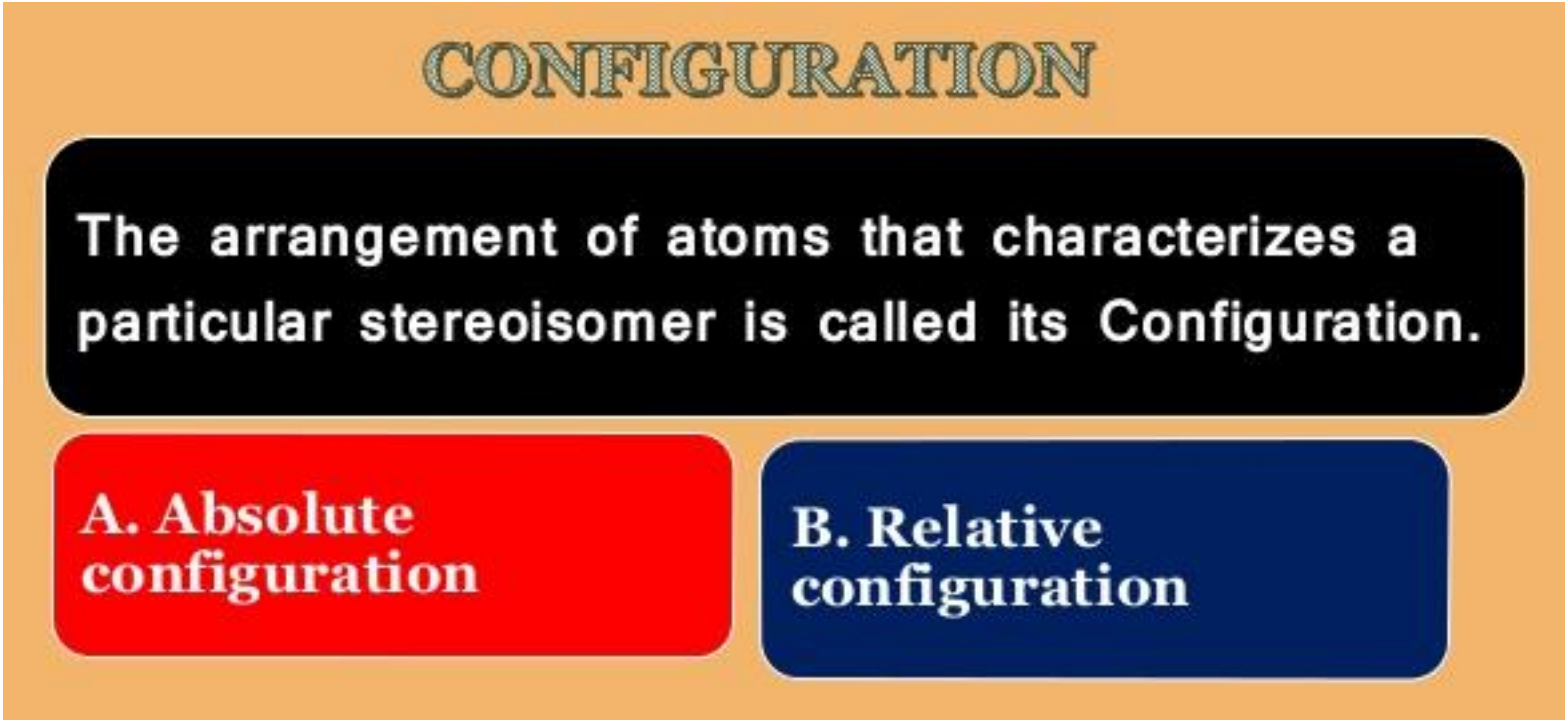
STEREOCHEMISTRY
Part-IV
Nomenclature of Organic Compounds

B.Sc Hons (Chemistry)
Sem-I , Paper CC-1

Dr. Indranil Chakraborty
Kharagpur College



CONFIGURATION

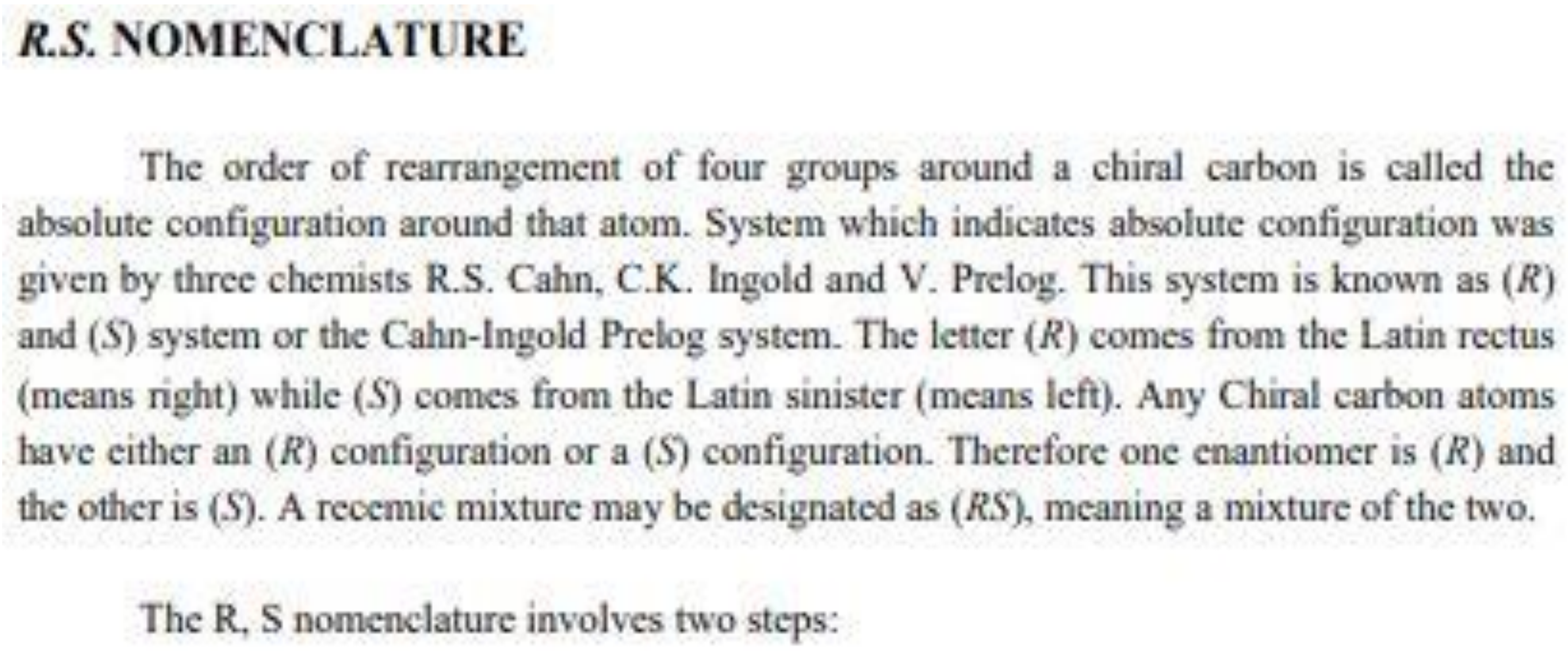
The arrangement of atoms that characterizes a particular stereoisomer is called its Configuration.

A. Absolute configuration

B. Relative configuration

Absolute Nomenclature

R/S NOMENCLATURE SYSTEM
(Cahn–Ingold–Prelog convention)



R.S. NOMENCLATURE

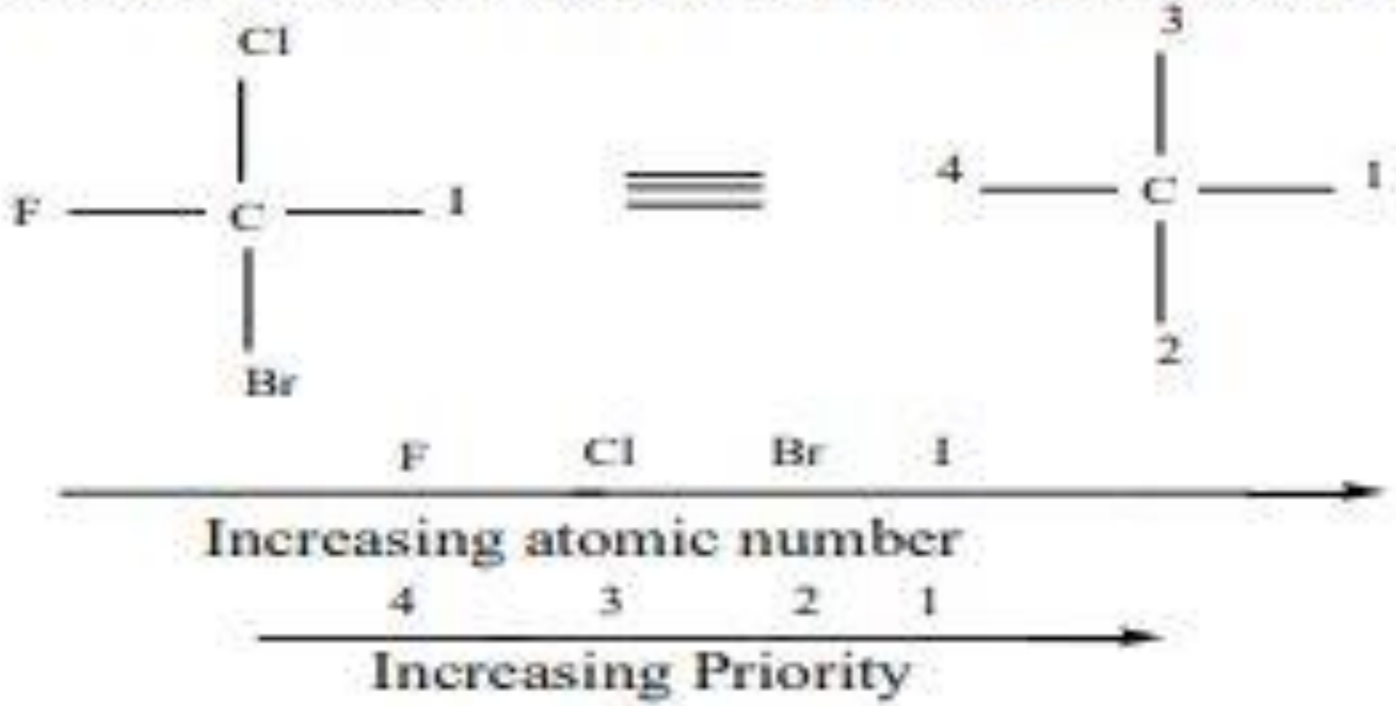
The order of rearrangement of four groups around a chiral carbon is called the absolute configuration around that atom. System which indicates absolute configuration was given by three chemists R.S. Cahn, C.K. Ingold and V. Prelog. This system is known as (*R*) and (*S*) system or the Cahn-Ingold Prelog system. The letter (*R*) comes from the Latin rectus (means right) while (*S*) comes from the Latin sinister (means left). Any Chiral carbon atoms have either an (*R*) configuration or a (*S*) configuration. Therefore one enantiomer is (*R*) and the other is (*S*). A recemic mixture may be designated as (*RS*), meaning a mixture of the two.

The R, S nomenclature involves two steps:

Step I: The four ligands (atom or groups) attached to the chiral centre are assigned a sequence of priority according to sequence rules.

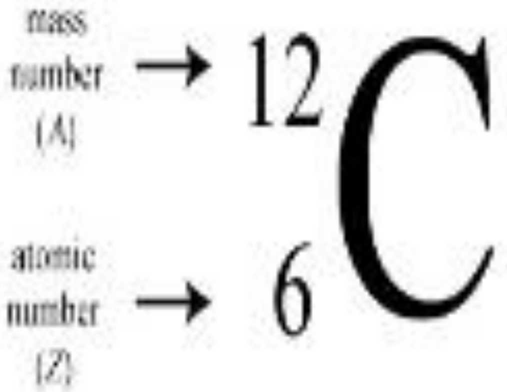
Rule 1: If all the four atoms directly attached to the chiral carbon are different, priority depends on their atomic number. The atom having highest atomic number gets the highest priority, i.e., (1).The atom with lowest atomic number is given lowest priority, i.e. (2), the group with next higher atomic number is given the next higher priority (3) and so on.

For example:



- ✓A substituent with a higher atomic number takes priority over a substituent with a lower atomic number.
- ✓ Hydrogen is the lowest priority substituent, because it has the lowest atomic number.

A)Isotopes (Same Atomic number but Different Mass number)



Atoms with highest ATOMIC MASS NUMBER is given first priority

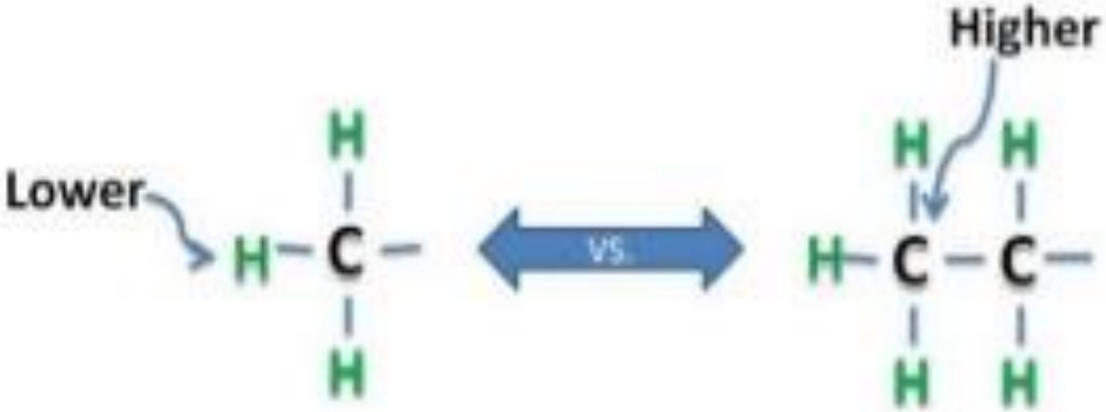
Rule 2: if two or more than two isotopes of the same element are present, the isotope of higher mass receives the higher priority.

$$ {}_1H^1 \qquad {}_1H^2 \qquad {}_1H^3 $$

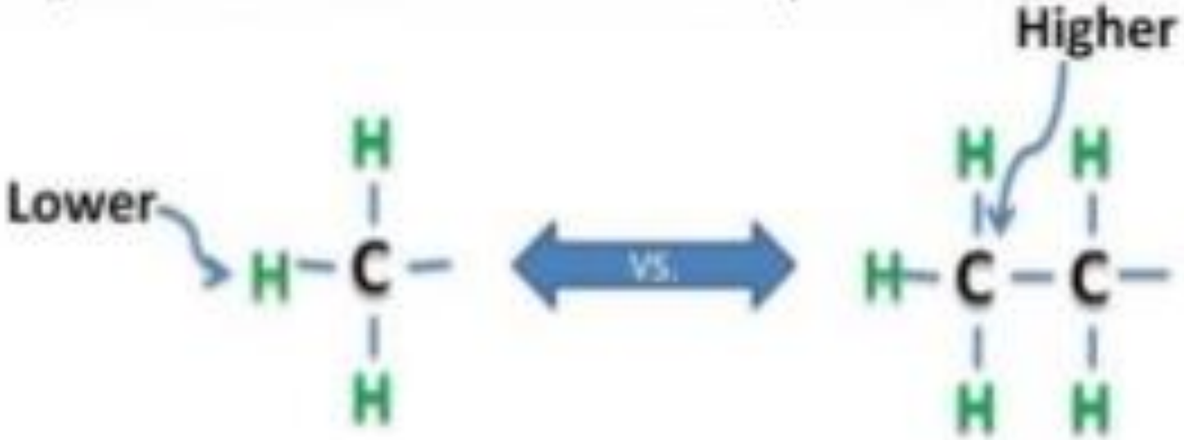
$$ \xrightarrow[\text{increasing priority}]{\qquad\qquad\qquad\qquad\qquad\qquad} $$

Rule 3: if two or more of the atoms directly bonded to the chiral carbon are identical, the atomic number of the next atom is used for priority assignment. If these atoms also have identical atoms attached to them, priority is determined at the first point of difference along the chain. The atom that has attached to it an atom of higher priority gets the higher priority.

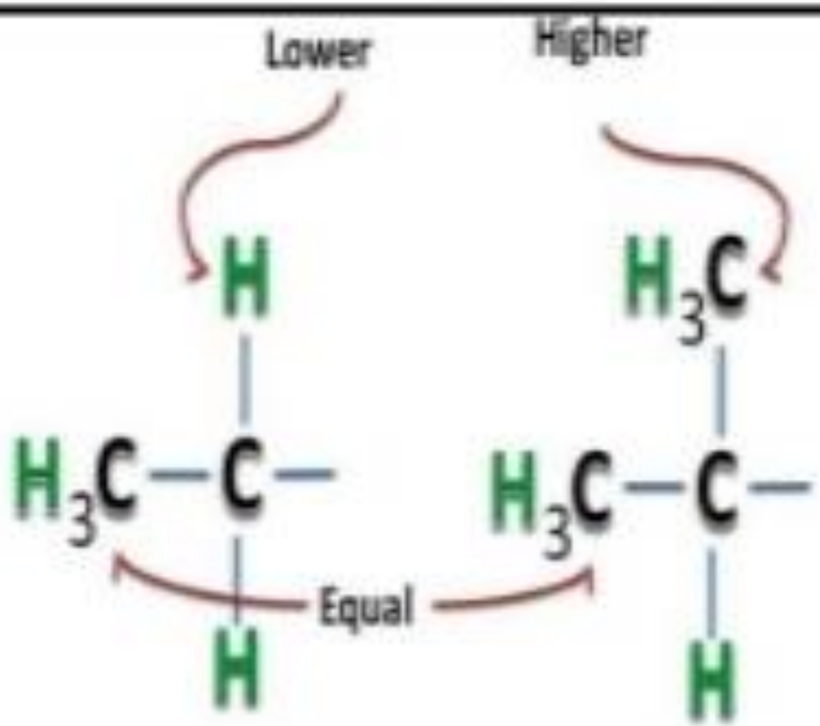
- If the two substituents are of equal rank, proceed along the two substituent chains until there is a point of difference.
- Determine the chain which has the first connection to an atom with the highest priority (the highest atomic number).
- That chain has the higher priority.
- If the chains are similar, proceed down the chain, until a point of difference.



Example: An ethyl substituent takes priority over a methyl substituent.

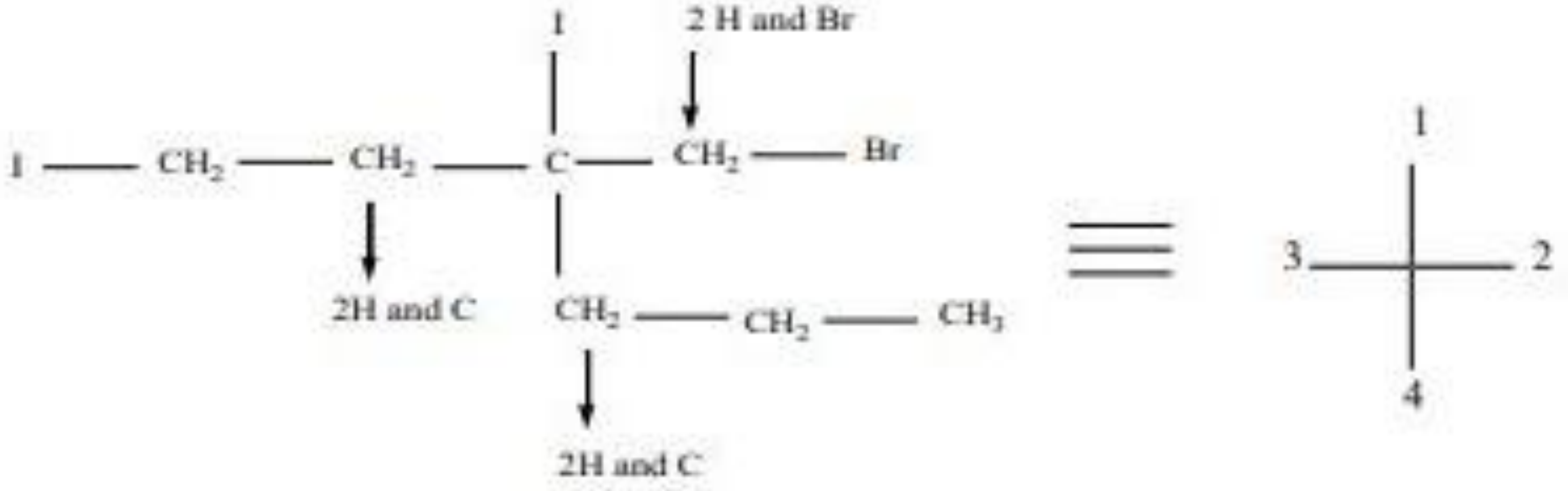


- At the connectivity of the stereocenter, both have a carbon atom, which are equal in rank.
- Methyl has only has hydrogen atoms attached to it, whereas the ethyl has another carbon atom.
- The carbon atom on the ethyl is the first point of difference and has a higher atomic number than hydrogen
- Therefore the ethyl takes priority over the methyl.



The "C-" (right) ranks higher than the "H-" (left) based on the <u>first point of difference</u> and thei relative molecular weights.

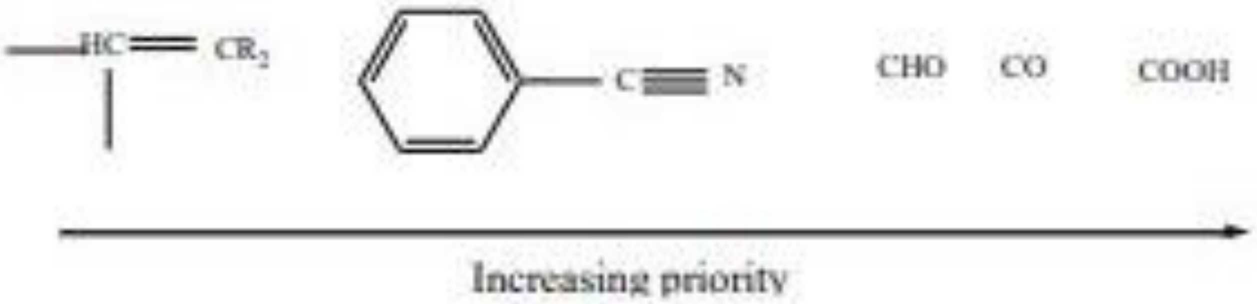
- ✓ 1-methylethyl substituent takes precedence over an ethyl substituent.
- ✓ Connected to the first carbon atom, ethyl only has one other carbon
- ✓ Whereas the 1-methylethyl has two carbon atoms attached to the first; this is the first point of difference.
- ✓ Therefore, 1-methylethyl ranks higher in priority than ethyl.



- In the above example, the atoms connected directly to the chiral carbon are iodine and three carbons.
- Iodine has the highest priority.
- Connectivity of other three carbons are 2H and Br, 2H and C and 2H and C.
- Bromine has the highest atomic number amongst C, H, Br and thus CH_2Br has highest priority among these three groups (*i.e.* priority number 2).
- The remaining two carbon are still identical (C and 2H) connected to the second carbon of these groups are 2H and I and 2H and C. Iodine has highest priority.
- Amongst these atoms, so that-CH_2-CH_2-I is next in priority list and CH_2-CH_2-CH_3 has the last priority.

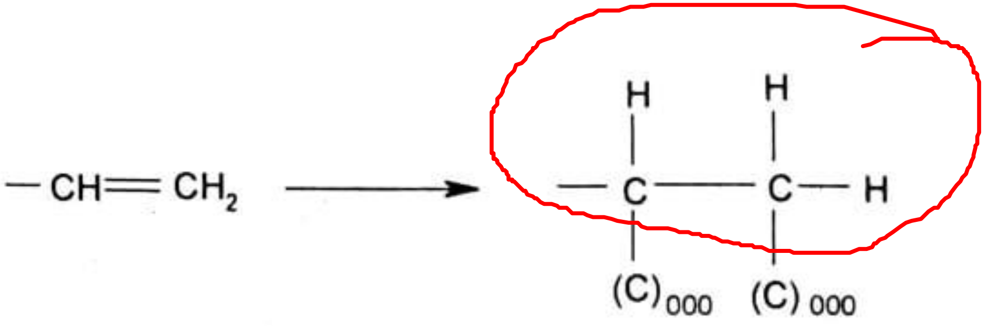
Rule 4: If a double or a triple bond is linked to chiral centre, the involved electrons are duplicated or triplicated respectively.

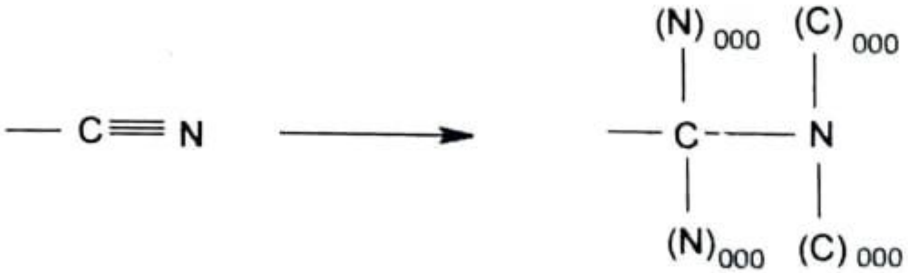
- By this rule, we obtain the following priority sequence:



- ✓ The compound containing double or triple bonded to an atom means that the atom is connected to the same atom twice.
- ✓ In such a case, follow the same method as above

3. For the purpose of assigning priority, double and triple bonds are considered by assuming that each such bonded atom is duplicated or triplicated from both sides of the multiple bond. The duplicated atoms are placed within parentheses and except for H atom, other duplicated atoms are made tetraliganded by phantom atoms (0) having atomic number zero. Phantom atoms(0) have lower priorities than H. For example, inflated forms of a few functional groups having multiple bonds are given below.





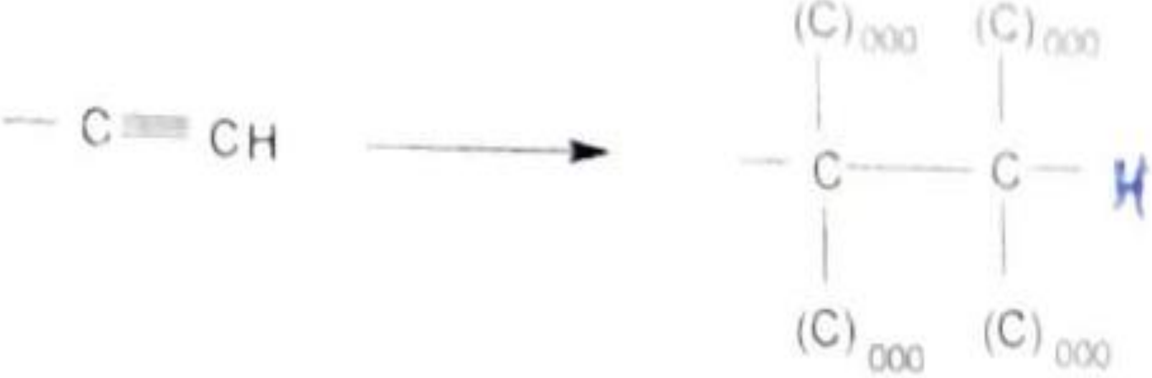
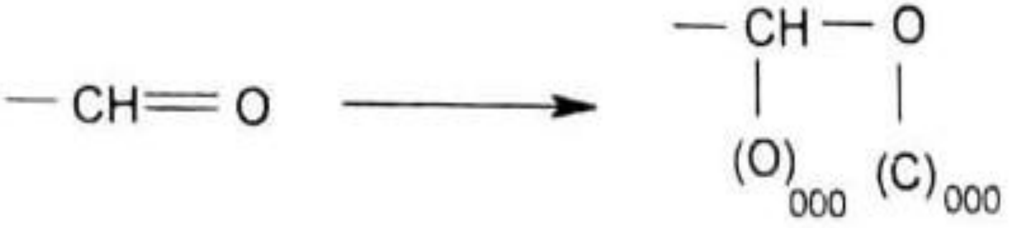


Fig. 3. 63

Uses of concept of phantom atoms are normally not required except in a few cases. For example, between -CH=O and -CH(OH)(OCH$_3$) , the hemiacetal group get the preference. When duplicated, the groups become,



It has already been mentioned that while searching for first differences between two bifurcated groups, one should proceed along that branch which has higher priority atoms. For example, to decide between -CHO and -CH(OH)OCH$_3$, the branches -CH-O-(C)$_{000}$ and -CH-O-CH$_3$ and not -CH-(O)$_{000}$ and -CHOH are to be taken into consideration. The last atom (carbon), in -CHO has three phantom atoms (o) whereas in CH(OH)OCH$_3$, there are three hydrogen atoms.

This rule allows to determine the relative priority of say, isopropyl and vinyl groups.

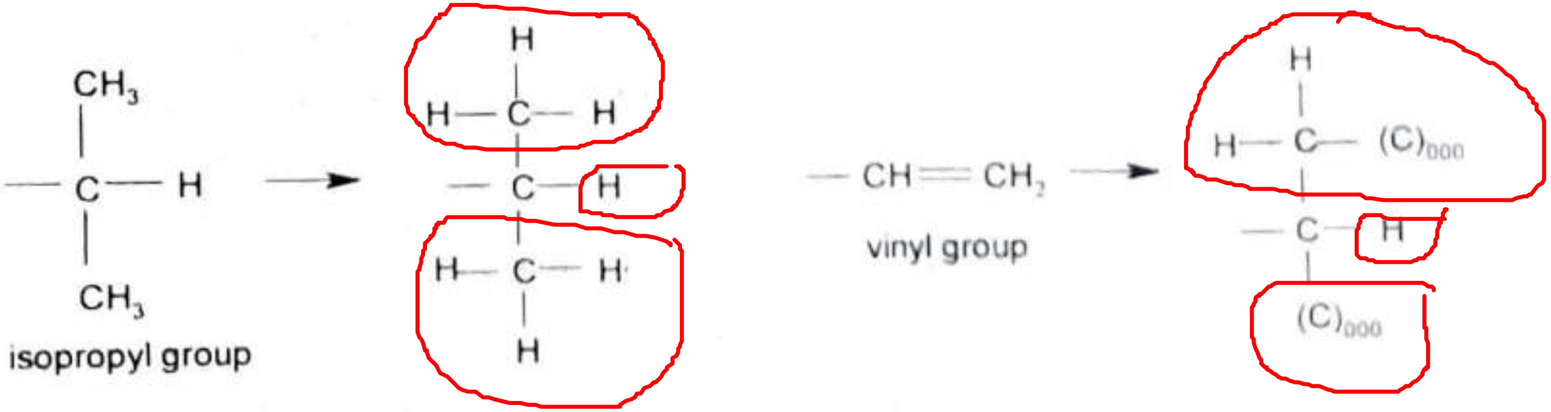
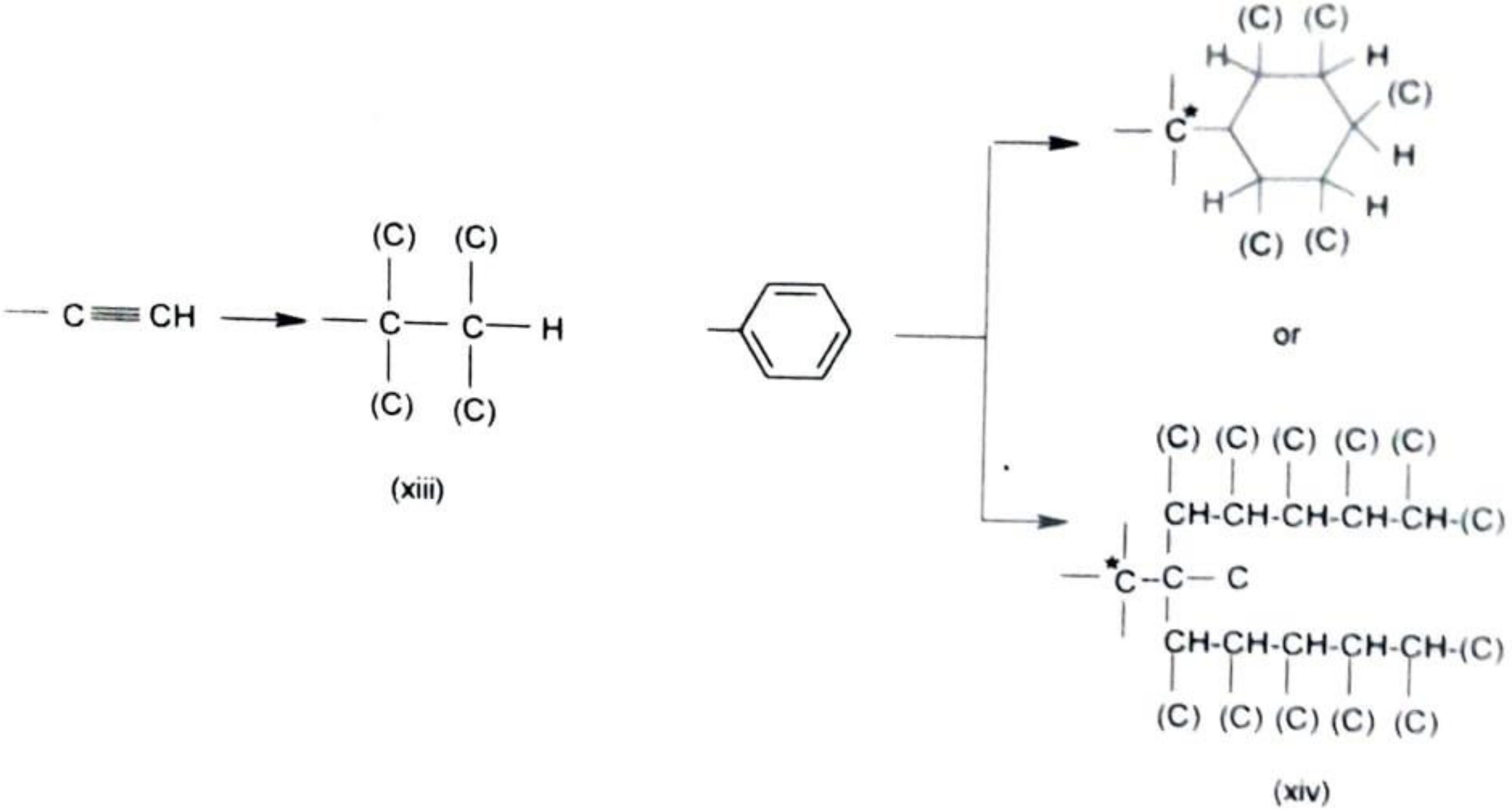


Fig. 3. 65

-CH=CH$_2$ group gets preference because, in isopropyl group, the terminal carbon contains three hydrogen atoms but in case of vinyl group, after replication, the terminal carbon contains two hydrogen and one carbon atom.

Again, between -C≡CH and -C$_6$H$_5$, phenyl group gets preference over ethynyl group. After replication, -C≡CH and -C$_6$H$_5$ are equivalent to (xiii) and (xiv) respectively. -C≡CH is equal to C(CC)-C(CCH)$_{000}$ but -C$_6$H$_5$ is equivalent to -C(CC)-C(CCH)C. Therefore, C$_6$H$_5$- gets priority over -C ≡CH.



(xiii)

(xiv)

Fig. 3. 66

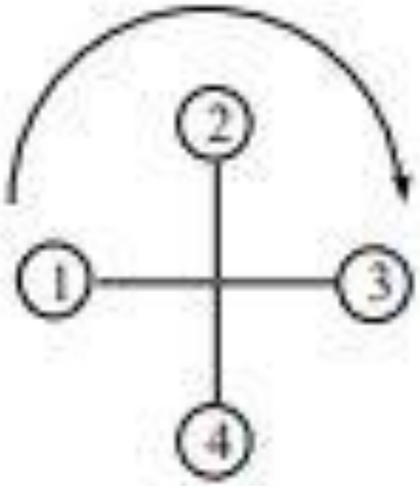
But in case of -C≡C-CH$_3$, it is equivalent to C(CC)-C(CCC)HHH and gets preference over -C$_6$H$_5$ which is equivalent to-C(CC)-C(CCH)C .

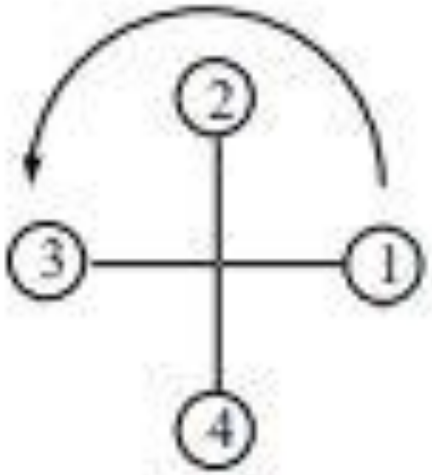
A list of common groups of increasing priority according to the above sequence rule is given below.

$I > Br > Cl > SO_2R > SOR > SR > SH > F > OCOR > OR > OH > NO_2 > NO > NHCOR$
$> NR_2 > NHR > NH_2 > CX_3$ (X=halogen) $COX > CO_2R > CO_2H > CONH_2 > COR > CHO$
$> CR_2OH > CH(OH)R > CH_2OH > C \equiv CR > C_6H_5 > CH \equiv C > C(R)=CR_2 > CR_3 >$
$CHR_2 > CH_2R > CH_3 > D > H >$ (. .) lone pair of electrons.

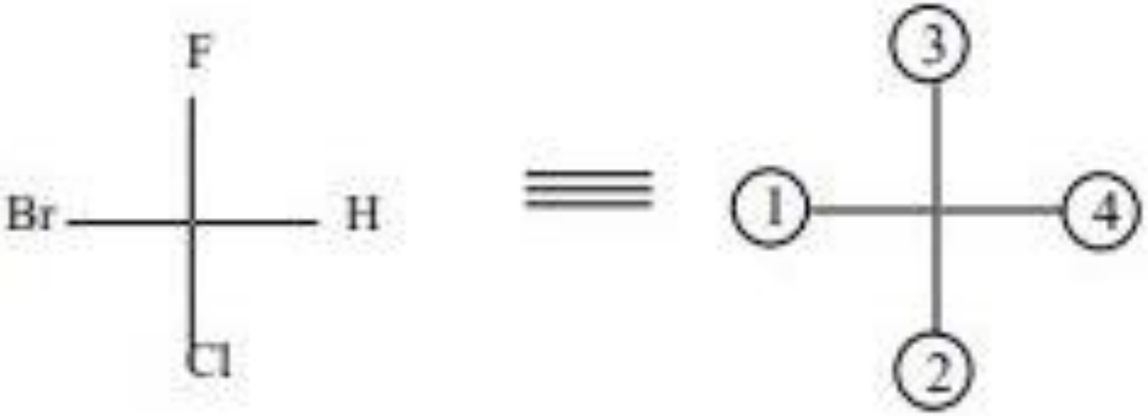
STEP-II: The molecule is then visualised so that the group of lowest priority (4) is directed away from the observer (at this position the lowest priority is at the bottom of the plane). The remaining three groups are in a plane facing the observer. If the eye travels clockwise as we look from the group of highest priority to the group of second and third priority (i.e. 1 → 2 → 3 with respect to 4) the configuration is designated R. If arrangement of groups is in anticlockwise direction, the configuration is designated as S.

For example:



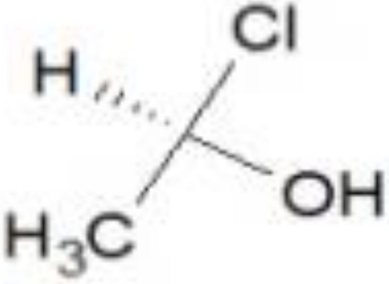


Let us apply the whole sequence to bromochlorofluoromethane.



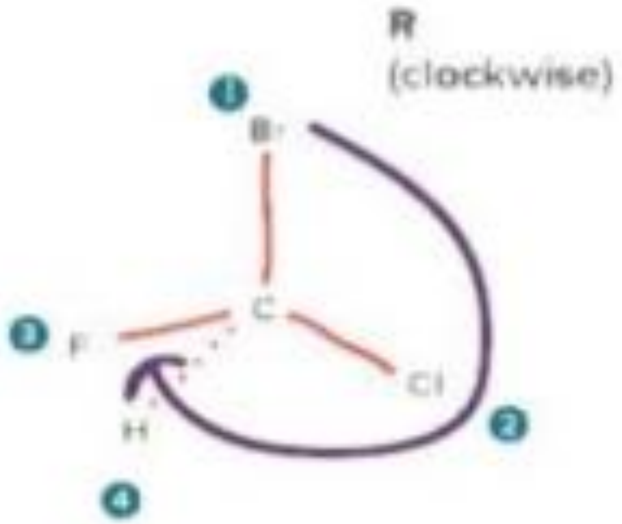
ii) The **lowest priority substituent** should always point away from the viewer (a dashed line indicates this).

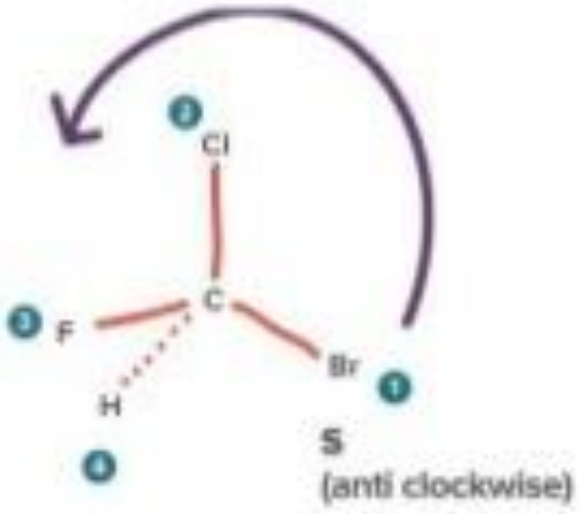
- ✓ Imagine a clock and a pole.
- ✓ Attach the pole to the back of the clock, so that when when looking at the face of the clock the pole points away from the viewer in the same way the lowest priority substituent should point away



iii) Draw an arrow from highest priority atom to the 2nd highest priority atom to the 3rd highest priority atom.

- ✓ The 4th highest priority atom is placed in the back, the arrow should appear like it is going across the face of a clock.
- ✓ If it is going Clockwise, then it is an R-enantiomer.
- ✓ If it is going Counter-clockwise, it is an S-enantiomer.

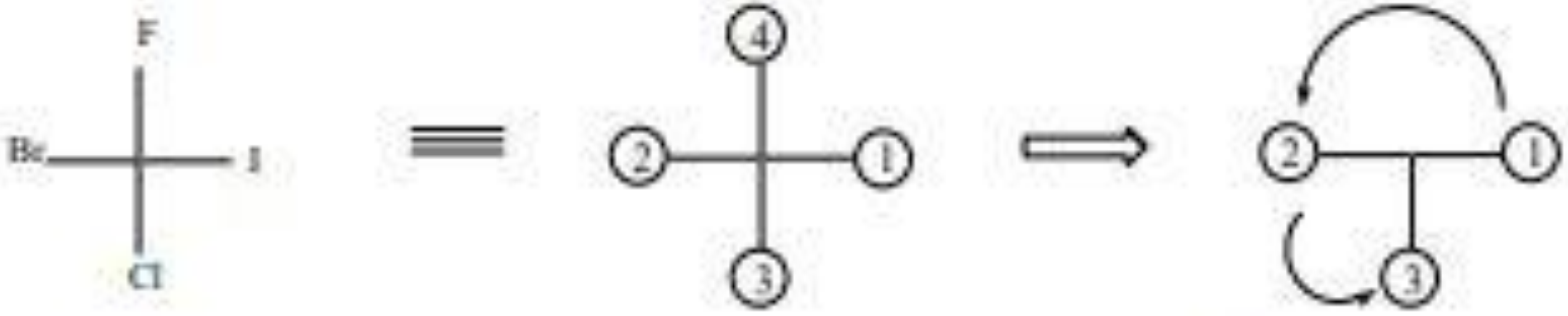




Fischer Projections

Case-I: R and S nomenclature from Fischer projection formula (Golden rule): If in a Fischer projection, the group of lowest priority (4) is on a vertical line, then the assignment of configuration is R for a clockwise sequence of 1 to 2to 3 and S for anticlockwise sequence.

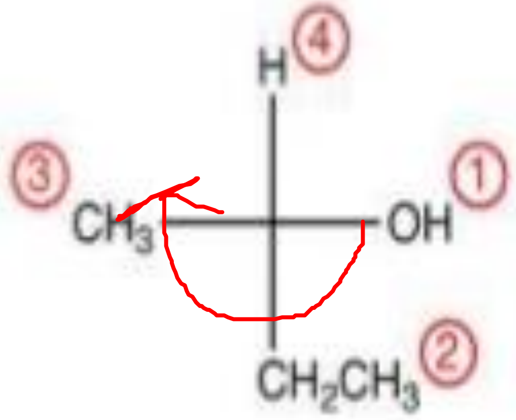
For example:



Anticlockwise arrangement
hence S- configuration

Step:1 :

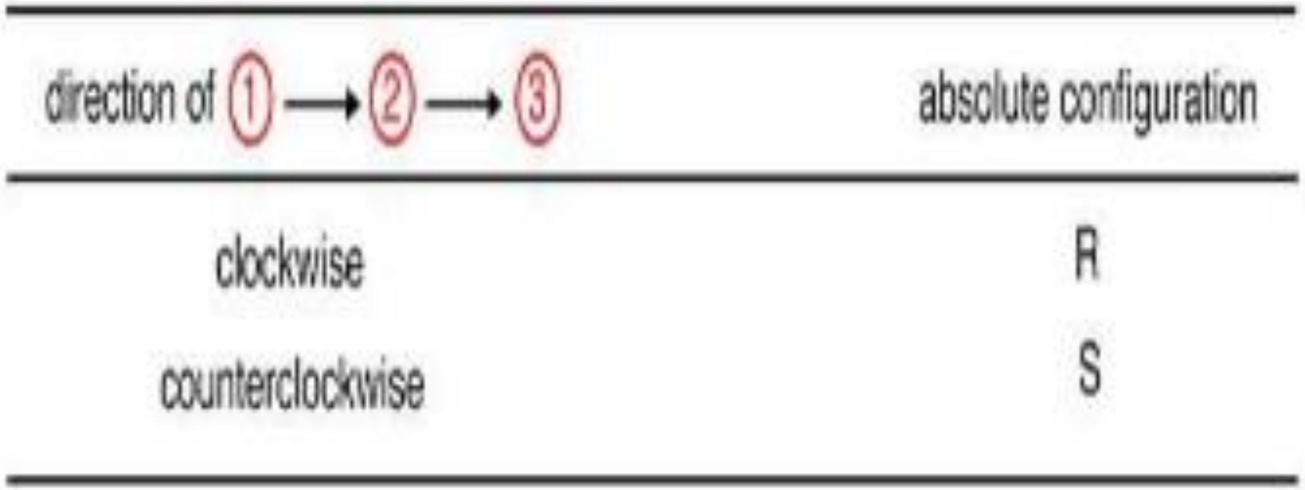
Assign priority numbers to the four ligands (groups) bonded to the chiral center using the CIP priority system.



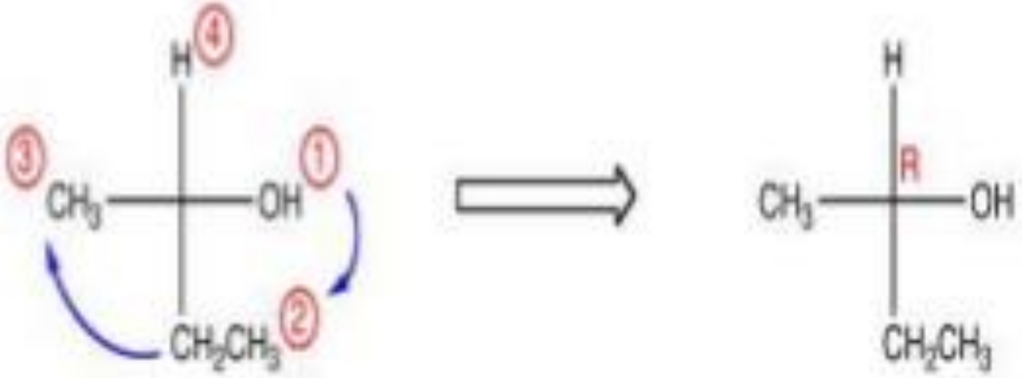
Step 2 – VERTICAL OPTION:

The lowest priority ligand is on a Vertical bond and it is pointing away from the viewer.

Trace the three highest-priority ligands starting at the highest-priority ligand (① → ② → ③) in the direction .



direction of ① → ② → ③	absolute configuration
clockwise	R
counterclockwise	S

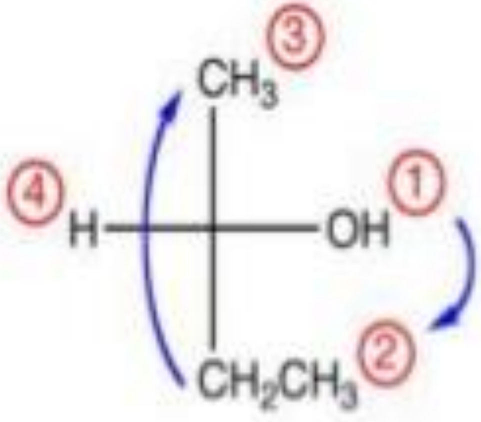


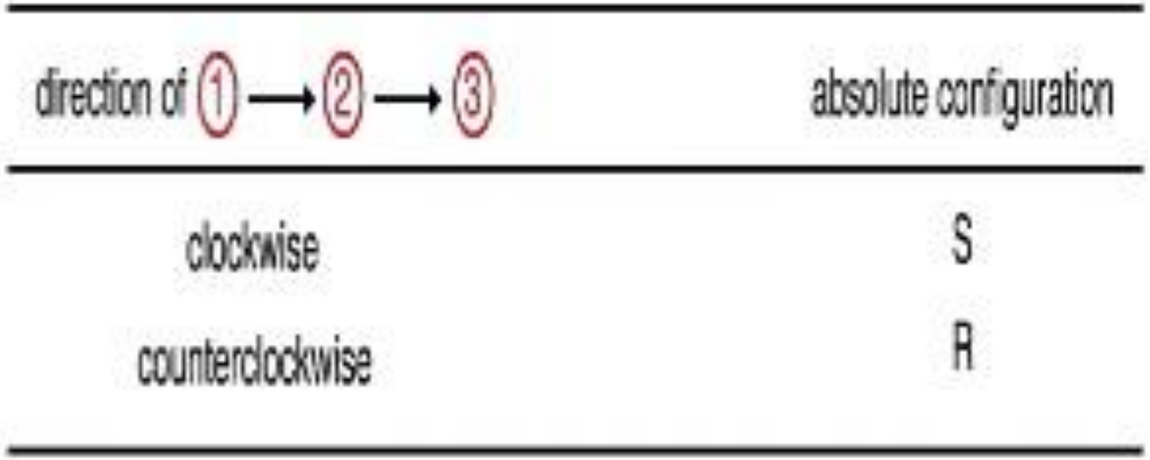
In the compound below, the movement is clockwise indicating an R-configuration.

The complete IUPAC name for this compound is (R)-butan-2-ol.

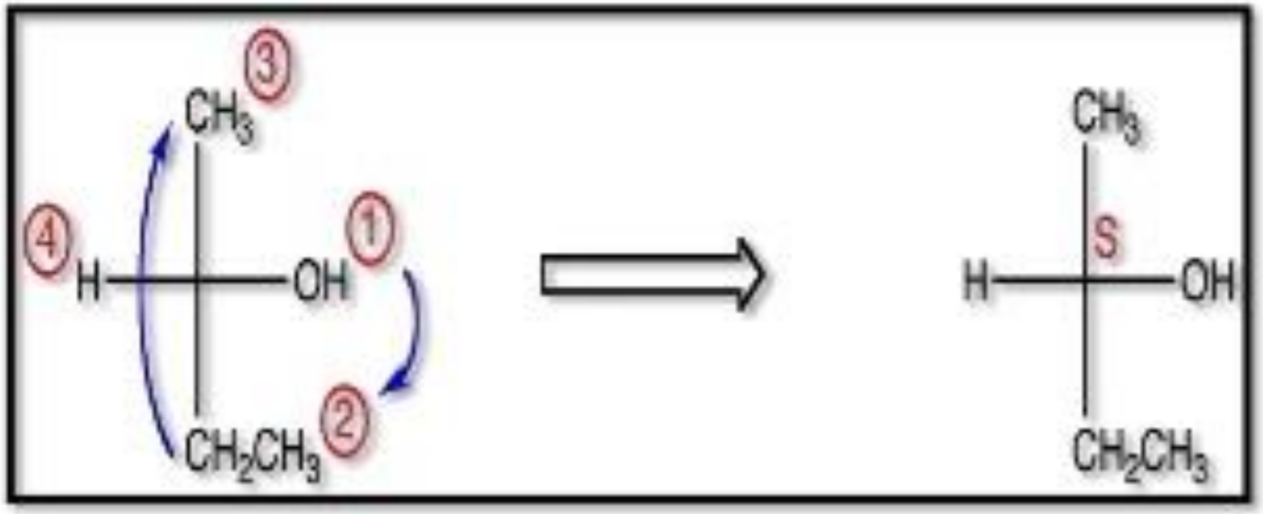
STEP 2 - HORIZONTAL OPTION

- If the lowest-priority ligand is on a Horizontal bond, then it is pointing toward the viewer.
- Trace the three highest-priority ligands starting at the highest-priority ligand (① → ② → ③) in the direction that will give wrong answer.
- Note in the table below that the configurations are reversed from the first example





direction of ① ⟶ ② ⟶ ③	absolute configuration
clockwise	S
counterclockwise	R



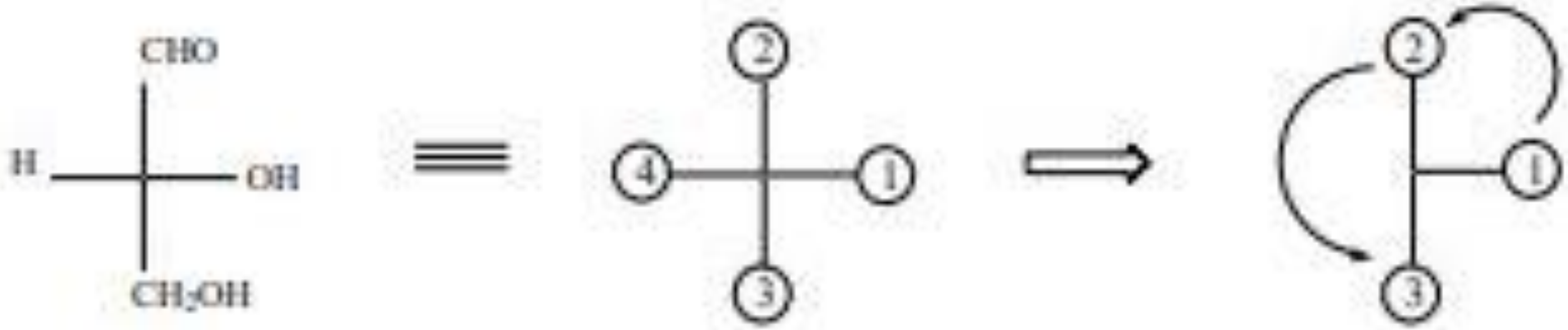
The movement is clockwise (R) which is wrong, so the actual configuration is S.

The complete IUPAC name for this compound is (S)-butan-2-ol.

LIMITATION.

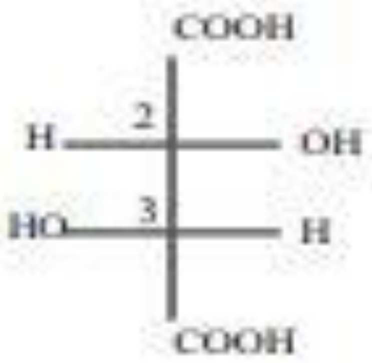
- A Fischer projection restricts a three-dimensional molecule into two dimensions.
- Consequently, there are limitations as to the operations that can be performed on a Fischer projection without changing the absolute configuration at chiral centers.

However, if the group of lowest priority is on horizontal line, then the assignment of configuration is S for a clockwise sequence of 1 to 2 to 3, and R for the anticlockwise sequence.

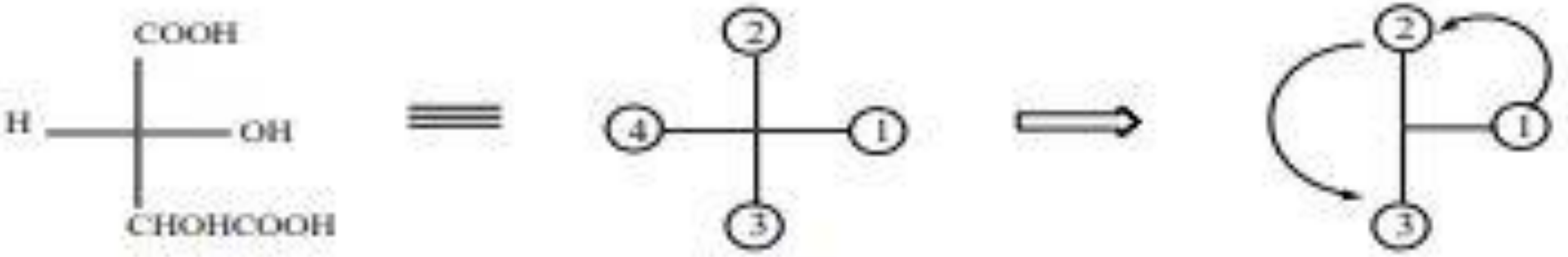


Anticlockwise arrangement
but lowest priority at horizontal
line hence R- configuration

When molecule contain two or more chiral centres, each chiral centre is assigned an R or S configuration according to the sequence and conversion rules. Thus (+) tartaric acid is (2R, 3R) (+) tartaric acid.

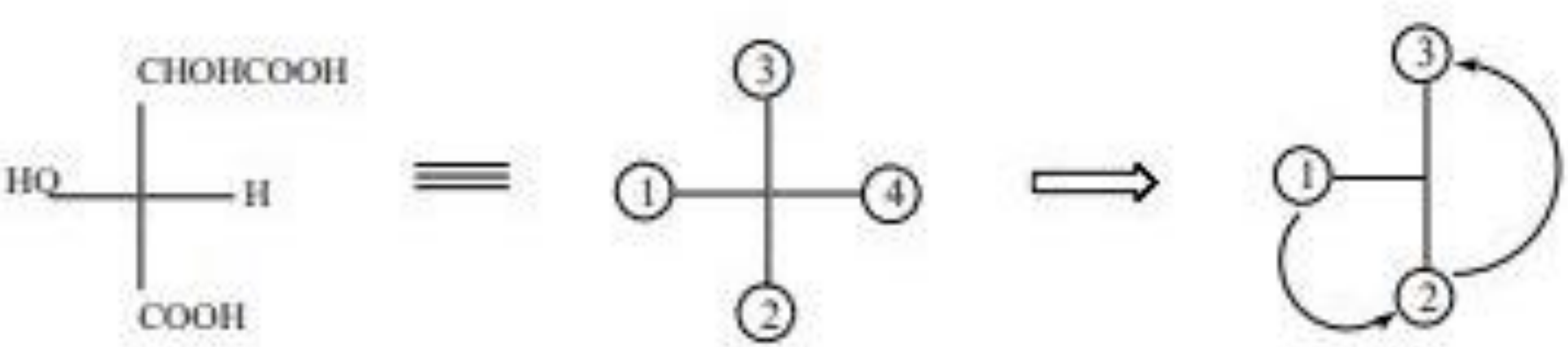


Configuration at chiral carbon - 2.



Anticlockwise arrangement
but lowest priority at horizontal
line hence R- configuration

Configuration at chiral carbon - 3.

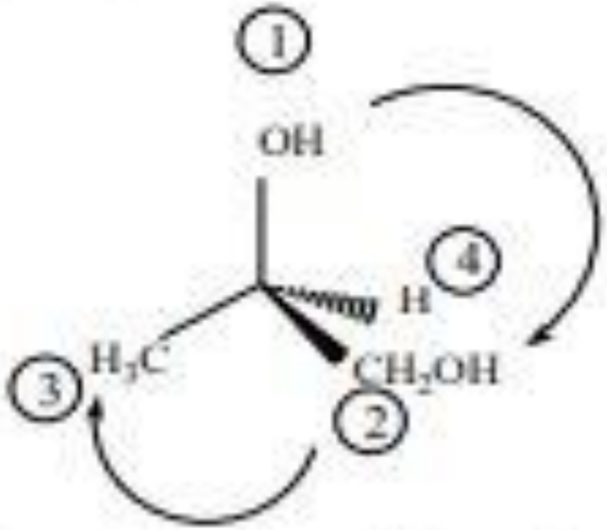


Anticlockwise arrangement
but lowest priority at horizontal
line hence R- configuration

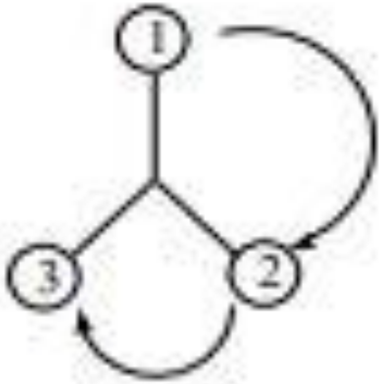
Flying Wedge

Case-II: R, S- nomenclature from flying-wedge formula.

- If the group of the lowest priority is away from the observer (i.e., bonded by dashed line) and the priority sequence (1 → 2 → 3) is clockwise, then the configuration is assigned as R. If the priority sequence is anticlockwise then the configuration is S.

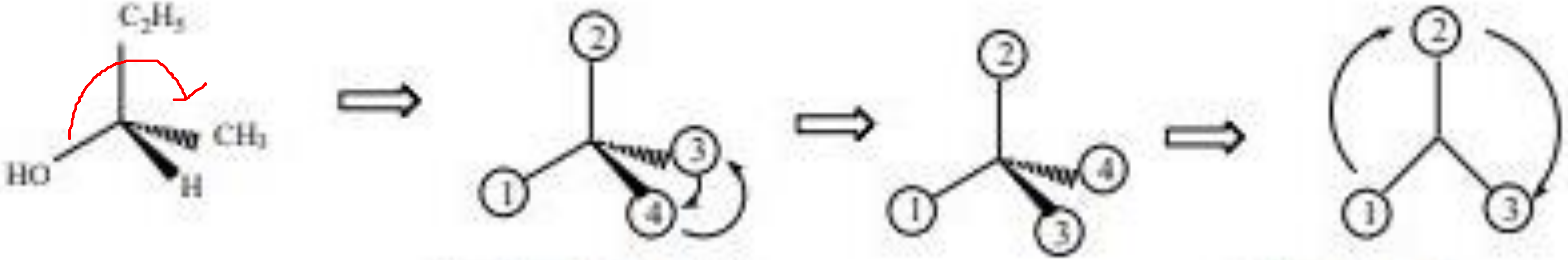


Lowest priority order is on deshed line



Clockwise arrangement thus configuration is R

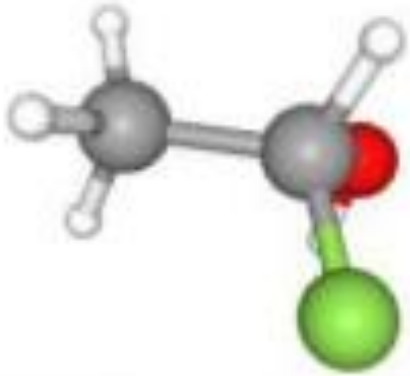
If the group of lowest priority is not bonded by dashed line then interchange a pair of groups so that the group with the lowest priority is bonded by dashed line. Now see the sequence (1 → 2 → 3), if it is clockwise then the configuration is assigned as S and if anticlockwise R. This is because you have interchanged a pair of groups and now you are determining the configuration of enantiomer of original molecule.

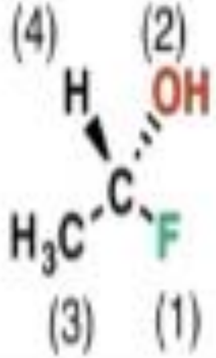


Least priority order is not bonded with deshed line , so interchange the group 3 and 4

This is R configuration, which means that the original compoundl has S configuration

Determining R/S when the #4 Substituent is in front (“Wedge”)





(R)-1-fluoroethanol

Priorities assigned based on atomic number.

F>O>C>H. So F is #1 and H is #4.

#4 priority is pointing **out** of the page (“wedge”).

#4 priority is on a **dash**:

- Clockwise = *R*
- Counter-clockwise = *S*

#4 priority is on a **wedge**:

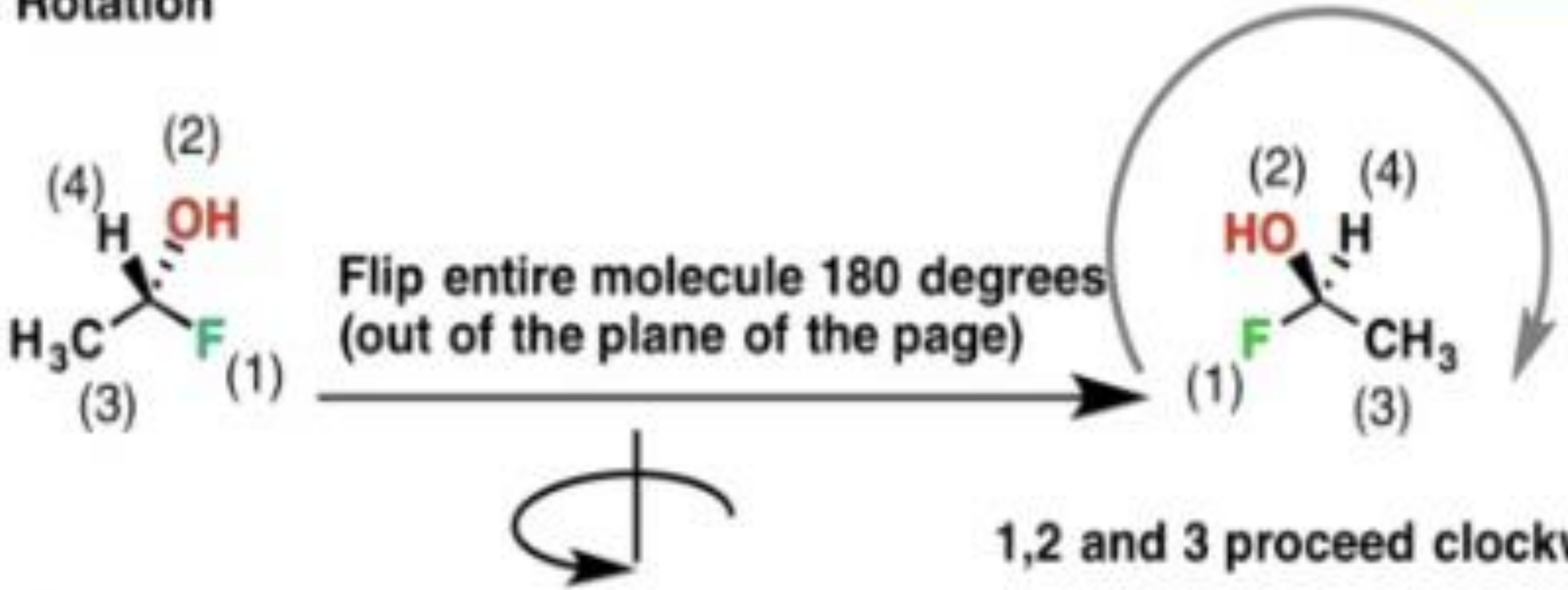
- Clockwise = *S*
- Counterclockwise = *R*

Determining (R)/(S) When The #4 Group Is On A Wedge

#4 priority is on a dash:

- *Clockwise = R*
- *Counter-clockwise = S*

1. Rotation



Flip entire molecule 180 degrees (out of the plane of the page)

1,2 and 3 proceed clockwise = *R*

This is the same molecule drawn from two different perspectives!

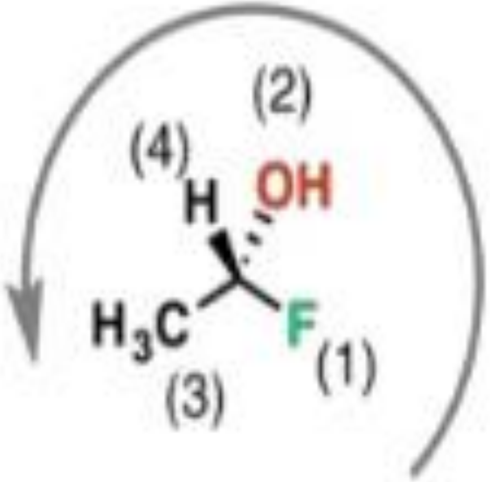
#4 priority is on a wedge:

- Clockwise = S
- Counterclockwise = R

Determining (R)/(S) When The #4 Group Is On A Wedge

2. Apply The "Opposite Rule"

We can get the same result if we just apply the opposite of the normal (R)/(S) rules.



1,2 and 3 proceed counter-clockwise. Looks like (S)

However, group #4 (H) is pointing out of the plane of the page

Therefore, flip the result

So in this case, flip (S) to give us the "real" configuration, R

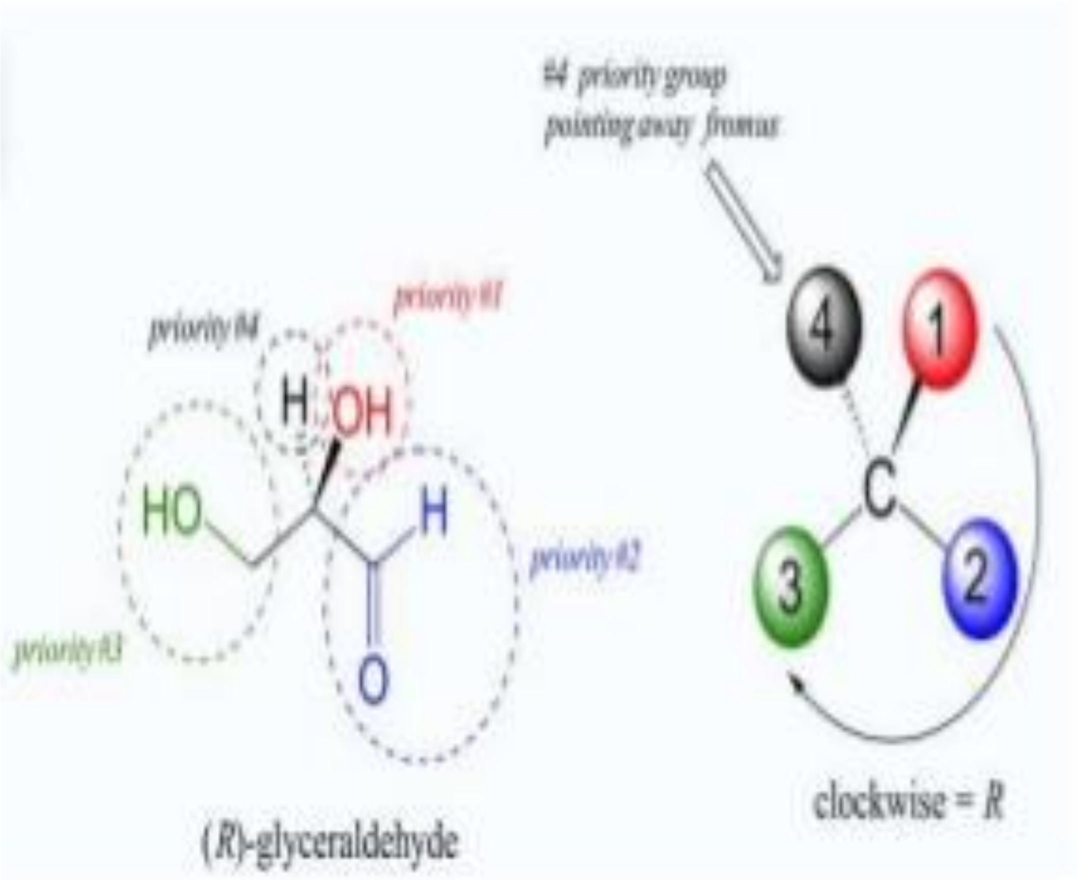
This is almost always easier than rotating the molecule

4/2 back + ve, 1/3 back –ve
4/2 front – ve, 1/3 front + ve

Lowest priority group	1 to 2 to 3	Configuration
Back /Away from the viewer	Clock wise	R
Back /Away from the viewer	Anti- Clock wise	S
Front / Close to the viewer	Clock wise	S
Front / Close to the viewer	Anti- Clock wise	R

Even back + ve, Even front – ve
Odd back – ve, Odd front + ve

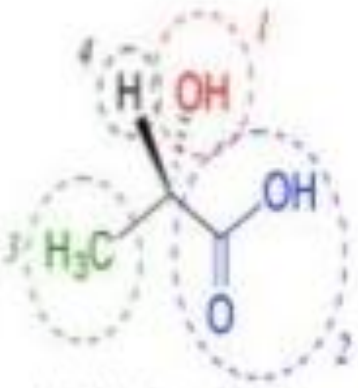
(R)-glyceraldehyde



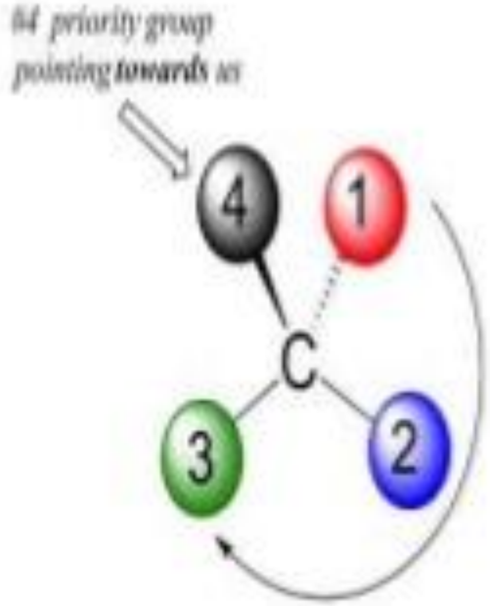
- ✓ Hydrogen(1) (#4) priority, and hydroxyl oxygen(8) priority (#1).
- ✓ Two carbon groups (6) has priority #2(aldehyde or methanol)
- ✓ On moving one more bond away from chiral center the aldehyde has an double bond to oxygen, while methanol group has a single bond to an oxygen.
- ✓ If the atom is the same, double bonds have a higher priority than single bonds.
- ✓ Aldehyde group is assigned #2 priority and the methanol group the #3 priority.
- ✓ #4 priority group (H) and it is pointed back away from us,

Trace a circle defined by the priority groups, circle is clockwise, this molecule is (R)-glyceraldehyde.

(S)-Lactic Acid.



(*S*)-lactic acid

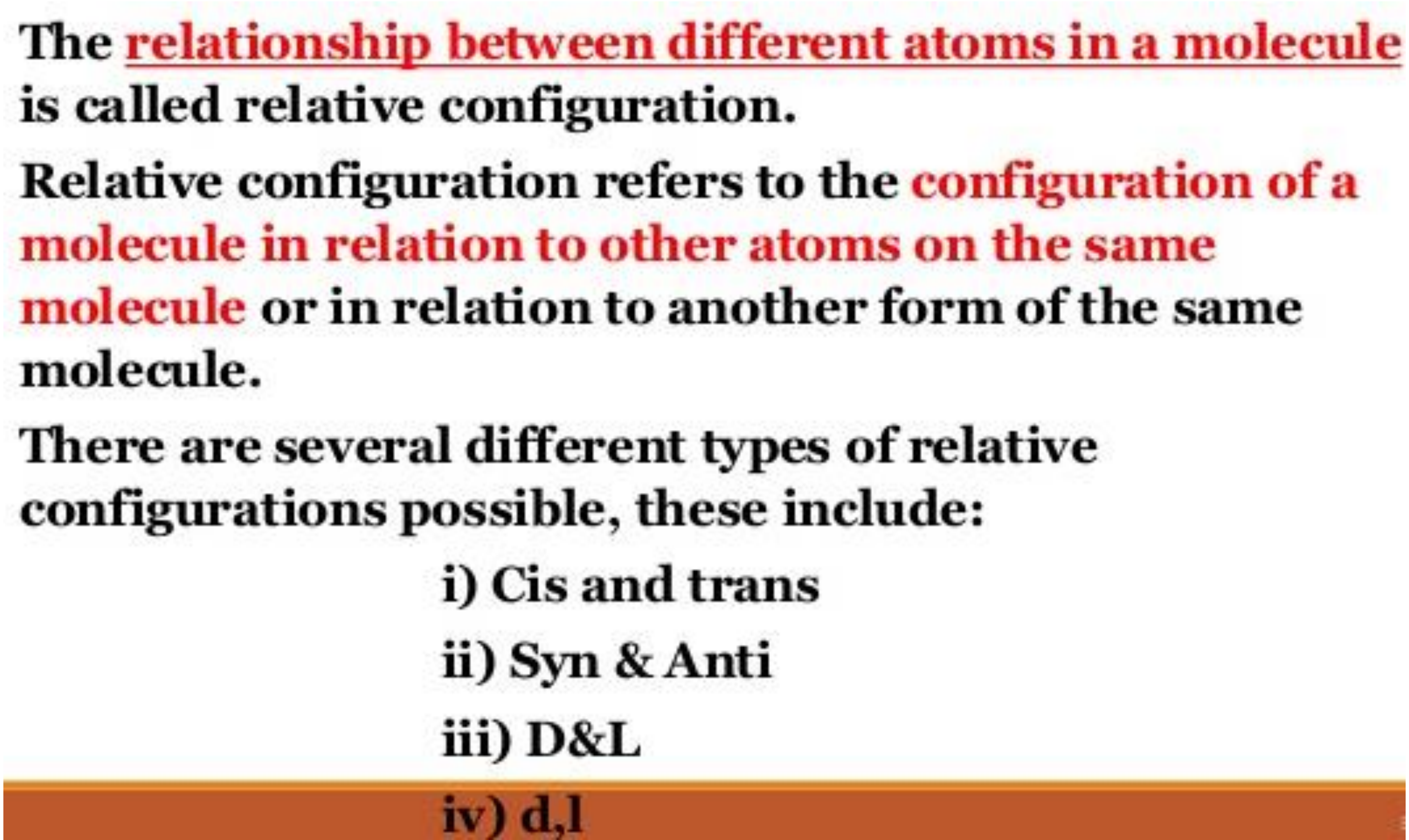


#4 priority group pointing **towards** us

clockwise = *S*

- ✓ H is the #4 substituent and OH is #1.
- ✓ Owing to its three bonds to oxygen, the carbon on the acid group takes priority #2, and the methyl group takes #3.
- ✓ The #4 group, hydrogen, happens to be drawn pointing *toward* us (out of the plane of the page) in this figure.
- ✓ The circle traced from #1 to #2 to #3 is clockwise,
- ✓ The chiral center has the *S* configuration.

Relative Configuration



The relationship between different atoms in a molecule is called relative configuration.

Relative configuration refers to the configuration of a molecule in relation to other atoms on the same molecule or in relation to another form of the same molecule.

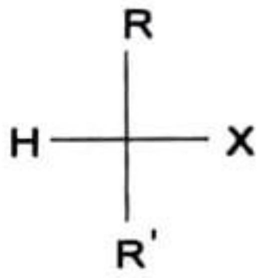
There are several different types of relative configurations possible, these include:

i) Cis and trans
ii) Syn & Anti
iii) D&L
iv) d,l

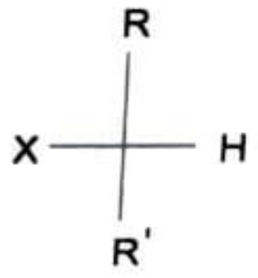
D/L system of nomenclature

The relationship between the configurations of two chiral molecules is the basis of this system. When two such molecules can be chemically interconverted (at least in principle) without breaking any bonds to the chiral centre, they are said to have the same relative configuration independent of the direction of rotation of the plane polarised light.

The simplest and oldest system of nomenclature of optical isomers having chiral centres is D, L-system (Fischer's method). In this system a molecule of the type $RCHXR'$ is written in *Fischer projection* with main longest chain, $R\text{-}C\text{-}R'$ as vertical chain with C-1 carbon (according to IUPAC nomenclature) at the top. Then if X is on the right side of the horizontal line, the designation used is D- and when X is on the left, it is called L-. Here X is taken to be a negative group.



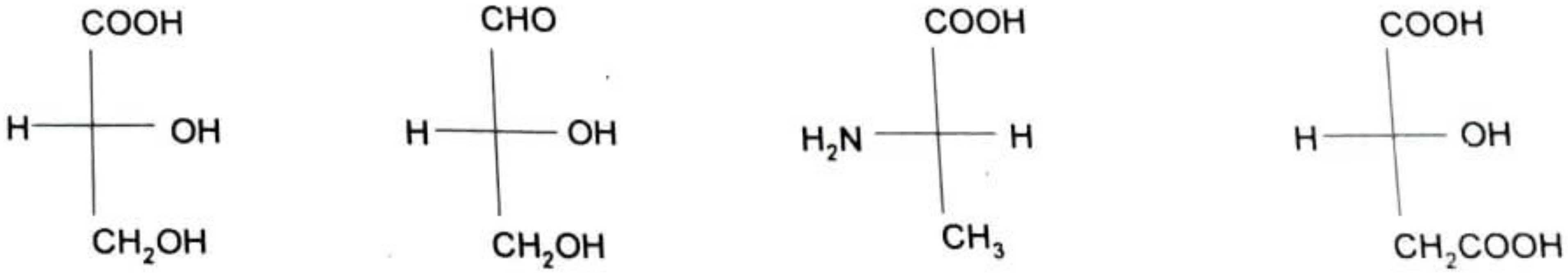
D - isomer



L- - isomer

R = placed arbitrarily at the top assuming its preference in IUPAC nomenclature

For example,

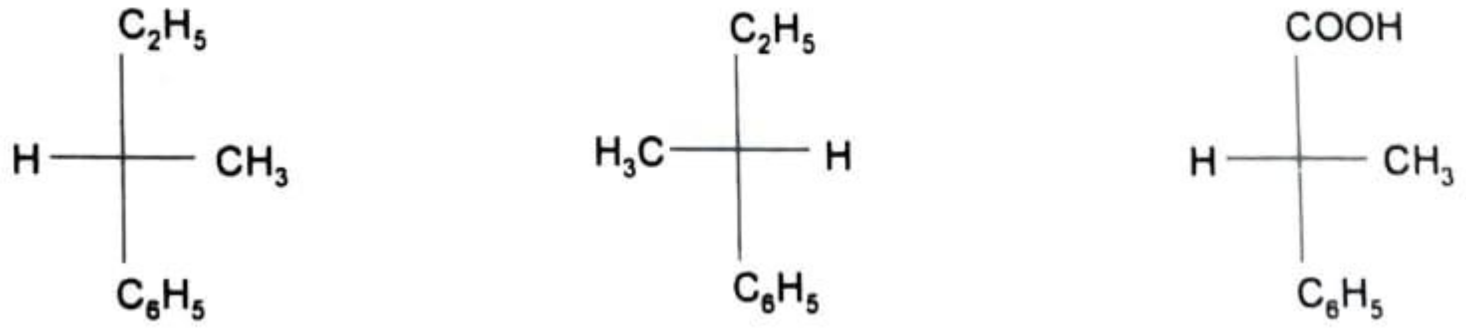


D - Glyceric acid D-Glyceraldehyde L - Alanine D-Malic acid

Fig. 3. 49

Rosanoff (1906) modified the system and his suggestion was to put the most oxidised carbon of the chain at the top of the Fischer projection. But it is not always possible to place the longest chain vertically along with the most oxidised group at the top. For example, 1-phenylbutyric acid cannot be written so, because here the longest chain and most oxidised carbon cannot be simultaneously placed at the top. In such cases, conventionally C-1 according to IUPAC nomenclature should be placed at the top to use D,L-system. However, neither Fischer nor Rosanoff has formulated any specific rule for these situations.

When the chiral centre contains a ring system, then total number of carbon atoms including the ring are taken into consideration to right down the main chain in Fischer projection. For example, when Ph-group is attached to the chiral centre then it is generally placed at the lower vertical bond in Fischer projection.



D-2-phenylbutane

L-2-Phenylbutane

D-2-Phenylpropanoic acid

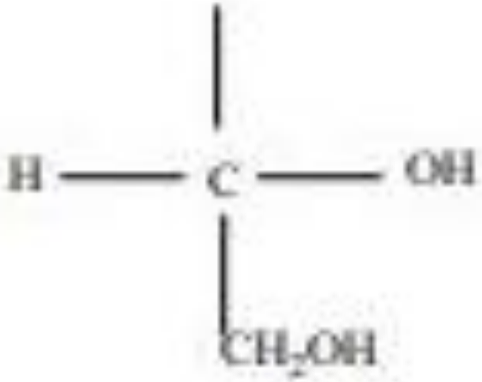
(Hydratropic acid)

Fig. 3. 50

When the chiral centre does not contain H atom as one of the ligands, and replaced by an alkyl group then D, L-naming depends on the orientation of the more electronegative group i.e., in the following examples, when the alkyl group is on the left then it is D-isomer and when on the right, it is L-isomer.

This nomenclature is mainly used in sugar chemistry or optically active polyhydric carbonyl compounds. This is a relative nomenclature because all the configurations described with respect to glyceraldehydes.

All sugars whose Fischer projection formula shows the OH group on the right hand side of the chiral atom belong to the D-series.

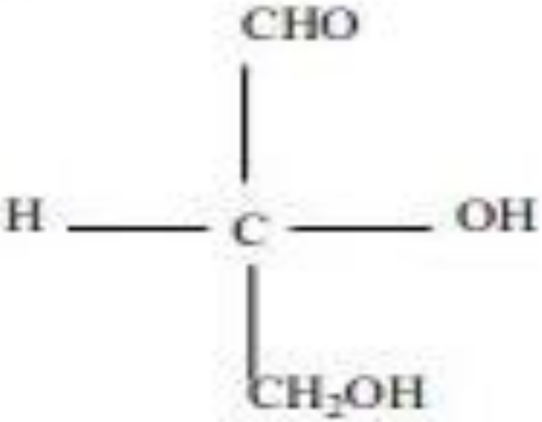


D-series.

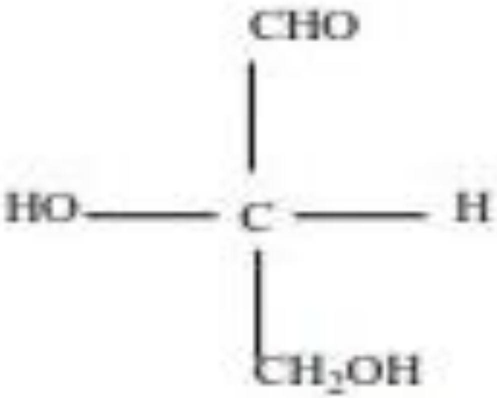
Similarly, if OH is on the left hand side, then the sugar belongs to the L-series.

L-series

Examples:

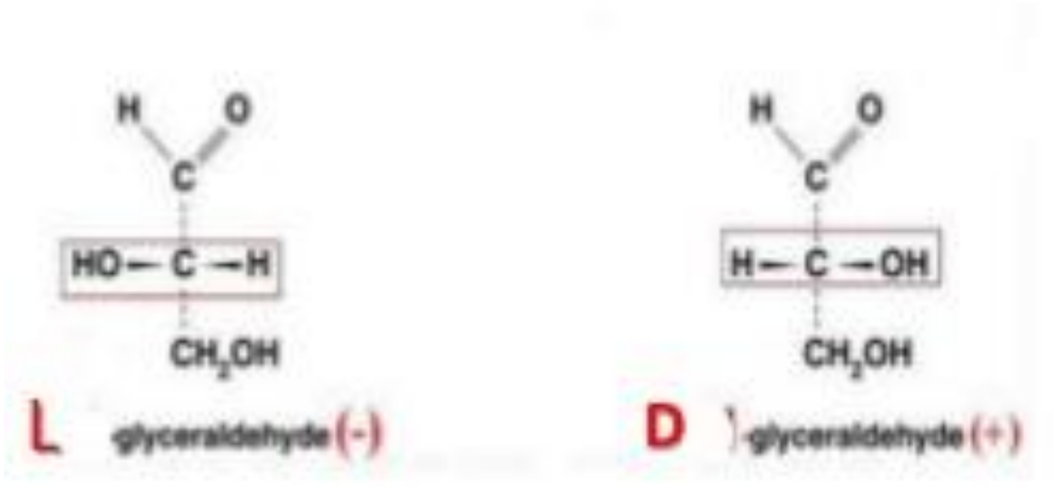


D(+) glyceraldehyde



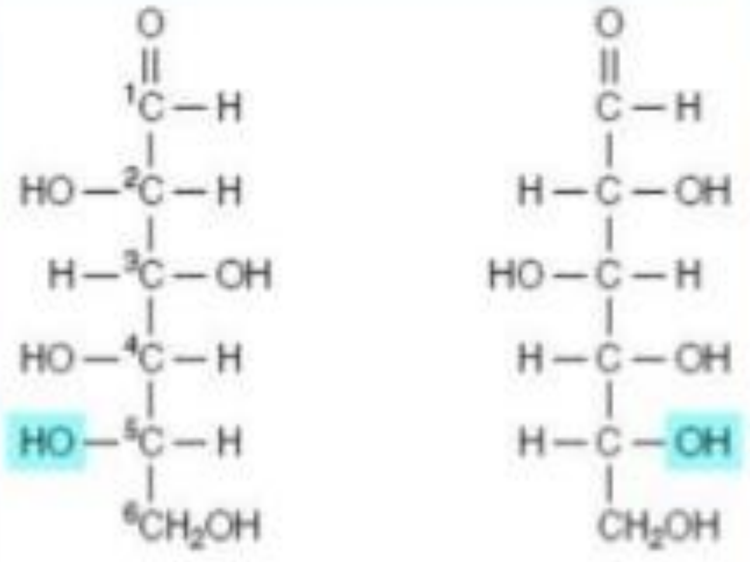
L(-) glyceraldehydes

iii) D & L NOMENCLATURE (Fischer–Rosanoff convention)



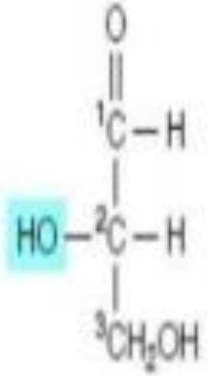
- ✓ When the –OH group on this carbon is on the right, then sugar is the D-isomer,
- ✓ When it is on the left, then it is the L-isomer

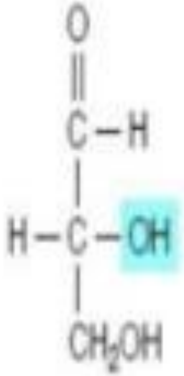
D & L NOMENCLATURE (More than one stereo center)

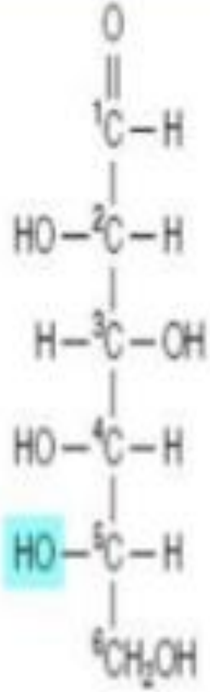


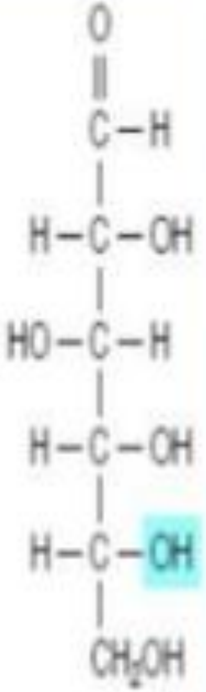
L-Glucose D-Glucose

- ✓ D & L convention is used to distinguish between enantiomers of chiral monosaccharides and chiral alpha-amino acids, based on the molecule drawn as a Fischer projections in a specific orientation.
- ✓ The Land D forms of the sugar depends on the orientation of the –H and –OH groups around the carbon atom adjacent to the terminal primary alcohol carbon(carbon 5 in glucose) determines whether the sugar belongs to the D or L series.
- ✓ The D-and L-notation is based on glyceraldehyde.
- ✓ **When the –OH group on this carbon is on the right, then sugar is the D-isomer,**


L-Glycerose
(L-glyceraldehyde)


D-Glycerose
(D-glyceraldehyde)

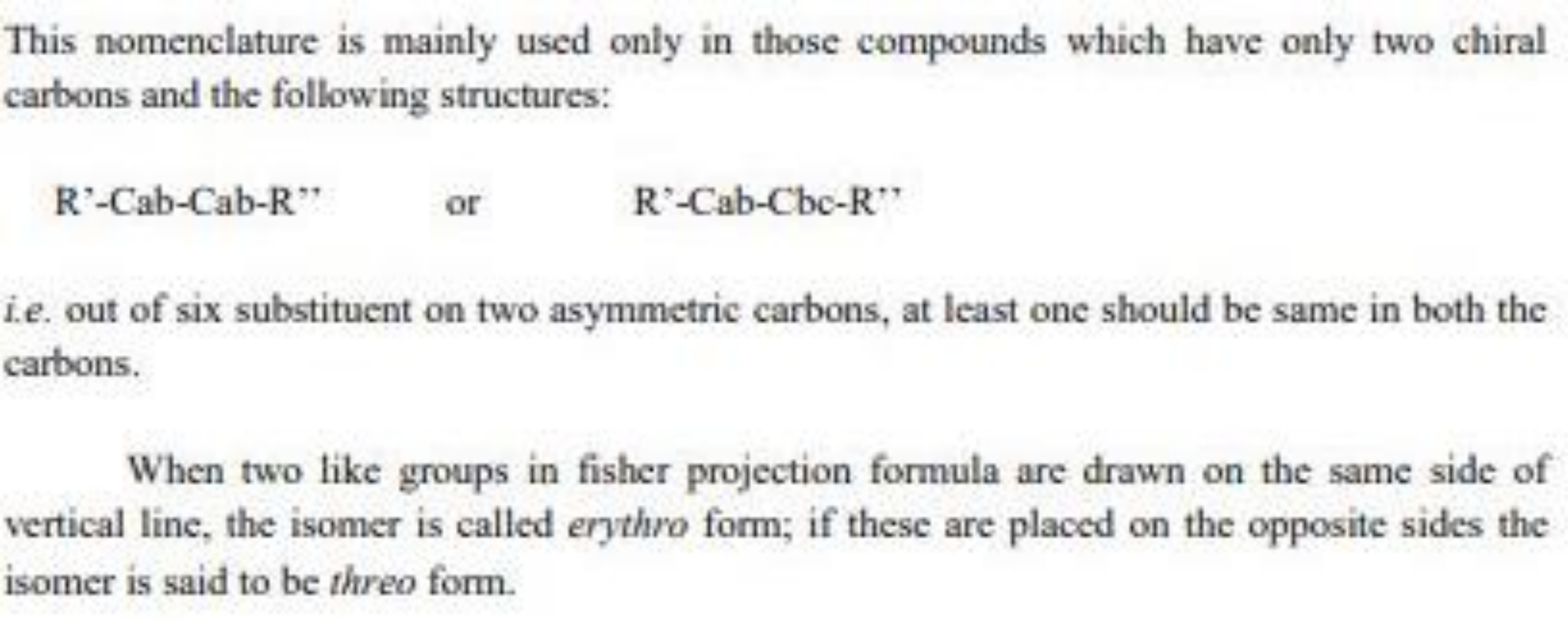

L-Glucose


D-Glucose

It must be noted that there is no relation between sign of rotation and (+, - or *d.l*) and configuration (D and L) of enentiomer.

Any compound that can be prepared from, or converted in to D(+) glyceraldehydes will belong to D-series and similarly any compound that can be prepared from, or converted in to L(-) glyceraldehydes will belongs to the L-series.

Threo/ Erythro nomenclature

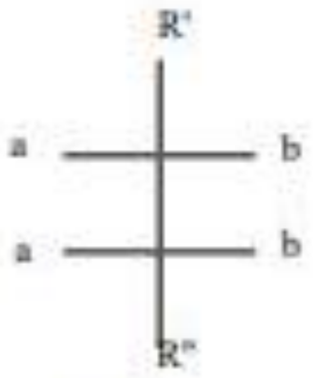


This nomenclature is mainly used only in those compounds which have only two chiral carbons and the following structures:

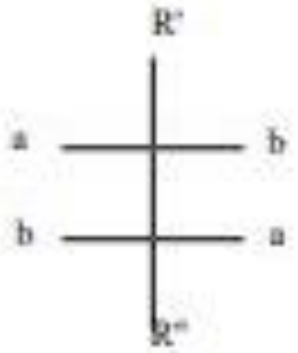
R’-Cab-Cab-R’’ or R’-Cab-Cbc-R’’

i.e. out of six substituent on two asymmetric carbons, at least one should be same in both the carbons.

When two like groups in fisher projection formula are drawn on the same side of vertical line, the isomer is called *erythro* form; if these are placed on the opposite sides the isomer is said to be *threo* form.

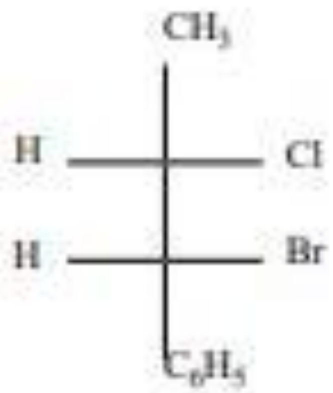


erythro form

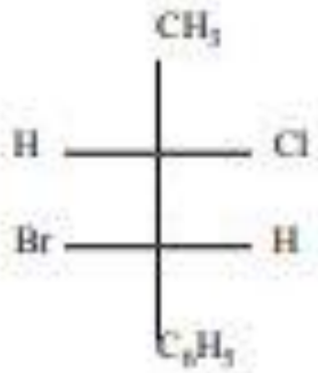


threo form

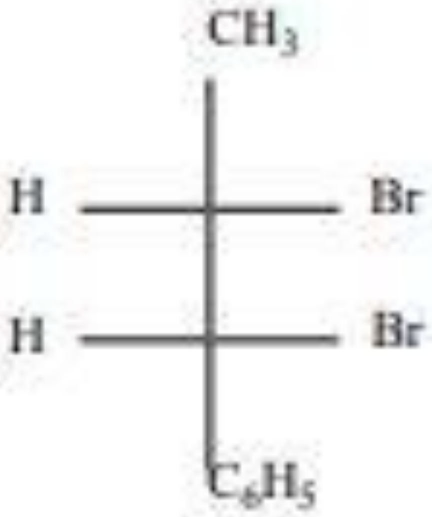
Following are some examples of *threo* and *erythro* form.



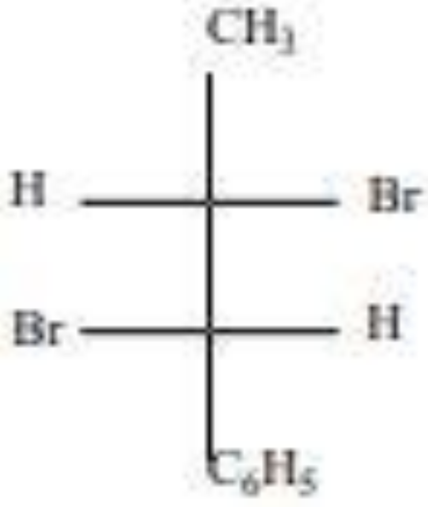
erythro form



threo form



erythro form



threo form