted by breaking and making of bonds.
- These are two types.....(A) Geometrical Isomerism and (B) Optical Isomerism.

3.2.2A. Geometrical Isomerism

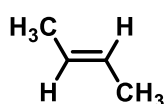
- It is obtained because of restricted rotation of atoms or groups around a covalent bond.
- It is further classified into two categories.....(I) *cis-trans* isomerism and (II) *E-Z* isomerism.

3.2.2A.I. Cis-trans Isomerism

- ❖ Cis-Trans isomerism in acyclic compounds: It is obtained in acyclic compounds due to restricted rotations of atoms or groups about carbon-carbon or carbon-hetero atom double bond
- ❖ In the compounds containing carbon-carbon double bond, if the identical atoms or groups lie on the same side of a π -plane, then the isomer is called cis-isomer, and if the identical atoms or groups lie on opposite sides of a π -plane, the stereoisomer is known as trans-isomer.

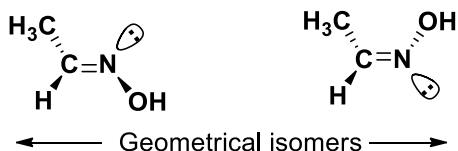


Cis-2-butene

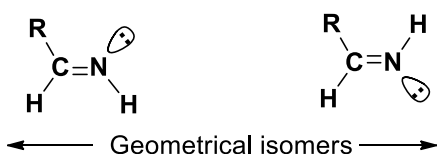


trans-2-butene

- The essential conditions for geometrical isomerism are....
 - The molecule must contain double bond.
 - The two atoms or groups attached to the same carbon atom must be different.
 - There are several functional groups, when present in a compound, involve geometrical isomerism although they do not contain carbon-carbon double bond
 - Oximes contain carbon-nitrogen double bond and may give rise to geometrical isomerism.

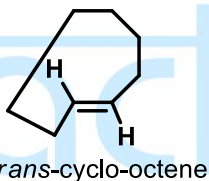
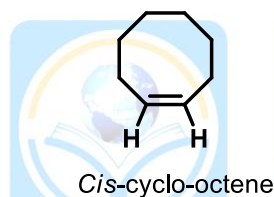


- Imines also contain carbon-nitrogen double bond may give rise to geometrical isomerism.



❖ ***Cis-trans isomerism in cycloalkenes:***

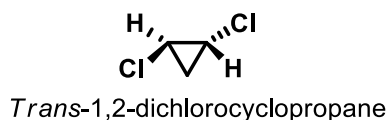
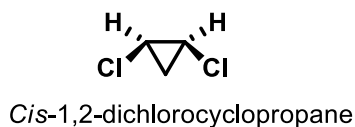
- Cycloalkenes are rigid and therefore exist in cis-form. If the cycloalkene becomes larger, then its flexibility increases and so trans-form exist.
- The smallest cycloalkene for which both cis- and trans-form exist in practice is cyclooctene.



- In larger cyclo-alkenes, trans-isomer exists well.

❖ ***Cis-trans isomerism in substituted cycloalkanes:***

The smaller cycloalkanes are rigid and if they are substituted properly, they may exist as *cis-trans* isomer. If identical atoms or groups are on the same side of the plane, they are called *cis*-isomer if its trans-isomer exist independently.



3.2.2A.II. E-Z Isomerism

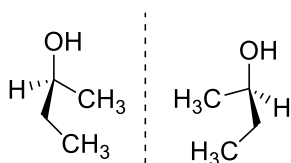
- If the atom or group of similar priority is on the same side of the π -plane, then it will be called Z-isomer. However, if the atom or the group of similar priority is on the opposite side of the π -plane, then it is known as E-isomer.
- The E-Z nomenclature is also applicable for cyclic compounds. If the higher priority groups are on the same side of the ring, then it is called Z-isomer, where as if the groups of higher priority are on the opposite side of the ring then the ring will be E.

3.2.2B. Optical Isomerism

- A substance which is not superimposable on its mirror image is called optically active compound and the phenomenon is known as optical isomerism.
- The instrument with the help of which optical activity is measured, is called polarimeter.
- The stereoisomer which rotates the plane polarized light in the clockwise direction is called “Dextrorotatory” and the other one which rotates the plane polarized light towards anticlockwise then it is called “Levorotatory”.
- Dextrorotatory isomer is designated as *d* or (+) and Levorotatory isomer is designated as *l* or (-).

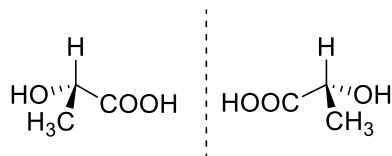
3.2.3. Chirality

- The compound which rotates the plane of plane polarized light is called optically active/chiral molecule and which does not rotate the plane of plane polarized light is called optically inactive/achiral compound.
- The above said property of a molecule is known as optical activity/chirality and optical inactivity/achirality.
- The carbon of a molecule with which four different atoms or groups of atoms are attached is called chiral carbon or asymmetric carbon or stereogenic centre or stereocentre or chiral centre.



3.2.4. Enantiomers

- The stereoisomers which are non superimposable on its mirror image are called enantiomers.

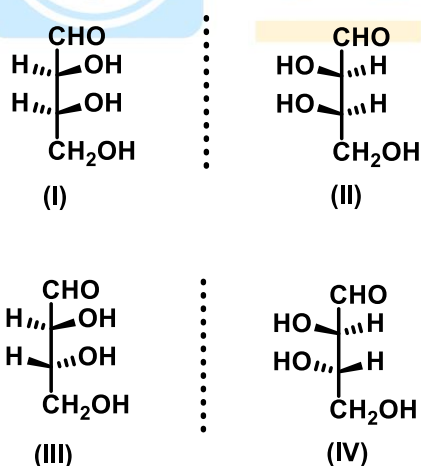


❖ Properties of enantiomers

- They have identical physical properties.
- Their specific optical rotation will be same in magnitude but the sign will be opposite (direction of rotation of the plane of plane polarized light).
- They have similar chemical action with optically inactive molecule, but they have huge difference in their action with optically active molecule.

3.2.5. Optical isomerism in compounds containing more than one chiral centre

- When a molecule has n number of chiral centres, the possible total number of stereoisomers will be 2^n . e.g. for 2,3,4-trihydroxybutanal has two chiral centres. Therefore, the total number of configurational isomer will be 2^2 or 4.

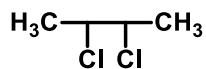


Structures (I), (II), (III) and (IV) are different configurational isomers; the set (I) and (II) & (III) and (IV) are pair of enantiomers.

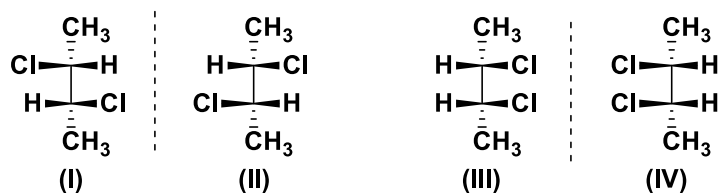
- A pair of stereoisomers which has no mirror image relationship is known as pair of diastereomers.

3.2.6. Meso compounds

A molecule with two chiral centres will not always have four possible stereoisomers. There may be three stereoisomers. This is due to the fact that some molecules with chiral centre are not chiral. e.g. 2,3-dichloro butane.



The different structures of 2,3-dichloro butane are as follows.....

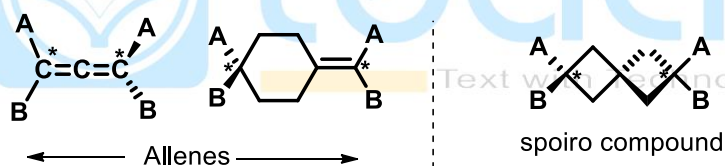


A pair of enantiomers
(non-superimposable)

(Identical molecule)

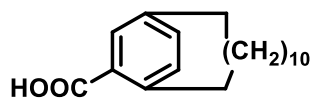
3.2.7. Optical activity due to chiral axis

There are some compounds which do not have chiral centre or chiral carbon, but the molecules are optically active. e.g. allenes and spiro compounds are optically active.



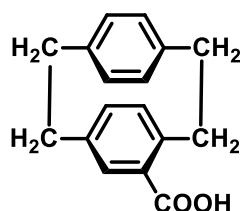
3.2.8. Chirality without a chiral atoms or centre

Some molecules are chiral although they do not have any chiral centre or axis. These are non-superimposable on their mirror images. One of such molecule is shown below.



If two para position of an aromatic compound is blocked by a polymethylene group, then the compound will be called ansa compound.

- Cyclophanes are very similar to ansa compounds where two aromatic rings are joined together to afford paracyclophanes, the structure of such compound is given below.



3.2.9. R-S system of nomenclature

There are two different stereoisomers for a molecule which has a chiral centre, if one is of R configuration, then the other stereoisomer will have S-configuration. This R/S configuration is proposed by Cahn, Ingold and Prelog. The rule of defining R/S configuration of a chiral molecule is called CIP rule.

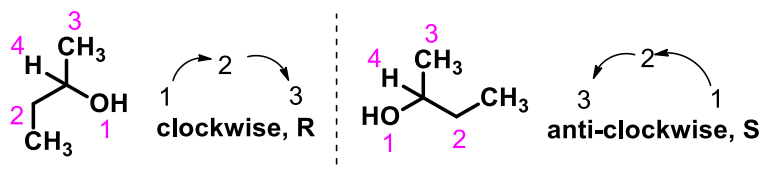
The different stereoisomers of a molecule can be expressed in terms of *R* and *S* configuration. This method was proposed by Cahn, Ingold and Prelog (CIP). This method involves the following steps

Step I: Identification of centre of chirality in the molecule.

Step II: The four atoms or group of atoms joined to the asymmetric centre are assigned as sequence of the priority by the sequence rules. These are governed by CIP rule which suggests that (a) the four substituent are listed decreasing order of atomic number, (b) If the relative priority of two groups is not decided by **rule a**, then the next atoms must be considered for priority assignment.

Step III: After assigning the priorities of the four groups or atoms attached to the asymmetric carbon atom the molecule is visualized in a position where the atom or group of atoms of lowest priority is directed away from us.

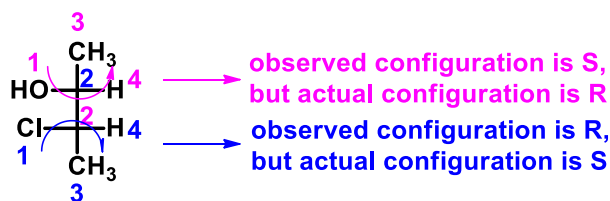
- If the sequence is left to right, i.e. clockwise, then it will be R (R stands for **rectus** which is a Latin word for right)
- If the sequence is right to left, i.e. anticlockwise, then it will be S (S stands for **sinister** which is a Latin word for left).



3.2.10. Assignment of R and S configuration from Fischer projection

In case of the presence of more than one chiral centres, to assign R and S-configuration, Fischer projection is very helpful. According to projection

- It is necessary to assign the priorities of the atoms or groups attached with the chiral carbon.
- If the group or atom of lowest priority is in the vertical line (upward or downward), then the observed configuration and actual configuration will be same.
- If the group or atom of lowest priority is in the horizontal line (right or left), then the observed configuration and actual configuration will be opposite.



3.2.11. Conformational Isomerism

The isomers which have same skeleton but differ in their position in three dimensional representation by virtue of rotation about single bond is known as conformational isomers or conformers and the phenomenon is known as conformational isomerism.

❖ Torsional Strain:

- The bond pair-bond pair repulsion is called torsional strain. Higher the torsional strain, lesser is the stability of the molecule.
- Torsional strain is the least in anti form. of a molecule.

❖ Angle Strain:

- When the bond angle of the bonding orbital is deviated from the usual bond angle due to molecular geometry is known as angle strain.
- Greater the angle strain, lesser is the stability of the conformation.

❖ van der Waals' or Sterik Strain:

- When the distance between any two substituent is less than the sum of their van der Waals' radii, then a repulsive force is generated which is known as van der Waals' or Sterik Strain.
- Generally, fully eclipsed conformation of any molecule has the highest van der Waals' or Sterik Strain, however, the anti form will have the least strain.

❖ Dipole-Dipole Interaction:

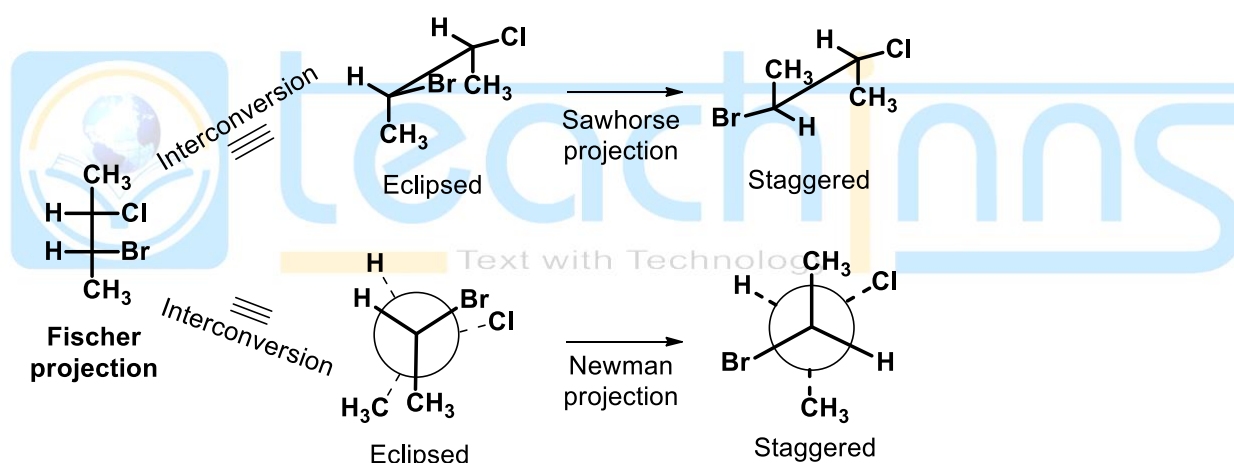
- Any two non-bonded substituents may undergo dipole-dipole interaction which can lead stabilization or destabilization of the molecule.
- If the dipole-dipole interaction is attractive, then, it will stabilize the molecule.
- If the dipole-dipole interaction is repulsive, then, it will destabilize the molecule.

3.2.12. Projections of Conformations

The conformations of any molecule can be represented two dimensionally on a paper by the following ways.....

1. Fisher projection
2. Newman projection
3. Sawhorse projection

• Interconversion of Fischer, Newman and Sawhorse projections



3.2.13. Some Important Terms of Stereochemistry

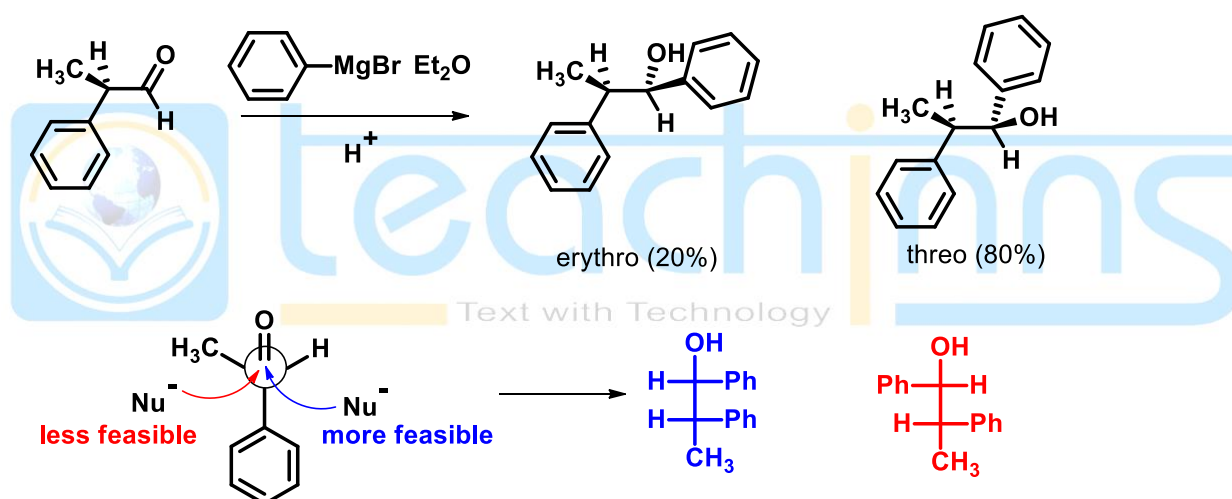
- Stereogenicity:** A compound in which an atom contains four different atoms or groups of atoms, is called stereogenic centre and this phenomenon is known as stereogenicity.
- Stereoselectivity:** A reaction in which a single reactant produces an unequal mixture of stereoisomers is called stereoselective reaction and this phenomenon is known as stereoselectivity.
- Enantioselectivity:** An enantioselective reaction is one in which one enantiomer is formed in preference to other, this phenomenon is known as enantioselectivity. The measurement of degree of selectivity of one enantiomer over the other is known as enantiomeric excess (*ee*).

- **Diastereoselectivity:** A diastereoselective reaction is one in which one isomer is formed in preference over other establishing the preferred relative stereochemistry and the phenomenon is known as diastereoselectivity. The measurement of formation of one isomer over other is done by diastereomeric excess (*de*).

3.2.14. Asymmetric Induction

When a reaction is carried out in presence of an optically active reagent, only one enantiomer or an excess of one enantiomer can be formed. The introduction of chirality is known as asymmetric induction.

- **Carbonyl Asymmetric Induction:** There are several models to describe the chiral induction during nucleophilic addition into carbonyl carbon. e.g (1) Cram's rule and (2) Felkin model.
- (1) **Cram's rule:** The nucleophile will attack the carbonyl carbon from the least hindered side.



(2) Felkin model:

