

Unit-2

Pharmaceutical Organic Chemistry-III

B.Pharma 4st Sem Notes

UNIT- II

Geometrical isomerism

- Nomenclature of geometrical isomers (Cis Trans, EZ, Syn Anti systems)
- Methods of determination of configuration of geometrical isomers.
- Conformational isomerism in Ethane, n-Butane and Cyclohexane. Stereo isomerism in biphenyl compounds (Atropisomerism) and conditions for optical activity.
- Stereospecific and stereoselective reactions



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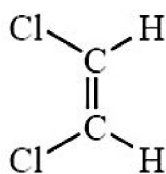
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Geometrical Isomerism:-

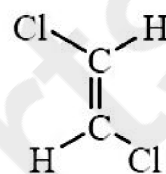
- The isomers which are having same structural formula but are differing in spatial arrangement of the groups or atoms around the double bond are termed as geometrical isomers and the phenomenon is termed as geometrical isomerism.

Or

- The isomerism which arises due to restricted (frozen) rotation about double bond in molecules or about single bond in cyclic compounds is known as geometrical or cis-trans isomerism.



cis-1,2-Dichloroethene ($C_2H_2Cl_2$)



trans-1,2-Dichloroethene ($C_2H_2Cl_2$)

- The Cis isomers is one in which two similar groups are on the same side of the double bond.
- The Trans isomers is one in which two similar groups are on the opposite sides of the double bond.

Condition for Geometrical isomerism:

A compound will show geometrical isomerism if fulfill following 3 condition-

- There should be atleast one double bond b/w carbon and carbon, carbon and nitrogen.
- There should be restricted rotation in double bond.
- There should be atleast one similar group b/w bath double bonded carbon.

Nomenclature of geometrical isomers (Cis Trans, EZ, Syn Anti systems):

1. Cis – trans:

If two different substituents are positioned at either end of the $C=C$ of an alkene, then they may exist as geometric isomers (stereoisomers).

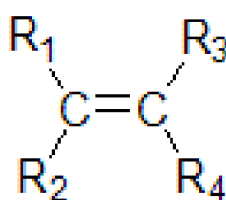
There is limited rotation of the double bond due to the pi bond, and therefore they are difficult to interconvert.

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- **Cis:** Indicates that the substituents are on the same side of the double bond or ring.
- **Trans:** Indicates that the substituents are on opposite sides of the double bond or ring.

Examples:

- Trans- and cis-isomers are not possible for terminal alkenes, i.e., those with a C=CH₂ unit.
- Neither the cis- nor the trans-isomers of a 1,1-symmetrical disubstituted alkene with a C=CR₂ unit can exist.
- There are cis- and trans-isomers of alkenes with the R₁-CH=CH-R₂ unit.
- The following alkene unit shows that the cis-and trans-isomers can exist only if R₁ and R₃ are not equal.



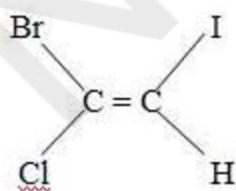
2. E Z Nomenclature:-

This nomenclature of geometrical isomers is more general and can be applied to all compounds.

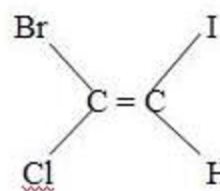
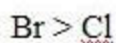
- **E:** Indicates "entgegen," which means "opposite" in German. It refers to the higher priority substituents being on opposite sides of the double bond or ring.
- **Z:** Indicates "zusammen," which means "together" in German. It refers to the higher priority substituents being on the same side of the double bond or ring.

It is based on Cahn-Ingold-Prelog System.

The group of highest priority on each carbon atom is identified by using the sequence rules.



Z form



E- form

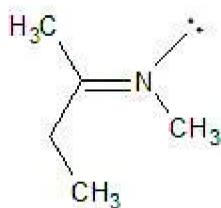
3. Syn-anti Systems:

This system is used particularly in coordination compounds or cyclic organic compounds.

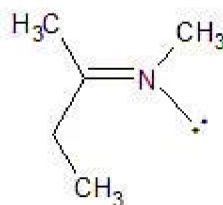
- **Syn:** Indicates that the substituents are on the same side of the ring or coordination complex.

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- **Anti:** Indicates that the substituents are on opposite sides of the ring or coordination complex.



syn



anti

Methods of determination of configuration of geometrical isomers.

- Determining the configuration of geometrical isomers often involves experimental techniques as well as theoretical considerations.

There are several methods used to determine the configuration

1. **Physical Properties**
2. **Cyclisation Method**
3. **Conversion Method**

1. Physical Method:

- The melting point and intensity of absorption of cis isomer are lower than trans isomer.
- The boiling point, solubility, Heat of combustion, heat of hydrogenation, density, refractive index, dipole moment and dissociation constant of cis isomer are greater than trans isomer.
- By the comparison of above these physical properties we can determine the configuration of isomers.

2. Cyclisation method:

- A cis isomer undergoes cyclisation much more readily than the trans isomers.

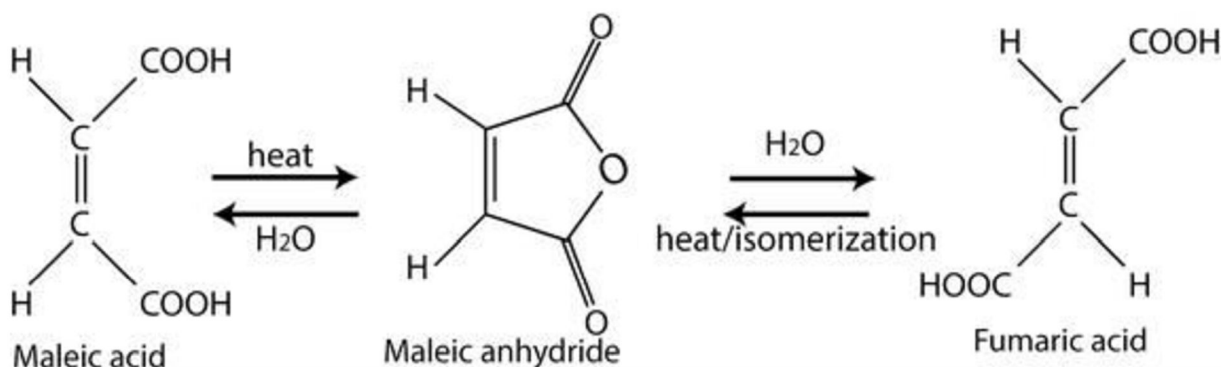
Example:

- Maleic acid forms a cyclic anhydride (maleic anhydride) when heated whereas fumaric acid does not form fumaric anhydride.

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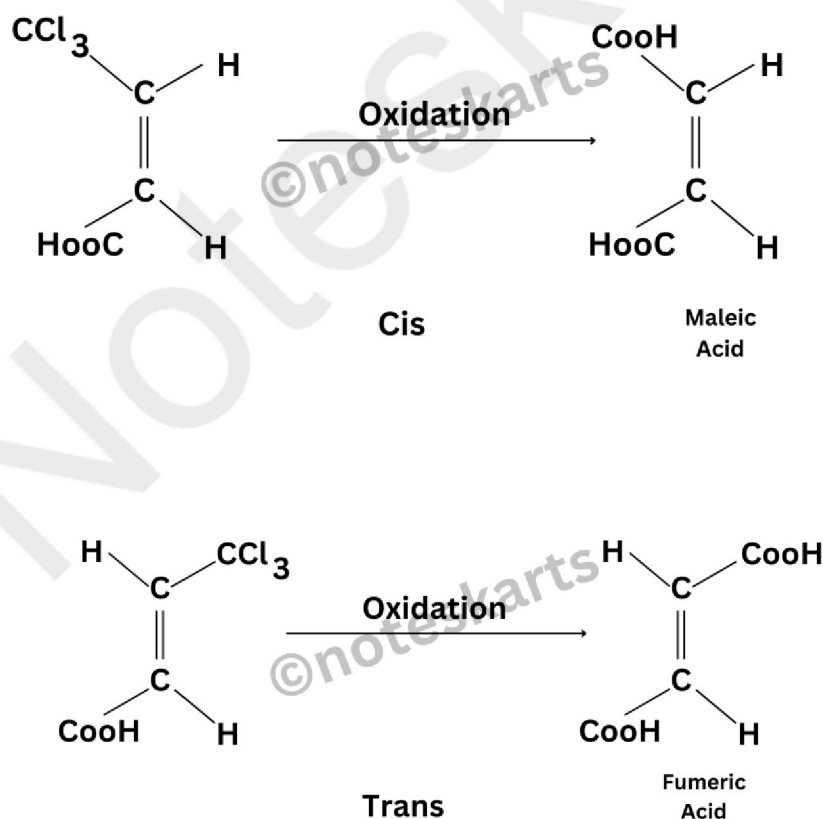
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3. Conversion Method:

- In this method the unknown compound is converted into the known compound after a chemical reaction, and by this conversion method we can determine the configuration of compounds.

Example:



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Conformational isomerism in Ethane, n-Butane and Cyclohexane. Stereo isomerism in biphenyl compounds (Atropisomerism) and conditions for optical activity.

Conformational isomerism:

- Conformational isomerism is a type of stereoisomerism that involves isomers that can be interconverted by rotating around single bonds.
- Conformational isomers, also known as conformers, are different spatial arrangements of atoms in a molecule.
- They have the same bond connectivity and configuration, if chiral .
- These different arrangements are obtained by rapid rotations around single bonds.

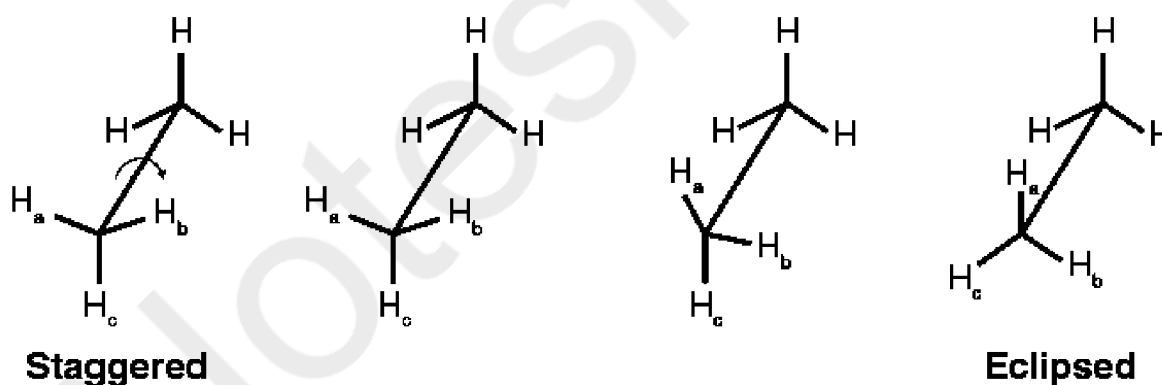
The structure of conformers is of two types:

1. Staggered:

- When torsional angle b/w 2 atom in dihedral molecules is 60°

2. Eclipsed:

- When torsional angle b/w 2 atom in dihedral molecules is 0°

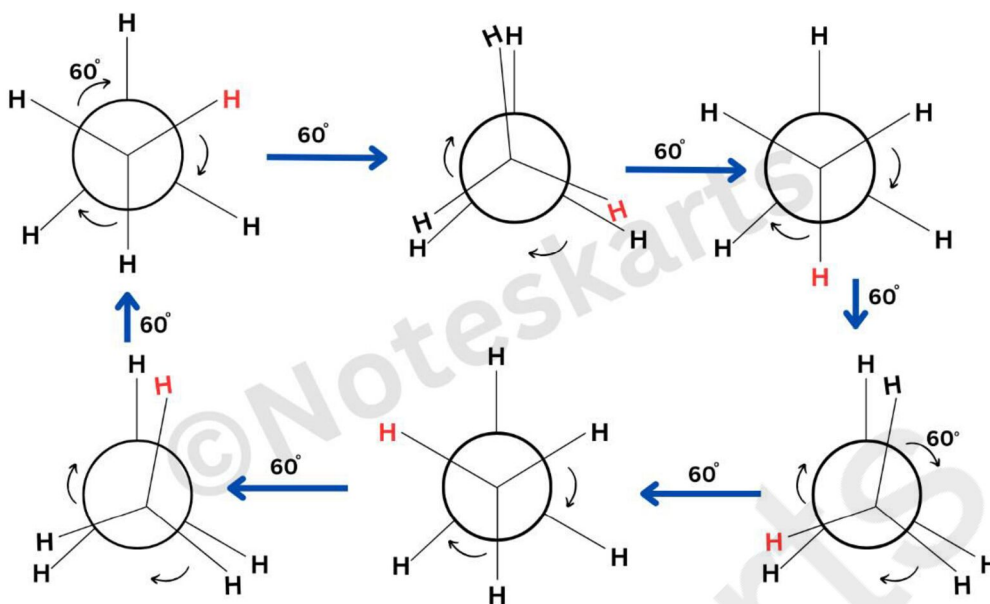


Conformational isomerism in Ethane:

1. Ethane:

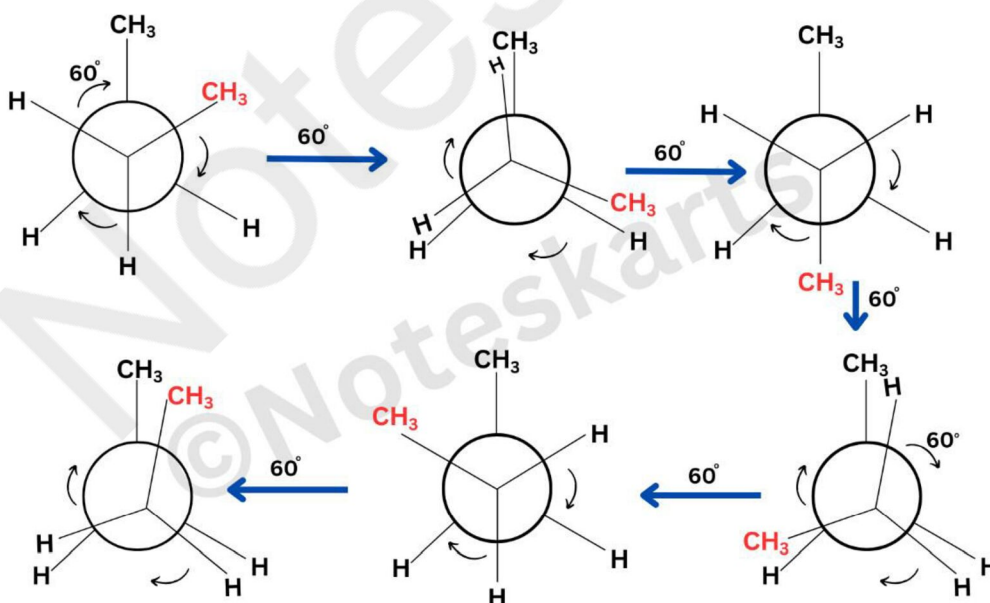
- Ethane is an organic chemical compound.
- It is a colourless and odourless gas at a standard temperature.
- In the structure of ethane 3 hydrogen is single bonded with bath carbon.
- In the spatial arrangements when band is rotated 60° then total 6 types of structure is obtained in which is staggered form and 3 is eclipsed.

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2. Butane:

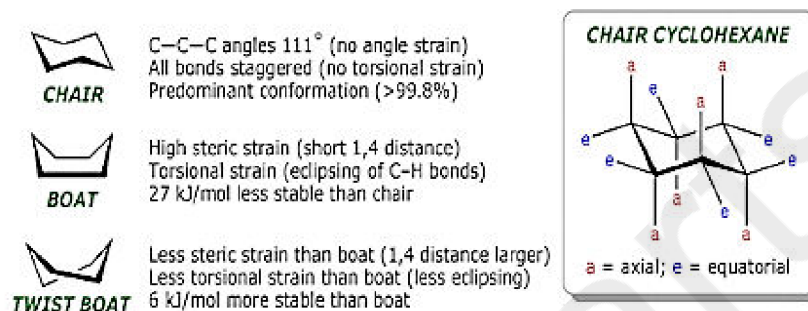
- In the structure of n-butane 2 hydrogen and 1 methyl group is present on each carbon.
- During conformational analysis after rotation of 60° in each time total 6 structure is formed in which full staggered is 1, fully eclipsed-1, partial staggered-2 and partial eclipsed-2.



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3. Cyclohexane:

- Cyclohexane is a cyclic compound which shows conformational analysis by rotation or straining of bands. Mohr and Sachse in 1890-91 gives the idea of conformational analysis in cyclohexane.
- The 3D conformation of Cyclohexane relieves all strain since it is not planar.
- The chair conformation is its most stable configuration.
- There is little activation barrier between cyclohexane's different chair conformations: 45 kJ/mol is required for the interconversion or flip of the chair.

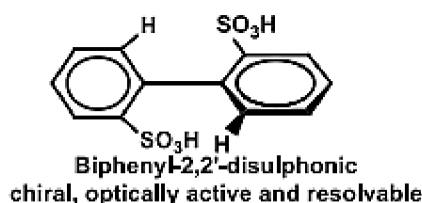


Stereo isomerism in biphenyl compounds (Atropisomerism) and conditions for optical activity.

Atropisomerism:

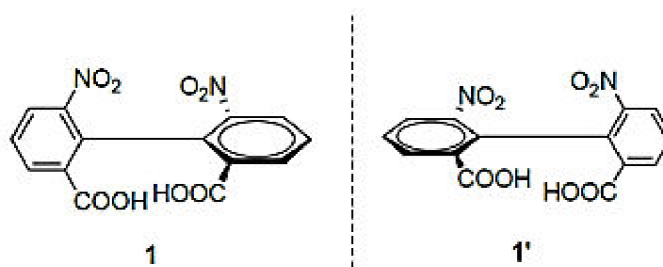
- A= Non
- Trop = Term
- Atropisomerism is a type of isomerism that occurs when a single bond cannot rotate due to steric hindrance.
- Atropisomerism is when isomers cannot be isolated under normal experimental conditions due to restricted rotation around a single bond.

Example -



Conditions for optical activity and for Atropisomerism:

- There should be any functional group at ortho position of rings (Substitution at ortho position with large size such as- Cl, Br, I, COOH, NO₂, SO₃H, etc.)



Enantiomers of the 6,6'-dinitrophenyl-2,2'-dicarboxylic acid

Conditions for Optical Activity:

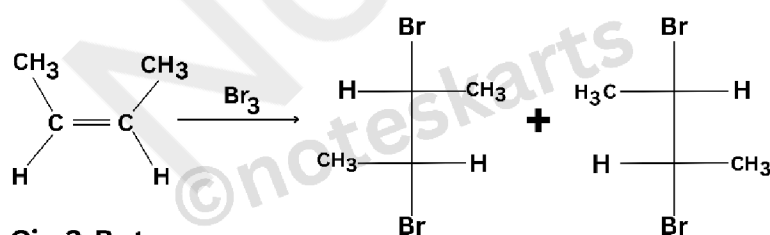
Optic activity requires the following conditions:

- Carbon atoms should be asymmetric in a compound
- There should not be any symmetry in the molecules
- Chiral axis should be present in the molecule.
- A chiral plane should be present in the molecule.
- Glyceraldehyde is an example of a material that is optically active.

Stereospecific and stereoselective reactions:

Stereospecific Reactions:

- Stereospecific reactions are chemical transformations where the stereochemistry of the reactants determines the stereochemistry of the products.
- In these reactions, both dextro and levo compounds can be synthesized in different proportion.



Racemic Mixture

Stereoselective reactions:

- These chemical reaction after which only one dextro or levo compound is formed and which is 100% selective they are called Stereoselective reactions.