

Organic Chemistry: Stereoisomers

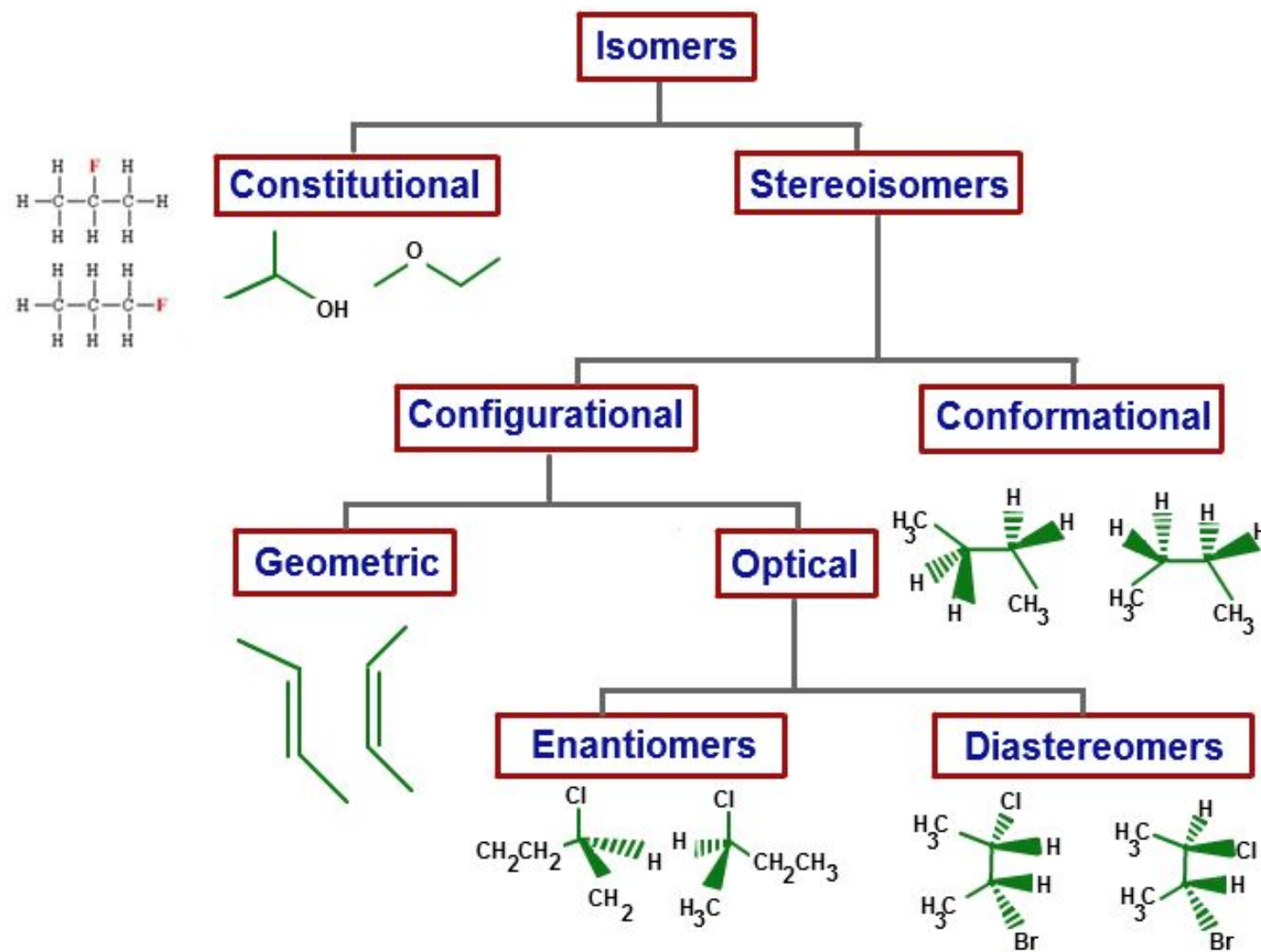
Dt. 20-12-2021

Stereochemistry

- Stereochemistry deals with three dimensional representation of molecule in space.
- This has sweeping implications in biological systems. For example, most drugs are often composed of a single stereoisomer of a compound.
- Among stereoisomers one may have positive effects on the body and another stereoisomer may not or could even be toxic.
- An example of this is the drug thalidomide which was used during the 1950s to suppress the morning sickness. The drug unfortunately, was prescribed as a mixture of stereoisomers, and while one stereoisomer actively worked on controlling morning sickness, the other stereoisomer caused serious birth defects.

Isomers

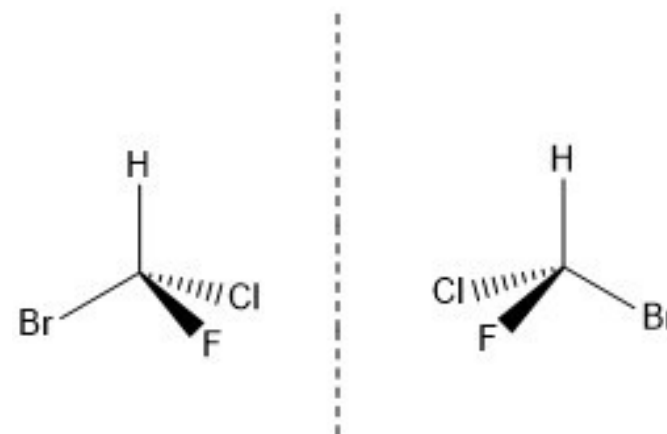
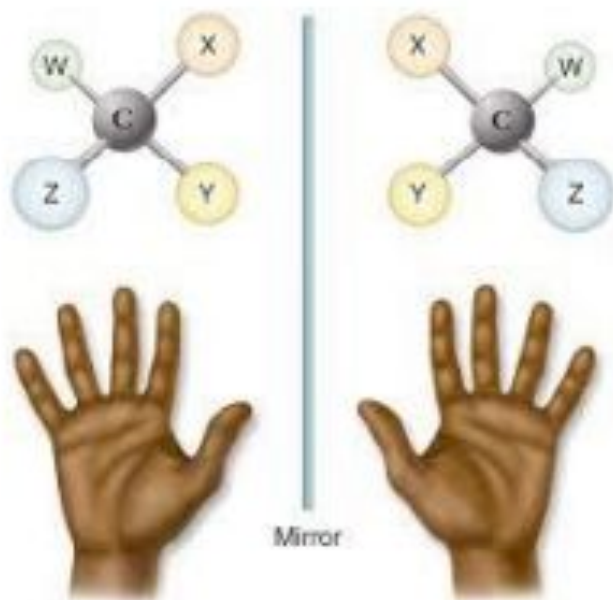
- Different compounds which have the same molecular formula. Here we will learn to make distinction between various kinds of isomers, especially the structural and stereoisomers.



TERMINOLOGY USED IN STEREOCHEMISTRY

CHIRALITY

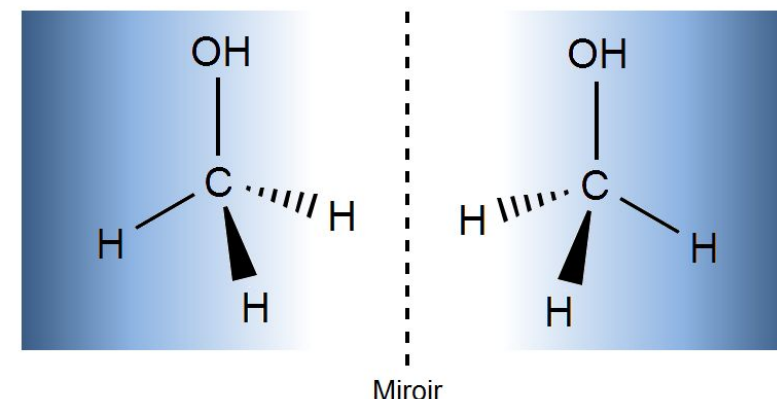
The term Chiral- The word chiral (Greek word Chier, meaning hand) is used for those objects which have right-handed and left-handed forms, i.e., molecules which have “handedness” and the general property of “handedness” is termed chirality. **An object which is not superimposable upon its mirror image is chiral.**



TERMINOLOGY USED IN STEREOCHEMISTRY

ACHIRAL

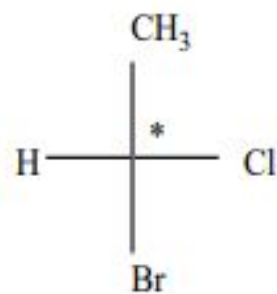
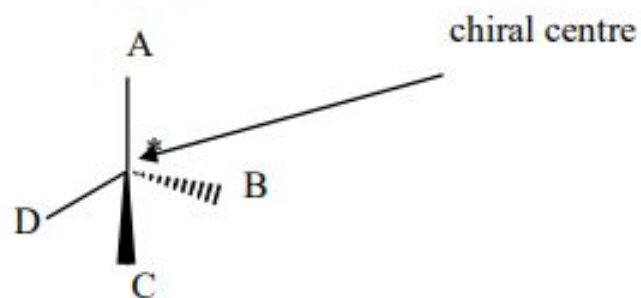
Object and molecules which are superimposable on their mirror images is achiral. Achiral molecule has internal plane of symmetry, a hypothetical plane which bisects an object or molecule into mirror-reflective halves. **An object or molecule with an internal plane of symmetry is achiral.**



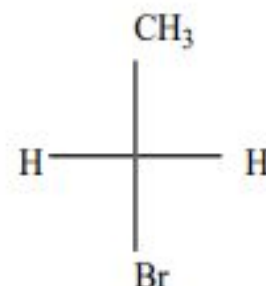
TERMINOLOGY USED IN STEREOCHEMISTRY

THE TERM ASYMMETRIC CENTER AND CHIRAL CENTER

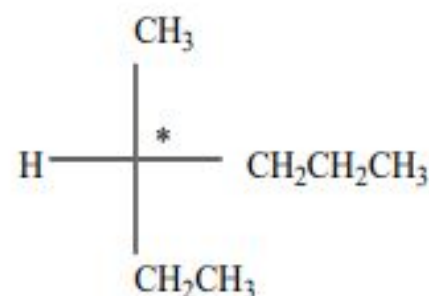
Terms are used to designate, a carbon atom bonded tetrahedrally to four different substituents in a chiral molecule: Asymmetric atom, chiral center or stereocenter.



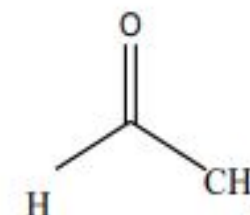
Chiral (asymmetric)
has four different
atoms bonded to
carbon



Achiral
does not have
four different
atoms bonded to
the carbon



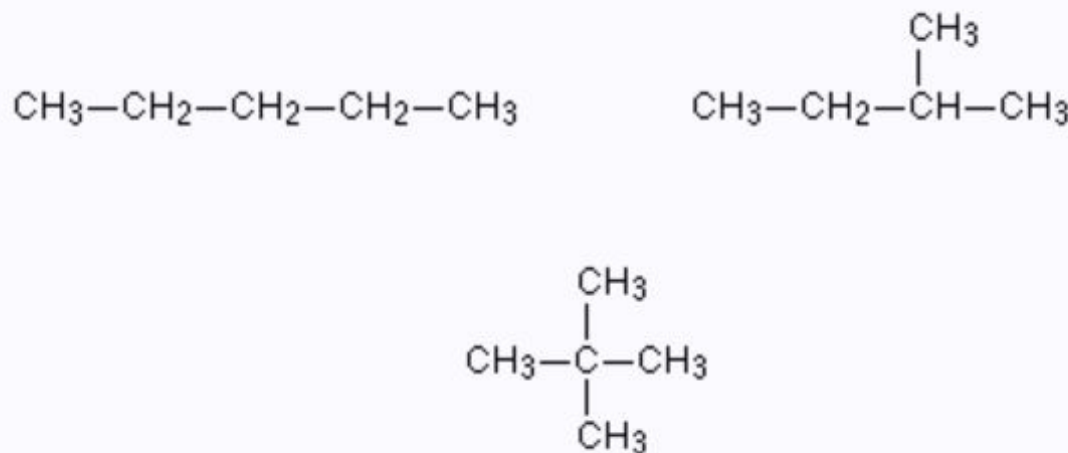
Chiral
has four different
groups bond to
the carbon



Achiral
only has three atoms
bonded to the
carbon

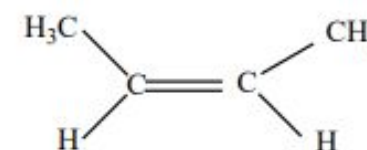
Structural isomers

- Isomers are molecules that have the same molecular formula, but have a different arrangement of the atoms in space. That excludes any different arrangements which are simply due to the molecule rotating as a whole, or rotating about particular bonds.
- In structural isomerism, the atoms are arranged in a completely different order. This is easier to see with specific examples. The names of the various forms of structural isomerism probably don't matter all that much, but you must be aware of the different possibilities when you come to draw isomers.

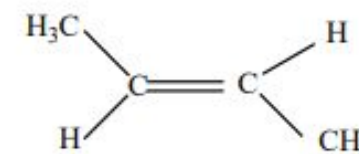


Structural isomers: Types

- Geometrical isomers occur as a result of restricted rotation about a carbon-carbon bond. This is also called cis-trans isomerism.
- This isomerism is exhibited by a variety of compounds such as compounds containing double bonds $C=C$, $C=N$, $N=N$, compounds containing cyclic structures or compounds containing restricted rotation due to steric hindrance.



Cis isomer



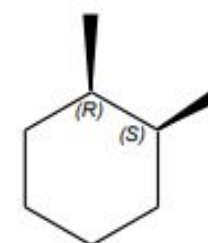
Trans isomer

Types 1: Chain Isomers

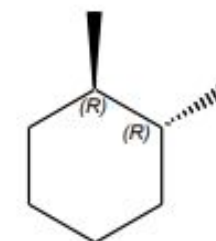
Type 2: Positional isomers

Type 3: Functional isomers

Type 4: Metamerism



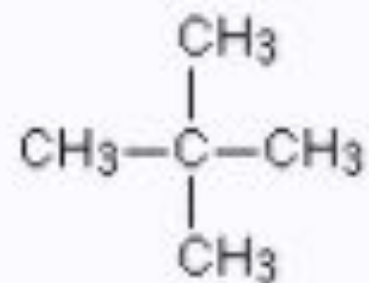
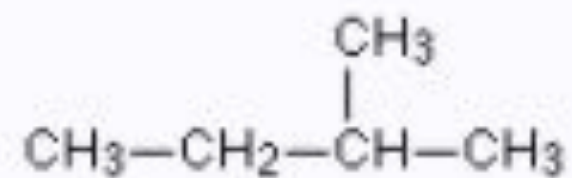
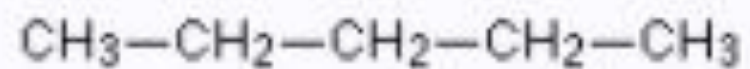
Cis isomer



Trans isomer

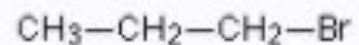
Types 1: Chain Isomers

Pentane, C_5H_{12} , has three chain isomers. If you think you can find any others, they are simply twisted versions of the ones below. If in doubt make some models

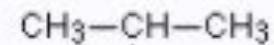


Type 2: Positional isomers

For example, there are two structural isomers with the molecular formula C_3H_7Br . In one of them the bromine atom is on the end of the chain, whereas in the other it's attached in the middle.



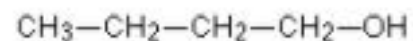
1-bromopropane



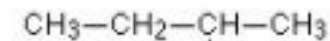
2-bromopropane

If you made a model, there is no way that you could twist one molecule to turn it into the other one. You would have to break the bromine off the end and re-attach it in the middle. At the same time, you would have to move a hydrogen from the middle to the end.

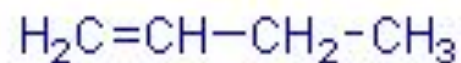
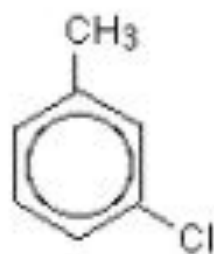
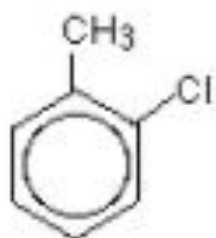
Another similar example occurs in alcohols such as C_4H_9OH



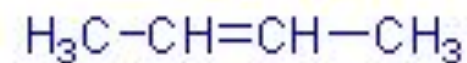
butan-1-ol



butan-2-ol



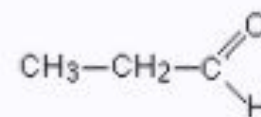
but-1-ene



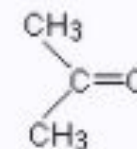
but-2-ene

Type 3: Functional isomers

A molecular formula C_3H_6O could be either propanal (an aldehyde) or propanone (a ketone).

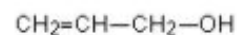


propanal

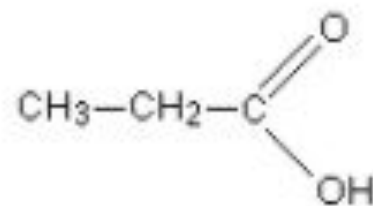


propanone

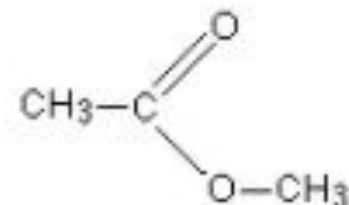
There are other possibilities as well for this same molecular formula - for example, you could have a carbon-carbon double bond (an alkene) and an -OH group (an alcohol) in the same molecule.



Another common example is illustrated by the molecular formula $C_3H_6O_2$. Amongst the several structural isomers of this are propanoic acid (a carboxylic acid) and methyl ethanoate (an ester).



propanoic acid



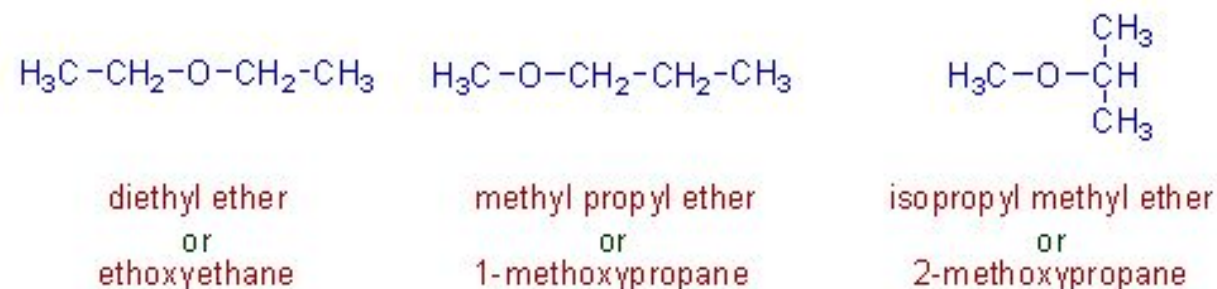
methyl ethanoate

Type 4: Metamerism

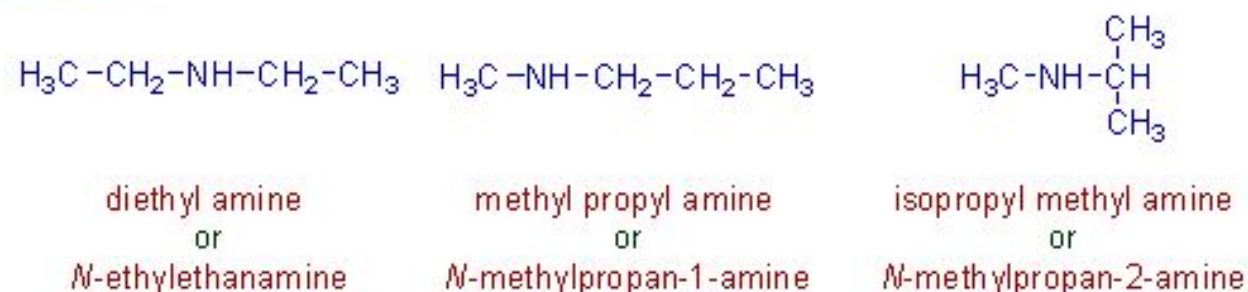
The **metamerism** arises when different alkyl groups are attached to same functional group.

E.g.

1) The following metamers contain the ether functional group. However they differ by the nature of alkyl groups attached to the oxygen atom



2) The metamerism is also possible in amines as shown below.

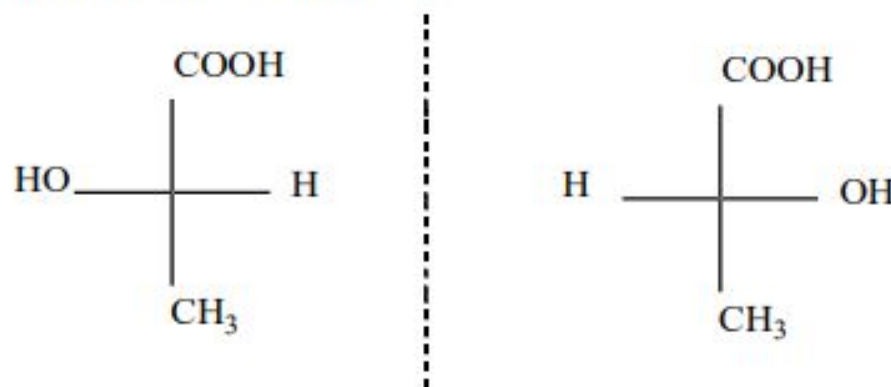


Stereoisomers

Isomers having the same molecular formula but different spatial arrangement of their atoms are known as stereoisomer. They are of following types:

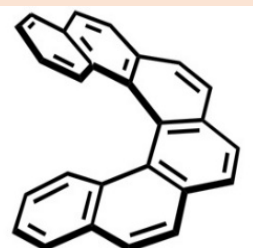
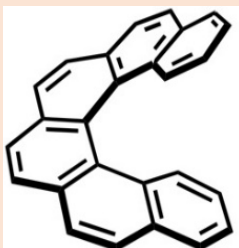
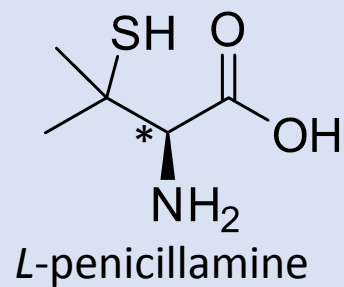
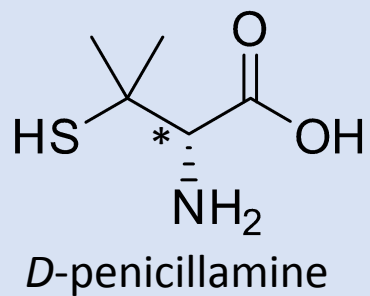
1. Enantiomers
2. Diastereomers

1. Enantiomers: Stereoisomers which are non superimposable mirror images of each other are called enantiomers. Chirality is necessary and sufficient condition for existence of enantiomers. These always exist as discrete pairs.

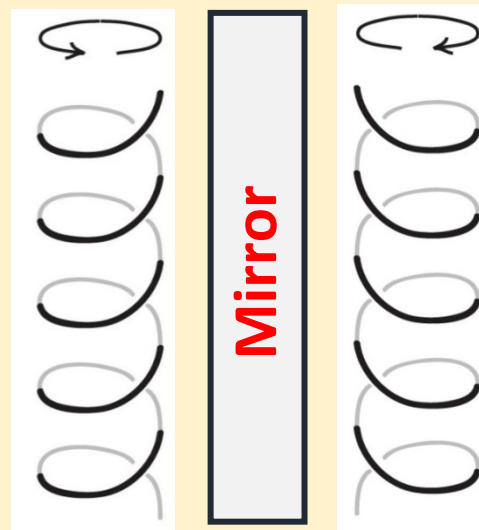


Two isomers of Lactic acid

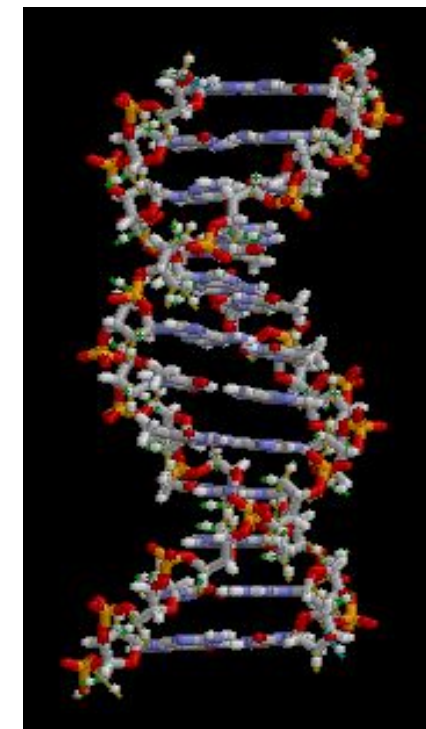
Stereoisomers- enantiomer



Helical isomers



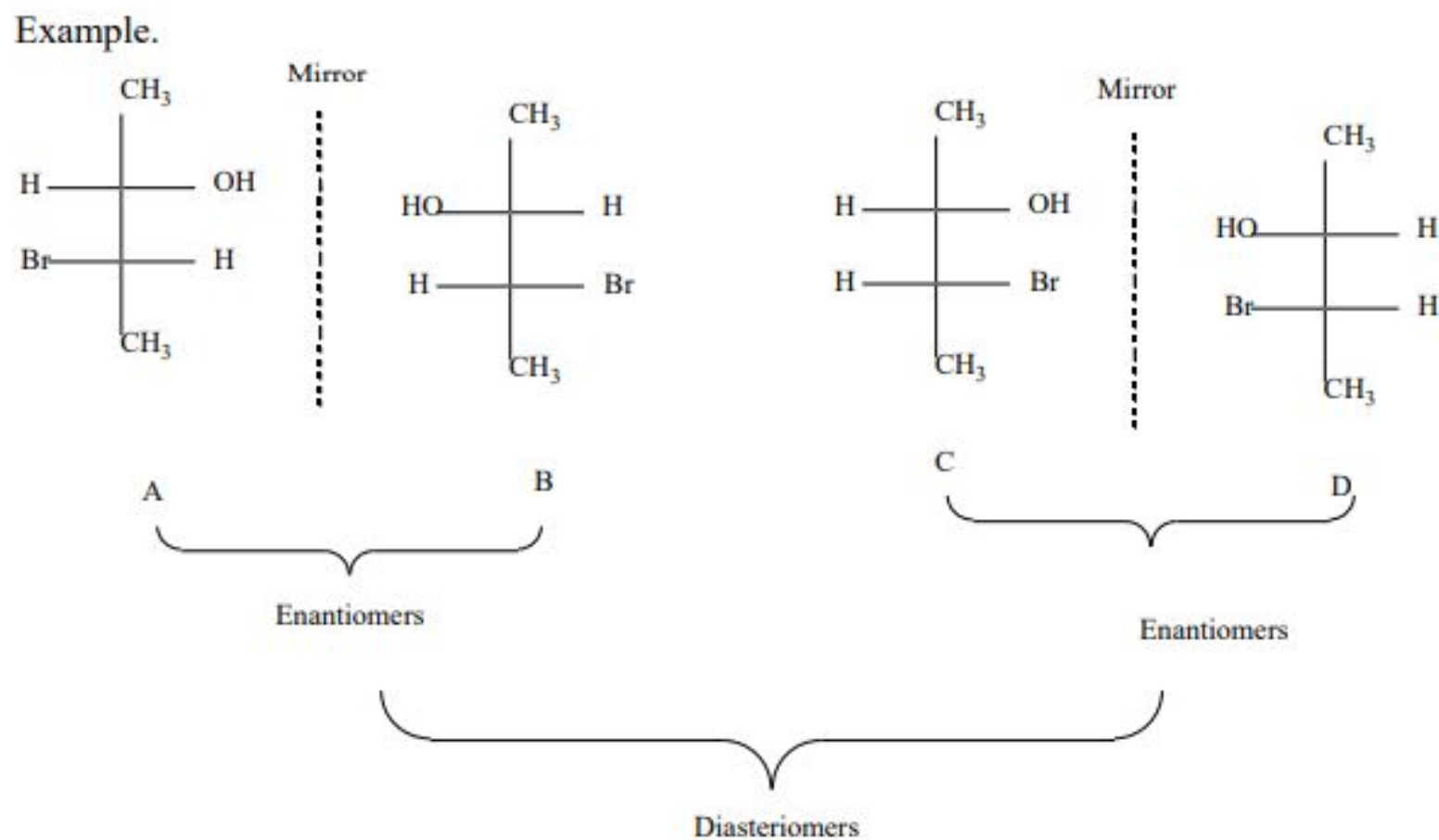
Anti-clock wise Clock-wise



DNA structure

Stereoisomers

2. Diastereomers: Stereoisomers that are not mirror images of each other are called diastereomers



Four isomers of 3-Bromo-2-butanol

REPRESENTATION OF THREE DIMENSIONAL MOLECULES

1. FLYING-WEDGE OR WEDGE-DASH PROJECTION



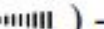
2. FISCHER PROJECTION

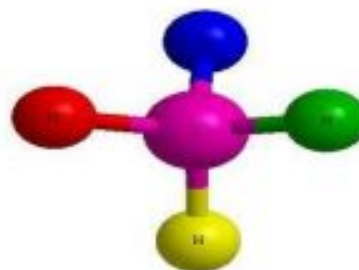
3. SAWHORSE FORMULA

4. NEWMAN PROJECTION

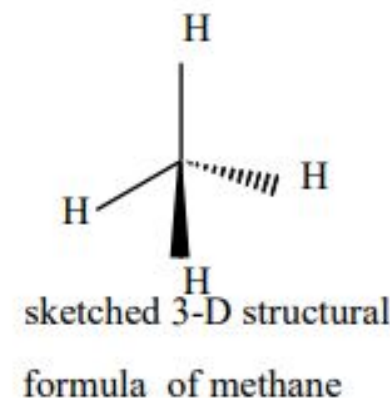
1. FLYING-WEDGE OR WEDGE-DASH PROJECTION

The Flying-Wedge Projection is the most widely used three dimensional representation of a molecule on a two dimensional surface (paper). This kind of representation is usually done for molecule containing chiral centre. In this type of representation three types of lines are used.

- A solid wedge or thick line () - it represents bond projection towards the observer or above the plane of paper.
- A continuous line or ordinary line () - it represents bond in the plane of paper.
- A dashed wedge or broken line () - it represents bond projection away from the observer or below the plane of paper. Example:- CH_4 (methane)



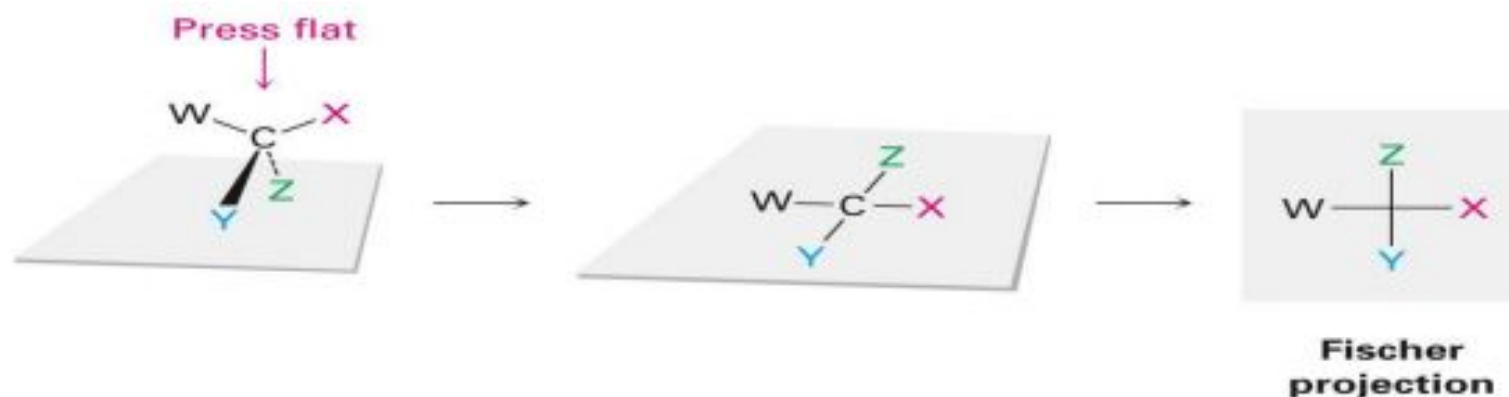
“Ball and stick” model
of 3-D structure of methane



REPRESENTATION OF THREE DIMENSIONAL MOLECULES

2. FISCHER PROJECTION

Fischer projection provide an easy way to draw three dimensional molecule on two dimensional paper and all the bonds are drawn as solid lines around asymmetric carbon atom.

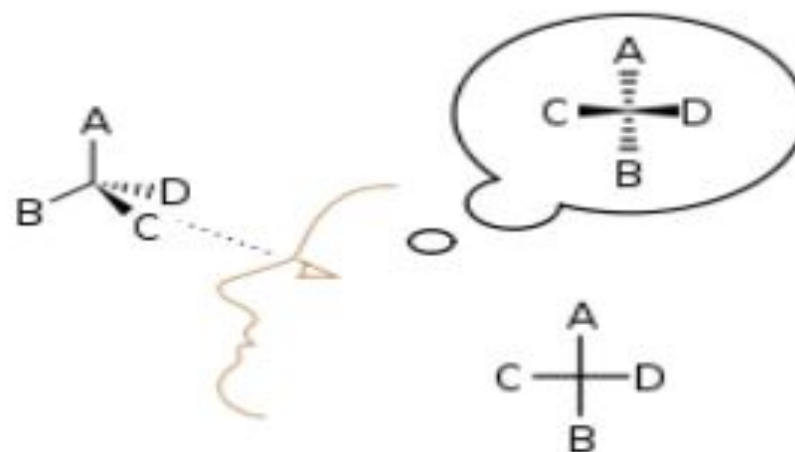


The Fischer rules for showing the arrangement around asymmetric carbon.

- The carbon chain of the compound is projected vertically, with the most oxidized carbon at the top or place the carbon number one at the top (as defined by nomenclature rule).
- The chiral carbon atom lies in the plane of the paper and usually omitted. The intersection of cross lines represents asymmetric carbon.
- The horizontal bonds attached to the chiral carbon are considered to be above the plane of paper or point towards the observer.
- The vertical bonds attached to the chiral carbon are considered to be below the plane of paper or point away from the observer.

REPRESENTATION OF THREE DIMENSIONAL MOLECULES

2. FISCHER PROJECTION



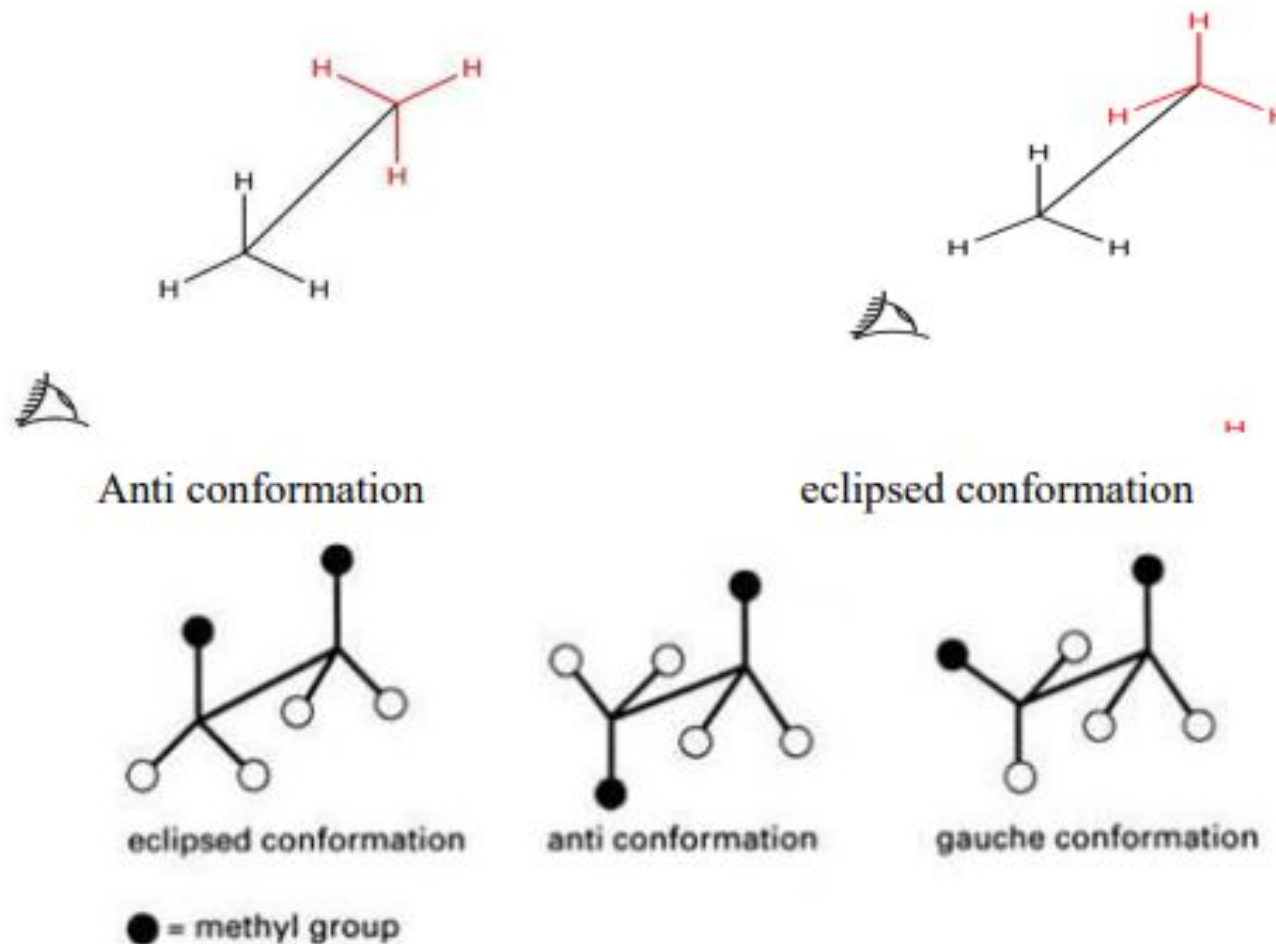
Example: glyceraldehyde



REPRESENTATION OF THREE DIMENSIONAL MOLECULES

3. SAWHORSE FORMULA

- The sawhorse formula indicates the arrangement of all the atoms or groups on two adjacent carbon atoms. The bonds between the two carbon atoms are drawn diagonally and of relatively greater length for the sake of clarity. The lower left hand carbon is taken as the front carbon or towards the observer and the upper right hand carbon as the back carbon or away from the observer.
e.g. ethane
- All parallel bonds in sawhorse formula are eclipsed and all anti parallel bonds are opposite or scattered. Gauche representation is that in which bulky groups are nearer to each other at 60° angles.

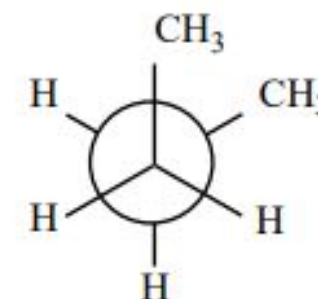
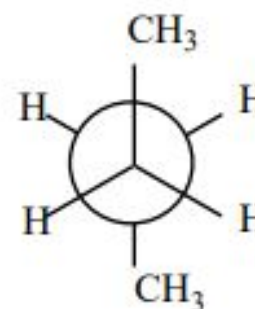
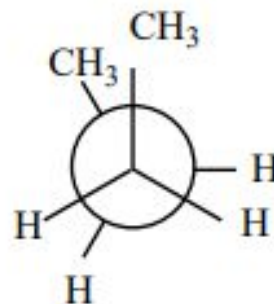


REPRESENTATION OF THREE DIMENSIONAL MOLECULES

4. NEWMAN PROJECTION

Newman devised a very simple method of projecting three dimensional formulas on two dimensional paper which are known as Newman projection.

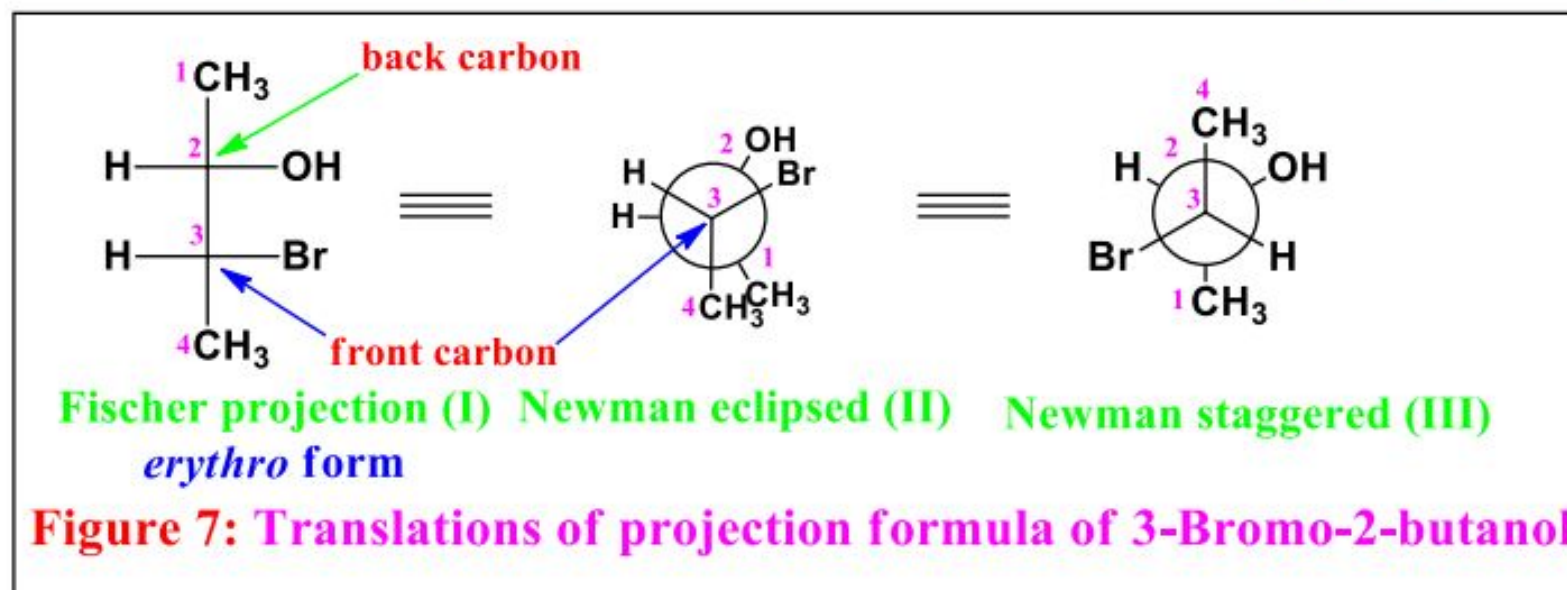
- In these formulae the molecule is viewed from the front or along the axis of a carbon-carbon bond.
- The carbon nearer to the eye is represented by a point and the carbon atom towards the rear by circle.
- The three atoms or groups on the carbon atoms are shown as being bonded to dot or circle by an angle of 120° to each other.
- In Newman formula all parallel bonds are eclipsed or all anti parallel or opposite bonds are staggered.



REPRESENTATION OF THREE DIMENSIONAL MOLECULES

4. NEWMAN PROJECTION

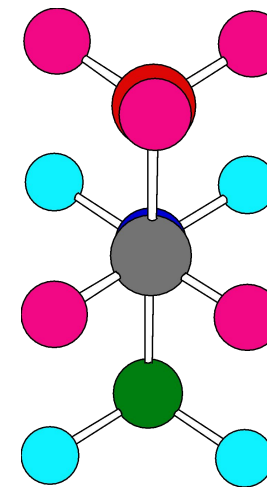
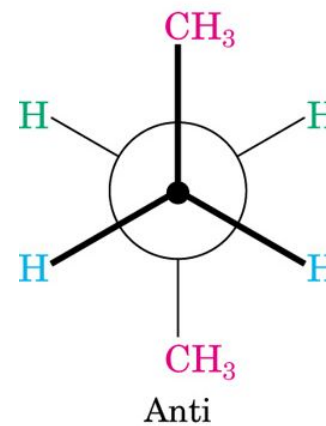
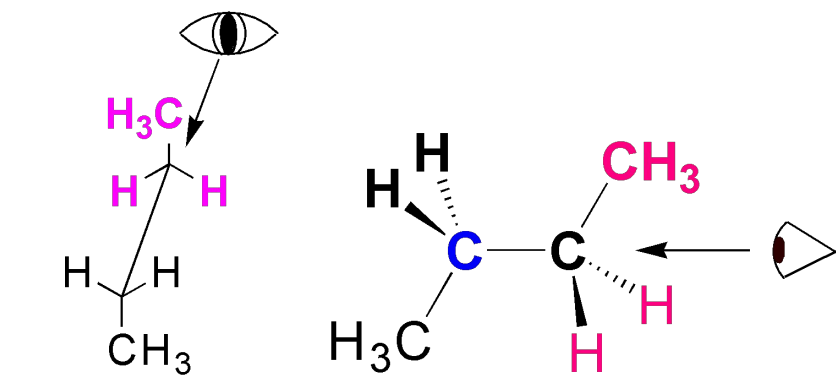
- The centre of the circle represents the front carbon atom and the circumference the back carbon atom. The remaining bonds on each carbon are shown by small straight lines at angles of 120° joined to the centre and to the circumference as shown in **Figure 7**.



Conformational analysis of n-butane

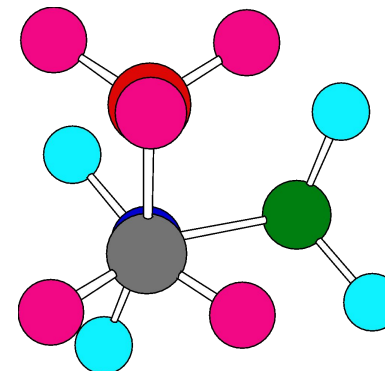
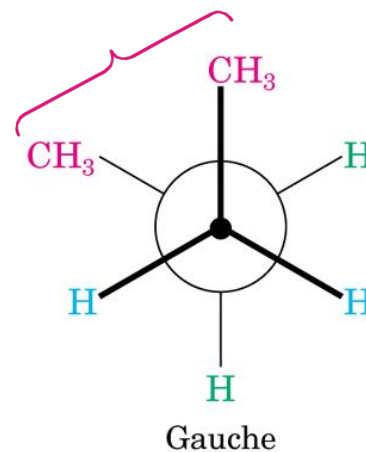
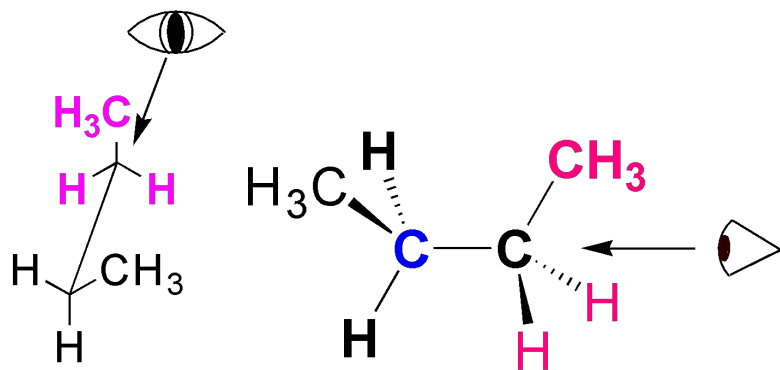
Conformational Analysis of

Butane



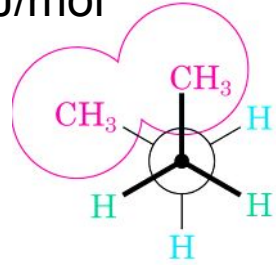
Staggered: gauche

3 KJ/mol

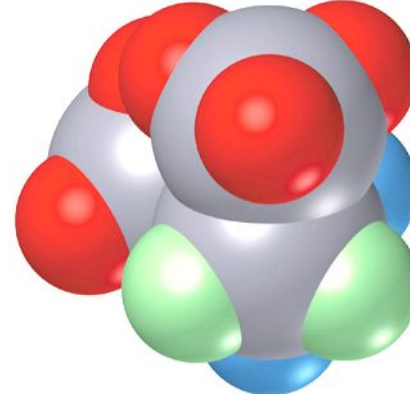
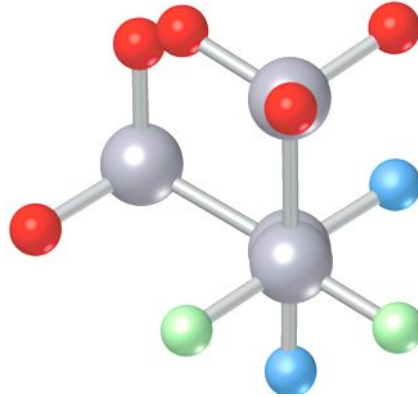


Steric Strain: repulsive interaction that occurs when two groups are closer than their atomic radii

3 KJ/mol

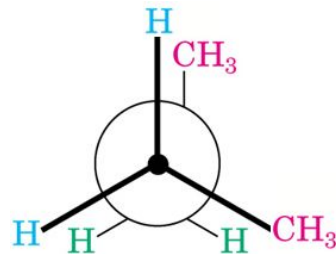
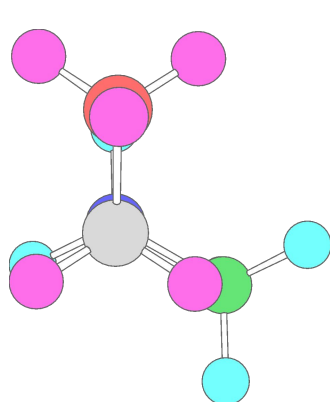


©2001 Brooks/Cole - Thomson Learning

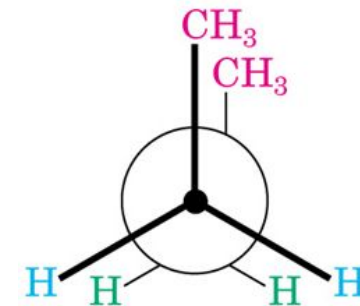
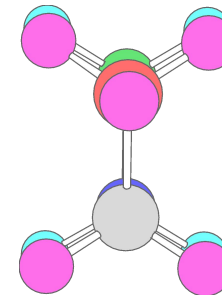


Eclipsed conformations of butane: rotational barrier of butane is 25 KJ/mol. A *CH₃-CH₃ eclipsing interaction is 17 KJ/mol.*

CH₃ - H



CH₃ - CH₃



Least stable eclipsed