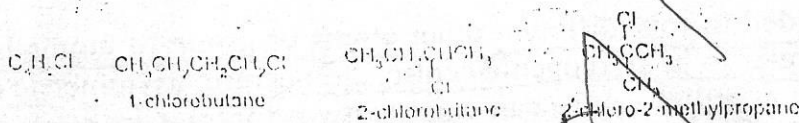
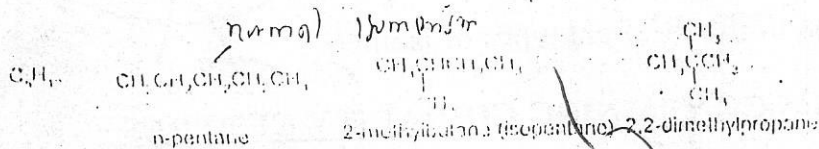
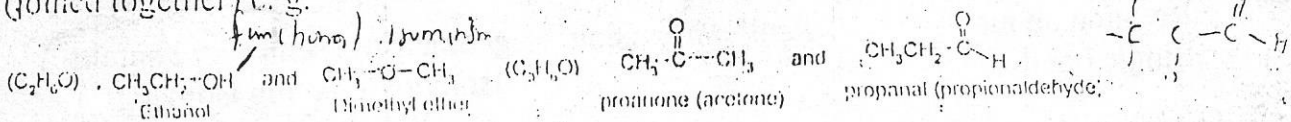


# ~~Handwritten~~ STEREOCHEMISTRY

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Isomerism is the existence of 2 or more compounds having the same molecular formula but different structural formula. There are 2 types constitutional isomers and stereoisomer

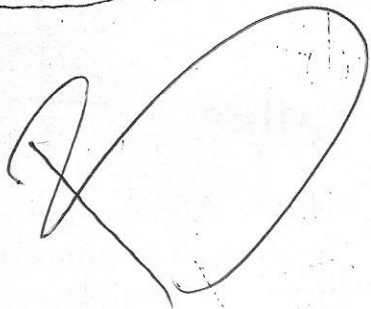
Constitutional (structural) isomers differ in the way their atoms are connected (joined together) e.g.



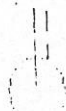
(C<sub>4</sub>H<sub>8</sub>O<sub>2</sub>)  
etc

On the other hand stereoisomers differ in the way their atoms are arranged in space i.e. the atoms are connected in the same way but differ in spatial arrangement in space.

There are two kinds of stereoisomer, conformational isomers and configurational isomers. Conformational isomers result from rotation about carbon-carbon single bonds and another kind is as a result of amine inversion. Conformational isomers interconvert rapidly at room temperature thus they cannot be separated. They are known as conformers e.g.

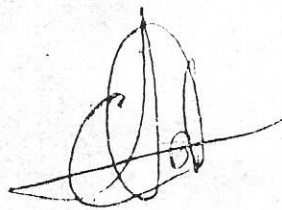


chair conformation of cyclohexane



boat conformation of cyclohexane

Configurational isomers on the other hand do not interconvert thus they are readily be separated. There are two kinds (Geometrical isomers and isomers that contain chirality centers)



08135609103

Tolu-my-in-law

# Isomers

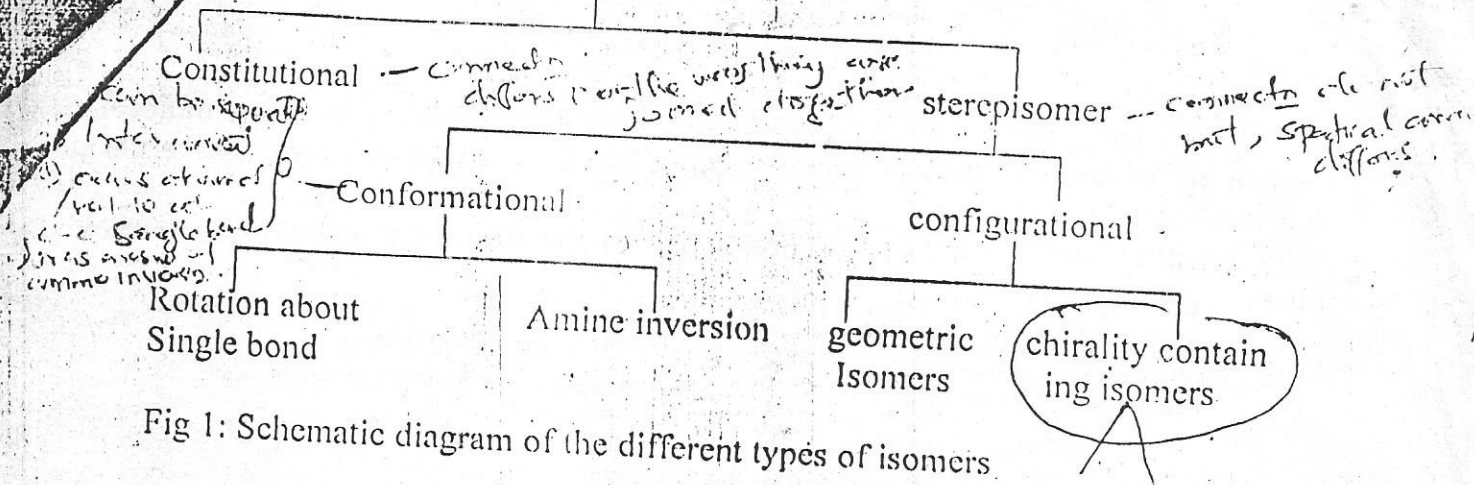
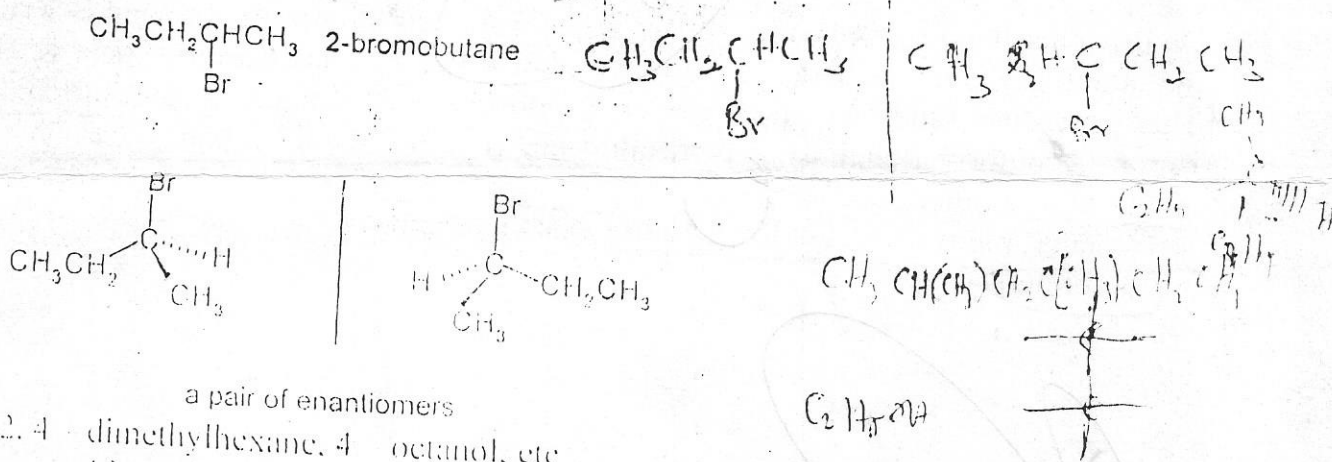


Fig 1: Schematic diagram of the different types of isomers

## ISOMERS CONTAINING CHIRALITY CENTRES.

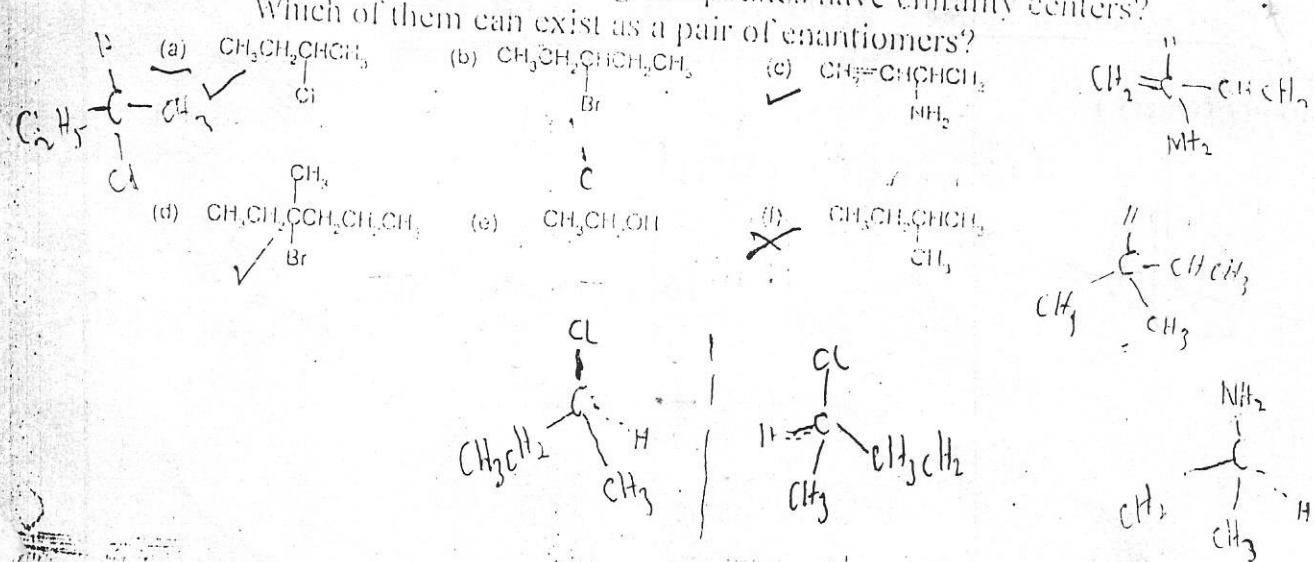
A carbon atom bonded to four different other atoms or group of atoms is known as chirality centre (also refer to as stereogenic centre, stereocentre, asymmetric carbon). A compound containing a chirality centre can exist as two different isomers. The two isomers cannot be super imposed. Just as you cannot super impose your left hand on your right hand e.g. 2-bromobutane



2, 4-dimethylhexane, 4-octanol, etc

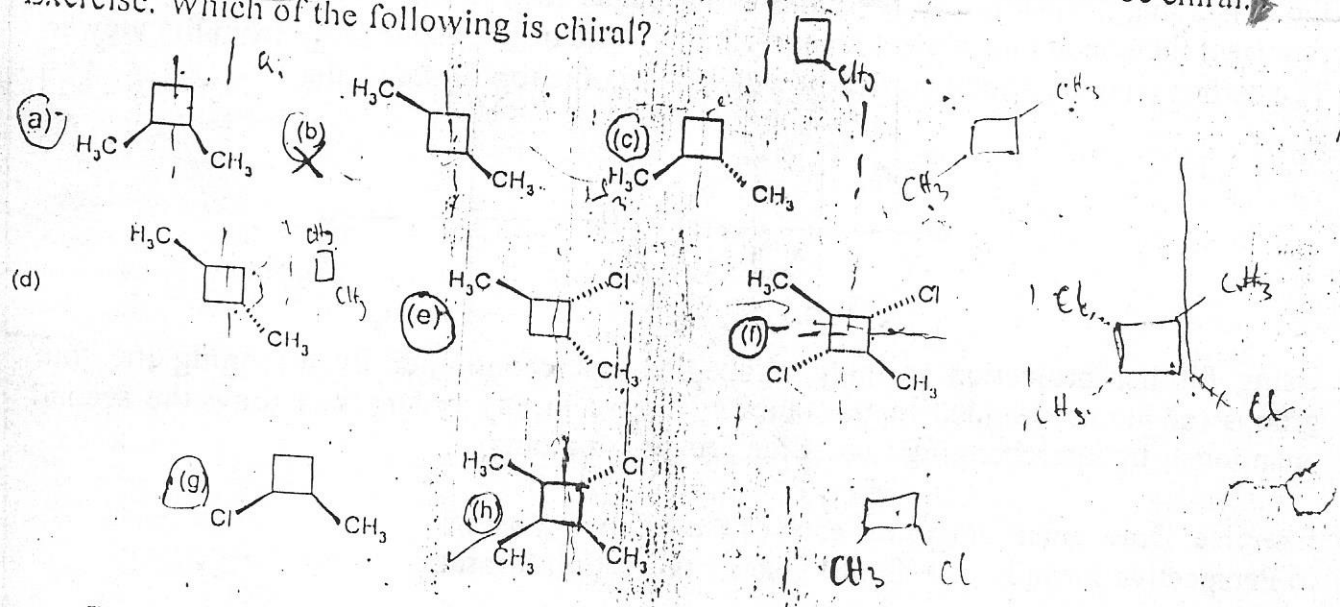
If a mirror is imagine between two isomers contain chirality centre, you will notice that they are mirror images of each others. A nonidentical (nonsuperimposable) mirror image is called an enantiomer of the original molecule. (Enantiomers is from the Greek word *enantion* meaning "opposite") Each of the isomers of 2-bromobutane is the enantiomer of the other.

Exercise: which of the following compounds have chirality centers?



A molecule that has a nonidentical mirror image is said to be chiral. A chiral molecule does not contain a plane of symmetry. (A plane of symmetry is a plane that cuts a molecule into two halves, each of which is a mirror image of the other.) Chiral objects do not contain a plane of symmetry e.g. hands, feet, shoes, etc. A molecule containing a plane of symmetry is said to be achiral, because if you cut the object in two halves along the plane symmetry, the left half is the mirror image of the right half, e.g. A fork, table, ladder etc. A chirality centre is what cause a molecule to be chiral.

Exercise. Which of the following is chiral?



DRAWING ENANTIOMERS

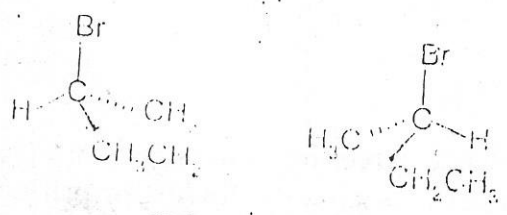
(There are two ways by which enantiomers can be drawn: The perspective formula and the Fischer projections formula.)

Perspective Formula

In perspective formula two lines are used to represent two of the bonds to the chirality center in the plane of the paper, one bond as a solid wedge coming out of the paper, and the fourth bond as a hatched wedge projecting back from the paper.

- lines ..... represent bonds on the plane of the paper
- solid wedges ..... represent bonds coming out of the paper
- hatched wedges ..... represent bonds projecting back from the paper

e.g. 2-bromobutane

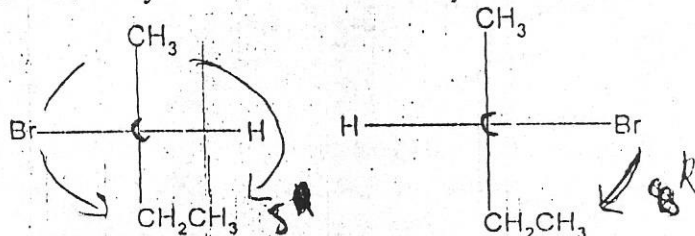


You may draw the first enantiomer by putting the four groups bonded to the chirality center in any order, and then draw the second enantiomer by making the mirror image of the first enantiomer.

Emil Fischer 1800

### Fischer projection formula

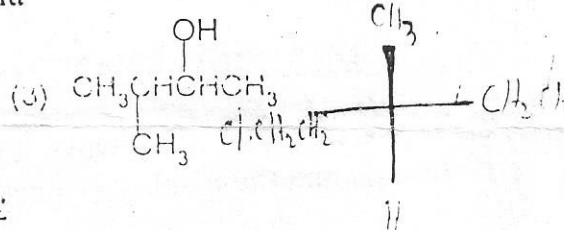
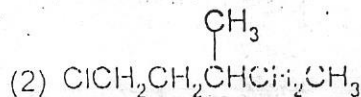
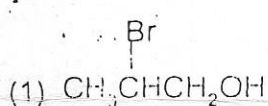
This is a modified method devised by Emil Fischer in 1800; the modification was by Viktor Meyer several years after Emil Fischer. Point of intersection of two perpendicular lines are used to represent the chirality centre, horizontal lines represent the bonds that project out of the plane of the paper toward the viewer and vertical line represent the bonds that project back from the plane of the paper away from the viewer. The carbon chain is drawn vertically with C - 1 at the top of the chain.



Using Fischer projection formula, draw the first enantiomer by arranging the four groups (or atoms) bonded to the chirality centre in any order, then draw the second enantiomer by interchanging two of the groups (or atoms)

Exercise: Draw enantiomers for each of the following using

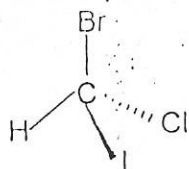
a) Perspective formula      b) Fischer projection formula



### Naming Enantiomers: R and S system of Nomenclature

To distinguish between two stereoisomers, a system of nomenclature that indicates the configuration (arrangement) of the groups (or atoms) about the chirality center was devised. Three chemists, Robert Sidney Cahn, Sir Christopher Ingold and Vladimir Prelog devised the *R* and *S* system of nomenclature of stereoisomers now known as Cahn - Ingold - Prelog system of nomenclature.

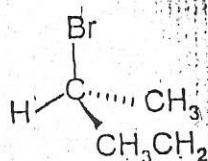
- The first step in the naming system; is to rank the groups (or atoms) that are bonded to the chirality center in order of priority. The priority depends on the atomic number of the atoms directly attached to the chirality centre. The greater the atomic number the higher the priority e.g. Bromochloriodomethane



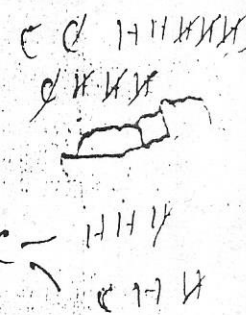
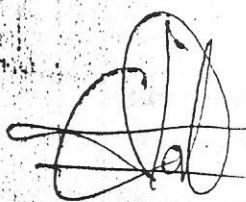
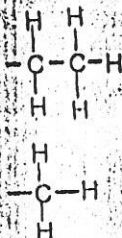
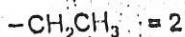
Iodine has the highest atomic number, so it will have the highest priority (priority 1) followed by Bromine, then chlorine and hydrogen will have the lowest priority.

1      2      iodine 3      hydrogen 4

In case there are two atoms directly bonded to the chirality center with same atomic number then the atomic number of the next bonded atom(s) will be considered e.g. 2-bromobutane.

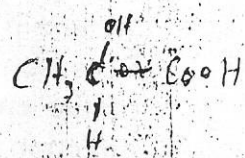
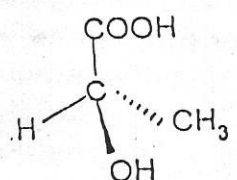


Atoms bonded to the chirality center are Br, C, C and H, obviously Bromine has the highest atomic number so will have the highest priority (priority No 1). To decide the next priority, we have to consider the atomic number of the next bonded atoms since two atoms bonded to the chirality center are carbon (one from an ethyl group and the other from a methyl group). One carbon is bonded to, H, H, and H (the methyl group) the other is bonded to C, H and H (the ethyl group). One H cancels in each of the two groups leaving C and H in the group and H and H in the methyl group, since carbon has greater atomic number than hydrogen, so the ethyl group has a higher priority than the methyl group i.e.

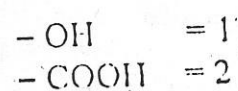


3. If an atom is doubly bonded to another atom, the priority system treats it as if it were singly bonded to two of those atoms and if triply bonded to another atom, the system treat it as if it were singly bonded to three of those atoms. e.g. lactic acid

OH > C=O



In lactic acid, hydroxyl group, (-OH) takes the highest priority since Oxygen has the greatest atomic number than other atoms directly bonded to the chirality center. There are 2 groups (carboxyl and methyl) each having carbon atoms directly bonded to the chirality center. The carbon of the methyl group is bonded to 3 H atoms while the carboxylic carbon is doubly bonded to oxygen and singly bonded to hydroxyl (-OH), therefore the carboxyl carbon is considered to be bonded to O, O and OH, thus the carboxyl group has the next higher priority.



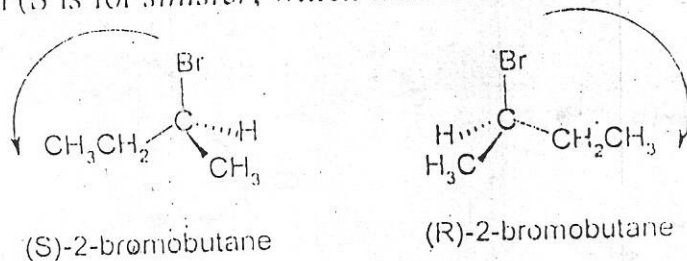
- CH<sub>3</sub> = 3

- H = 4

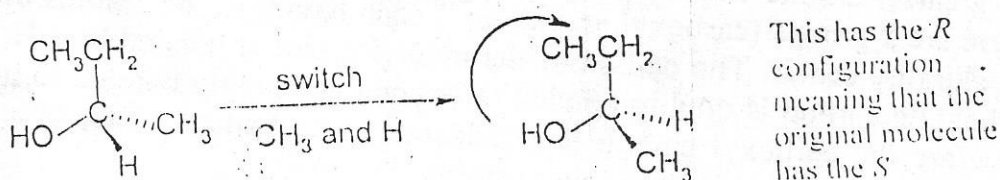
Exercise: Assign priority numbers to the following group

- a) - CH<sub>2</sub>OH      - CH<sub>3</sub>      - CH<sub>2</sub>CH<sub>2</sub>OH      - H  
b) - CH=O      - OH      - CH<sub>3</sub>      - CH<sub>2</sub>OH  
c) - CH(CH<sub>3</sub>)<sub>2</sub>      - CH<sub>2</sub>CH<sub>2</sub>Br      - Cl      - CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Br  
d) - CH=CH<sub>2</sub>      - CH<sub>2</sub>CH<sub>3</sub>      - CH<sub>3</sub>      -

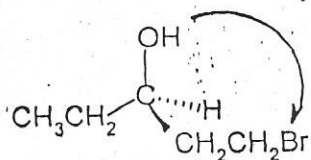
Having assign priority to the groups (or atoms) around the chirality center then the next step is to orient the molecule so that the group (or atom) with the lowest priority (priority 4) is directed away from you. Then draw an imaginary arrow from the group (or atom) with the highest priority (priority 1) to the group atom with the next highest priority (priority 2). If the arrow points in a clockwise direction the chirality centre has the *R* configuration (*R* is for *Rectus*, which means "Right" in Latin). If the arrow points in a counter clockwise direction, the chirality center has the *S* configuration (*S* is for *sinister*, which means "Left" in Latin) e.g.



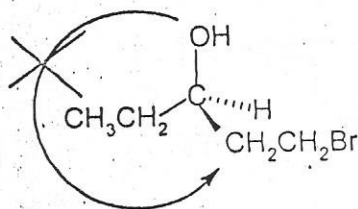
In the example above the atom of the lowest priority (4) is bonded by a hatched wedge. If the group (or atom) of the lowest priority (4) is not bonded by a hatched wedge, then first switch a pair of groups so that group 4 is bonded by a hatched wedge. Then proceed to determine that configuration as above, i.e. Draw a curved arrow from the group with the highest priority (1) to the group with the second highest priority (2). Because you have switched a pair of groups, you are now determining the configuration of the enantiomer of the original molecule. So if the arrow points in a clockwise direction, the enantiomer (with the switched) pair has the *R* configuration, which means the original molecule, has the *S* configuration. Therefore, if the arrow point in a counter clockwise direction, the enantiomer (with the switched pair) has the *S* configuration, which means the original molecule, has the *R* configuration e.g.



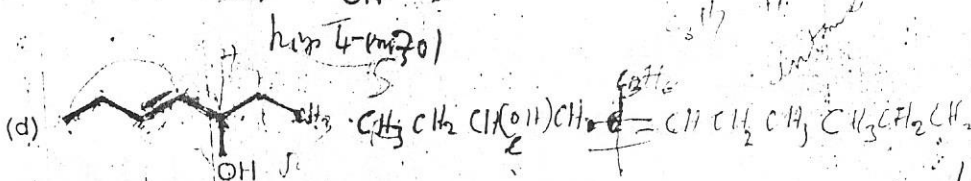
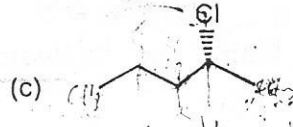
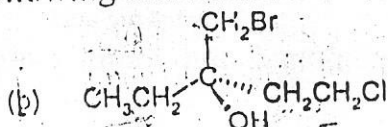
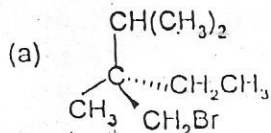
In drawing the arrow from group 1 to group 2, you can draw past the group with the lowest priority (4), but never draw past the group with the next lowest priority (3) i.e.



(R)-1-bromopentan-3-ol

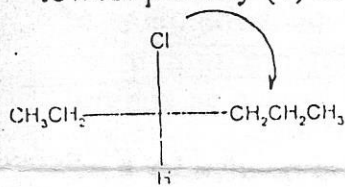


Exercise: Indicate whether the following sometimes has the *R* or *S* configuration?

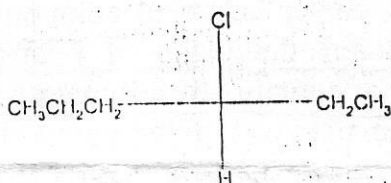


To determine the configuration of a compound in a Fischer projection formula, use the following rules.

1. Draw an arrow from the group (or atom) with the highest priority (1) to the group (or atom) with the next highest priority (2). If the arrow points in a clockwise direction, the enantiomer has the *R* configuration; if it points in a counter clockwise direction, the enantiomer has the *S* configuration provided that the group with the lowest priority (4) is on a vertical bond e.g.

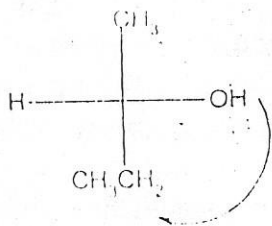


(R)-3-chlorohexane

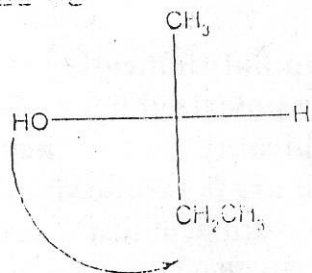


(S)-2-chlorohexane

2. If the group (or atom) with the lowest priority is on a horizontal bond, the answer you get by determining the direction of the arrow will be opposite of the correct answer. (You may use the following mnemonic to remember the conversion) i.e. if you assume that a clockwise arrow specifies an *R* configuration and a counter clockwise arrow specifies an *S* configuration, the answer you get is Very true if the lowest priority (substituent) is on a Vertical bond and horribly wrong if the lowest priority (substituent) is on a Horizontal bond e.g.

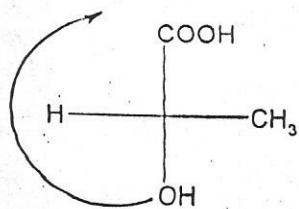


(S)-2-butanol

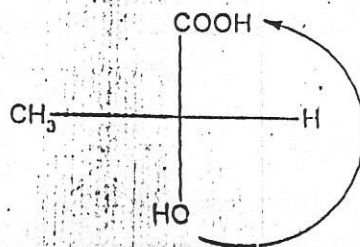


(R)-2-butanol

In drawing the arrow from group 1 to group 2, you can draw past the group with the lowest priority (4), but never draw past the group with the next lowest priority (3) e.g.

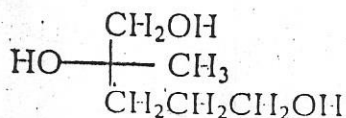


(S)-lactic acid



(R)-lactic acid

Exercise: Name the following compound and indicate whether it has the R or S configuration.



### OPTICAL ROTATION

Deals with polarized light

Optical rotation is a phenomenon observed when a molecule rotates the plane of polarization. Enantiomers are the same in all respect physically i.e. same boiling & melting points, solubilities etc. the only exception are those properties that depends on how group bonded to chirality center are arranged in space. One of such properties that make a difference is the way they interact with polarized light.

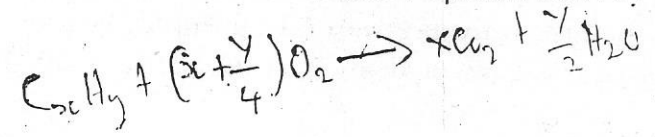
Compounds containing chirality center i.e chiral compound rotates the plane of polarization, such compound that rotates the plane of polarization are said to be optically active. Compounds that do not contain chirality center are known as achiral compound and they do not rotate the plane of polarization thus they are optically inactive.

A chiral compound will rotate the plane of polarization in either clockwise or a counter clockwise direction. If one enantiomer rotates the plane of polarization in a clockwise direction, its mirror image will rotate the plane of polarization exactly the same amount in a counter clockwise direction. An optically active compound that rotates the plane of polarization in a clockwise direction is called dextrorotatory and indicated by (+). On the other hand an optically active compound that rotates the plane of polarization in a counter clockwise direction is said to be levorotatory and is indicated by (-). Dextro and levo are Latin prefixes for "to the right" and "to the left" respectively.

Note: (+) and (-) are symbols indicating the direction in which an optically active compound rotates plane polarized light whereas R and S indicate the arrangement of the group about a chirality center, they are not synonymous. Some compound with the R configuration are (+) while some are (-).

Polarimeter is an instrument that is used to measure the amount that an optically active compound rotates the plane of polarized light.

Assignment: Describe how polarimeter is used to measure optical activity and draw the instrument.





$$\frac{[\alpha]_D^{25}}{c} = \frac{[\alpha]_D^{25}}{l \cdot c}$$

Rotation

Specific rotation of a compound is "the number of degree of rotation caused by a solution of 1.0g of the compound per mL of solution in a sample tube 1.0 dm long at a specified temperature and wavelength".

Specific rotation can be calculated from the following formula.

$$[\alpha]_{\lambda}^T = \alpha / lc$$

$$([\alpha]_{\lambda}^T) = \alpha / lc$$

- Where  $[\alpha]$  = Specific rotation
- T = Temperature in °C
- $\lambda$  = wavelength of the incident light
- $\alpha$  = Observed rotation
- l = length of sample tube in decimeters
- C = Concentration of the sample in grams per milliliter of solution.

$$([\alpha]_{\lambda}^{25}) = \frac{2.0}{25 \times 1.0} = \alpha = +134 = 28$$

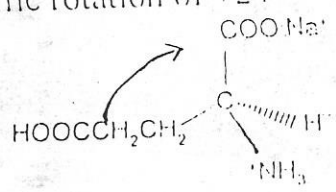
$$\lambda = 0.005970$$

e.g. The observed rotation of 2.0g of a compound in 10 mL of solution in a polarimeter tube 25cm long is +134°. What is the specific rotation of the compound?

Racemic Mixture

A mixture of equal amount of a pair of enantiomers is called a racemic mixture, a racemic modification or a racemate. Racemic mixtures are optically in-active and are indicated as (±). For example (±) -2- bromobutane contains the (+) and the (-) in equal amount.

e.g. (S) - (+) - monosodium glutamate (MSG) is a flavor enhancer used in many foods; it has a specific rotation of +2.4°



*{msg} for monosodium glutamate*

- a) What is the specific rotation of (R) - (-) - monosodium glutamate
- b) What is the specific rotation of a racemic mixture of MSG?

Optical Purity

Optical purity or enantiomeric excess is the ratio of the observed specific rotation of a compound to the specific rotation of the pure enantiomer of that compound. Optical purity tells us how much of each enantiomer is present in an isolated or prepared compound. An enantiomerically pure sample means there is one enantiomer present. If a sample of an optically active compound has an observed specific rotation of 0°, then the sample contains a racemic mixture. If however the observed specific rotation deviates from the value of a pure enantiomer, then the sample contains a mixture of the enantiomer in an unequal proportion.

Optical purity (enantiomeric excess) can be determined mathematically as

$$\text{Optical purity} = \frac{\text{Observed Specific rotation}}{\text{Specific rotation of the pure enantiomer}}$$

*optical purity =  $\frac{d}{[\alpha]}$*

e.g. The specific rotation of (S) - (+) - 2- bromobutane is +23.1°. A sample of 2- bromobutane has an observed specific rotation of +9.2°, what is its optical purity.

$$\text{Optical purity} = \frac{+9.2^\circ}{+23.1^\circ} = 0.40$$

i.e. the sample is 40% pure.

From the calculation above, since the observed specific rotation is positive, then we know that the sample contains excess (S)-(+)-2-bromobutane. The mixture is 40% optically pure meaning that 40% of the mixture is excess *S* enantiomer and 60% is a racemic mixture. Half of the racemic mixture plus the amount of excess enantiomer equals the amount of the *S* enantiomer in the mixture. Thus 70% of the mixture is the *S* enantiomer (i.e.  $\frac{1}{2} \times 60 + 40$ ) and 30% is the *R* enantiomer.

Exercises: (1) (+)-mandelic acid has a specific rotation of  $+158^\circ$  what would be the observed specific rotation of each of the following?

- 25% (-)-mandelic acid and 75% (+)-mandelic acid
- 50% (-)-mandelic acid and 50% (+)-mandelic acid
- 75% (-)-mandelic acid and 25% (+)-mandelic acid

(2) The specific rotation of (R)-(+)-glyceraldehyde is  $+8.7^\circ$ . If the observed specific rotation of a mixture of (R)-(+)-glyceraldehyde and (S)-(-)-glyceraldehyde is  $+1.4^\circ$ . What percent of glyceraldehydes is present as the *R* enantiomer?

(3) A solution prepared by mixing 10 mL of a 0.10M solution of the *R* enantiomer and 30 mL of a 0.10M solution of the *S* enantiomer was found to have an observed specific rotation of  $+4.8^\circ$ . What is the specific rotation of each of the enantiomer?

**SOLUTION:** One mmol (millimole; 10 mL  $\times$  0.10M) of the *R* enantiomer is mixed with 3 mmol of the *S* enantiomer; 1 mmol of the *R* enantiomer plus 1 mmol of the *S* enantiomer will form 2 mmol of a racemic mixture. There will be 2 mmol of *S* enantiomer left over. Therefore 2 mmol out of 4 mmol is excess *S* enantiomer ( $2/4 = 0.50$ ). The solution is 50% optically pure.

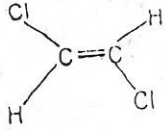
$$\begin{aligned} \text{Optical purity} = 0.50 &= \frac{\text{Obs. SP. ROT.}}{\text{SP. ROT. of Pure enantiomer}} \\ &= \frac{+4.8^\circ}{x} \\ x &= +9.6^\circ \end{aligned}$$

The *S* enantiomer has a specific rotation of  $+9.6^\circ$ ; the *R* enantiomer has a specific rotation of  $-9.6^\circ$ .

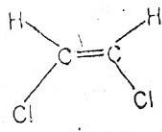
### GEOMETRICAL ISOMERS

Geometrical isomerism is a phenomenon in which 2 compounds possess the same structural formula but differ in spatial arrangements of the group around the double bond. The isomer with similar group on the same side is known as -cis, while that with

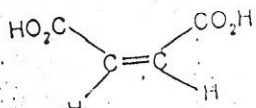
Similar groups on opposite sides is trans. (thus it is also known as the cis - trans isomer)  
 e.g. 1, 2 - dichloro ethane; maleic and fumaric acid.



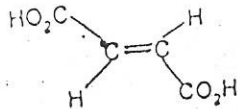
trans-1,2-dichloroethene



cis-1,2-dichloroethene



maleic acid

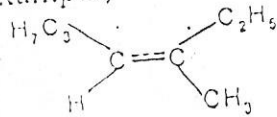


fumaric acid

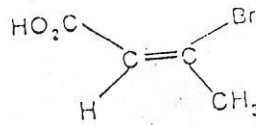
maleic is trans, which fumaric is cis. (both fumaric acid)

E - Z systems of designating geometric isomers

If the alkene is di or tetra substituted the use of cis and trans becomes meaningless. For example,



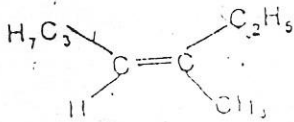
3-methyl-3-heptene



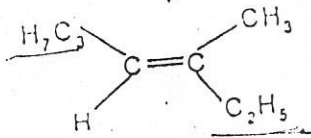
3-bromobut-2-enoic acid

It is not possible to decide trans or cis isomer in the two examples above, therefore, the E - Z convention was design for such isomers. In these systems the substituent are given priority according to the atomic number of the atom directly attached to the carbon atom. (Based on Cahn - Ingold - Prelog system.)

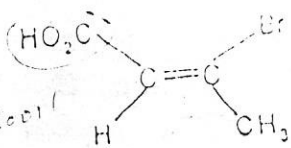
Then the group of higher priority on one carbon is compared with the group of higher priority on the other carbon atom. If both the groups of higher priority are on the same side of the double bond the alkene isomer is designated as Z (German: Zusammen meaning 'together') isomer but if the group of higher priority are on the opposite sides of the double bond, the alkene is designated as E (German: Entgegen meaning 'opposite') isomer. e.g.



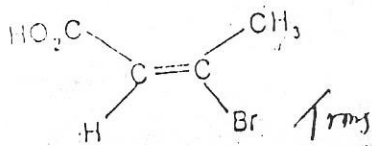
Z-3-methyl-3-heptene



E-3-methylhept-3-ene



Z-3-bromobut-2-enoic acid



E-3-bromo-2-butenic acid

**FURTHER READING**

1. Paula Yurkanis Bruice: Organic Chemistry, 3<sup>rd</sup> edition (2001), Prentice Hall, New Jersey.
2. K. S. Tewari, N. K. Vishnoi and S. N. Mehrotra: A text book of Organic Chemistry, 2<sup>nd</sup> edition, (2002). Vikas Publishing House PVT Ltd, New Delhi.