

STEREOCHEMISTRY

Part-V

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

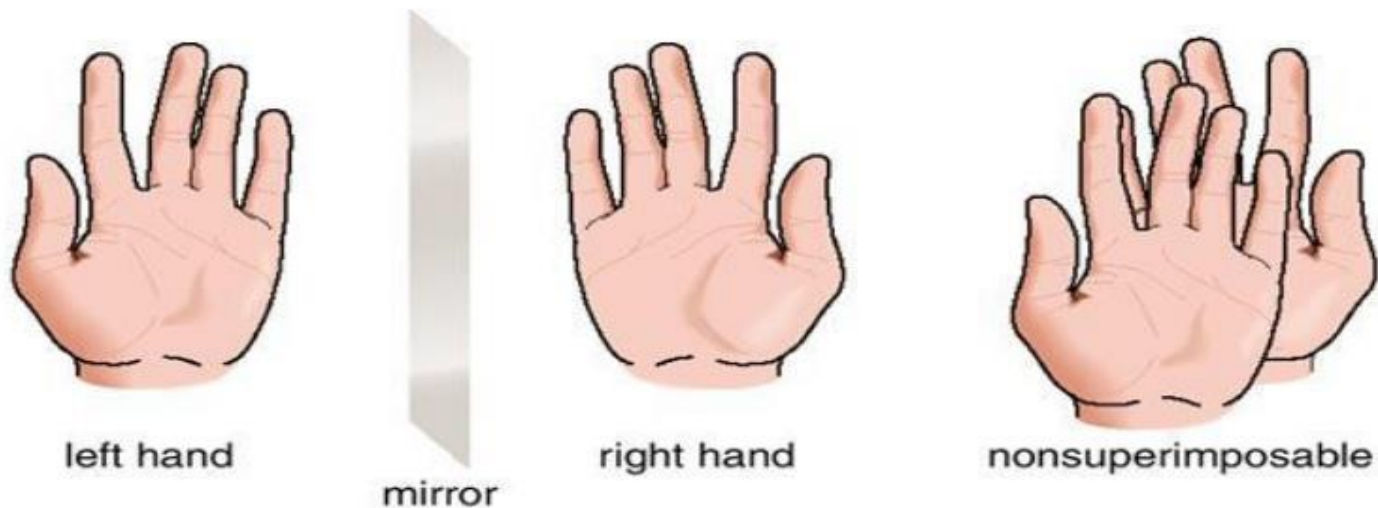
Dr. Indranil Chakraborty
Kharagpur College

Chirality and chiral molecules

Chiral compounds

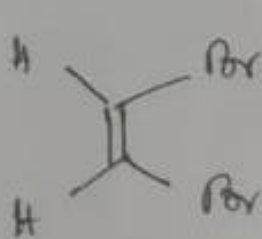
- o Has chiral center
- o Has no element of symmetry
- o The compound and its mirror image are Non superimposable.

N.B. The compound and its mirror image called **Enantiomers**



Nomenclature of cis-trans isomers

- * If an alkene contains similar substituent on each carbon on the same side of the double bond, the isomer is called cis-isomer. When similar substituents are on opposite side of the double bond, they are called trans isomers.



Cis-1,2-dibromo
ethene



Trans-1,2-dibromo
ethene.

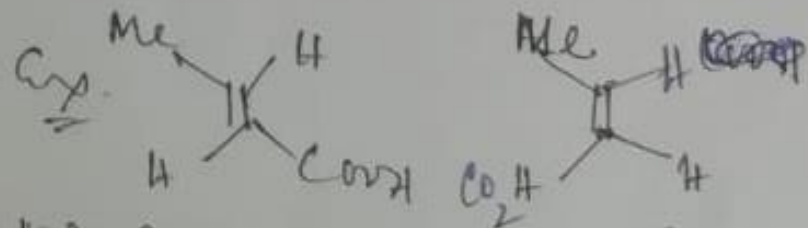
- * When all the four groups on sp^2 carbon are different or different type of nomenclature other than cis-trans is required and this is called E-Z nomenclature.

Let, we have a compound $R_1R_2C=CR_3R_4$. The first job is to make an order of precedence³ of the groups R_1 & R_2 and R_3 & R_4 as per CIP rule & sequence

Let- we also consider that $R_1 > R_2$ and $R_3 > R_4$. Now the isomer where R_1 and R_3 are on the same side of the double bond, is known as Z isomer and where R_1 and R_3 are on the opposite side is called E isomer. (Z = cis like; E = trans like)

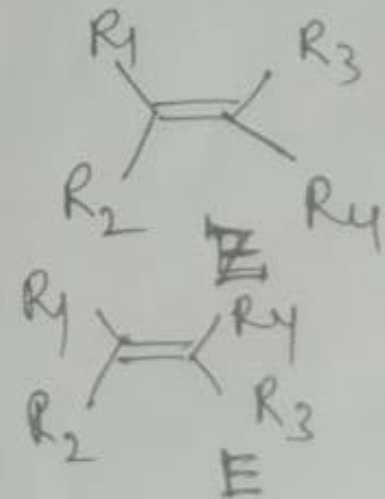
Z \Rightarrow German, ZUSAMMEN = Together

E \Rightarrow German, ENTGEGEN = Opposite

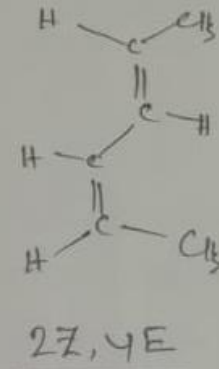
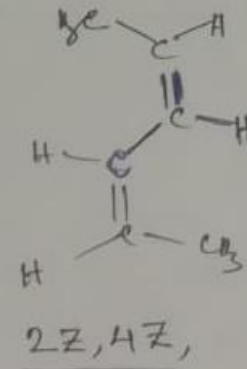
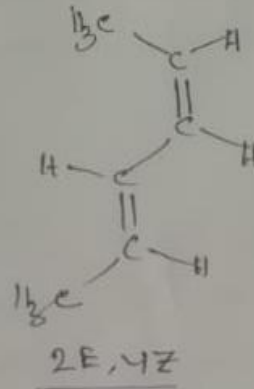
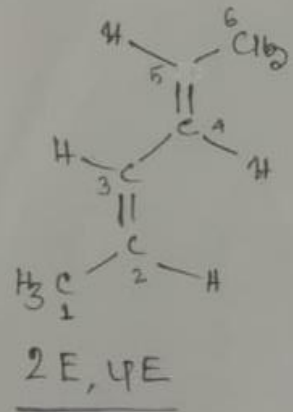


(E)-2 Butenoic acid : (Z)-2 Butenoic acid.

$Me > H$; $CO_2H > H$.

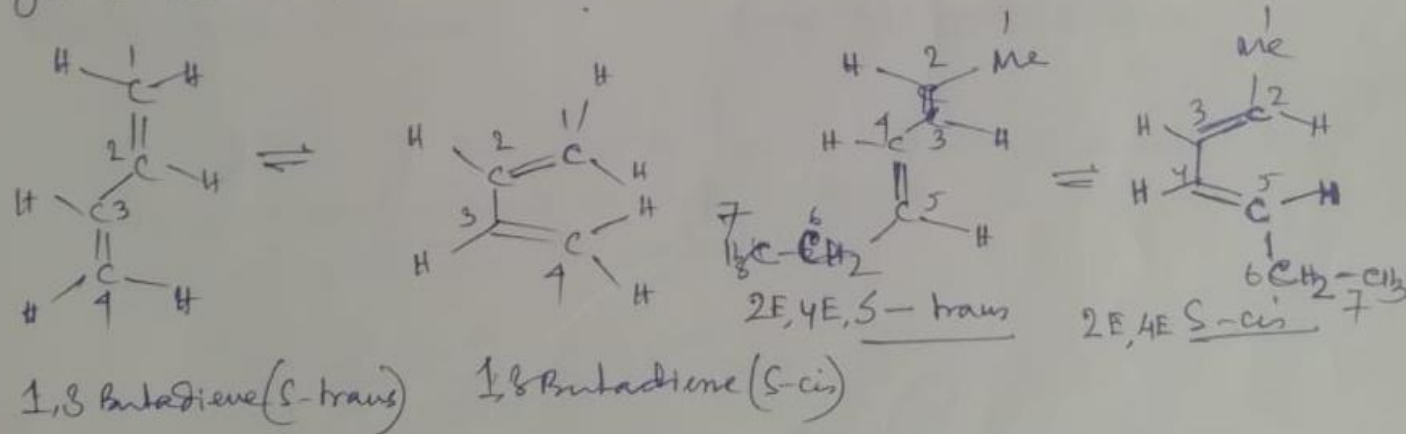


When cis-trans isomers contain more than one double bond nomenclature is done specifying the configuration of each double bond.



Hexa-2,4-diene

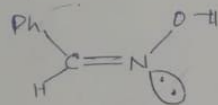
Acyclic conjugated dienes can be written in different conformations by rotating the C-C single bond that joins the two double bonds.



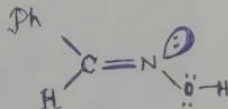
Stereochemical nomenclature of oximes

Compounds containing $C=N$ or $N=N$ can also show cis-trans isomerism. In oxime chemistry the terms cis and trans is replaced by the terms syn and anti respectively.

In aldoximes. The isomer where the hydrogen atom and the hydroxyl groups are on the same side of the double bond is called syn, and the anti form is that isomer that containing OH gr and H atom on opposite side of the double bond.

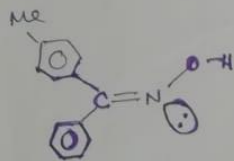


Anti-Benzaldoxime

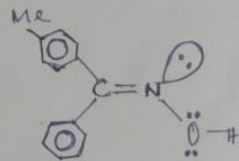


Syn-Benzaldoxime

In Ketoximes the prefix syn or anti indicates the configurational relationship between the first group mentioned and the OH group.

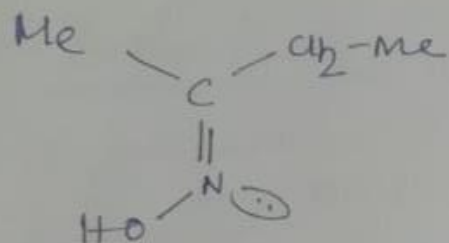


Syn-1-phenyl-4-methylphenylketoxime
or
anti-phenyl-p-tolylketoxime
or
Z-phenyl-p-tolylketoxime

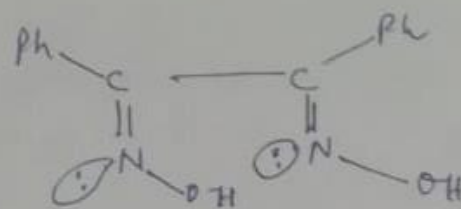


Syn-phenyl-p-tolylketoxime
or
anti-p-tolyl-phenylketoxime
or
E-phenyl-p-tolylketoxime

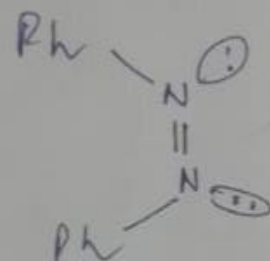
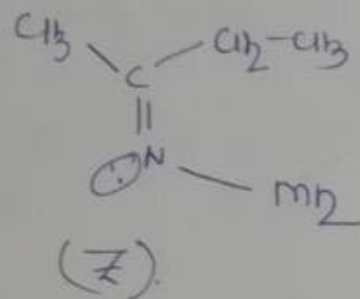
[In E-Z nomenclature in fact the p-tolyl gr has greater priority over phenyl and OH gr has priority over lone pair. Thus oximes can also be named as E/Z-]



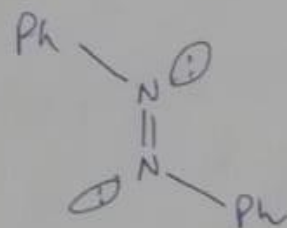
(E) - Butanone oxime



(Z, E) - Benzil dioxime



Syn
or
Z Azobenzene



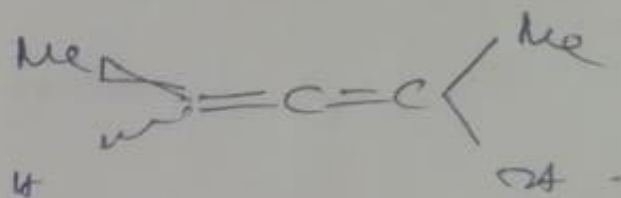
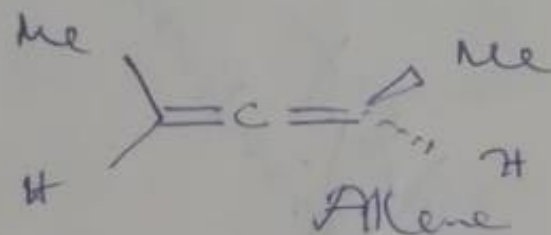
anti azobenzene
or
E - Azobenzene

Chirality Other than Chiral Centre.

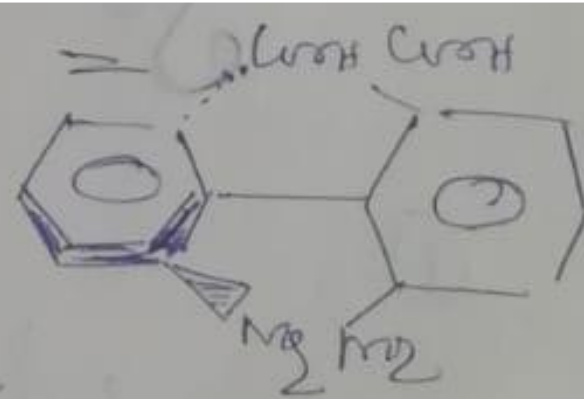
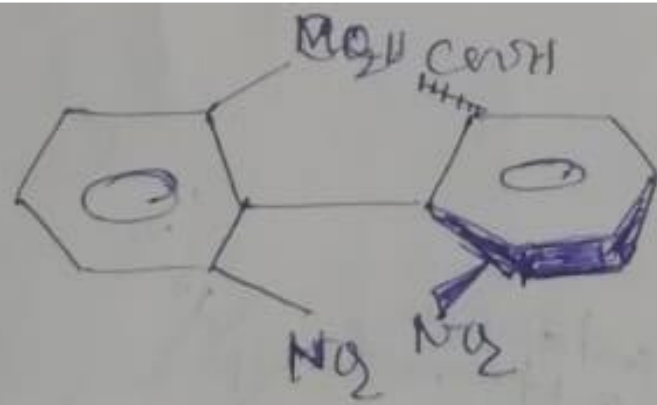
⑩ Axial Chirality \Rightarrow Allenes and Spiroanes.
(suitably substituted).

~~And unlike groups in each terminus~~

Each terminus should carry ~~unlike~~ a pair of unlike groups (although the set may be identical).

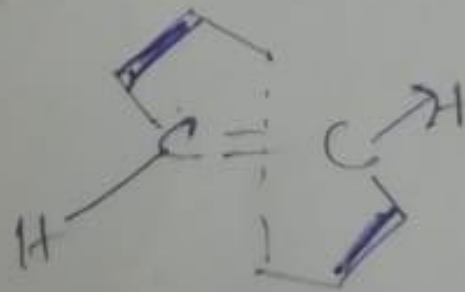
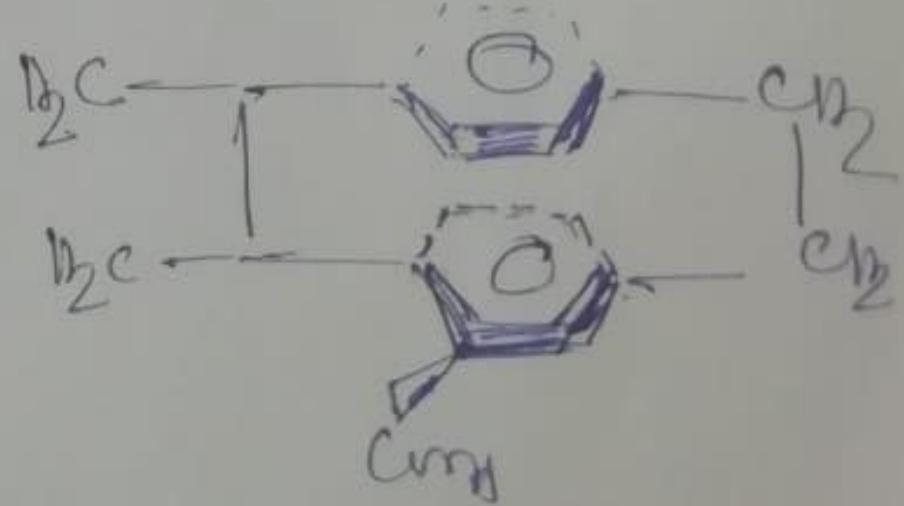
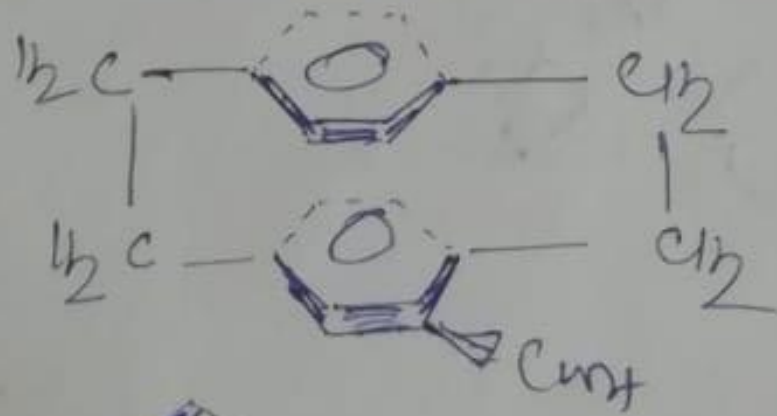


Spiroanes.



Bisphenol
=

Planar Chiralität



The necessary & sufficient condition of optical activity \Rightarrow

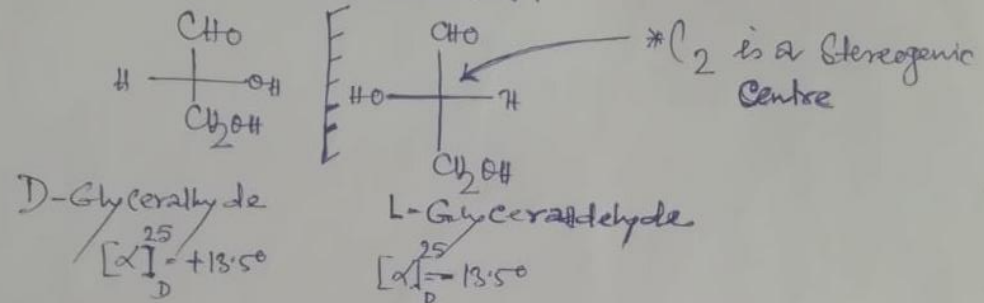
The molecule should not be superimposable on its mirror image, so as to show measurable optical rotation.

From symmetry point of view the molecule should be at least dissymmetric i.e. it must not contain plane of symmetry (σ), centre of symmetry (i) and alternating axis of symmetry (S_n), but may or may not contain C_n .

Thus in one sentence it can be said that Chirality is the necessary and sufficient condition for showing optical activity.

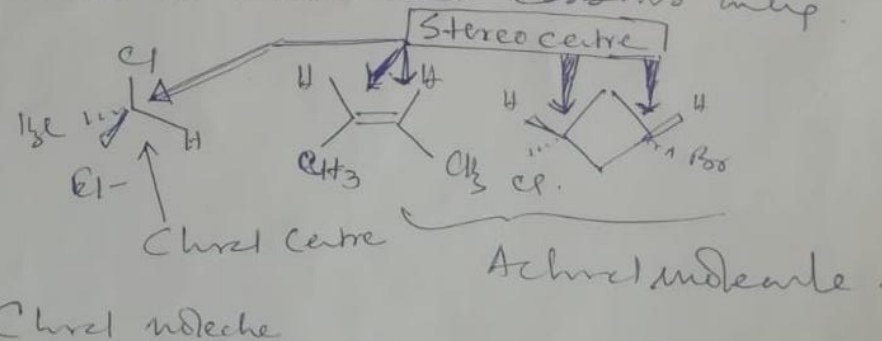
Stereogenic Centre \Rightarrow or Stereocentre \Rightarrow

An atom having groups of such nature that an interchange of any two groups can produce a stereoisomer.



Chiral Centre or asymmetric centres are replaced by the term Stereocentre or Stereogenic Centre i.e. Centre giving rise to stereoisomer.

Thus all Chiral Centres are stereocentres but all stereocentres need not necessarily be Chiral Centres, because Chiral Centres are restricted to saturated carbons only.

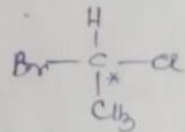
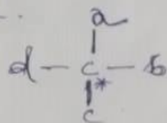


Optical Isomers. The stereoisomers that are capable of rotating the plane of a plane polarised light are said to be optically active isomers or optical isomers.

Conditions for optical activity

A molecule will be optically active if it is not superimposable on its mirror image, such molecules are called chiral molecules. Chirality arises due to the presence of chiral centre/chiral axis/chiral plane.

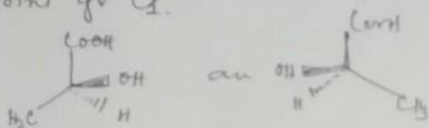
Chiral Centre: A carbon atom to which four different atoms or groups are present.



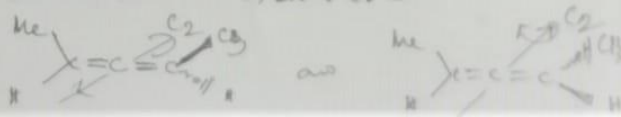
Chiral axis and Chiral plane can be discussed later.

Optical activity is also related to the presence and absence of certain symmetry elements. That's why two terms Disymmetric and Asymmetric molecules can be taken into consideration.

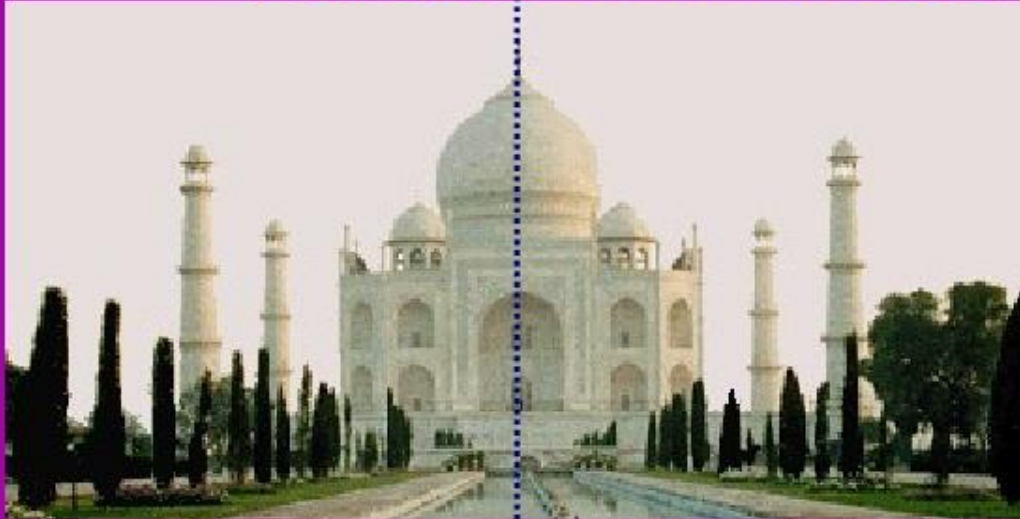
Asymmetric molecules are those which do not contain any symmetry elements (σ , S_n , C_n , i absent). These belong to point group C_1 .



Disymmetric molecules on the other hand contain only C_n but do not contain σ , S_n or i .



Monuments & Symmetry.



Symmetry exists in architecture all around the world.

One of the best known examples of this is the Taj Mahal.

If an object is reflected in water many people believe the image has line symmetry.

But is it really a 'mirror image'? Is it really symmetrical?
What are your thoughts?
The image can be rotational symmetry.



❖ The organic compound becomes optically active if :

- contain chiral center or chiral axis
- not contain element of symmetry

Chiral center

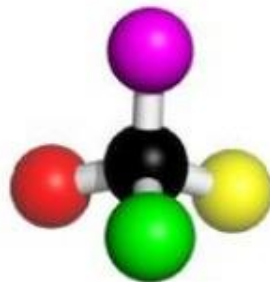
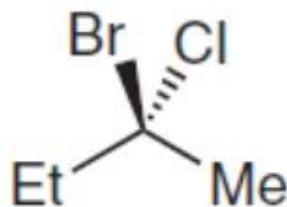
❖ **Chiral center** called **Streo**center and **stereogenic center**

❖ **Chiral center:** atom connected to four different groups.

❖ If the atom is **carbon**, it is called **chiral carbon**

❖ **Chiral carbon:** it is **tetrahedral (SP³) carbon**, connected to four different groups.

e.g. 1

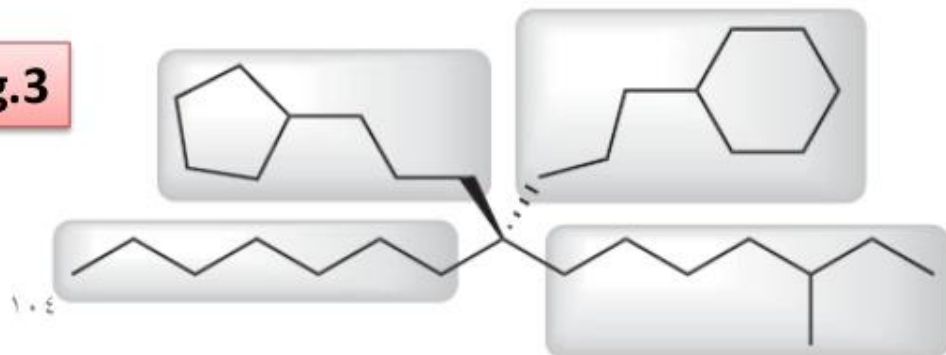


e.g. 2



Not a stereocenter

e.g.3

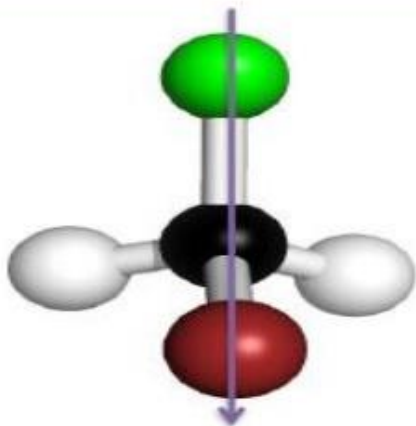


Element of symmetry

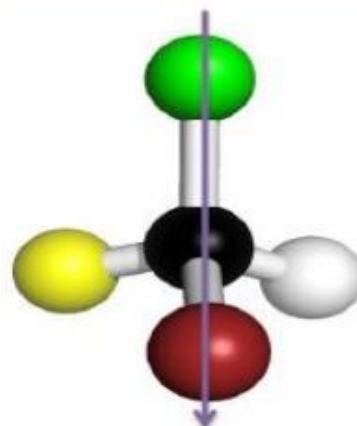
- Plane of symmetry
- Center of symmetry

1- Plane of symmetry

- ❖ plane of symmetry (internal mirror plane) is a **mirror plane that cuts the molecule into two halves**, so that one half of the molecule is a reflection of the other half.
- ❖ The plane may pass through **atoms, between atoms, or both**



Has Plane of symmetry, **achiral**
This molecule has **two identical halves**



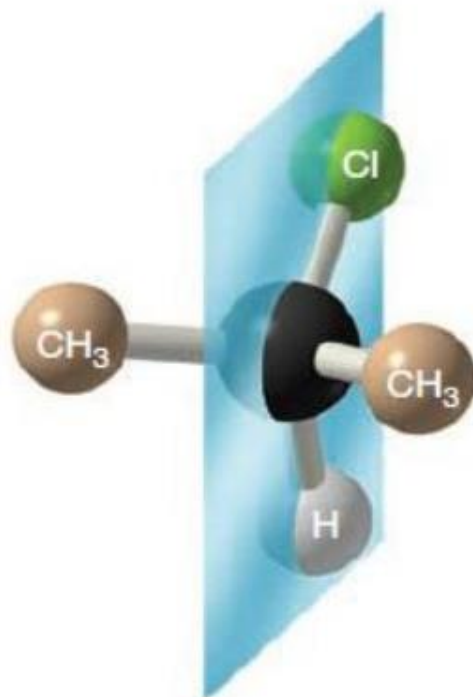
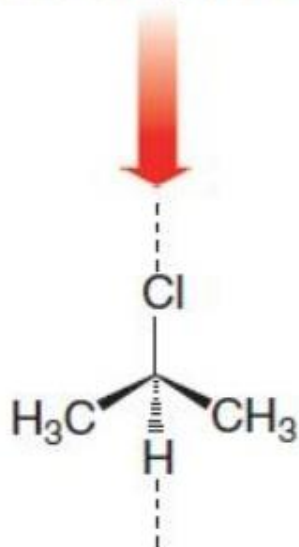
Has NO Plane of symmetry, **chiral**
This molecule has **not two identical halves**

Example

(a) 2-Chloropropane **has a plane of symmetry** and is **achiral**.

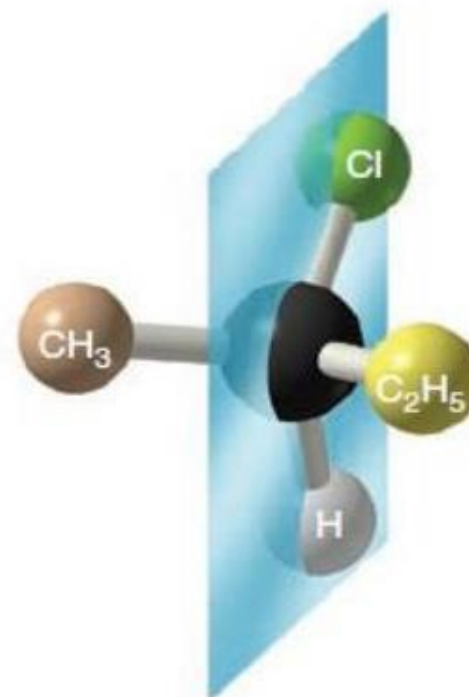
(b) 2-Chlorobutane does **not possess a plane of symmetry** and is **chiral**.

Plane of symmetry



Achiral

(a)



Chiral

(b)

❖ The compound have plane of symmetry is:

Optically inactive and called **Meso compound**

example

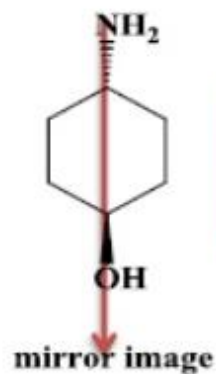
➤ *cis-1,2-dimethylcyclohexane*

This molecule has a plane of symmetry cutting the molecule in half. Everything on the left side of the plane is mirrored by everything on the right side.



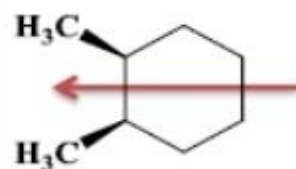
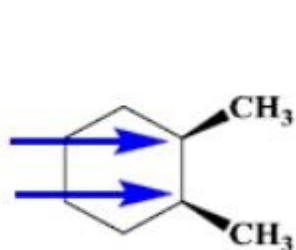
❖ Classify each of the following pairs as **chiral** or **achiral**

a)

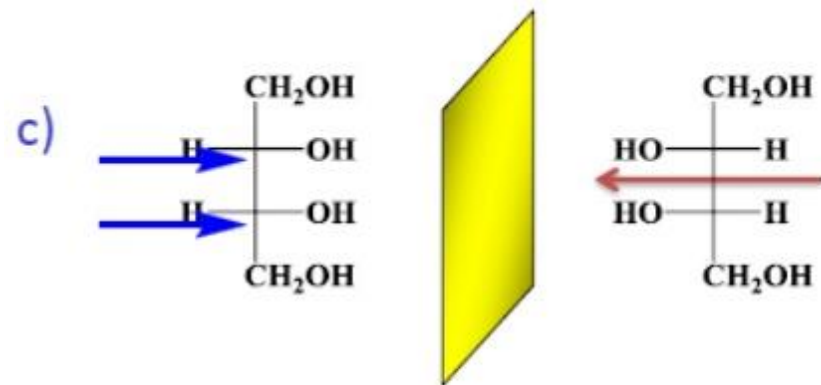


Achiral: the molecule has plane of symmetry,
Not has chiral carbon

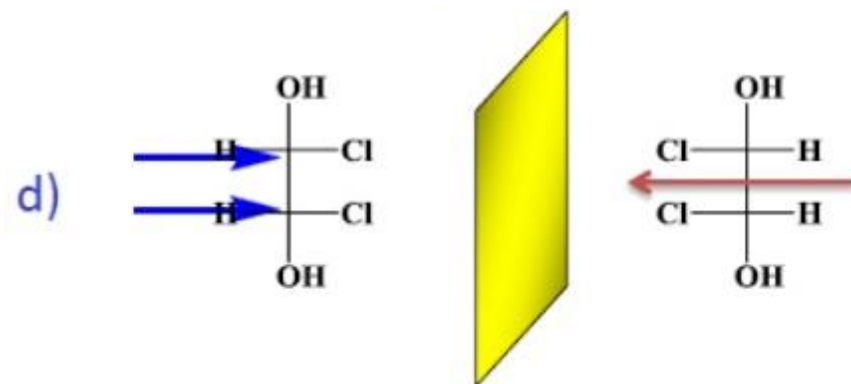
b)



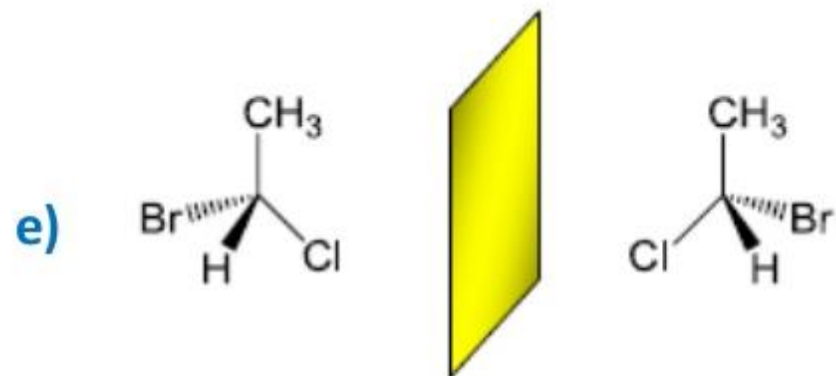
Achiral: the molecule has plane of symmetry



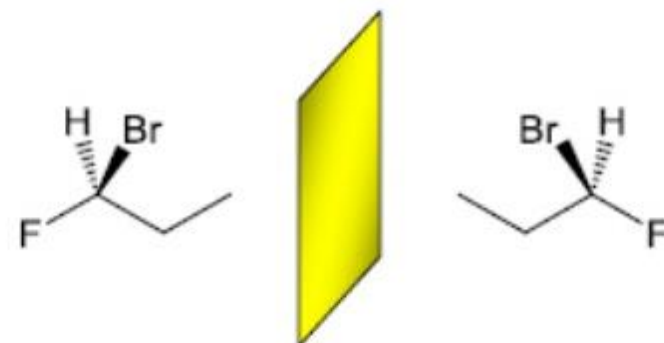
Achiral: the molecule has plane of symmetry



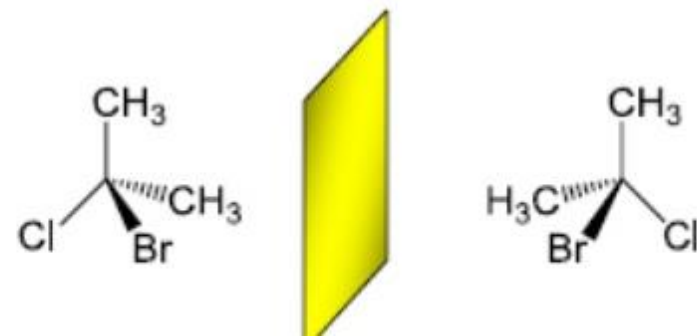
Achiral: the molecule has plane of symmetry



f)

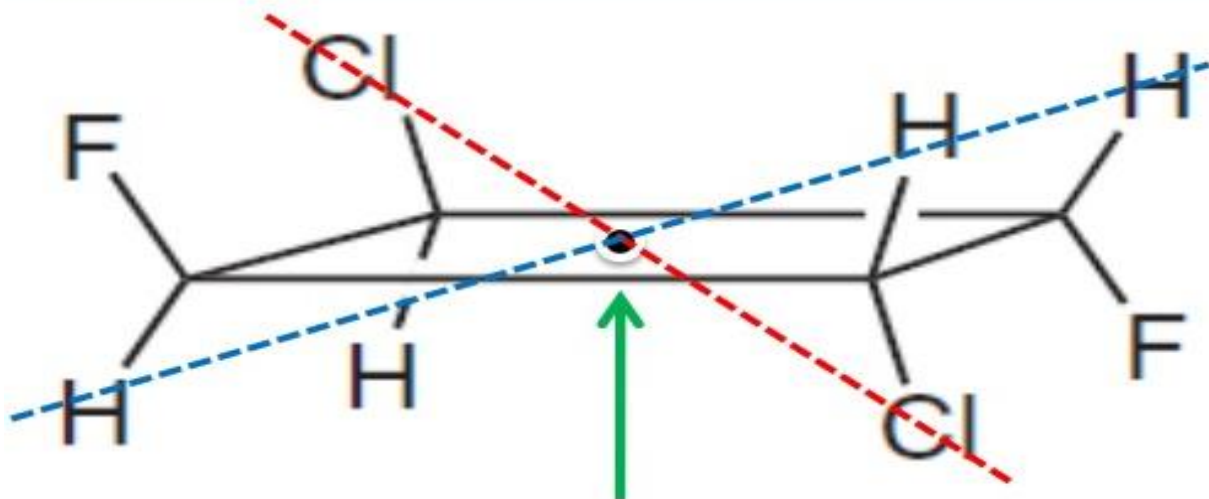


g)

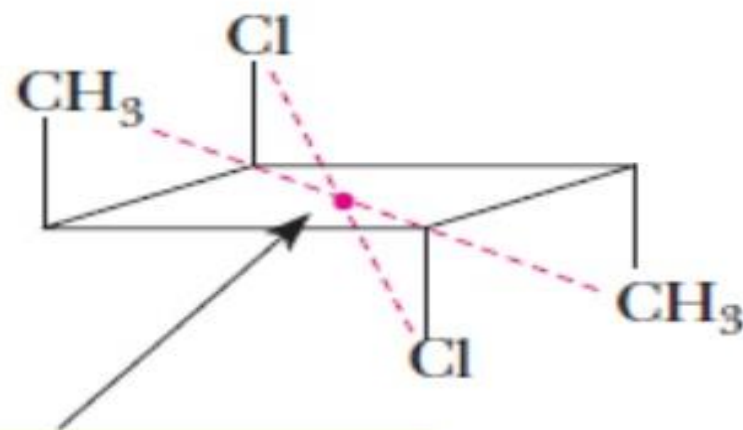


2- Center of symmetry

➤ It is the point in the center of molecule to which a line can be drawn from any atom such that when extended an **equal distance** past the center, the line **meets another atom of the same kind**



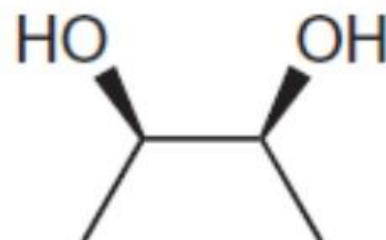
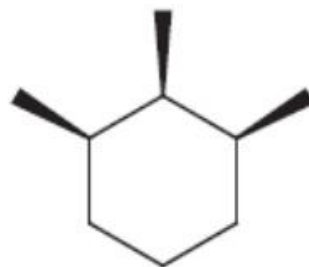
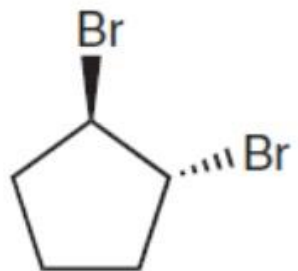
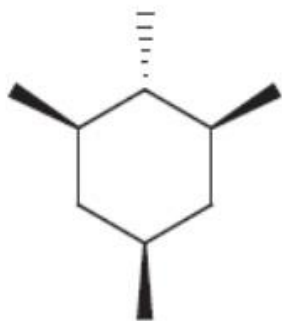
Center of symmetry



Center of symmetry

Q. Trans-3,6-dimethyl-2,5-diketopiperazine is optically inactive while Cis-3,6-dimethyl-2,5-diketopiperazine is optically active. Why??

Q. Identify which of the following compounds is a *meso* compound.



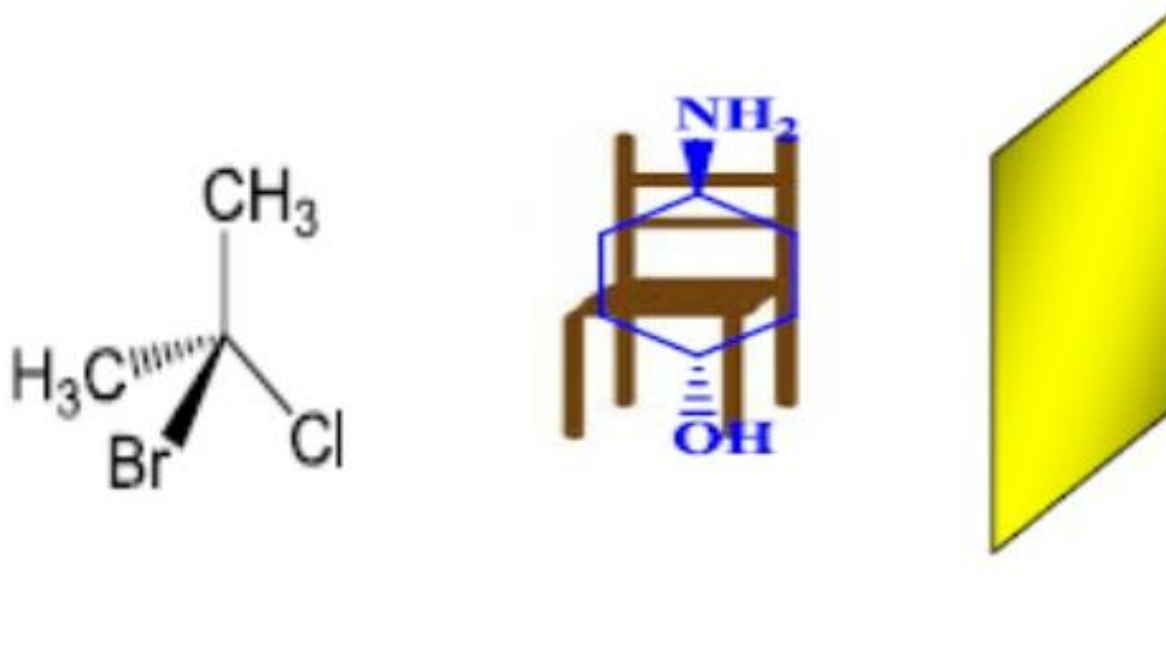
Achiral compounds

- o Has **No** chiral center
- o May contain chiral center but the compound and its mirror image are **Superimposable**
- o **Has** element of symmetry (**Plane of symmetry or center of symmetry**)

N.B: Achiral compound is **optically inactive**



Achiral compound, not contain chiral center



Achiral compound, has Plane of symmetry, superimposable

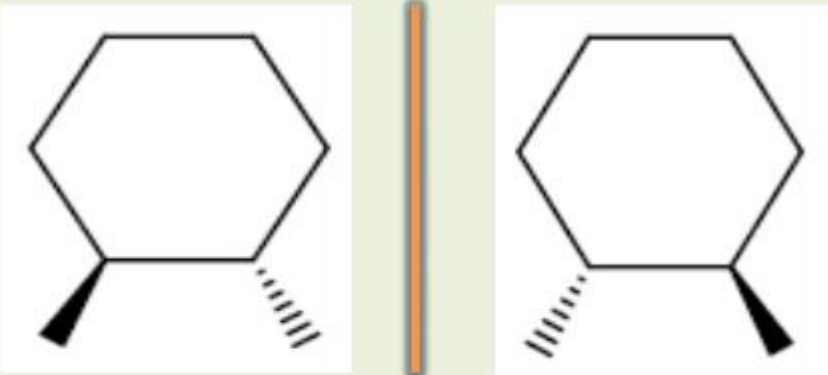
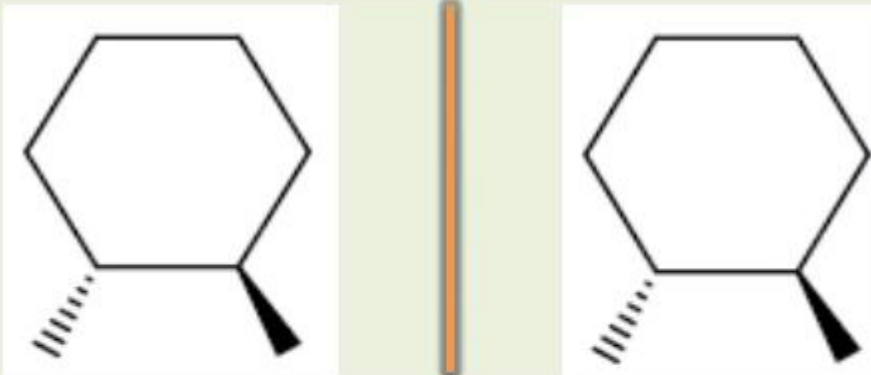


The glass and its mirror image are superposable.



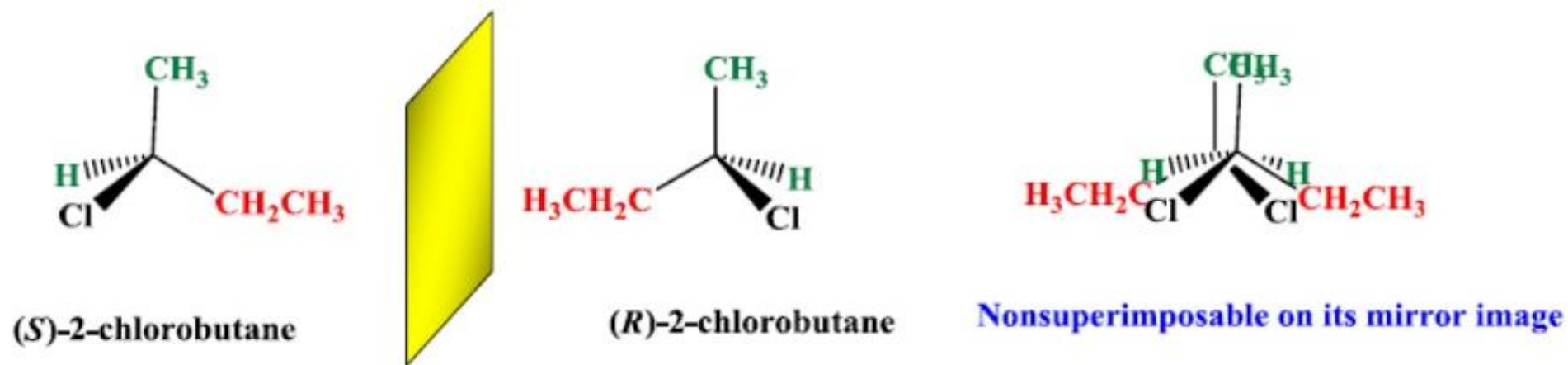
This mug is chiral.

Chiral compounds Vs. Achiral compounds

Chiral compounds	Achiral compounds
	
Has chiral center	Has No chiral center
the compound and its mirror image are NOT Superimposable	May contain chiral center but the compound and its mirror image are Superimposable
Has NO element of symmetry (Plane of symmetry or center of symmetry)	Has element of symmetry (Plane of symmetry or center of symmetry)
optically active	optically inactive

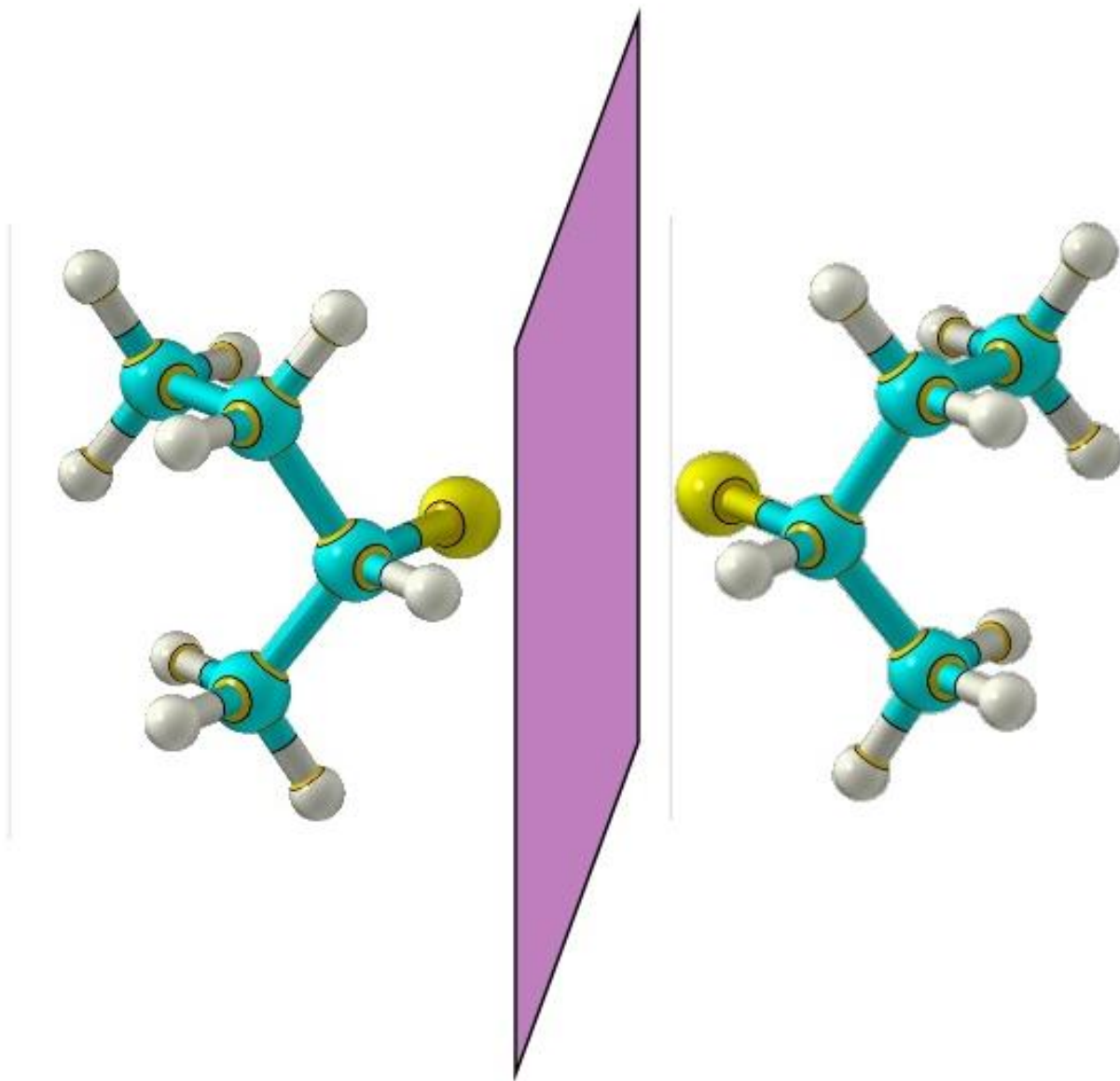
Enantiomers

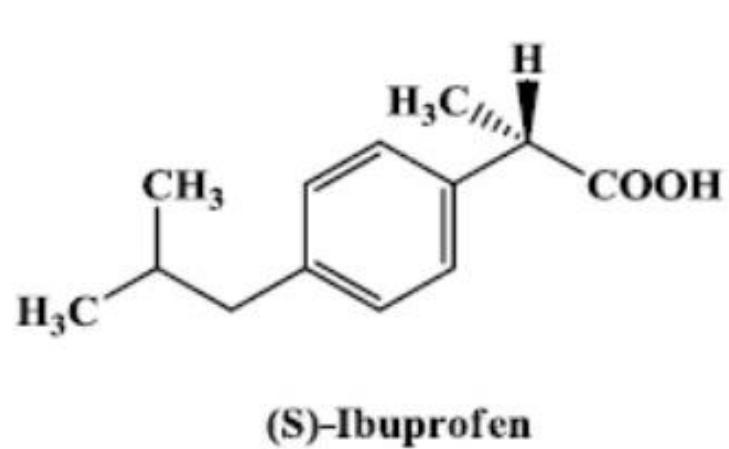
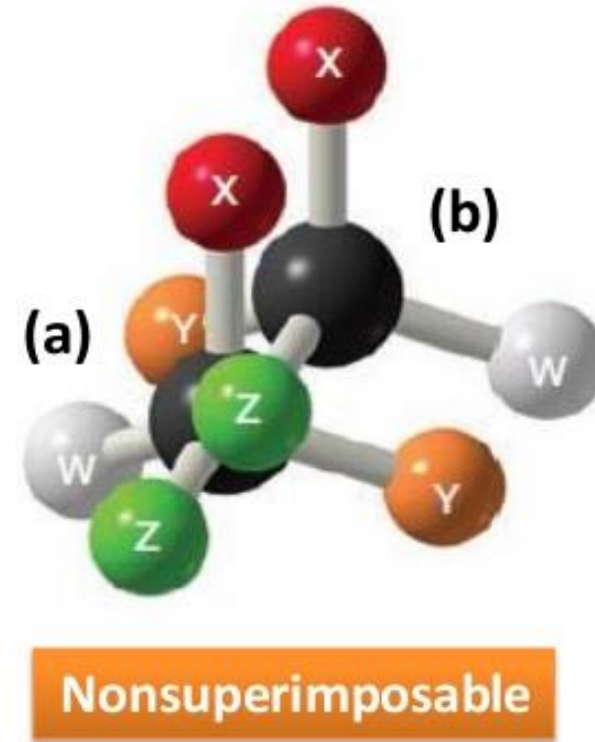
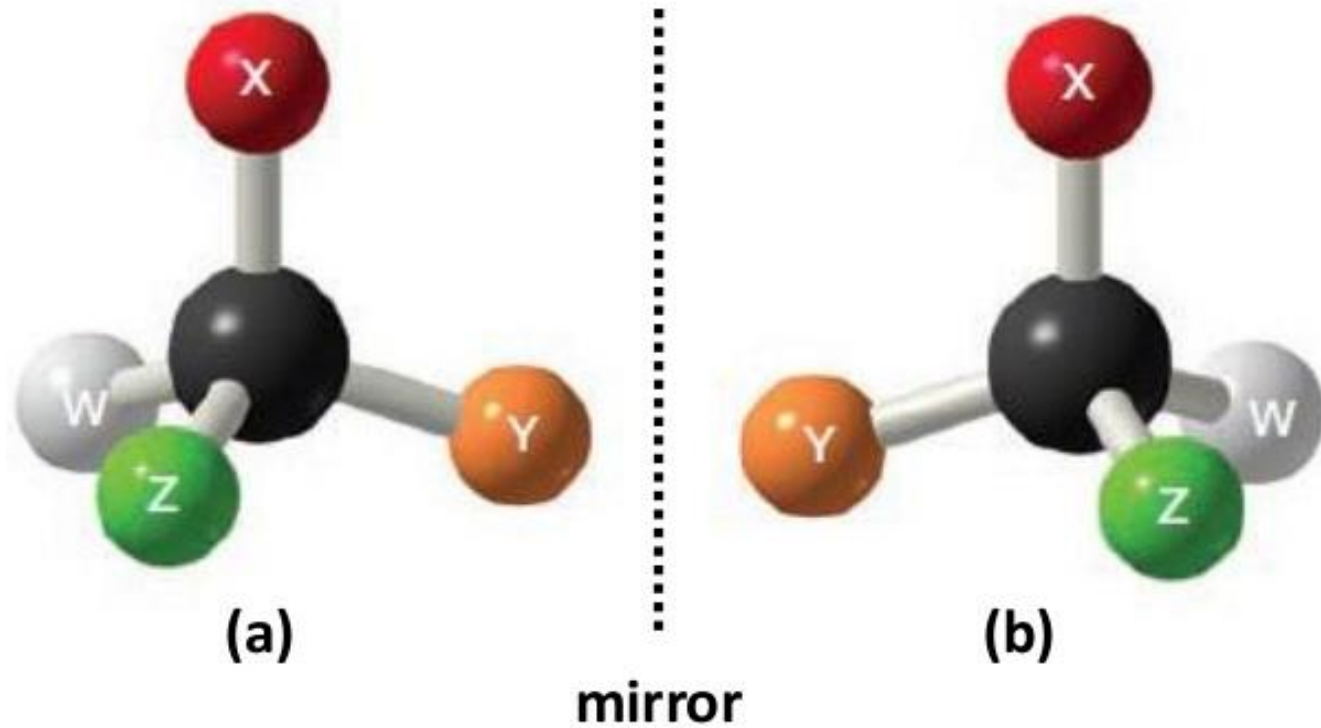
- ❖ **Enantiomers:** stereoisomer compounds with the **same connectivity, different arrangement of atoms in space**
 - Have one or more **chiral center**
 - **Lacks plane of symmetry**
 - **Non super-imposable** on its mirror image
 - Have **same physical and chemical properties**
 - Rotate the plane of polarized light by exactly **the same number of degrees but in opposite directions**
 - **Different in pharmacological actions**



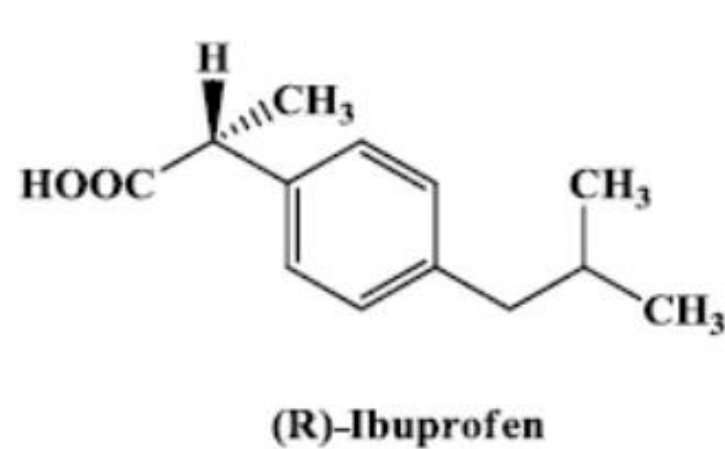
Enantiomer

Enantiomers: Non super-imposable on its mirror image

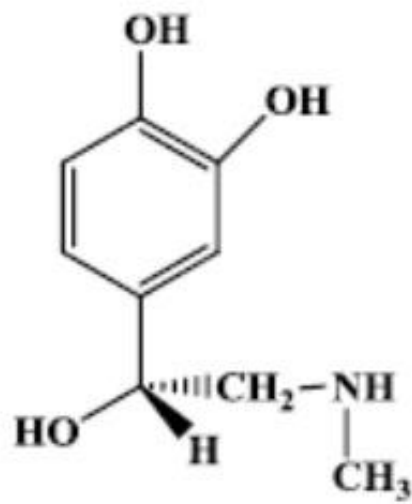




Inhibits platelet thromboxane production twice as effectively as does the racemate

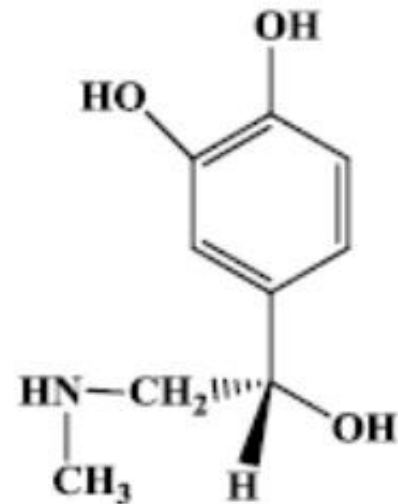


Racemizes to the S-form and does not cause G.I. lesions



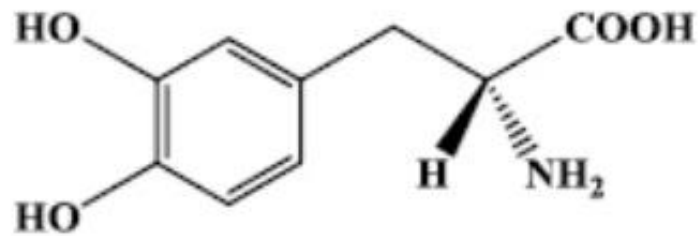
(R)-(-)-Epinephrine

Fit the enzyme active site



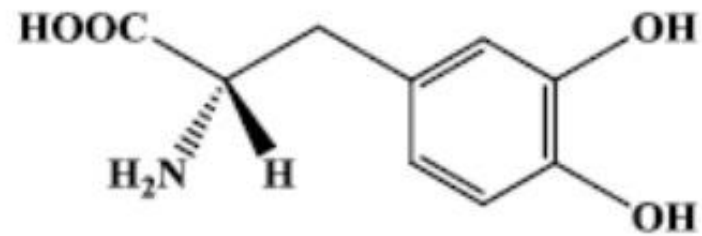
(S)-(+)-Epinephrine

Does not fit the enzyme active site



(R)-L-DOPA

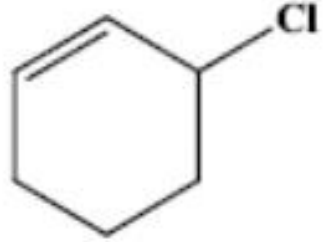
No biological effect



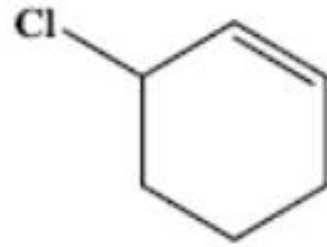
(S)-L-DOPA

Used for the treatment of Parkinson disease

Enantiomer

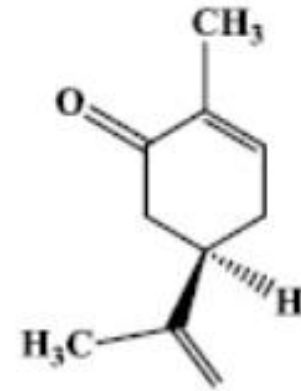


3-Chlorocyclohexene

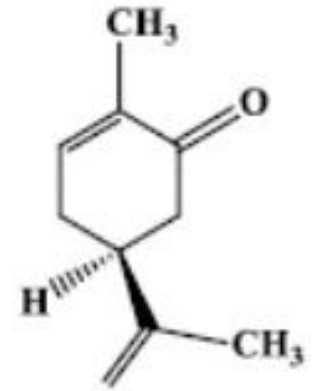


3-Chlorocyclohexene

Enantiomer

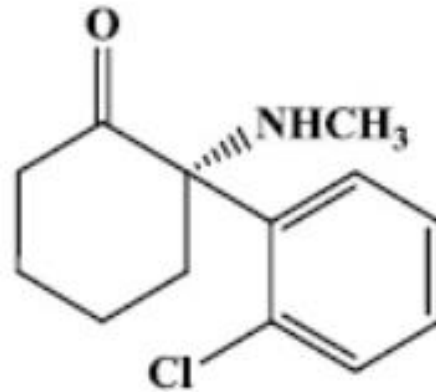


(R)-(-)-Carvone
Caraway seeds



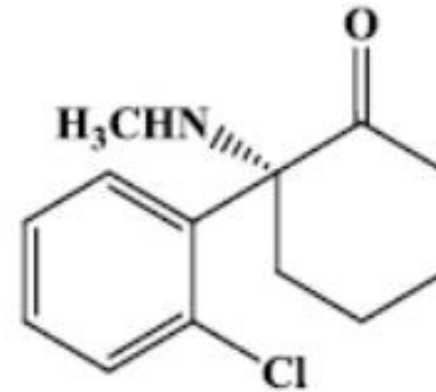
(S)-(+)-Carvone
Caraway seeds

Enantiomer



R-(-)-Ketamine

Causes spontaneous motor
activity and post-emergent
distress



S-(+)-Ketamine

2-4 times more potent than R-
ketamine in anaesthesia

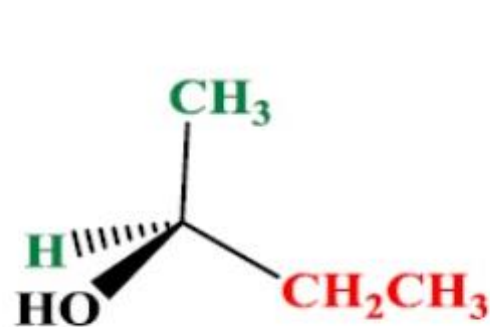
Racemic mixture

- ❖ **Racemic mixture**: mixture containing equal amounts of two enantiomers.
- It is **Optically inactive** ($\alpha = 0$) due to (+) enantiomer cancel the optical activity of (-) enantiomer.
- sample that is **optically inactive** can be either an **achiral substance** or a **racemic mixture**
- **Racemic mixtures** are designated using the prefix



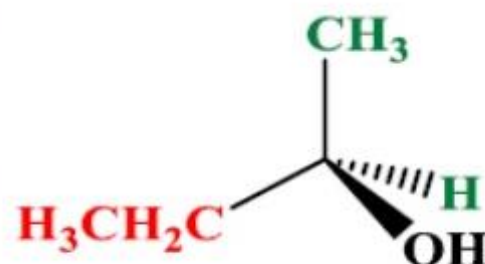
e.g

(+)-2-butanol



(S)-(+)-2-butanol

+ 13.5° rotation



(R)-(-)-2-butanol

- 13.5° rotation

Nomenclature of Enantiomers (R,S System)

❖ Determination of **chiral carbon**

❖ Arrangement of **substituents about chiral center**:

1. Rank the atoms bonded to the chiral center by **atomic number** based on

Cahn-Ingold-Prelog sequence rules

{ H-(1) < C- (6) < N-(7) < O-(8) < F-(9) < S-(16) < Cl-(17) < Br-(35) < I-(53) }

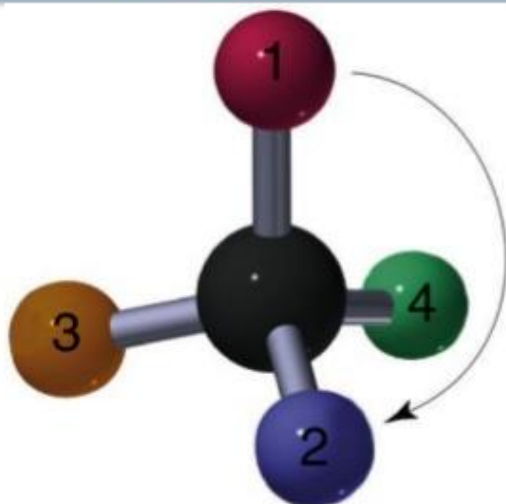
2. If the **groups attached to the chiral center are not different**, the sequence is determined **at the first point of difference**

3. The group attached to the chiral center with the **highest atomic number = 1**, next = 2, etc.

4. Rotate the **lowest priority group to the back**

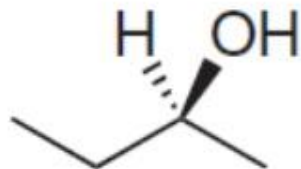
5. Draw a curve from group of **highest priority through the group of second priority to group of third priority**

6. **R** (Latin rectus) = **right** turn and **S** (Latin sinister) = **left** turn



→				
C	N	O	F	
P	S	Cl		
		Br		
		I		
				↑

e.g.

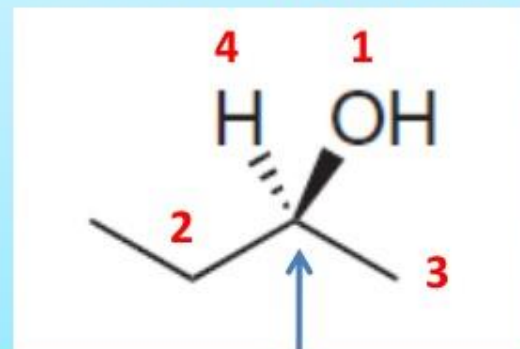


- The four atoms attached to the stereocenter are C, C, O, and H
- We rank them from 1 to 4 based on atomic number.
- When comparing the four atoms in the example above, we see that **oxygen** has the highest atomic number, so we give it the first priority—we give it the number **1**. **Hydrogen** is the **smallest** atom, so it will always get the number **4** (**lowest priority**) when a stereocenter has a hydrogen atom.

The carbon atom on the **left side** of the stereocenter has three bonds (**C, H, and H**) the carbon atom on the **right side** of the stereocenter.

It has three bonds (**H, H, and H**).

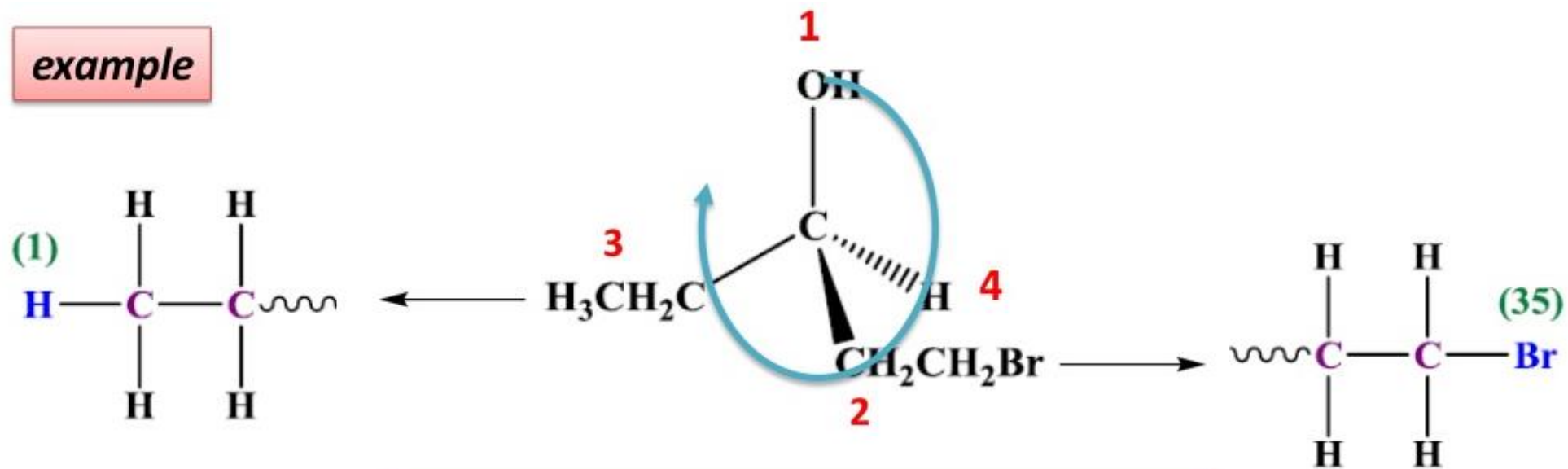
The **carbon in left side** get the no. **2** and the **carbon in right side** get the no. **3**



chiral carbon

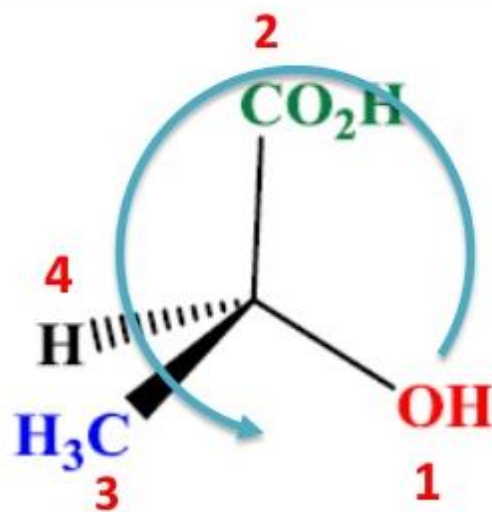
➤ If the group of lowest priority is on hatched or horizontal line, follow as normal, but reverse the R and S

example



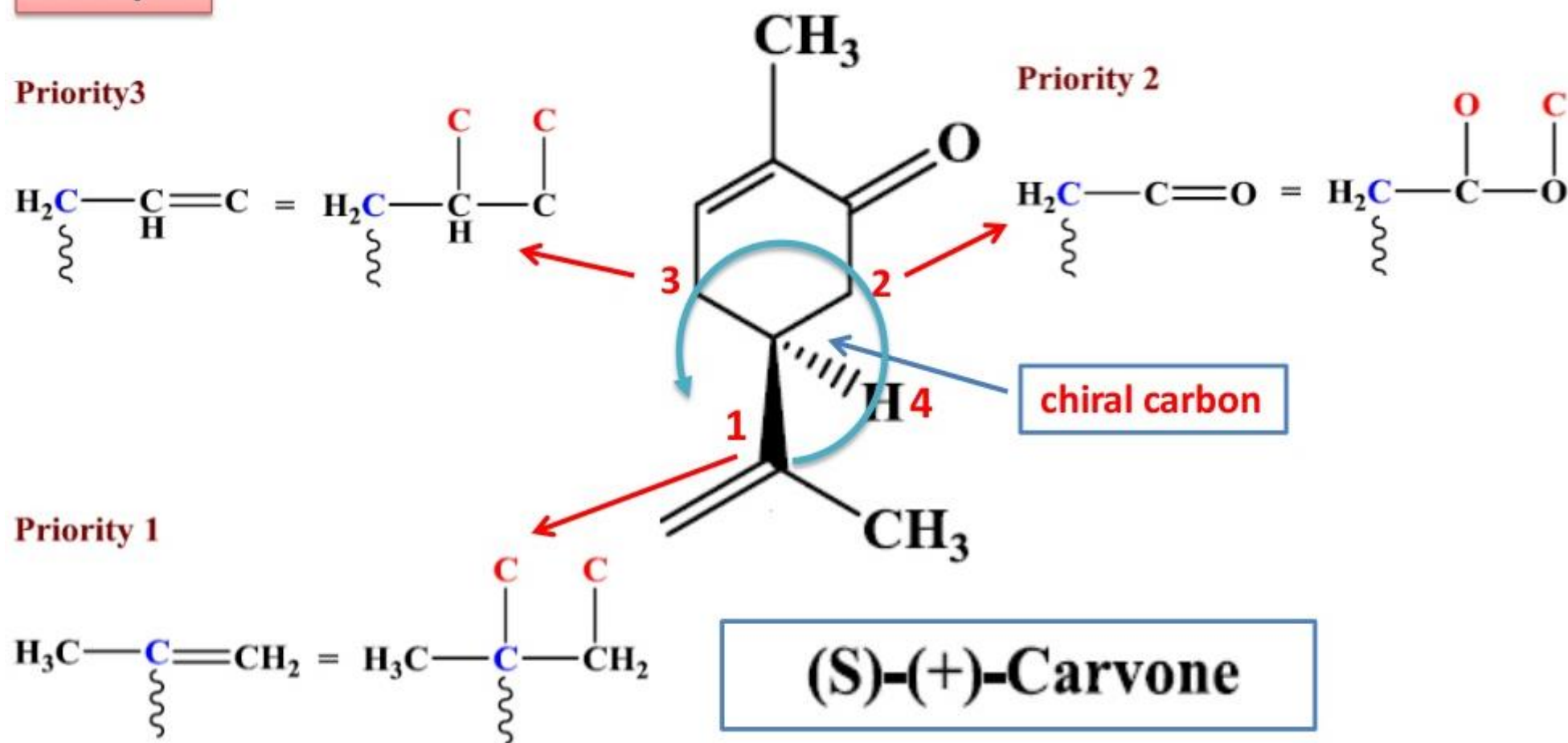
(R)-1-Bromopentane-3-ol

example

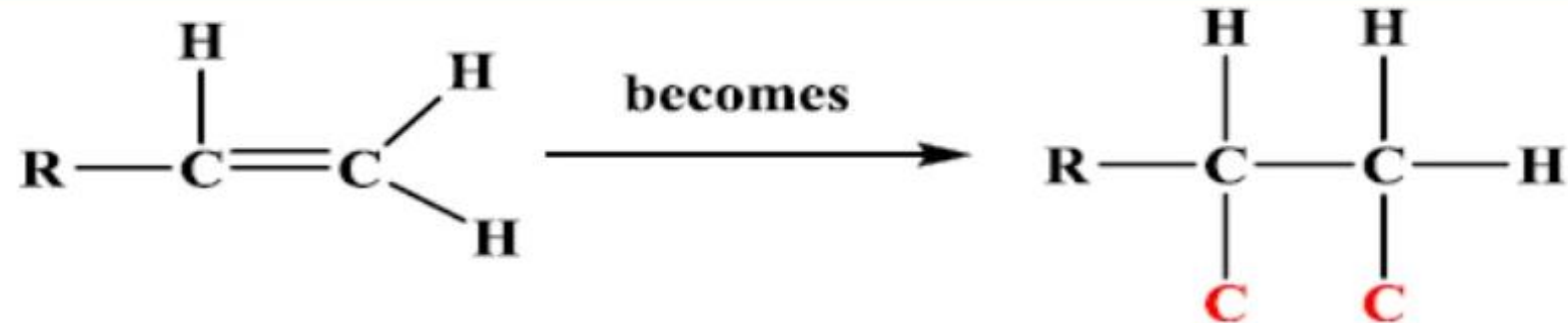


(S)-Lactic acid

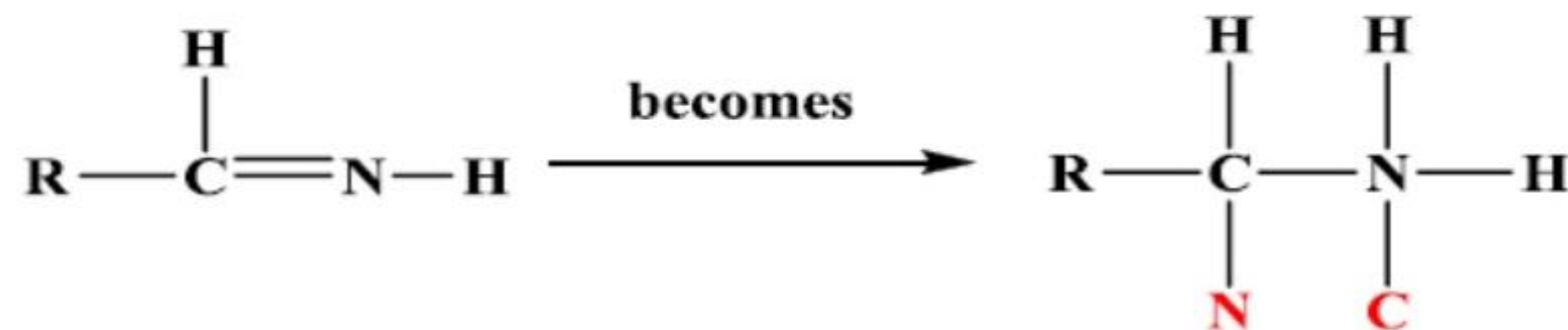
example



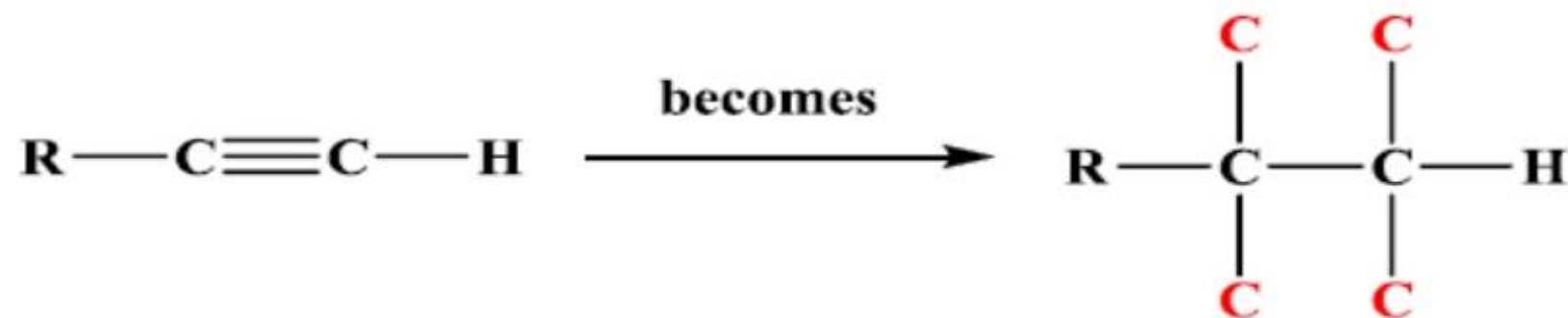
❖ Double and triple bonds are treated like bonds to duplicate atoms.



break and duplicate



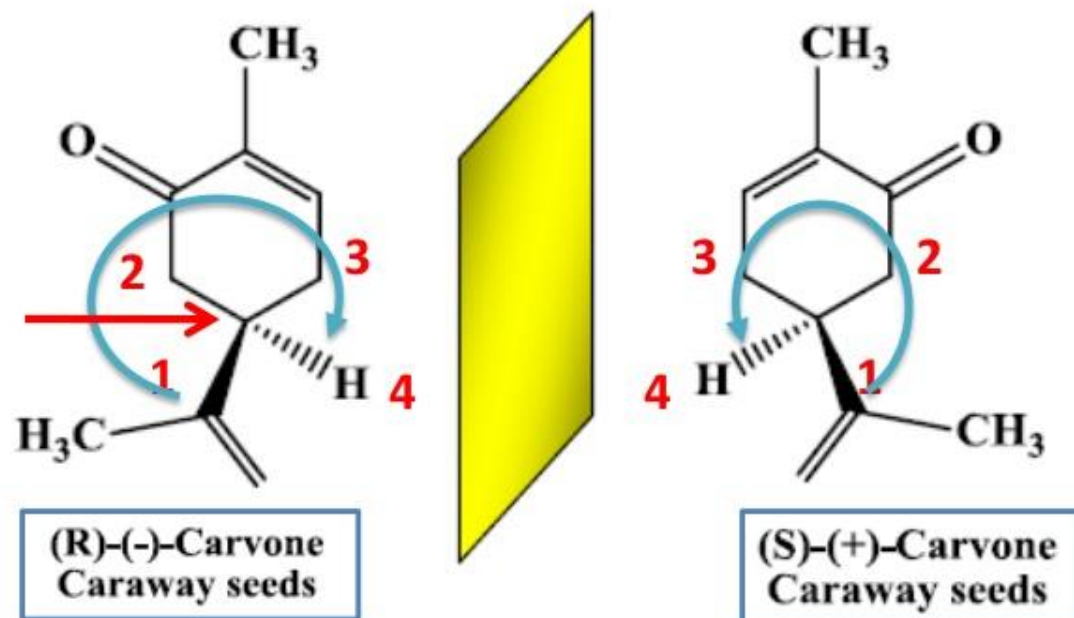
break and duplicate



break and duplicate

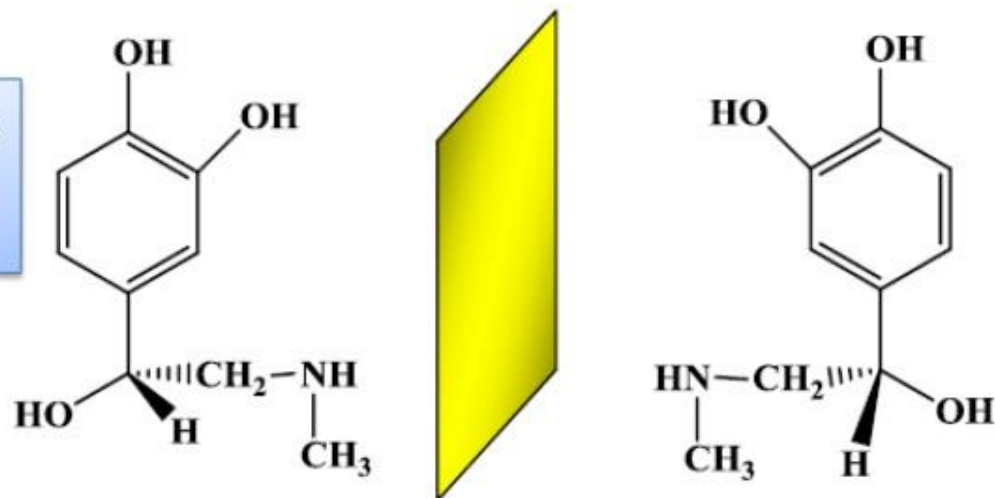
Enantiomers are different in configuration, one of them is (R) and another is (S) Or one of them is (S) and another is (R).

e.g.1

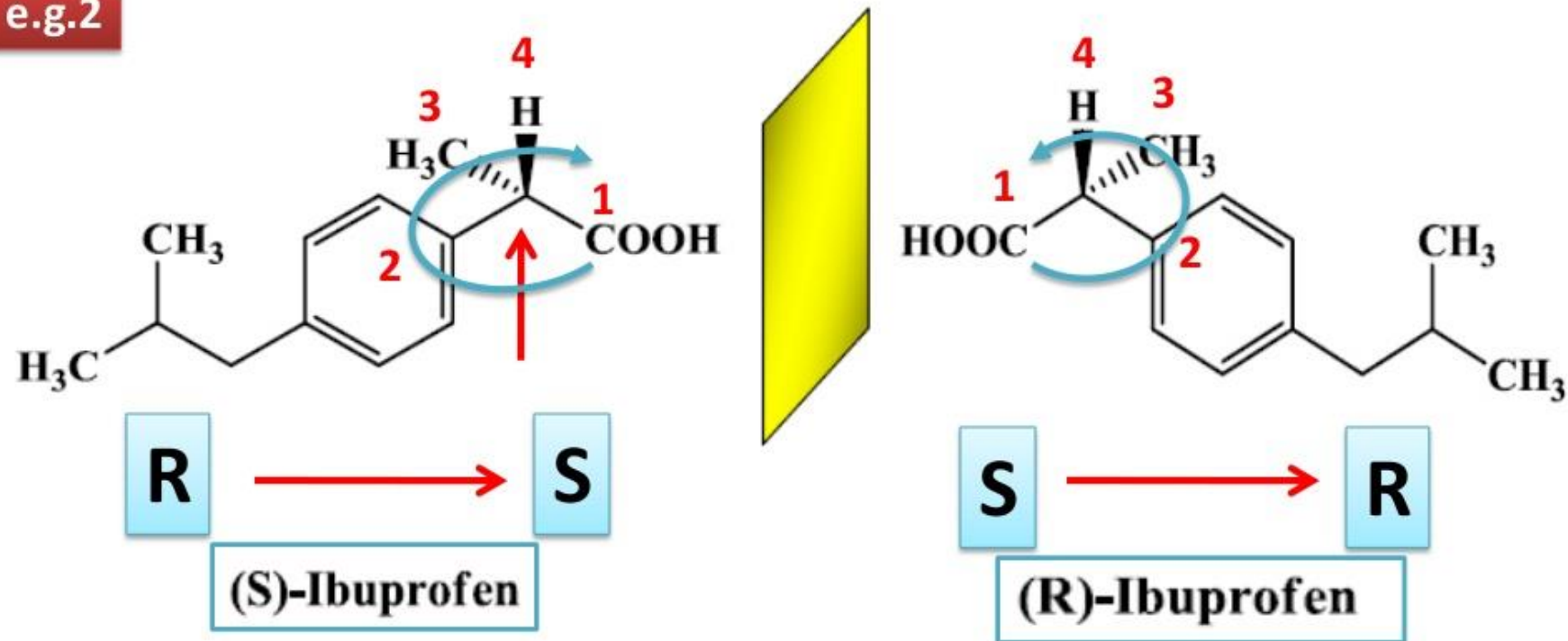


QUESTION

Name the following
Compound using
R,S system

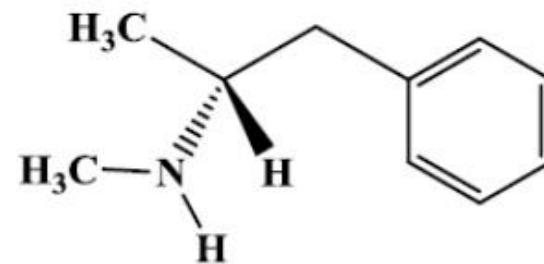
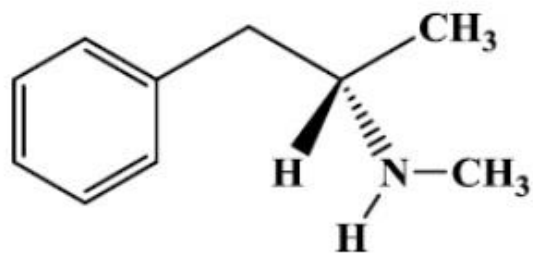


e.g.2

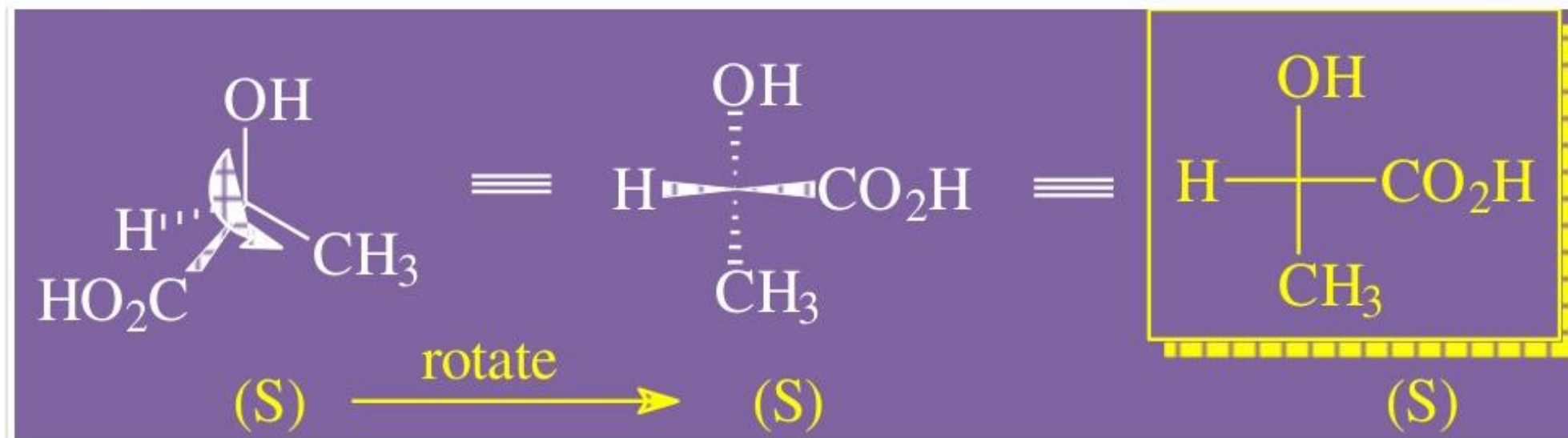


QUESTION

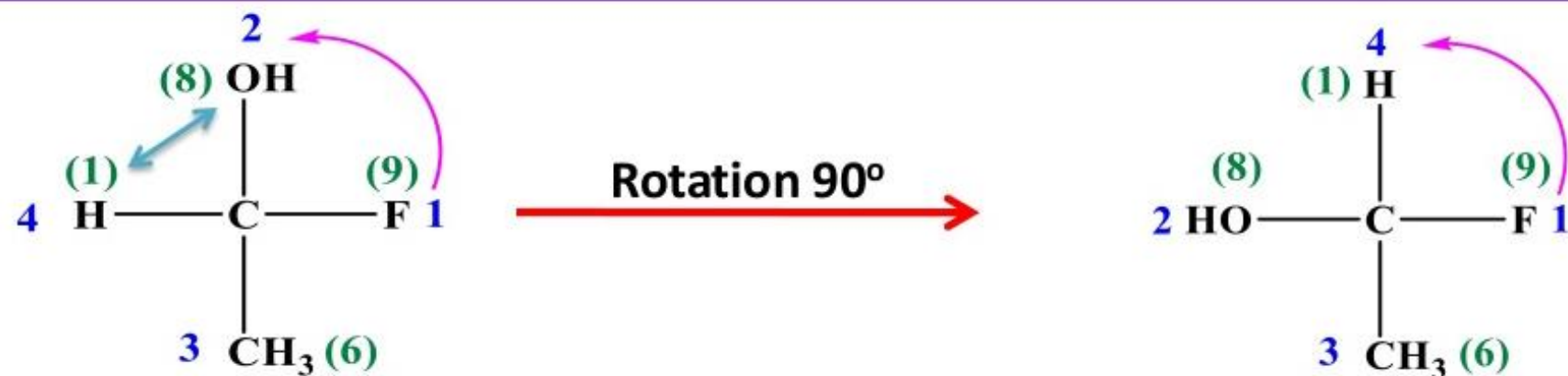
Name the following Compound using R,S system



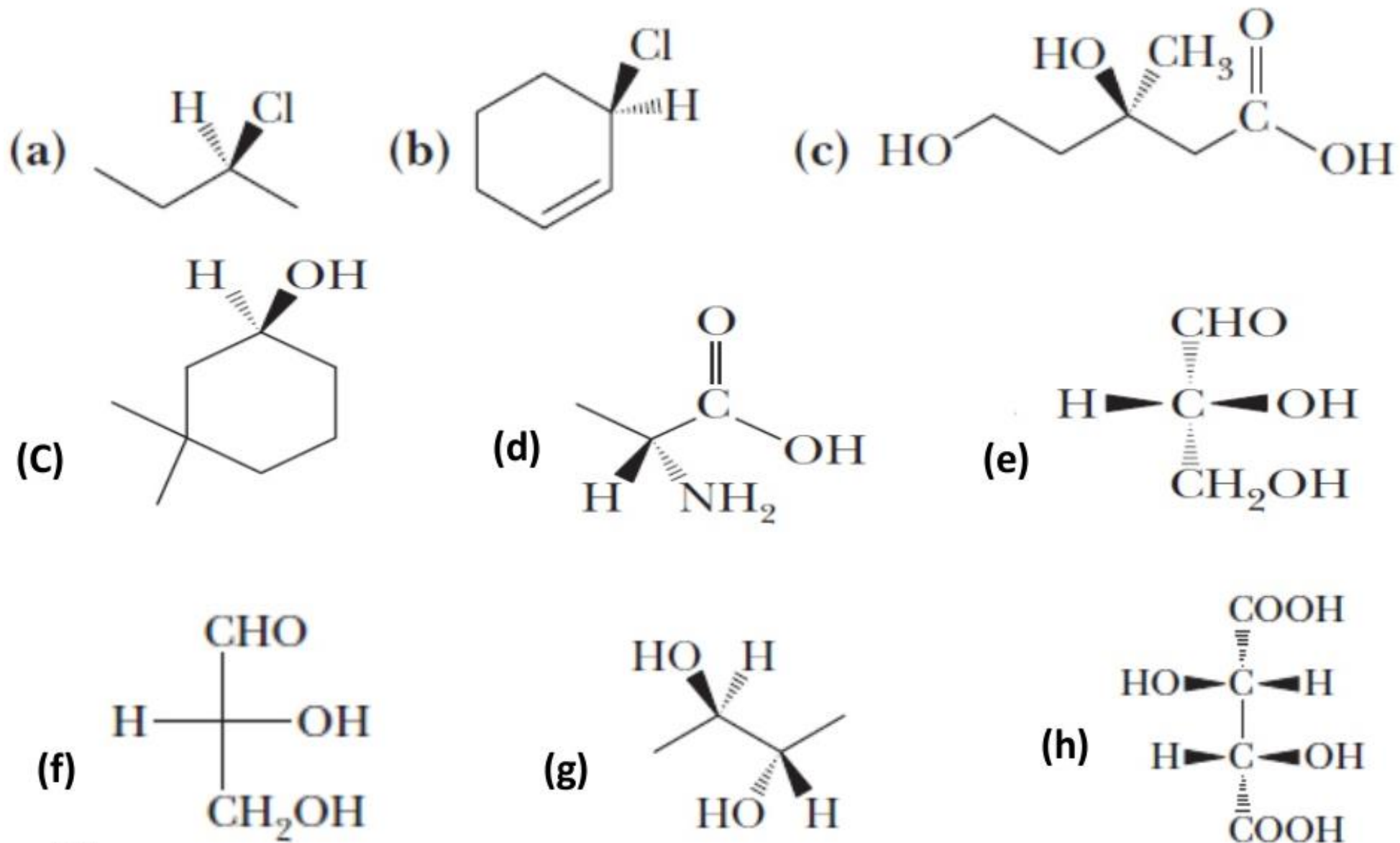
Assigning Absolute Configuration to Fischer Projections



Rotation of the Projection 90° Reverses Absolute Configuration



Q. Assign an R or S configuration to the chiral center in each molecule:

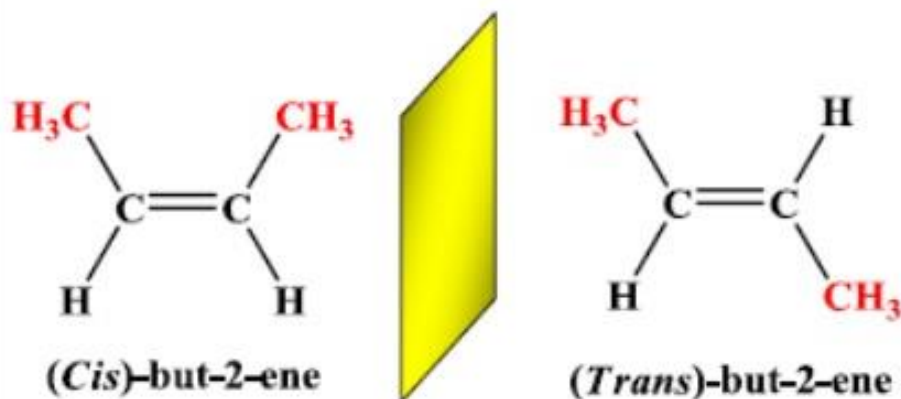


Diastereomers

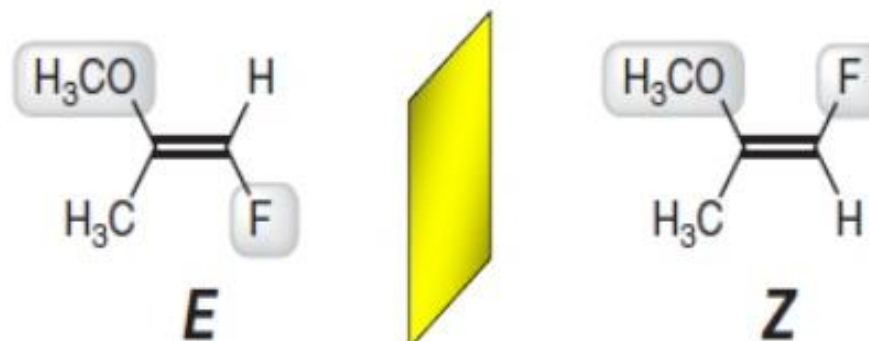
❖ **Diastereomers:** are **stereoisomers** those are **not mirror images** and have **different physical and chemical properties (unlike enantiomers)**

❖ Types of diastereomers

1- Cis-trans and E, Z isomers



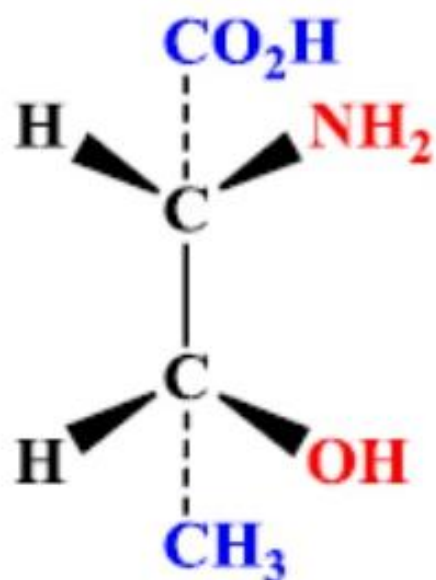
Diastereomers (non-mirror-image)



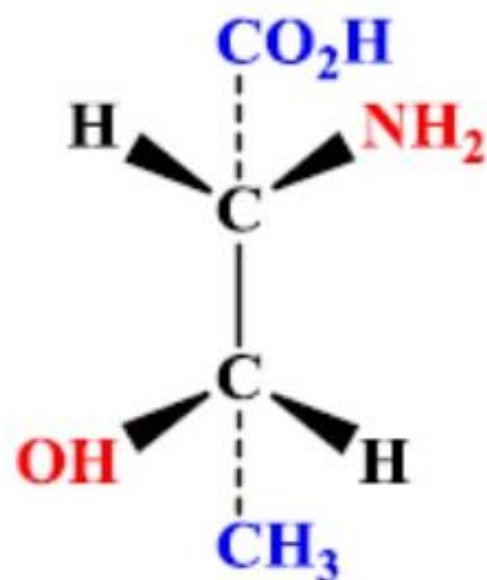
Diastereomers (non-mirror image)

2-Conformational isomers (R/S isomers)

Diastereomers have **more than one chiral center**

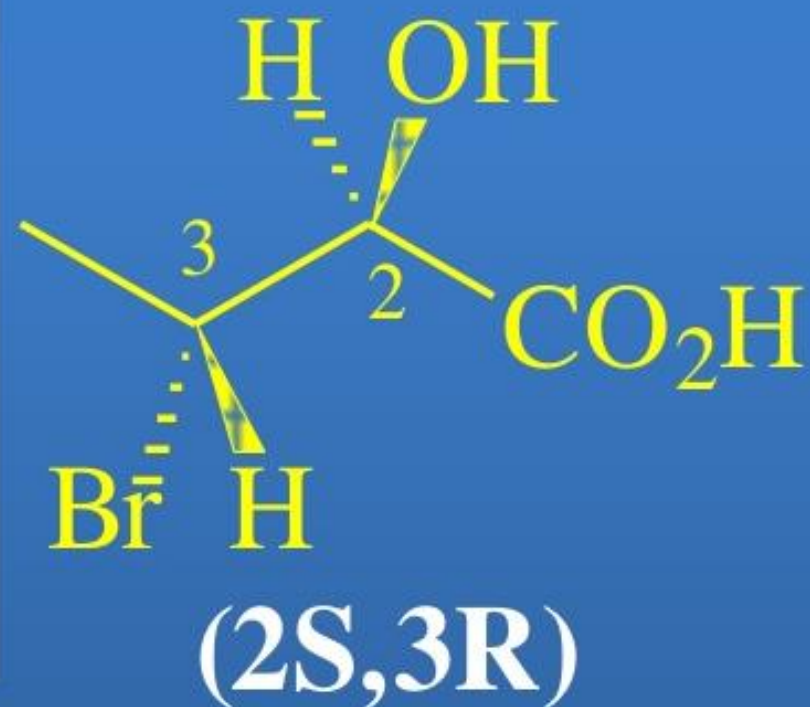
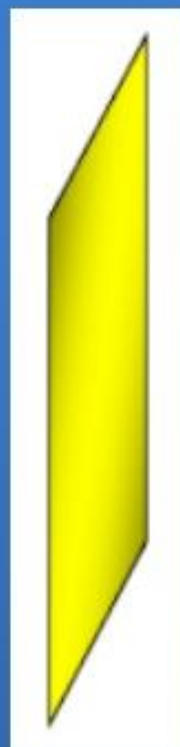


(2R,3R)-2-amino-3-hydroxybutanoic acid



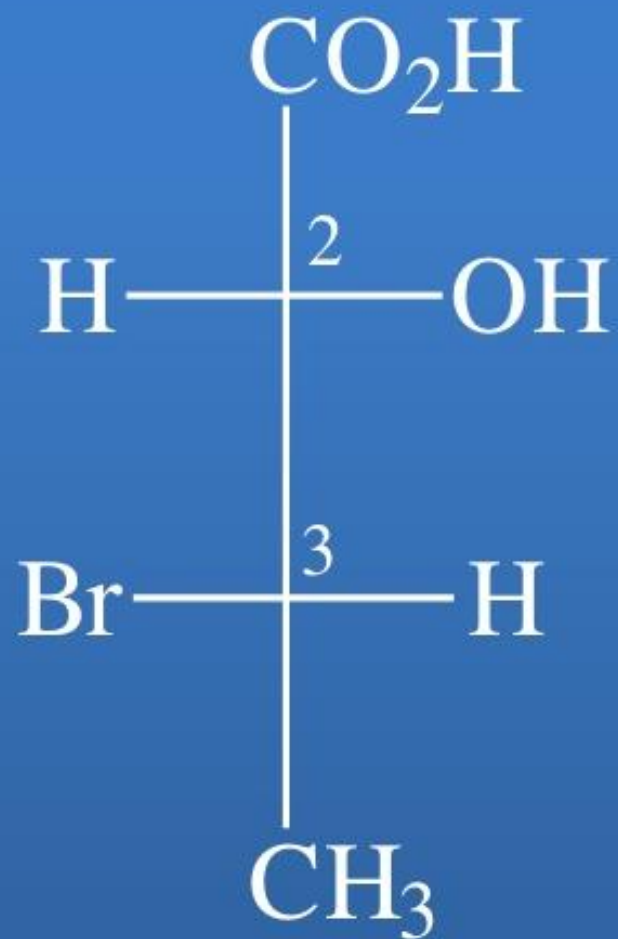
(2R,3S)-2-amino-3-hydroxybutanoic acid

Diastereomers (non-mirror-image)

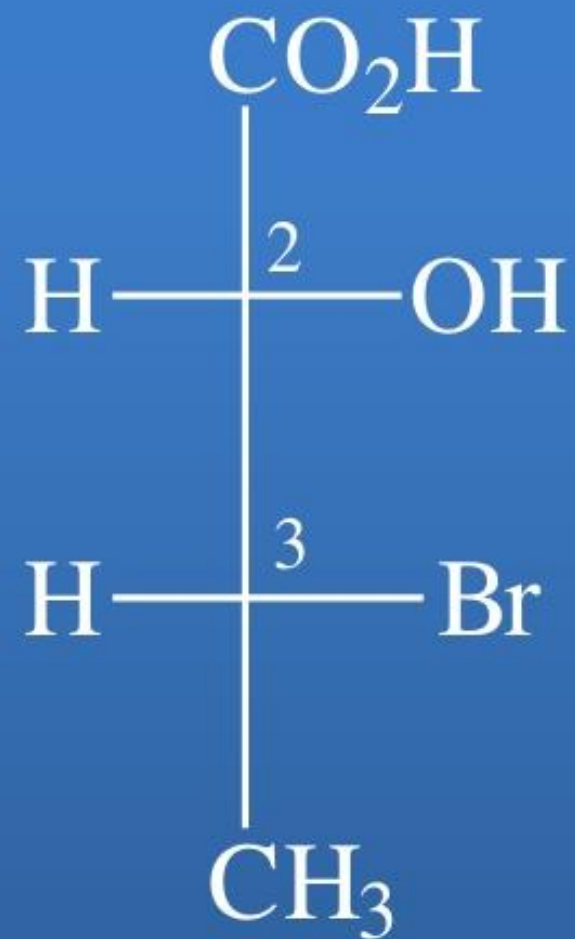
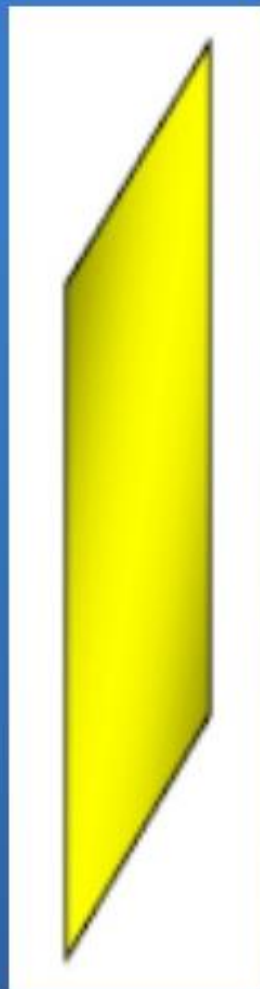


same stereochemistry at C₂ (S)
 opposite stereochemistry at C₃

Diastereomers (non-mirror image)



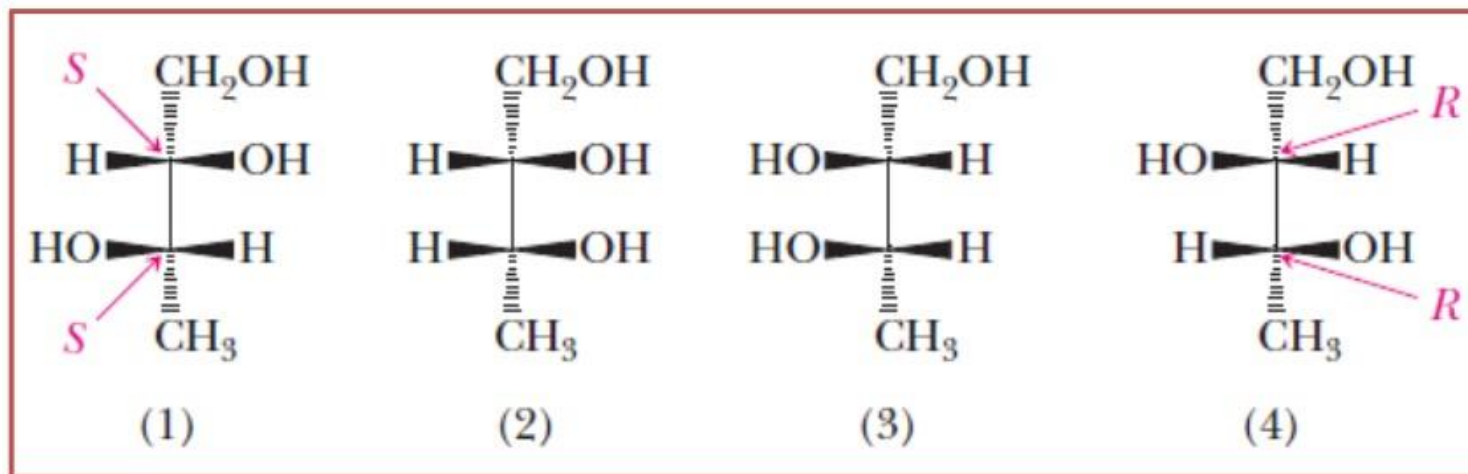
(2S,3S)



(2S,3R)

Diastereomers (non-mirror image)

Q. Following are stereo representations for the four stereo isomers of 1,2,3-butanetriol. *R* and *S* configurations are given for the chiral centers in (1) and (4).



- (a) Write the IUPAC names for each compound showing the *R* or *S* configuration of each chiral center.
- (b) Which molecules are enantiomers?
- (c) Which molecules are diastereomers?

- (a) (1) (2S,3S)-1,2,3-Butanetriol
(2) (2S,3R)-1,2,3-Butanetriol
(3) (2R,3S)-1,2,3-Butanetriol
(4) (2R,3R)-1,2,3-Butanetriol

(b) **Enantiomers** are stereoisomers that are nonsuperposable mirror images.

As you see from their configurations, **compounds (1) and (4)** are one pair of enantiomers and **compounds (2) and (3)** are a second pair of enantiomers.

(c) **Diastereomers** are stereoisomers that are not mirror images.

Compounds (1) and (2), (1) and (3), (2) and (4), and (3) and (4) are pairs of diastereomers.

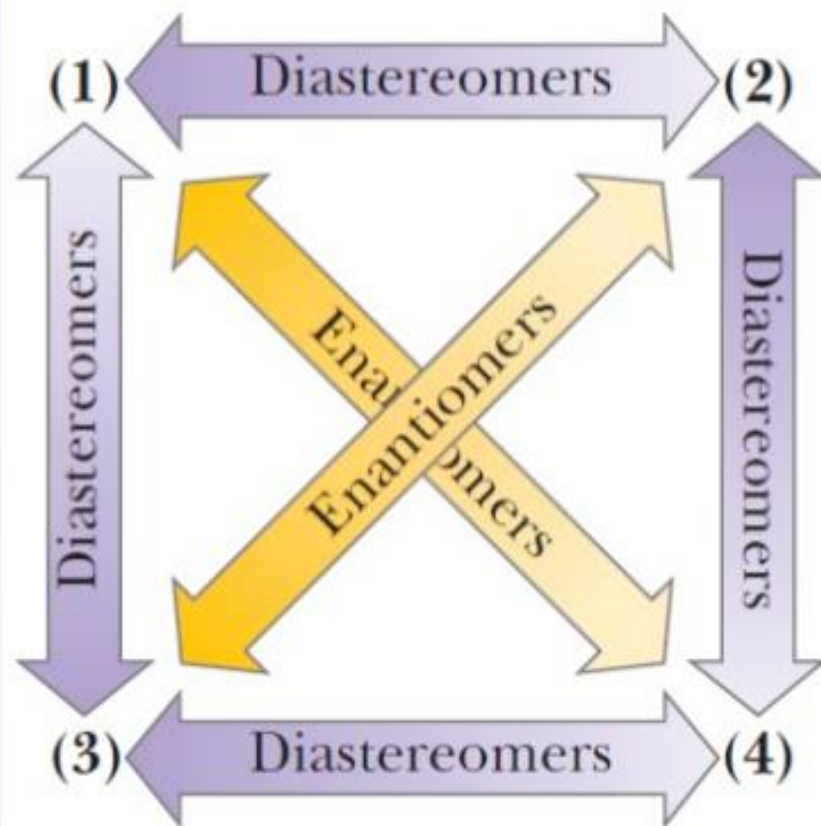


diagram that shows the relationships among these isomers.