Chapter –III
Stereochemistry of Organic Compounds

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Introduction:

Isomerism: Various organic compounds represented by the same molecular formula are called as Isomers. The phenomenon which exhibits the existence of **two or more chemical compounds** with the **same molecular formula** but having **different properties** owing to a **different arrangement of atoms** within the molecule is termed as **isomerism**.

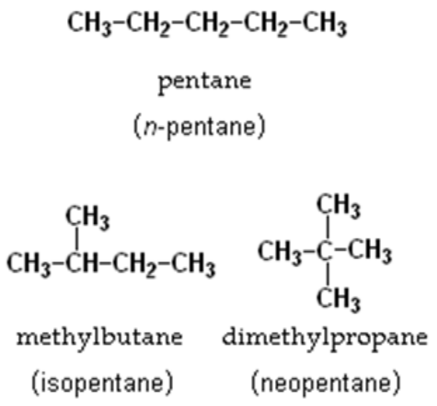
Isomerism is classified into two types.

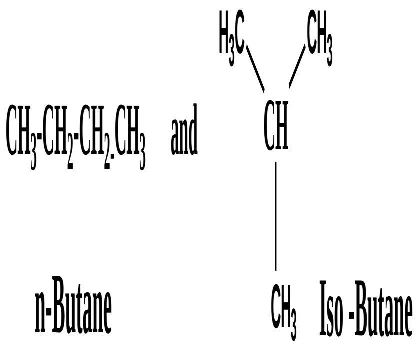
A) Structural Isomerism
B) Stereoisomerism

Structural Isomerism: It is isomerism exhibited by the compounds having the **same molecular formula** but **different structural formulae**.

Structural isomerism is further classified into six categories.

1) Chain or Nuclear isomerism: When two or more compounds have the same molecular formula but differ in the branching of carbon atoms. It is also known as skeletal isomerism shows differently branched structures.

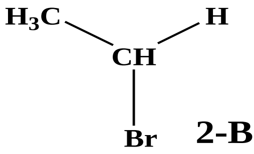




2) Position Isomerism: This type of structural isomerism is caused by the difference in position of same substituent in the same carbon chain. e.g. Bromopropane exhibits following two position isomers, that are the positions of the functional groups or substituent atoms are different in position isomers.

CH_3-CH_2-CH_2-Br

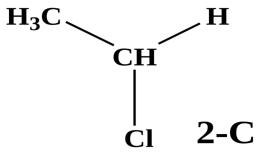
1-Bromo propane



2-Bromo propane

CH_3-CH_2-CH_2-Cl

1-Chloro propane



2-Chloro propane

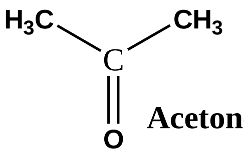
3) Functional isomerism: It refers to the compounds that have the same chemical formula but different functional groups attached to them. It is also known as functional group isomerism.

CH_3-CH_2-OH

Ethanol

CH_3-O-CH_3

Dimethyl ether



Acetone

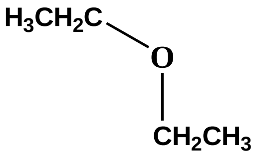
CH_3-CH_2-CHO

n-Propionaldehyde

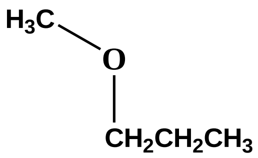
4) Metamerism: This type of structural isomerism is exhibited by members of the same homologues series. These members differ in the nature of alkyl group attached to the polyvalent atom (e.g. C,O,N) of the functional group.

Example: 1) $C_4H_{10}O$ can be represented as ethoxy-ethane ($C_2H_5OC_2H_5$) and Methoxy-propane ($CH_3OC_3H_7$).

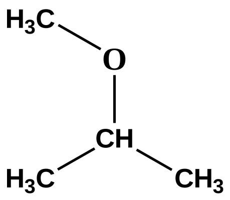
2) Ether with Molecular formula $C_4H_{10}O$ shows following three metamers (Isomeric ethers)



Diethyl ether

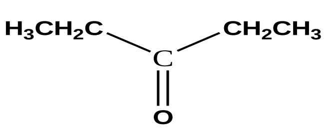


Methyl n-propyl ether

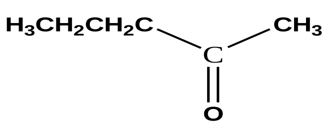


Methyl iso-propyl ether

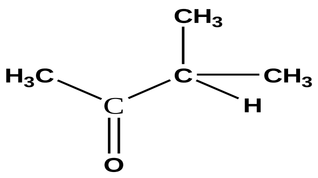
3)



Diethyl Ketone



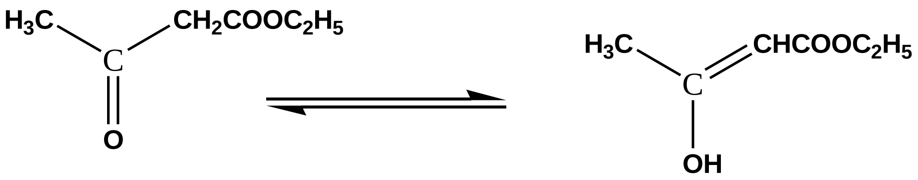
Methyl n-propyl ketone



Methyl iso-propyl ketone

5) Tautomerism: It is a kind of dynamic isomerism wherein one isomer is constantly changing into the other and vice-versa. Tautomerism is caused by the wandering of a labile hydrogen atom between two polyvalent atoms.

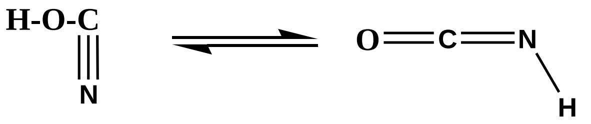
Examples are 1) Acetoacetic ester exists in two keto-enol tautomers.



Keto form

Enol form

2) Cyanic acid and isocynanic acid are tautomers.



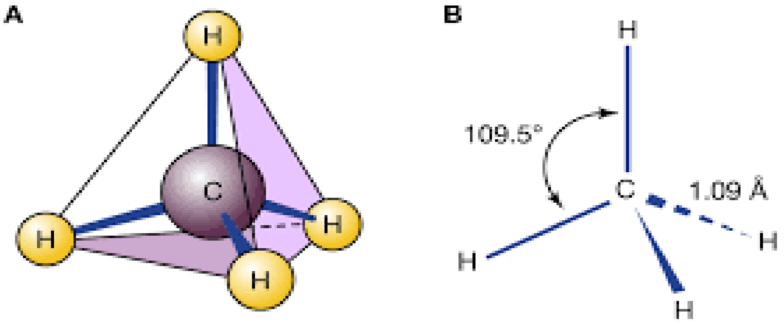
Cynanic acid

Isocynanic acid

Stereoisomerism:

- Isomerism exhibited by **two or more compounds** with the **same molecular and structural formulae** but **different configuration** (i.e. spatial arrangement of atoms or groups in a molecule) is termed "**Stereoisomerism**".
- Isomers that have the **same constitution** but **differ in the spatial arrangement** of their atoms or groups of atoms are called "**Stereoisomers**".
- **Stereochemistry** refers to **Chemistry of molecules in three dimensions**.
- The foundations of Organic Stereochemistry were laid by Jacobus van't Hoff and Charles Le Bel in 1874. Independently of each other, that is beginning of stereochemistry that is concerned with the study of structures of molecules in three dimensions.

- van't Hoff the first Nobel prize in Chemistry in 1901 and Le Bel (Both are marked as the beginner of Stereochemistry) proposed that the four bonds of the carbon atom in methane, are arranged in a way so as to point towards the corners of a regular tetrahedron.



Tetrahedral structure of Methane

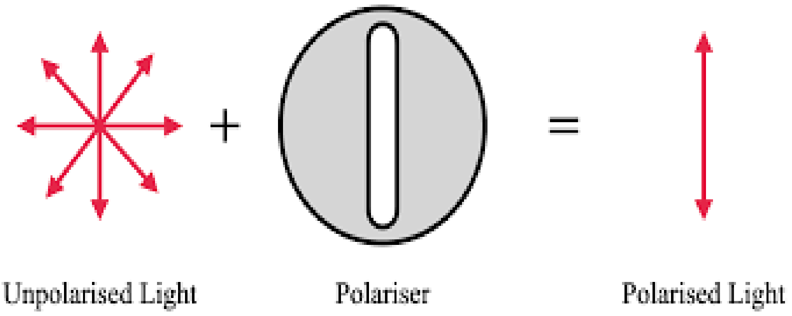
Stereoisomerism is of two types:

1) Geometrical isomerism   2) Optical isomerism.

Optical Isomerism:

1) Plane polarized light:

- Light is the transverse wave motion. Ordinary light consists of electromagnetic waves vibrating in all planes perpendicular to the Path of propagation (i.e. direction in which light travels.)
- Such a ray of light when passed through Nicol prism emerges out vibrating only in one plane. So, a ray of light whose vibrations take place only in one plane is called as plane polarized light (PPL).



2) Optical activity: The property of a substance of rotating the plane of PPL either towards left or right is called as optical activity.

3) Enantiomers /enantiomorphs /optical stereoisomers or optical antipodes: Compounds which are mirror images of each other and non-superimposable are called as enantiomers or enantiomorphs or optical stereoisomers or optical antipodes.

4) Dextrorotatory enantiomers (d) or (+) : The enantiomer which rotates the plane of PPL towards right hand side (clockwise) is called as dextrorotatory and is designated as d or (+).

5) Laevorotatory enantiomers (l) or (-): The enantiomer which rotates the plane of PPL towards left hand side (anticlockwise) is called as laevorotatory and is designated as l or (-).

Properties of enantiomers:

1) Enantiomers generally have identical physical properties or identical achiral properties such as melting point, boiling point, density, solubility in water, UV, infrared absorptions and NMR spectra.

2) Enantiomers generally have identical physical properties such as melting point, boiling point, infrared absorptions and NMR spectra.

3) This is because the intermolecular interactions between opposite enantiomers that are between the R and S enantiomers may be different to those between like enantiomers that are between two molecules both of 'R' or both of 'S' stereochemistry.

4) Enantiomers rotates plane polarized light (optical active)

5) Enantiomers have same rate of reaction with achiral reagents.

6) Chemical and biochemical reactions of Enantiomers are stereospecific.

7) Enantiomers react at different rates with chiral reagents.

6) Optical activity and its examples:

- It has been found that only those crystalline or molecular structures which are not superimposable on their mirror images are optically active.
- Substances like quartz, sodium chlorate, benzil etc. are optically active in the solid 'state only. Quartz exists in two crystalline forms, one of which is dextrorotatory and the other laevorotatory. These two forms are mirror images of each other and non-superimposable. Such pairs of crystals are said to be enantiomorphs.
- When quartz crystals are fused, optical activity is lost. Fusion causes only change in physical state. Therefore, optical activity is entirely due to asymmetry of the crystalline structure.
- Thus, substances like quartz, sodium chlorate, benzil etc. are optically active only in solid state: vaporization, fusion or solutions in a solvent cause's loss of optical activity.
- There are many substances like glucose, tartaric acid etc. are optically active in the solid, fused, gaseous or dissolved state. In such cases, optical activity is entirely due to the asymmetry of the molecular structure.

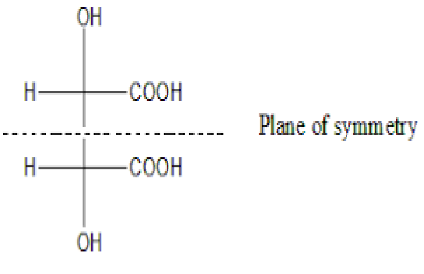
7) Optical Isomerism: Optical isomerism is the isomerism exhibited by the compounds having the same molecular and structural formulae but different configuration and because of molecular asymmetry; these compounds rotate the plane of PPL.

8) Asymmetric carbon or stereogenic center: A carbon atom of which four valencies are satisfied by linking with four different atoms or groups is called as asymmetric carbon atom and a molecule possessing carbon atom is called as asymmetric molecule.

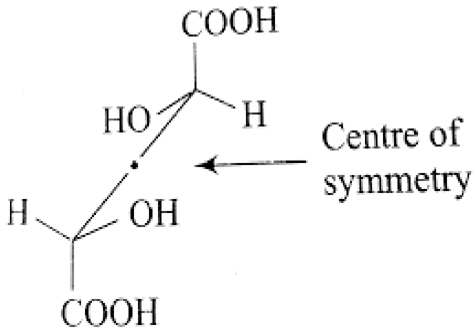
(Actually it is the group as a whole which is asymmetric; a carbon atom cannot be asymmetric.) Carbon atom is also called as stereogenic center and is indicated by asterisk*.

- The majority of optically active organic compounds contain one or more asymmetric carbon atoms. It should be remembered that the **essential requirement for optical activity is the asymmetry of the molecule**:
- **Note:** A molecule **even containing two or more asymmetric carbon** atoms **shows optical inactivity.**

For e.g. **Meso tartaric acid**, though it contains two asymmetric carbon atoms, is **optical inactive because it possesses plane of symmetry**.



Meso tartaric acid



The test of superimposing a formula on its mirror image indicates whether the molecule is symmetric or not. The most satisfactory way in which superimposibility may be ascertained, is to build up models of the molecule and its mirror image. Usually this is not convenient and so, in practice it is determined by knowing whether the molecule possesses a plane of symmetry or center of symmetry or alternating axis of symmetry.

9) Asymmetric/dissymmetric molecule or chiral molecule: A molecule having none of the above elements of symmetry is termed as asymmetric molecule which is optically active.

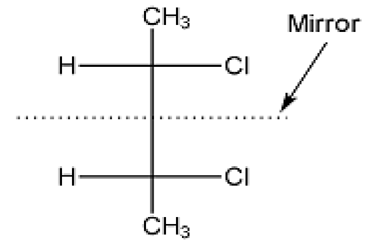
10) Symmetric or achiral molecule: If the molecule contains at least one of elements of symmetry (Plane, center, simple or proper and alternating axis), the molecule is symmetric or achiral which is optically inactive.

Stereochemistry is primarily concerned with molecular geometry which is best described in terms of symmetry.

- In order to study the symmetry of a molecule. Certain operations such as rotation and reflection are performed. If by performing these operations. An arrangement is obtained which is indistinguishable from the original structure of molecule, the operation is called as symmetry operation and the molecule is said to possess an element of symmetry.
- Symmetry of a molecule is described in terms of **four symmetry operations** and **four corresponding elements of symmetry**.
  i) Plane of symmetry
  ii) Centre of symmetry,
  iii) Simple or proper or proper axis of Symmetry.
  iv) Alternating axis of symmetry

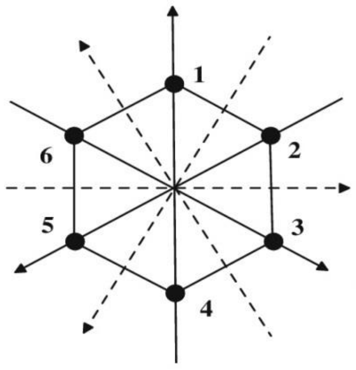
1) Plane of symmetry: It is a plane which divides the molecule (or an object) into two halves which are mirror image of each other. In other words, reflection of the two half parts of the molecule across the reflection plane gives a structure indistinguishable from the original molecule. The plane is called as ‘s’ plane and the operation is called as ‘σ’ operation.

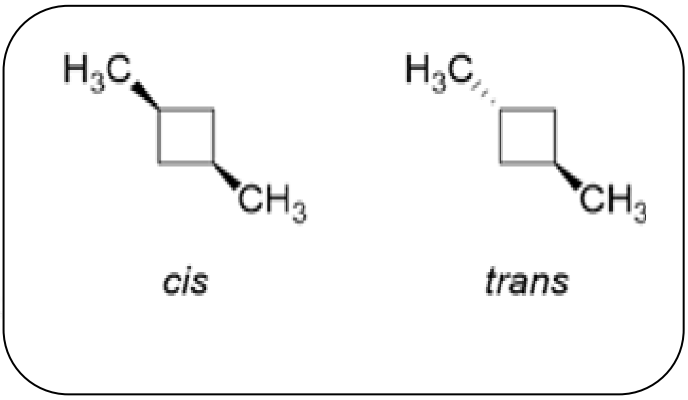
Examples 1) **meso-2,3-dichlorobutane**



meso-2,3-dichlorobutane

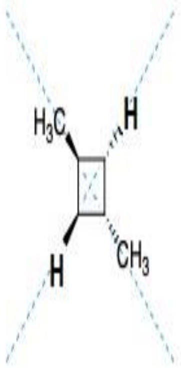
2) **Benzene** has one horizontal plane (the molecular plane) and six vertical planes, out of which three ‘s’ planes pass through opposite atoms and another set of three ‘s; planes pass through the opposite bonds.



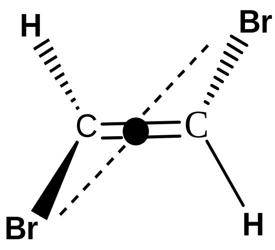


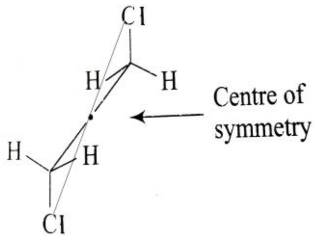
2) Centre of symmetry: It is a point within a molecule such that if an atom or point is joined to it and the line drawn to an equal distance beyond. It meets an equivalent atom. In other words, inversion of all atoms in the molecule through the point gives an arrangement indistinguishable from the original molecule. Centre of symmetry is designated as 'I' and the operation as 'i' operation.

Example 1) Trans-1,3 dimethyl cyclobutane has one center of symmetry at the entre of the ring.



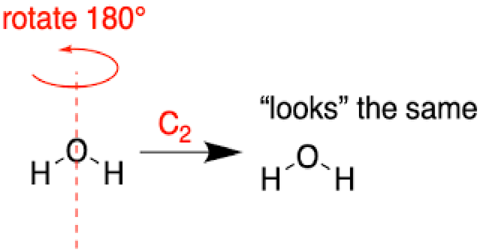
Example 2) Trans-dibromo ethene has one center of symmetry at the midpoint of C=C bond. **Example 3)** staggered ethylene dichloride possesses one center of symmetry.



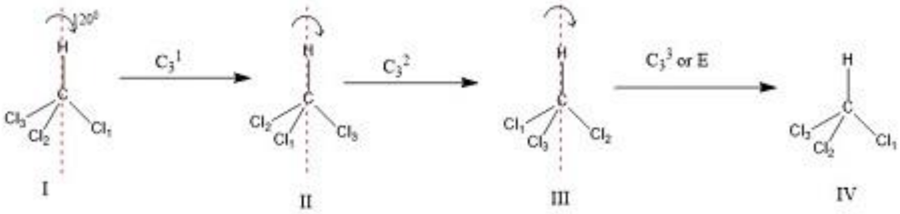


3) Simple or proper axis of symmetry (proper rotation axis): An n-fold simple axis of symmetry is an axis such that, when a structure possessing this axis, is rotated by an angle of 2π / n that is 360/n) around the axis, another identical structure results. Rotation usually taken as clockwise. The axis is designated as Cn and the operation is called as Cn operation) the operation, if repeated n times leads to an orientation identical with the original.

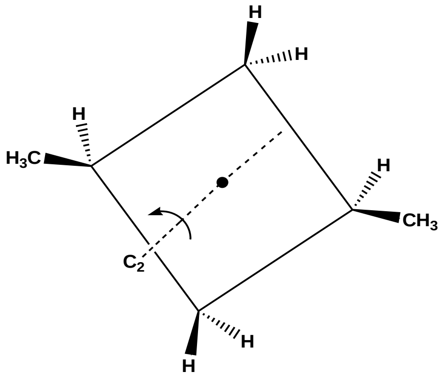
1) water molecule has one two fold simple axis of symmetry. (C-2) bisecting the H-O-H angle.



Example 2) Chloroform has one C_3 axis along C-H bond.



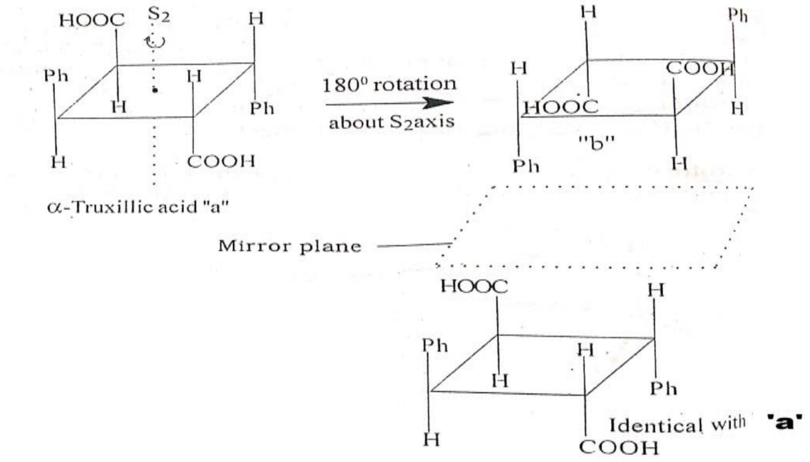
Example 3) Cis -1,3 dimethyl cyclobutane has one C_2 axis (vertical)



4) Alternating axis of symmetry (Rotation-Reflection axis): An n-fold alternating axis of symmetry is an axis such that, when the structure possessing this axis is rotated around the axis by an angle of 2π /n (360/n) and then reflected across a plane at right angles to the axis, another identical structure results. It is designated and the operation is designated as ‘Sn’ operation.

Many compounds which possess this symmetry element found to be inactive.

Example 1) α-Truxillic acid has ‘S_2 axis which passes through the center of and perpendicular to the cyclobutane ring. The following show that the structure "a" by rotation through 180^0 through a plane perpendicular to the axis produces structure "b". Reflection structure "b" across a plane at right angles to the axis, produces equivalent structure as that of "a".



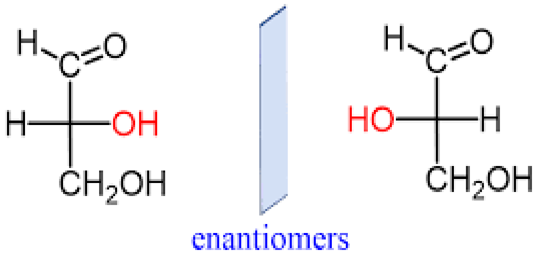
Specification of configuration: The arrangement of atoms or groups that characterizes a particular stereo-isomer is called its configuration. Two systems are used to designate the configuration of a molecule.

1) Relative configuration (D-L Notational system)
2) Absolute configuration (R-S Notational system)

1) Relative configuration (D-L Notational system):

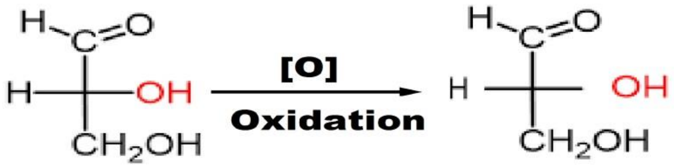
The configuration of a compound **with reference to arbitrarily assigned configuration**, of a reference substance is known as its relative configuration. The reference substances chosen by **Rosanoff in 1906** were (+) and (-) forms of glyceraldehyde. CHO.CHOH.CH_2OH.

- The enantiomer having-OH group on the right when the aldehyde group is placed at the top, is assigned **'D' configuration.**
- If the OH group is at the left, it is assigned **'L' configuration.**



D-glyceraldehyde L-glyceraldehyde

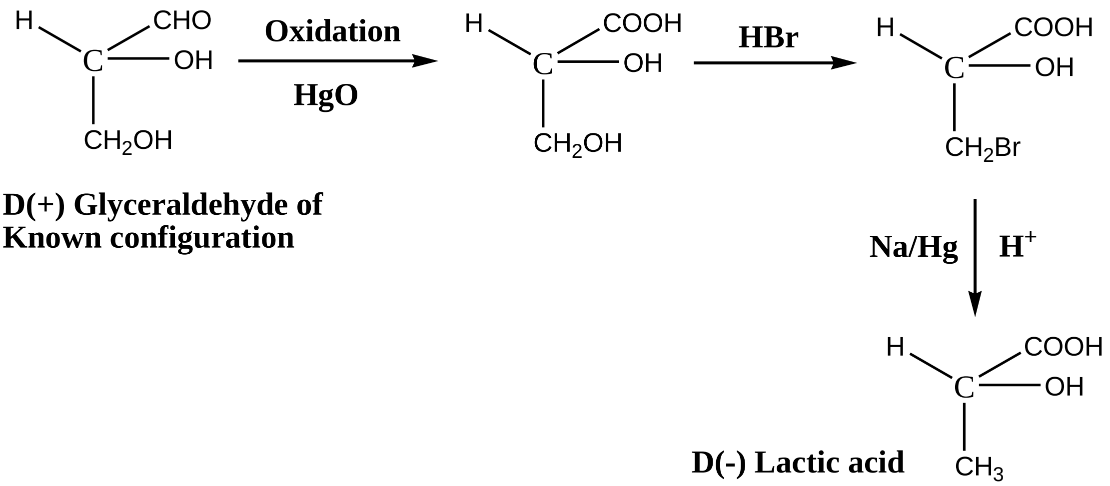
- Any compound that can be prepared from or converted to D-(+) glyceraldehyde will belong to D-Series and similarly any compound that can be prepared from or converted into L (-) glyceraldehyde will belong to L-series.
- For example Glyceric acid prepared from dextrorotatory D-glyceraldehyde belongs to D-Series which is leavorotatory.



D-(+) glyceraldehyde L-(-) glyceraldehyde

- **It should be noted that**
  1) 'D' and 'L' are configurational symbols and there can be 'D' (+) and 'D'(-) compounds. Similarly, there can be 'L' (+) and 'L'(-) compounds
  2) (+) and (-) i.e. d & l refer to the rotation of the plane of Polarized light. It is a physical property.

Lactic acid prepared by the following series of reactions from D (+) glyceraldehyde, has D- configuration which is laevorotatory.

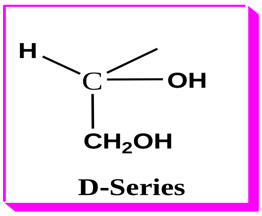


D(+) Glyceraldehyde of Known configuration

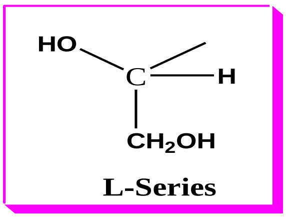
D(-) Lactic acid

Similarly, lactic acid prepared from L(-) glyceraldehye will have L(+)configuration.

In case of compounds containing, more than one, asymmetric Carbon atom, while representing relative configurational relationship, the asymmetric carbon atom of glyceraldehyde is always drawn at the bottom and the rest of the molecule is then built up.

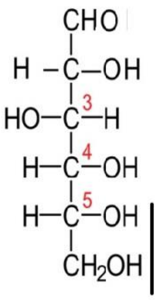


D-Series

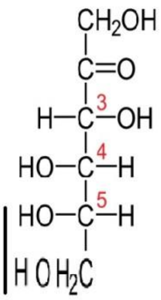


L-Series

Glucose and fructose having following structural formulae represent 'D' and 'L' configurations respectively.



D(+) Glucose



L(+) Fructose

Absolute configuration (CIP/R-S notational system):

- The configuration of an asymmetric carbon is the **specification of the relative spatial placement** of the four groups attached.
- The absolute configuration, in particular, **specifies the order of priority of atoms or groups,** attached to asymmetric carbon atom. On this basis, we can distinguish the two enantiomers and thereby define their chirality;

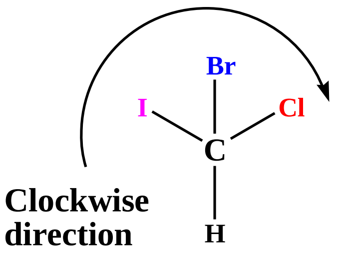
- R.S. Cahn (The Chemical Society, London) Sir Christopher Ingold (University college-London) and V. Prelog (Zurich) proposed a scheme of representation of optical isomers on paper by using prefix **‘R’**, derived from Greek word **Rectus meaning right** and prefix **‘S’**, derived from Greek word **sinister meaning left**. The system is known as **Cahn-Ingold-Prelog (CIP)** system of nomenclature after the names of authors.
- In R-S notational system, configurations are assigned to the molecules according to the following sequence rules.

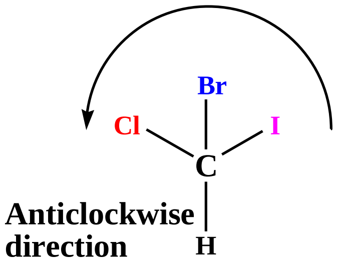
Sequence rule I: A sequence of priority is assigned to the four different atoms or groups attached to the chiral carbon atom. **Priority is based on atomic numbers**. An atom with **higher atomic number gets higher priority.**

Example 1) In case of Bromo chloro iodo methane the sequence of priority is I > Br > C1 > H.

In the arrangement, if I → Br → Cl traces a right handed turn (Clockwise), the configuration is ‘R’. If traces a left handed turn (anticlockwise), the configuration is ‘S’.

‘R’ and ‘Configuration of the above molecule in the form of two dimensional Fisher projection structures, can be represented as follows,

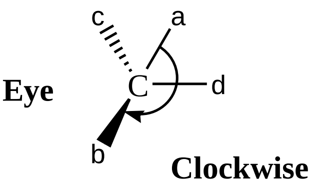




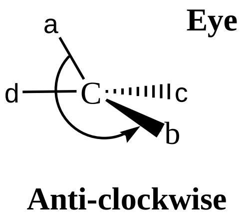
Note: *In two dimensional Fischer structure, horizontal lines represent bonds rising above the plane of the paper (towards observer) and vertical tunes represent bonds projecting behind the plane of the paper (away from the observer).*

‘R’ and ‘S’ configurations in tetrahedral structures, can be represented by observing the following rules.

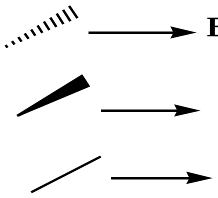
- Visualize the tetrahedral structure orientated so that the atom or group of atoms of lowest priority (d) is directed away from us and observe the arrangement of the remaining atoms or groups of atoms
- if, in proceeding from the atom or group of highest priority (a) to atom or group of second priority (b) and then to the third (c),
- Our eye travels in a clockwise direction, the configuration is specified ‘R’; if anticlockwise, the configuration is specified ‘S’.



R-Configuration



S-Configuration

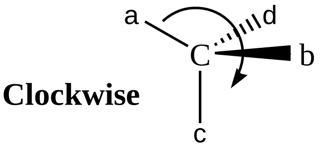


Broken line represents behind the plane of paper

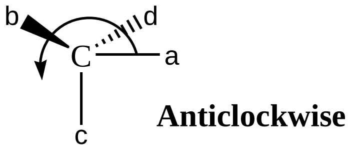
Dark wedge line represents infront of the plane of paper

Solid line represents in the plane of paper

- Projecting the **atom or group of lowest priority (d) behind the plane of paper** and **visualizing the structure from the front side**, ’R’ and ‘S’ configurations in the form of three dimensional tetrahedral structures, can be represented as follows.



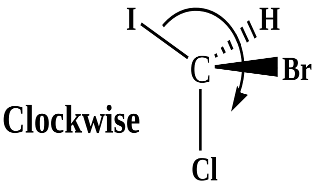
R-Configuration



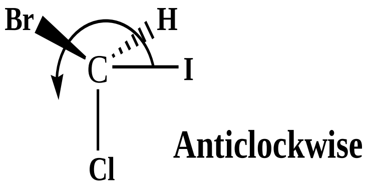
S-Configuration

*(**Note:** The position of atom or group of atoms of lowest priority (d) is to be ignored while deciding the sequence of priority for a. b & c.)*

On this basis, R and S configurations of Bromo chloro iodo methane can be represented as,



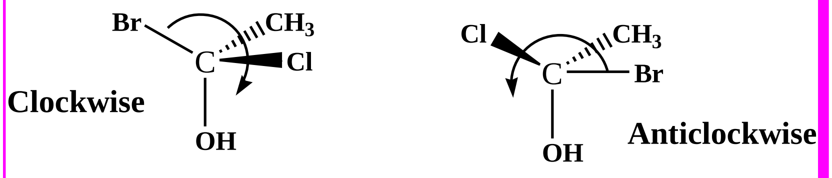
R-Configuration



S-Configuration

Similarly ‘R’ and ‘S’ configurations of the following compounds can be represented as, 1)**1-Bromo-1-chloro ethanol.**

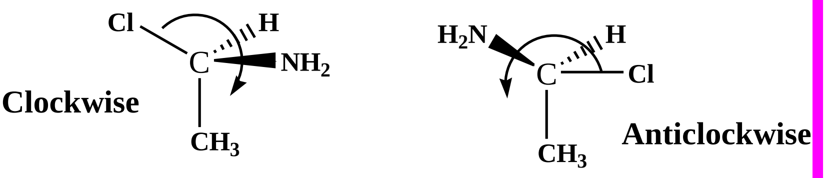
In this compound sequence of priority is Br > Cl > OH > CH_3



R-Configuration **S-Configuration**

2) 1-chloro ethylamine.

In this compound sequence of priority is Cl > NH_2 >CH_3 > H



R-Configuration **S-Configuration**

3)1-chloro-1-propanol.

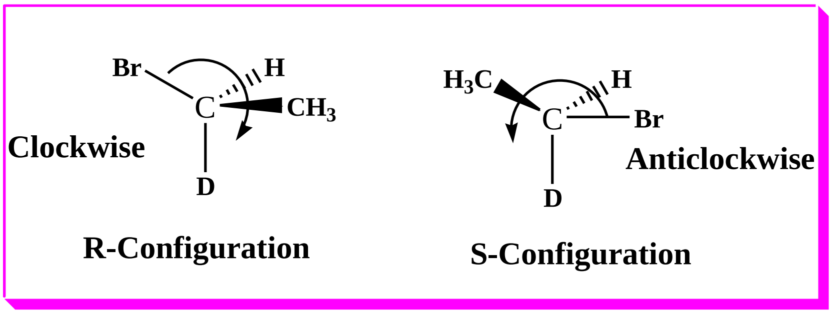
In this compound sequence of priority is Cl > OH >CH_3CH_2> H

R-Configuration **S-Configuration**

Sequence rule II: If two atoms are isotopes of the same element the atom of higher mass number gets the higher priority.

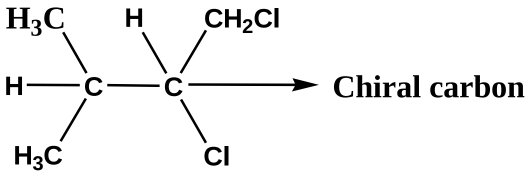
For example: In **α-deutero ethyl bromide** the sequence of priority is Br > CH_3 > D > H.

Hence 'R' and 'S' configurations can be represented as,

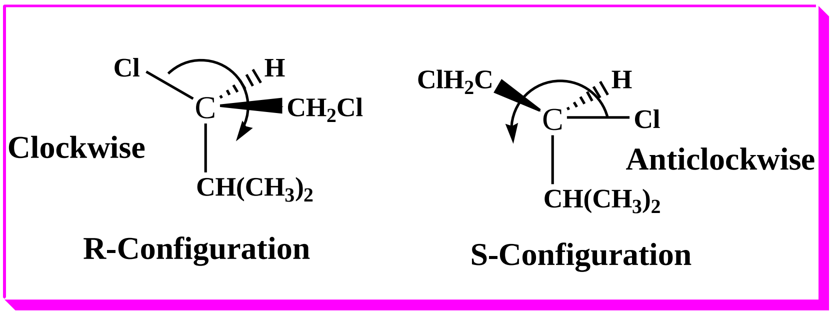


Sequence rule III: If two or more atoms attached to chiral carbon atom are the same, sequence rule -I cannot decide the priority, in such cases, compare the second atoms attached to each of these first atoms.

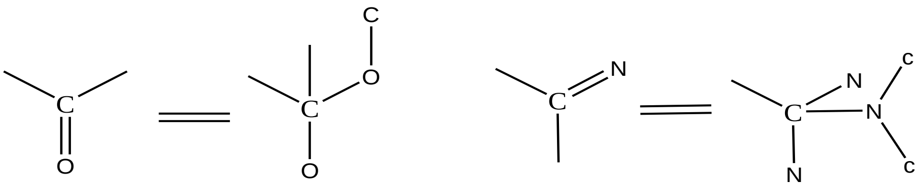
For example in **1,2 dichloro-3-methylbutane**



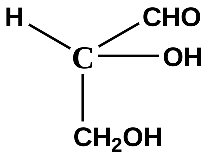
- Carbon atom ‘2’ is chiral. Two atoms (carbon atoms 1 and 3) attached to chiral center are same.
- In CH_2Cl, second atoms are H, H and Cl while in $(CH_3)_2C$-H group, second atoms are C,C and H. Among these atoms, Cl has higher atomic number.
- Hence –CH_2Cl group gets priority over $(CH_3)_2C$-H group (Isopropyl group) hence, in this compound, sequence of priority is, Cl > CH_2Cl > $(CH_3)_2CH$- > H. On this basis ‘R’ and ‘S’ configuration can be represented as,

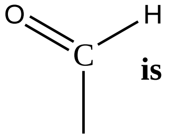


Sequence rule IV: If a molecule contains group with multiple bond (a double or triple bond) then for the purpose of determining priority, both atoms of that group are considered to be duplicated or triplicated.

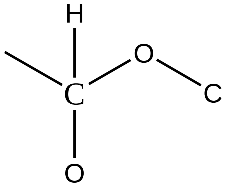


For example in **Glyceraldehyde,**



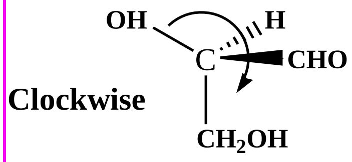


is equivalent to

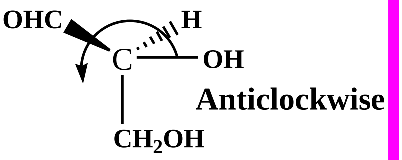


that is in -CHO group

- Second atoms attached to carbon atom are H, O and O. In –CH_2OH, second atoms are H, O and H. Hence.-CHO group gets priority over –CH_2OH.
- Sequence of priority is -OH > -CHO > -CH_2OH > H.,
- Hence ‘R’ and ‘S’ configuration of Glyceraldehyde can be represented as,

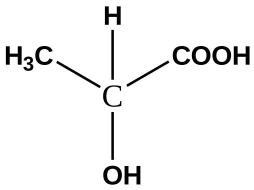


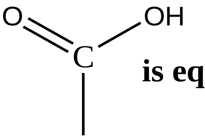
R-Configuration



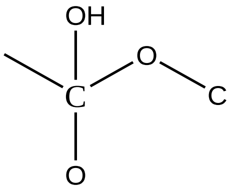
S-Configuration

Similarly in **Lactic acid**



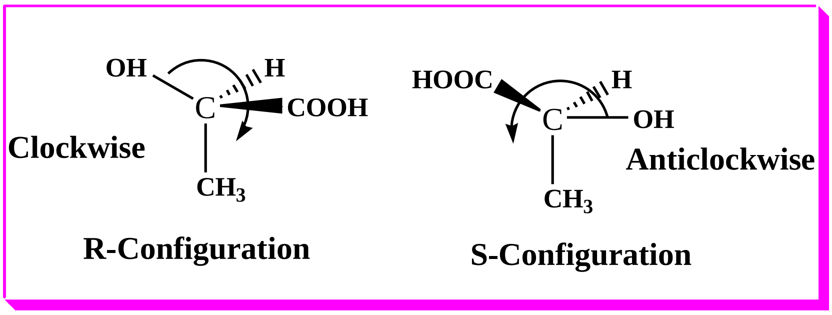


is equivalent to



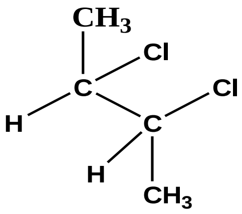
that is in -COOH group

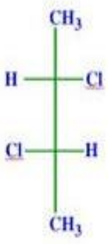
- That is second atoms in –COOH group are O, O and O. In CH_3 group, second atoms are H, H and H. Hence,-COOH group get priority over –CH_3.
- Sequence of priority is -OH > -COOH > -CH_3 > H., Hence ‘R’ and ‘S’ configuration of Lactic acid can be represented as,



Chiral and achiral molecules with two stereogenic centers:

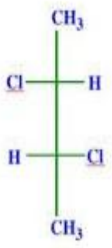
2, 3-Dichlorobutane contains two chiral centers (carbon 2 and 3).These two chiral centers occupy equivalent positions along the carbon chain. Optical stereoisomers exhibited by 2, 3-dichlorobutane in the form of two dimensional Fisher projection formulae can be represented as follows,





1

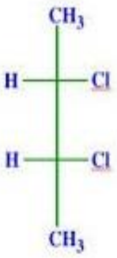
S,S



2

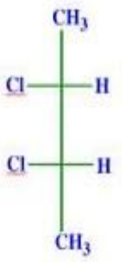
R,R

- ➢ In optical stereoisomers 'I' form, both chiral centers exhibit S,S configurations while in stereoisomer 'II' form, both chiral centers exhibit R,R configurations.
- ➢ Both 'I' and 'II' stereoisomers are mirror images of each other and non-superimposable. Hence, 'I' and 'II' forms are **optically active enantiomers.**



3

2S,3R



4

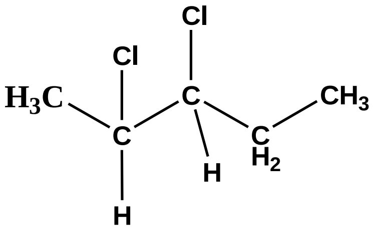
2R,3S

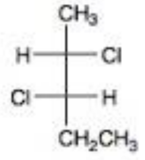
- ✓ In III and IV stereoisomers both chiral centers possess opposite configuration. (In III 2S, 3R and in IV 2R, 3S).III form is superimposable with its mirror image IV form.
- ✓ Moreover, both III and IV forms possess plane of symmetry. Hence these forms become achiral molecules and they do not exhibit optical activity that is **they are optically inactive.**
- ✓ Molecule that has chiral centers but itself is achiral is called as '**Mesoform'.**

Note:

- In Fischer projection formula when atom or group of **lower priority** (e.g. H) is on the **horizontal line**, the **configuration opposite to the configuration** exhibited by chiral center is considered, e.g In figure of 'I' form, arrows indicate R,R configuration for both chiral centers but they are considered as S,S.
- Similarly, In II-form, both chiral centers represent R, R configurations.
- When atom or **group of lowest priority** (e.g. H) in Fischer Structure is **on the vertical line**, **no change in configuration** is made.

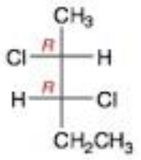
Similarly, stereoisomers of 2,3-dichloro pentane





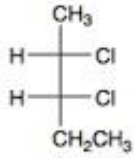
2S,3S

I



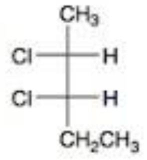
2R,3R

II



2S,3R

III



2R,3S

IV

2,3 dicloropentane contains two chiral centers (carbon atom 2 and 3).

- According to sequence rules, the order of priority of atoms or groups attached to carbon '2' is, -Cl > $-CHClCH_2CH_3$ > $-CH_3$ > H
- and for carbon 3 is -Cl > $-CHClCH_3$ > $-CH_2CH_3$ > H.

- **Structure I (2S, 3S) and II (2R, 3R) stereoisomers** are **mirror images of each other** and **non-superimposable**. Therefore they are **enantiomers**. They **do not possess plane of symmetry**. Hence, they are **optically active.**
- **Structure III (2S, 3R) and IV (2R, 3S) stereoisomers** are **also mirror images of each other** and **non-superimposable**. Therefore, they are **enantiomers**. Two chiral centers have **different groups**. They **do not possess plane of symmetry**. Hence, they are **optically active.**
- Structure or form **I and II are non-superimposable on III** form **but they are not mirror images of each other**. Therefore, they are **not enantiomers**. **Such stereoisomers**

which are not mirror images of each other but non-superimposable, are **called as ‘Distereoisomers’**. Thus, compound **III is a distereoisomer of I and II.** Similarly compound **IV is a distereoisomer of I and II.**

Properties of Distereoisomers:

1) Distereoisomers differ in their physical properties like B.P., M.P., densities, refractive index and solubility in the given solvent.

2) They have similar chemical properties but chemical reactions are not identical.

3) When two distereoisomer differ from each other at only one stereo center they are epimers. Each stereo center gives rise to two different configurations and thus typically increases the number of stereoisomers by a factor of two.

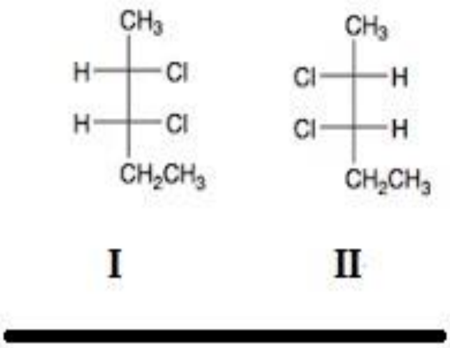
4) They are similar, but they are not mirror images.

5) Enantiomers have opposite configuration at all chiral centers; Distereoisomers are opposite at some but not all chiral centers.

Threo and erythro Diastereomers:

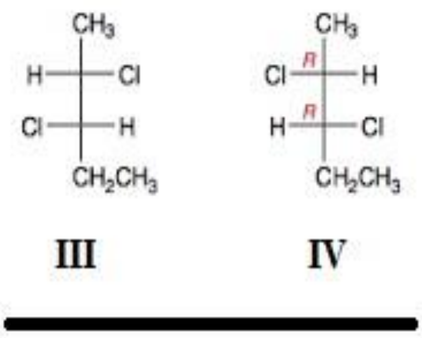
Organic chemists use an **informal nomenclature system** based on Fischer projections to **distinguish between Distereoisomers,**

- When the **carbon chain is vertical** and **similar substituents are on the side** of the Fischer projection, the molecule is described as the **"erythrose" diastereoisomer**.
- When similar substituents are **on opposite sides** of the Fischer projection, the molecule is described as the "**threose**" distereoisomer.
- Thus for example, stereoìsomers of **2, 3-dichloropentane** can be represented as,



I **II**

Erythrose

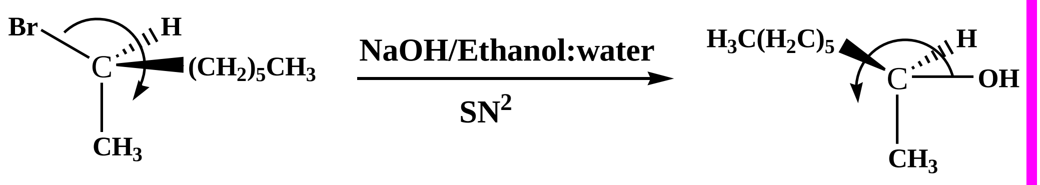


III **IV**

Threose

Stereochemistry of Nucleophilic aliphatic substitution reaction (S_N1 and S_N2):

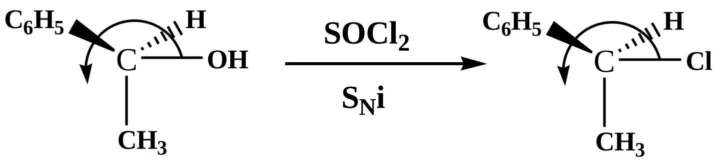
1) R(-)2-bromo-octane (A molecule containing one stereogenic/asymmetric center) on hydrolysis with NaOH solution gives S(+) 2-octanol.



R(-)2-Bromo-octane **S(+) 2-Octanol**

It is **S_N2 reaction** and the nucleophile **attacks the substrate from the side opposite to the bond of the leaving group**. This is called "**backside displacement** or substitution with **inversion of configuration or Walden inversion**"

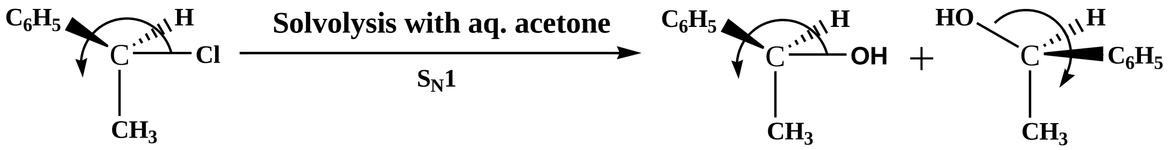
2) (S) 1-phenyl ethanol on treatment with thionyl chloride ($SOCl_2$) gives (S) 1-phenyl ethyl chloride.



(S) 1-phenyl ethanol **(S) 1-phenyl ethyl chloride**

In this reaction, nucleophile attacks the substrate at the same face from which the leaving group departs. This is called "front side displacement or substitution with retention of configuration" Such reaction is designated as S_Ni (Internal Nucleophilic substitution).

3) (S) 1-phenyl ethyl chloride on solvolysis with aq. acetone gives a mixture of (S) 1-phenyl ethanol and (R) 1-phenyl ethanol.(Solvolysis is a Nucleophilic substitution in which the nucleophile is molecule of solvent).



(S) 1-phenyl ethyl chloride
(optically active)

(S) 1-phenyl ethanol **R-1-phenyl ethanol**

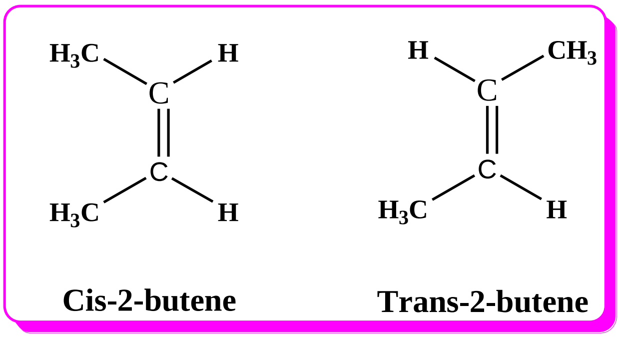
It is **S_N1 reaction** and takes place with **formation of racemic mixture i.e. racemization** (A reaction that transforms an optically active compound into a racemic mixture is said to proceed with racemization).

This reaction proceeds through the **formation of an intermediate carbocation**, because of it trigonal planar configuration, reacts with water (nucleophile) **with equal rates from either side to form the dextro and laevo (R and S)** enantiomers of 1-phenyl ethanol in equal amounts in the form of **racemic mixture** which is **optically inactive.**

Geometrical Isomerism:

Definition: It is the isomerism exhibited by compounds having the **same molecular** and **structural formulae** but they **differ in spatial arrangement of atoms or groups** around the **doubly bonded carbon atoms**.

e.g. **2-Butene** exhibits following two geometrical isomers.

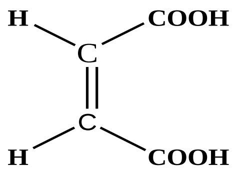


- Compounds having **similar** or identical **groups on the same side** are called as **cis compounds**.
- Compounds having **similar** or identical **groups on the opposite side** are called as **trans compounds.**
- **Properties of Geometrical isomerism:**
  1) These geometrical isomers differ in their physical properties and chemical reactions.
  2) The presence of double bond restricts the rotation and also a change from one form to another.
  3) Geometrical isomers are not mirror images of each other. Therefore, they are not enantiomer but may be considered as Distereoisomers.
  4) Physical properties of geometrical isomers depend on

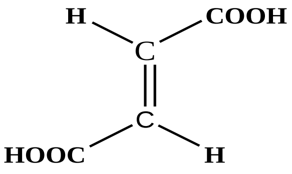
     a) The polarity of the molecules: Cis isomer has a net dipole moment and dipole – dipole attractions between its molecule, whereas, trans isomer which is nonpolar has only vander Waals forces. Thus B.P. of cis is therefore higher than trans.

b) The shape or symmetry of molecules: The trans isomer are packed closely due to greater symmetry, so intermolecular forces are more effective then cis isomer, so M.P. of trans isomer is therefore higher.

e.g. Maleic and Fumaric acids represents **cis and trans forms** respectively.



Maleic acid
(cis-Butenedioic acid)



Fumaric acid
(trans-Butenedioic acid)

It is easy to name the geometrical isomers if the two groups are identical. But when all four groups are different, then nomenclature of geometrical isomers becomes difficult.

A new system of nomenclature of geometrical isomers, called the 'E' and 'Z' nomenclature system has been introduced to name geometrical isomers with four different groups.

E-Z Nomenclature:

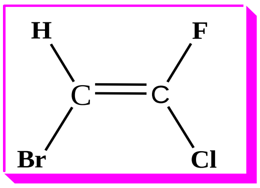
'E' label has been derived from the **German word 'entgegen'** meaning **opposite** and

'Z' label has been derived from the **German word 'zusammen'** meaning **follow together**.

In E-Z nomenclature system, configurations are assigned according to the following sequence rules.

Rule I: When two different atoms or groups are attached to the double bonded carbon atoms, then the sequence of priority of atoms or groups at each carbon atom is decided on the basis of atomic numbers.

e.g. In **1-bromo-2-chloro-2-fluro ethane.**

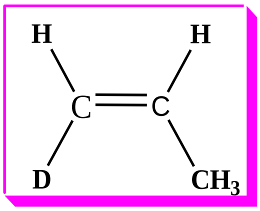


Sequence of priority of atoms

at carbon '1 'is , Br > H and

at carbon '2' is . Cl > F

If two atoms attached to double bonded carbon atom are isotopes of the same element, atom of higher mass number gets higher priority. **e.g. 1-deutero propene.**



Sequence of priority of atoms

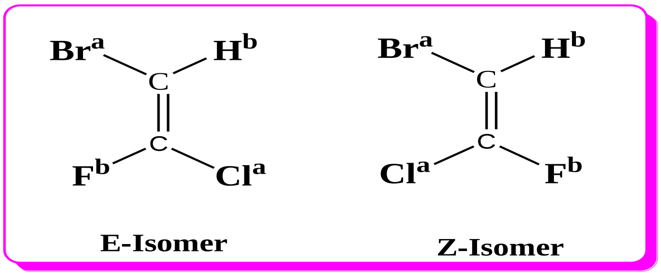
at carbon ‘1 ‘is , D > H and

at carbon ‘2’ is , $CH_3 > H$

Rule II:

- Let us designate **atoms or groups** with **higher atomic number** at **each double bonded** carbon atom **as "a"**
- And **atoms or groups** with **lower atomic numbers** at **each double bonded** carbon atom **as "b"**.
- The geometrical isomer in which **two "a"** atoms or groups are **on the same side**, is **designated as ‘Z’** and
- Another in which **two "a" atoms or groups** are **on opposite side**, is **designated as ‘E’.**

On the basis of these rules, ‘E’ and ‘Z’ forms of 1-bromo-2-chloro2-fluoro ethene can be represented as follows.

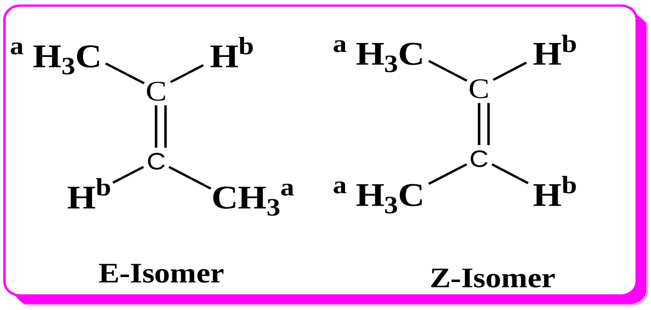


E-Isomer **Z-Isomer**

In ‘E’ form, two higher priorities “a” groups are on opposite while in ‘Z’ form, they are on same side.

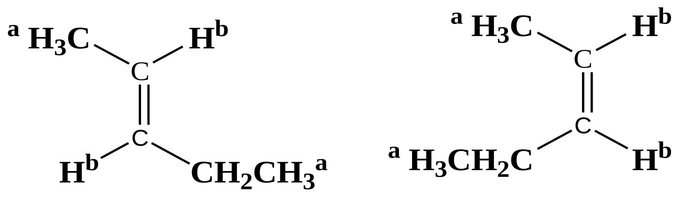
Other examples are,

1) **2-Butene:**



E-Isomer **Z-Isomer**

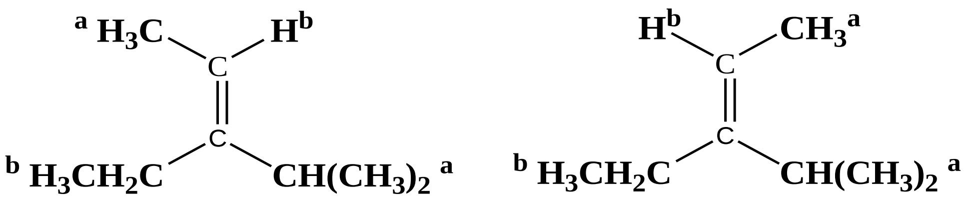
2) 2-Pentene:



E-Isomer **Z-Isomer**

3) 3-Ethyl-4-methyl-2-pentene:

Sequence of priority at carbon ‘2’ is CH_3 > H and at carbon ‘3’ is $–CH(CH_3)_2 > -CH_2CH_3$.

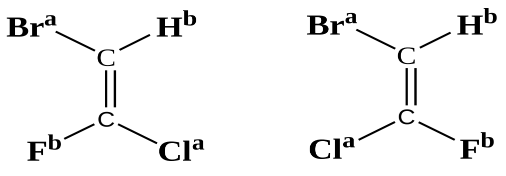


E-Isomer **Z-Isomer**

Rule II:

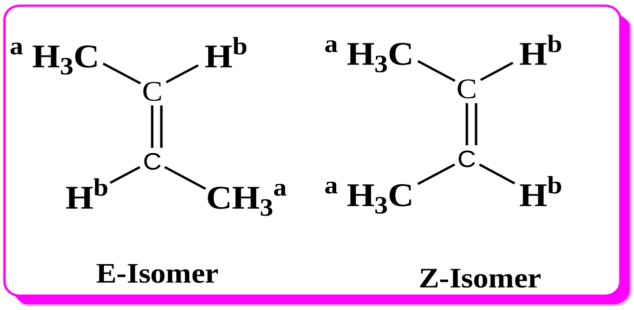
- Let us designate **atoms or groups with higher atomic number** at each double bonded carbon atom as "**a**" and **atoms or groups with lower atomic numbers** at each double bonded carbon atom as "**b**".
- The geometrical isomer in which **two "a" atoms or groups are on the same side**, is designated **as ‘Z’** and
- Another in which **two "a" atoms or groups are on opposite side**, is designated **as ‘E’**.

For e.g. ‘E’ and ‘Z’ forms of 1-bromo-2-chloro 2-fluoro ethene can be represented as follows.



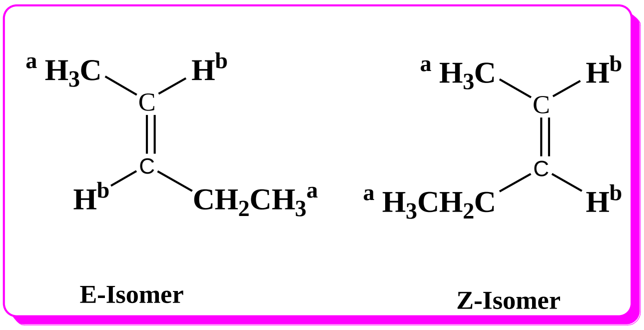
E-Isomer **Z-Isomer**

Example 2) 2-Butene:



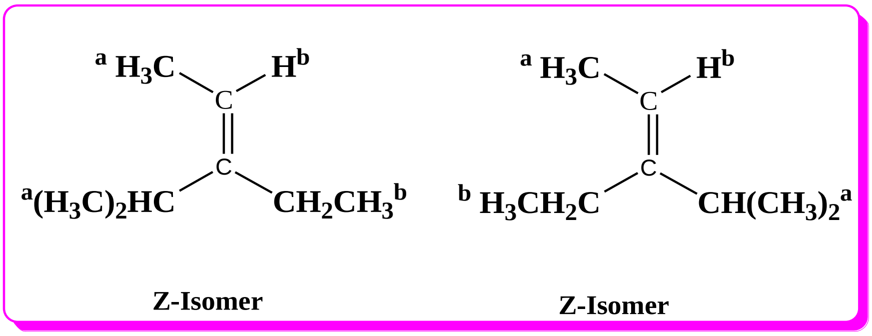
E-Isomer **Z-Isomer**

Example 3) 2-pentene:



E-Isomer **Z-Isomer**

Example 4) 3-ethyl-4-methyl-2pentene:

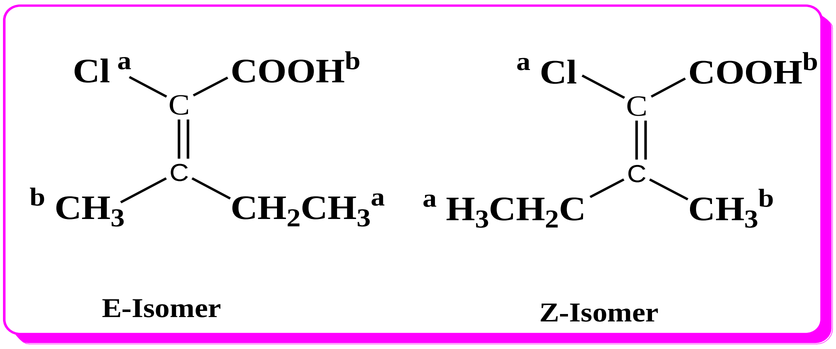


Z-Isomer **Z-Isomer**

* Sequence of priority at carbon ‘2’ **is CH_3 >H.**

* Sequence of priority at carbon ‘3’ **is –$CH(CH_3)_2$ > CH_2CH_3.**

Example 5) 2-chloro-3-methyl-2-pentenoic acid:



E-Isomer **Z-Isomer**

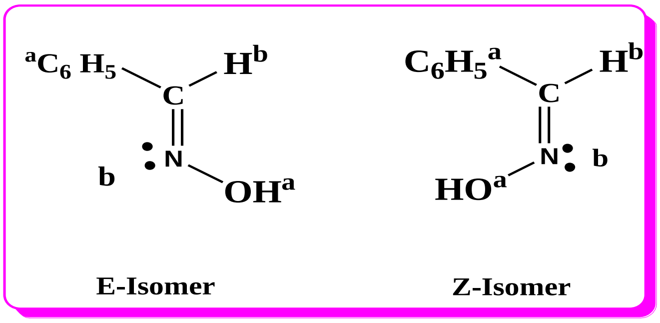
* Sequence of priority at carbon ‘2’ **is -Cl >-COOH.**

* Sequence of priority at carbon ‘3’ **is –$CH_2\,CH_3$ > -CH_3.**

Rule III: Geometric isomerism in oximes:

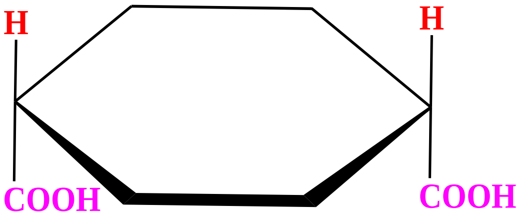
- If in a compound, one of double bonded atom is not having any substituent, then, While deciding priority, that vacant position is considered to have an atomic number zero.
- e.g. in **Benzaldoxime** at nitrogen atom, there is only -OH group & another position is vacant. Hence, -OH group is designated as "a" and vacant position as "b".
- At double bonded carbon atom, C_6H_5 is "a"& H is "b".

Therefore, E & Z forms of Benzaldoxime can be represented as follows,

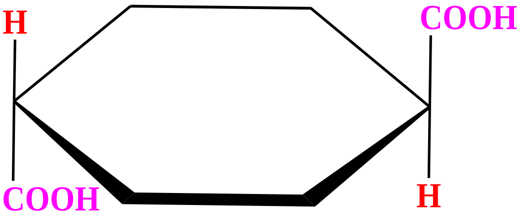


Geometric isomerism in alicyclic compounds:

In substituted alicyclic compounds, due to the restricted rotation about a ring, geometrical isomerism may also develop. Thus. 4-cyclohexane dicarboxylic acid exists in cis and trans forms.

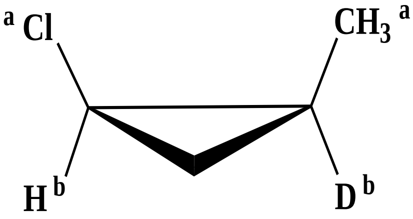


Cis-form (Z)

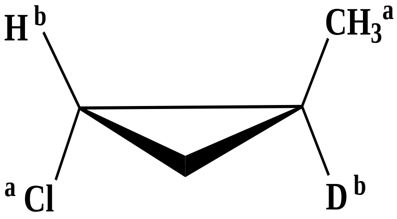


Cis-form (Z)

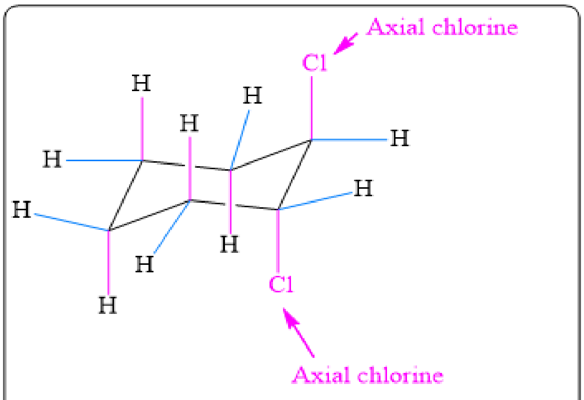
When two different atoms or groups are attached to the two carbon atoms of alicyclic ring, then the sequence of priority of atoms or groups is decided on the basis of atomic numbers. Accordingly,they are designated as "a" or "b", followed by ‘E’ and ‘Z’ nomenclature.



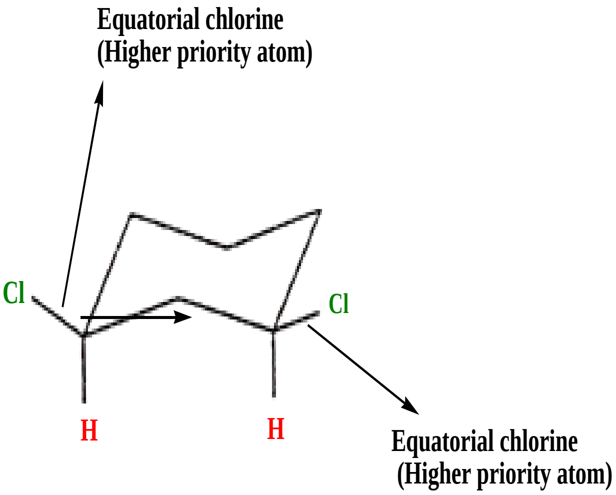
Z



E

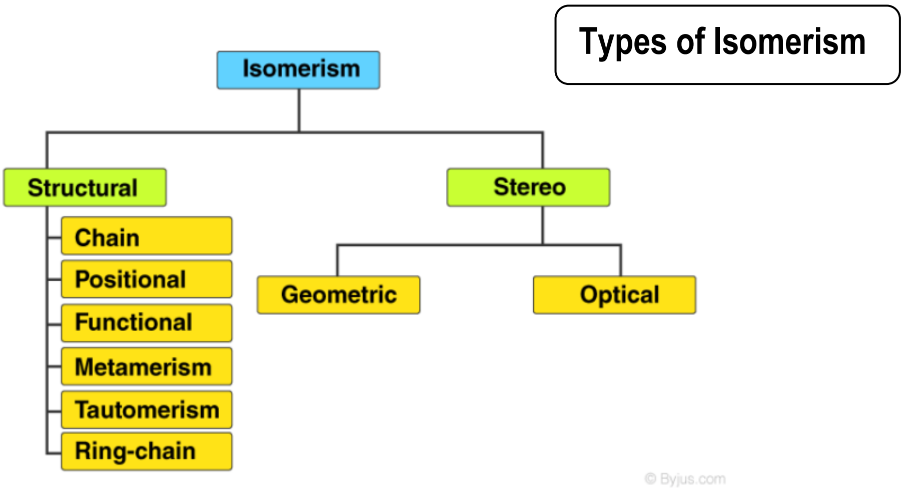


trans-1,2-Dichlorocyclohexane



Z/Cis 1,2 dichlorocyclohexane

Flow Diagram for Isomerism:



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DEPARTMENT OF CHEMISTRY

Question Bank

Class: B.Sc. Semester –I

Name of Paper: Organic Chemistry (Paper –II) CHE-102

Title of Chapter: Stereochemistry of Organic Compounds.

Questions:

Q.1. what do you understand by Isomerism? Give its classification.

Q.2 Write 'E' and 'Z' configuration for the following compounds.

a) 1-Bromo-2-chloro-2-fluro ethene
b) 2-Butene
c) 2chloro-3-methyl-2-pentenoic acid
d) 2-pentene
e) Benzaldoxime
f) 1-bromo-1-chloropropene
g) 1-bromo-1,2-dichloroethene
h)

Q.3. Define the terms.

a) Enantiomers
b) Stereogenic Centre
c) Optical Isomerism
d) Plane polarized light (PPL)

Q.4. Explain a) Plane of symmetry
b) Centre of symmetry with suitable examples.

Q.5 Write notes on following

a) Simple axis of symmetry
b) Sequence rules for R-S notational system.
c) Relative configuration (D-L notational system)
d) Alternating axis of symmetry

e) Racemic mixture

Q.6. Draw ‘R’ and ‘S’ configuration of the following

a) Bromo-chloro-iodo methane
b) Deutero ethyl bromide
c) 1-chloro ethyl amine
d) Glyceraldehyde
e) Lactic acid
f) 1,2-dichloro-3-methyl butane
g) Alanine ($HOOC-CH-CH_3-NH_2$)
h)

Q.7 Distinguish the following with suitable examples.

a) Distereoisomers and Tautomerism
b) Chiral and achiral molecules
c) Meso form and racemic form
d) Enantiomer and distereoisomer

Q.8.Discuss the in detail optical isomerism exhibited by 2,3-dichlorobutane.

Q.9 What is stereochemistry.

Q.10 what are isomers?

Q.11Draw the structures of cis and trans 1,2-dichorocyclopentane and apply the principles for chirality on it.(Which on is chiral and achiral)

Q.12 In what respect stereoisomers differ from one another

Q.13 what are distereoisomers? Explain giving the example of 2-bromo-3-chlorobutane.

Q.14 How can one recognize a meso compound? Explain giving suitable examples.

Q.15 what is optical activity?

Q.16 Comment on the chirality of 1,1-dichlorocyclopropane and 1,1,2-trichlorocyclopropane.

Q.17 Comment on the chirality of cis and trans-1,3-dimethyl-cyclobutane,whih of these is a meso compound ?

Q.18 In how many stereoisomeric forms 1,2-dimethylcyclopentane can exists ? Is there any meso compound?

Multiple choice questions:

1. Compounds which have different arrangements of atoms in space while having same atoms bonded to each other are said to have

a) Position isomerism

b) Functional group isomerism

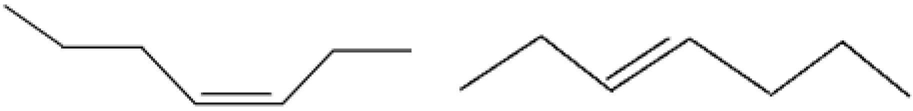
c) Chain isomerism

d) Stereoisomerism

2. Which of the following can make difference in optical isomers?

a) Heat b) temperature c) polarized light d) pressure

3. Which of the following terms best describes the following pair of molecules?



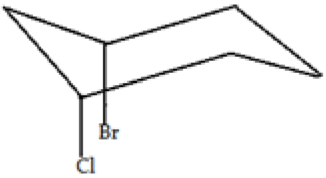
a) Isomers

b) Constitutional isomers

c) Configurational isomers

d) Geometrical isomers

4. What is the relationship between the two groups in the following molecules?



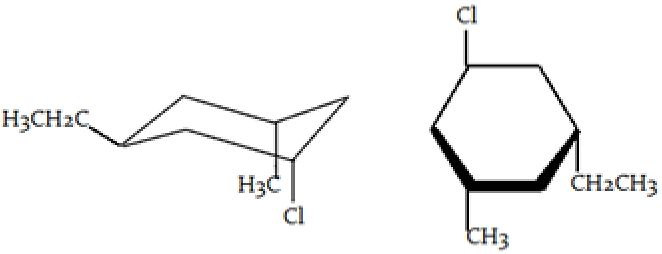
a) They are equatorial to one another

b) They are axial to one another

c) They are cis to one another

d) They are trans to one another

5. What is the stereochemical relationship between the following two molecules?



a) Geometrical isomers

b) Enantiomers

c) Diastereomers

<u>d) Identical</u>

6. Which of the following is an alkane which can exhibit optical activity?

a) Neopentane

b) Isopentane

c) 3–Methylpentane

d) 3–Methylhexane

7. Which of the following statements most accurately describes the stereochemistry between the various cyclohexanes?

a) Cis-1,2-dichlorocyclohexane and trans-1,2-dichlorocyclohexane rotate plane-polarized light in opposite directions, and together in equal proportions form a racemic mixture.

b) The diaxial and diequatorial forms of trans-1,3-dichlorohexane can be separated by their differing physical properties.

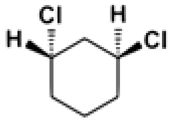
c) Only cis-1,4-dichlorocyclohexane is achiral due to a plane of symmetry, and cis-1,4-dichlorocyclohexane is diastereomeric to trans-1,4-dichlorocyclohexane.

d) The conformational isomers of trans-1,2-dichlorocyclohexane are enantiomers, which are not interconvertible, but resolvable.

Answer: d

Explanation: In the below given diagram of trans-1,3-dichlorohexane the chlorines cannot be positioned diaxial or diequatorial but can only be axial and equatorial or vice versa. Additionally, if they were diastereomers or structural isomers, then they could be separated by physical means.

8. Which of the following are meso compounds?



trans-1,3

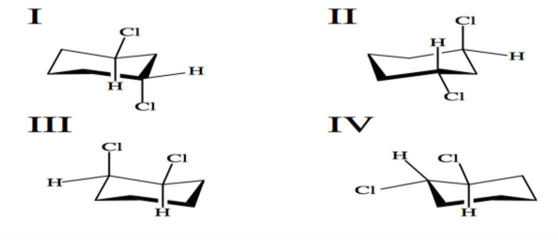
a) 2,4-dichloropentane

b) 1,3-dimethylcyclopentane

c) 2,3-dichloropentane

d) a and b are correct

9. Which of the given chair conformations represents a meso compound?



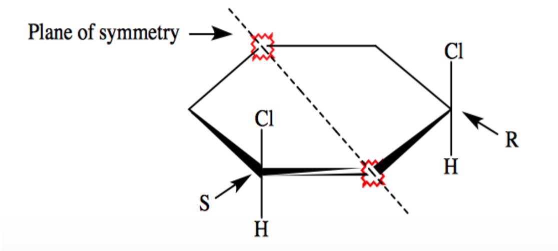
a) III b) I c) II d) None of these

10. Which of these molecules is a meso compound?

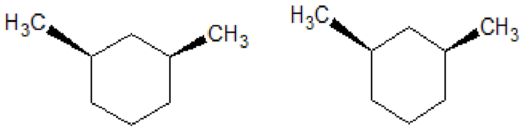
a) II only b) II & III c) III only d) IV only

Explanation:

A molecule is meso if it contains at least two stereocenters, but is rendered optically inactive by internal structural symmetry. In other words, a meso compound may be split in half in some way such that portions on either side of an imaginary line are mirror images. Note: The absolute configurations of a meso compound with two stereocenters are opposite (R/S). The internal symmetry that makes molecule III a meso compound is best conveyed through a Haworth projection:



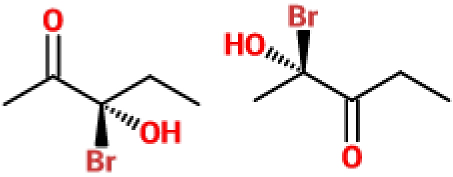
11. The given molecules are ____________.



a) Constitutional isomers b) conformers c) stereoisomers d) identical

Explanation: Stereoisomers have different orientations around a single stereocenter. The two molecules are stereoisomers. Specifically, these molecules are epimers, meaning that they differ at only one stereocenter. Constitutional isomers have the same molecular formula, but different structures. Conformers have different rotations around a single bond. The molecules are clearly not identical.

12. The molecules shown below are best described as ___________.



a) Isomers b) Diastereomers c) epimers d) enantiomers

Explanation: The molecules in this problem are isomers because they each have unique configurations and do not share the same funcitonal groups at the same carbon positions. Enantiomers are reflections of each other. Diastereomers are stereoisomers that differ at one or more stereocenters, while epimers are stereoisomers that differ at only one stereocenter.

13. How many distinct groups must a carbon have to be chiral?

a) Three b) one c) Four d) five

14. What are the terms that are symbolized by E and Z when notating alkene isomerism?

a) Electronic, Zwitterionic b) Elemental, Zeolitic

c) Elastomeric, Zymurgic d) Entgegen, Zusammen

15. Monosubstituted alkenes show E/Z isomerism.

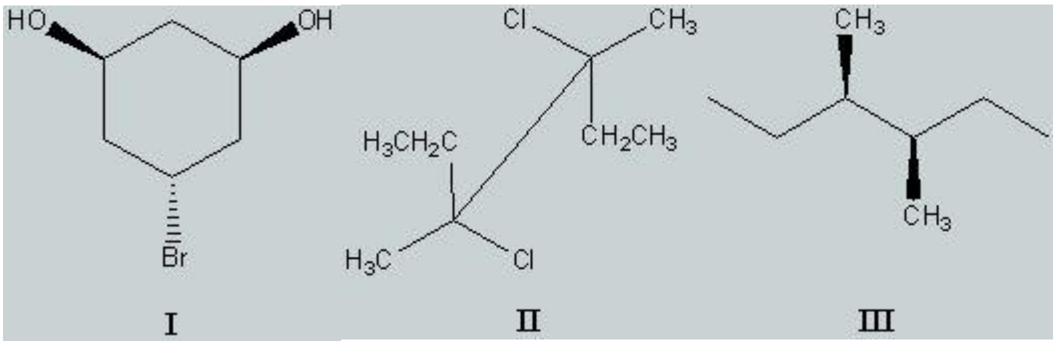
a) True b) False

16. What type of stereochemistry do SN^1 reactions show?

a) Racemization b) Retention of Configuration

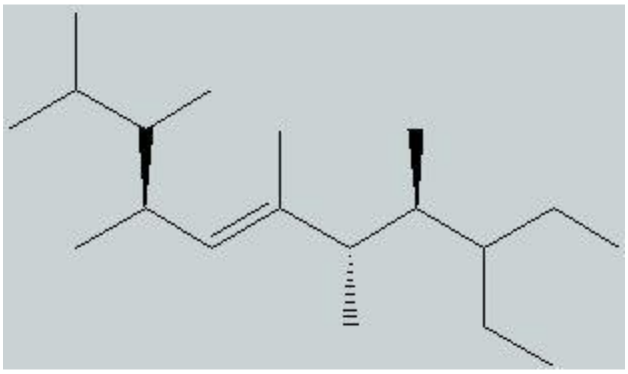
c) Inversion of Configuration d) Cis/trans isomerism

17. Which of the following three molecules is (are) achiral?



a) I only b) II only c) I and II d) I ,II and III

18. How many chiral atoms does the following molecule have?

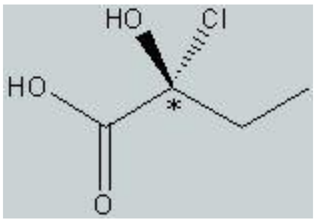


a) Three (3). b) Four (4) c) Five (5) d) Six (6)

19. Which of the following terms best describes the following pair of molecules?

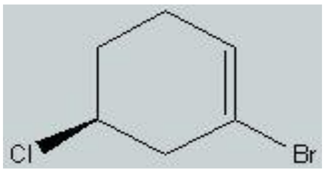
a) Isomers. b) ● Constitutional isomers c) ○ Configurational isomers d) Geometric isomers.

20. Which group on the atom marked with an asterisk (*) has the highest priority in the molecule below?



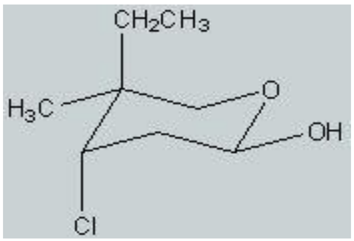
a) Alcohol b) Chlorine c) Ethyl group d) The carboxylic acid group

21. What is the spatial orientation of the double bond in the molecule below?



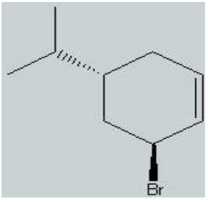
a) Cis b) Trans c) E d) Z

22. . In the molecule below, how many stereocenters have an S orientation?



a) Zero (0) b) one (1) c) Two(2) d) Three (3)

23. What is the complete name of the molecule below, if the base name of the molecule is 3-bromo-5-isopropylcyclohexene?



a (R)-bromo-(5,R)-isopropyl-Z-cyclohexene.

b) (3,S)-bromo-(5,S)-isopropyl-Z-cyclohexene

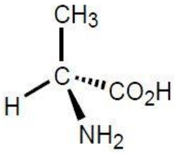
c) (3,S)-bromo-(5,R)-isopropyl-E-cyclohexene.

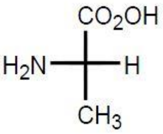
d) (3,S)-bromo-(5,R)-isopropyl-Z-cyclohexene

24. How many asymmetric carbons are present in the compound below?

a) One b) two c) three d) four

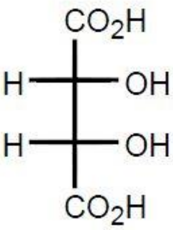
25. Which of the following terms best describes the pair of compounds shown: enantiomers, Diastereomers, or the same compound?





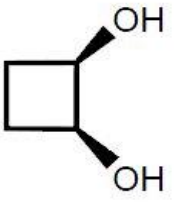
a) Enantiomers b) Disteromers c) Same compounds d) threo compound

26. How many asymmetric carbons are present in the compound below?



a) One b) two c) three d) four

27. Is the molecule shown chiral or achiral?



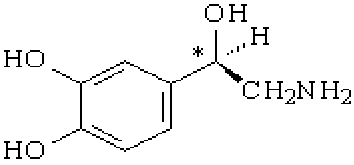
a) Chiral b) Achiral

Ans: Molecule is achiral (because it possesses of axis of symmetry)

28. Optically active molecules which rotate plane-polarized light in a counterclockwise direction are said to be

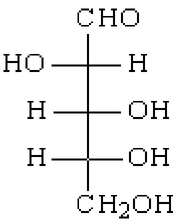
a) Levorotary b) of R configuration c) dextrorotary d) of S configuration

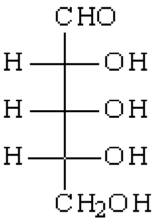
29. Assign 'R' or 'S' configuration to the chiral carbon marked with an asterisk



a) R b) S c) E d) Z

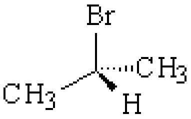
30. Assign the correct term describing the relationship to the following two isomers





a) enantiomers b) diastereomers c) identical d) Dissimilar

31. What is the stereochemistry of the following compound.



a) R b) S c) Meso d) Not chiral

32. Which of the following groups has the highest priority according to the Cahn-Ingold-Prelog sequence rules?

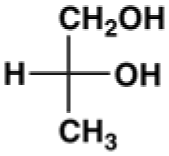
a) CH_3 b) CH_2Cl c) CH_2OH d) CHO

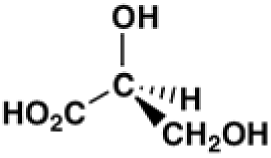
33. Which of the following groups has the highest priority according to the Cahn-Ingold-Prelog sequence rules?

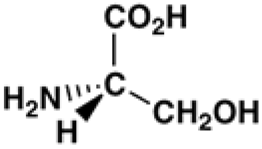
a)CΞCH b) $CH{=}CH_2$ c) $CH(OH)CH_3$ d)CH_2CH_2OH

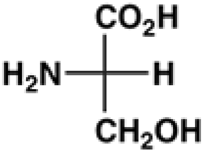
34. Which of the following has the (*R*) configuration?

a)

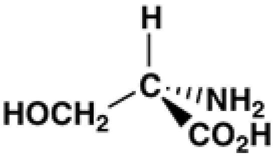


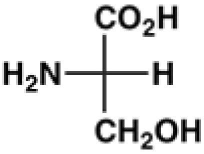
b)


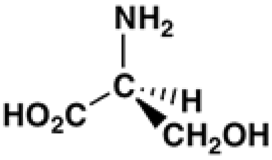
c)


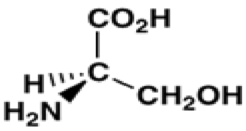
d)


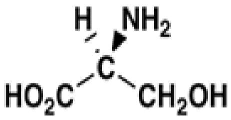
35. Which compound is the enantiomer of the following?



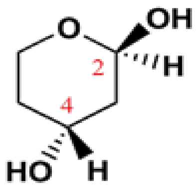
a)


b)


c) 

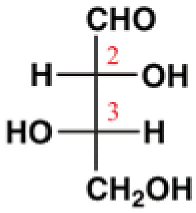
d) 

36. Which is the correct assignment of chirality at C2 and C4 of the following molecule?



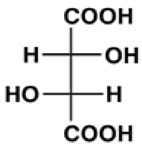
a) 2s,4R b)2R,4R c) 2S,4R d)2R,4S

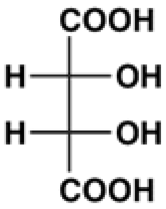
37. Which is the correct assignment of chirality at C2 and C3 of the following molecule?

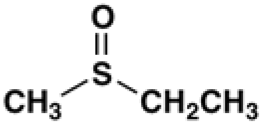


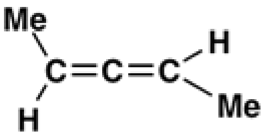
a) 2S,3R b)2,3R c) 2S,3R d)2R,3S

38. Which of the following compounds is achiral?

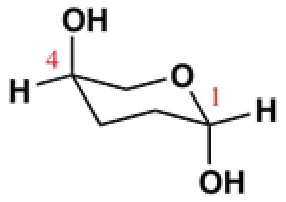
a) 

b) 

c) 

d) 

39. Which is the correct assignment of chirality at C1 and C4 of the following molecule?



a) 1S,4R b) 1R,4R c) 1R,4S d)1S,4S

40.2,3 dibromopropanol has -------asymmetric carbons

a) one b) two c) three d) four

41. Which the following compounds can show geometrical isomerism?

1) 2-pentene

2) 1,3-dibromocyclobutene

3) 1,1,2-trichloropropene

4) 2-methyl-3-heptene

a) 1 and 2 b) 1,2 and 3 c) 1,2 and 4 d) 1,2,3 and 4

42. According to perspective formula, the solid wedge indicates the group which is

a) towards reader

b) Away from reader

c) In plane of paper

d) none

43. Choose the functional groups which can act as functional isomers

1) R-CHO 2) R-COOH 3) RCOR 4) R-OH

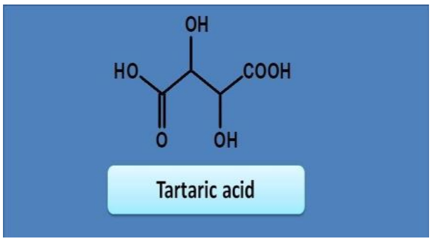
a) 1 and 4 b) 1 and 3 c) 1 and 2 d) 3 and 4

44. Stereocenter is a

a) Carbon attached to similar groups b) carbon attached to four different groups

c) carbon where interchange of groups gives isomer d) carbon having restricted rotation

45. How many stereoisomers are possible for the following structure?



a) two b) four c) three d) eight

46. Diastereomers are

a) Mirror images b) Non-superimposable c) Non mirror images d)Super imposable

47. Enantiomers will have

1) Same physical properties 2) same chemical properties

3) Different physical properties 4) Different chemical properties

a) 1 and 3 correct b) 2 and 4 correct c) 3 and 4 correct d) 1 and 2 correct

48. Erythro enantiomer will have

a) Similar group on same side b) Similar group on different side

c) Different groups on two chiral carbon d) Two chiral center with plane of symmetry

49. A pure single compound with chiral carbons has shown optical activity as zero. The compound may be

a) Dextro b) Laevo c) Meso d) Racemic

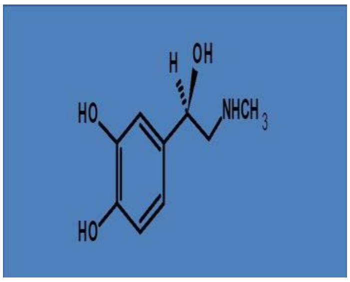
50. Diastereomers will have

1) Similar Physical properties 2) Similar chemical properties

3) Different Physical properties 4) Different chemical properties

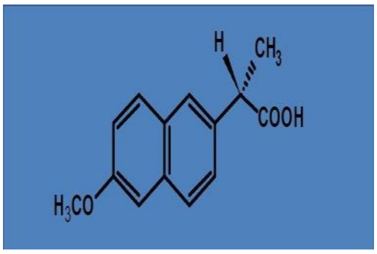
a) 1 and 4 b) 2 and 4 c) 1 and 3 d) 2 and 3

51. What is the configuration of the following structure



a) 2R b) 2S c) 1R d) 1S

52. The configuration of the above Naproxen drug is



a) 1R b) 1S c) 2R d) 2S

53. The functional isomers of ethers are

a) Ketones b) Aldehydes c) Alcohols d) Esters

54. Which of the following compounds can exhibit geometrical isomerism?

a) 1-Hexene b) 2-Methyl-2-pentene c) 3-Methyl-1-pentene d) 2-Hexene

55. Which of the following pairs of compounds are tautomers ?

a) Propanol and propanone b) 1-Propanol and 2-propanol

c) Ethanol and vinyl alcohol d) Vinyl alcohol and ethanol.