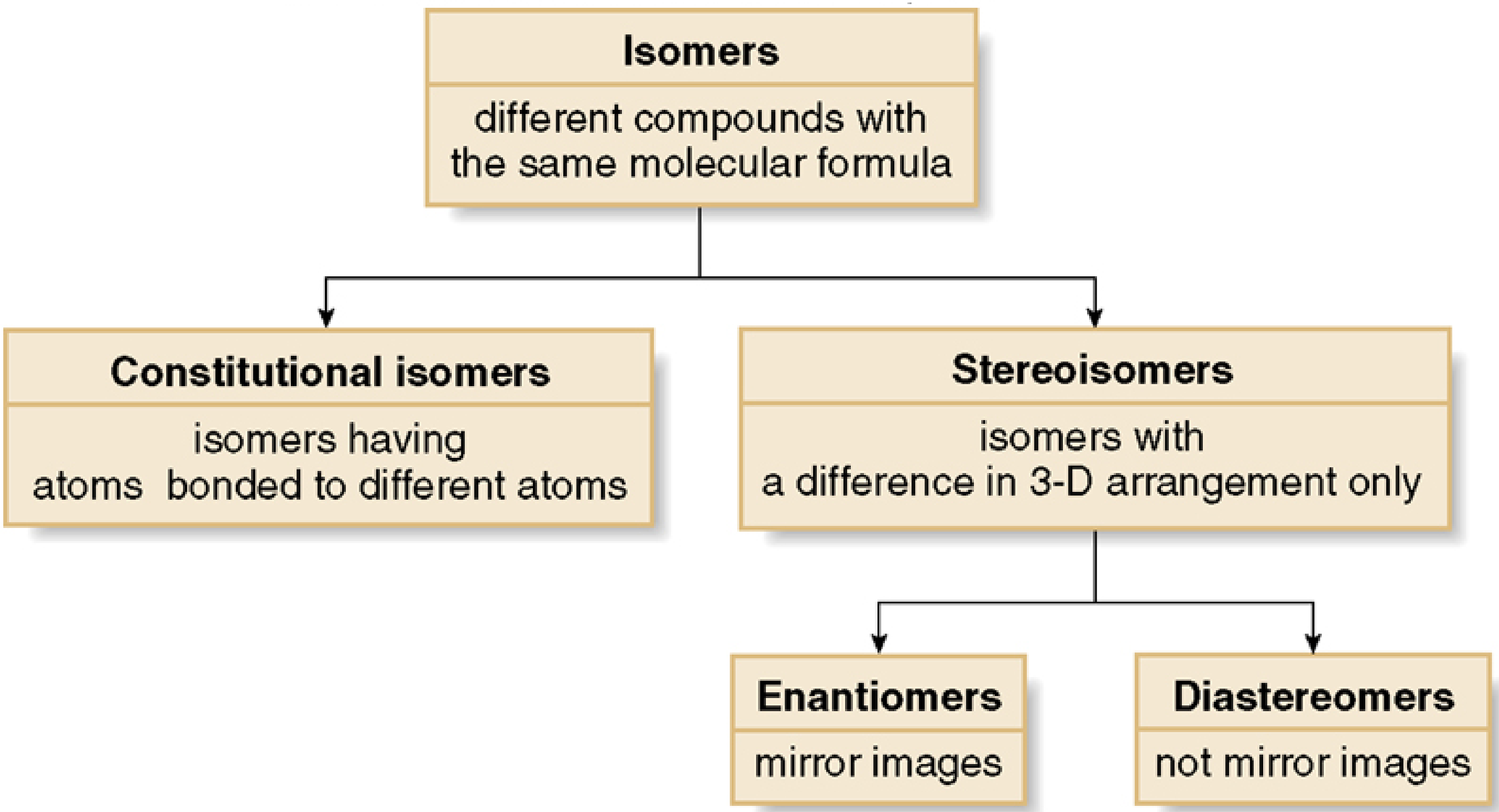
CYI101
Common CHEMISTRY(Organic)

Stereochemistry: Concept of chirality, Stereoisomers

20th December 2021/Sec G & H


Isomers
different compounds with
the same molecular formula
Constitutional isomers
isomers having
atoms bonded to different atoms
Stereoisomers
isomers with
a difference in 3-D arrangement only
Enantiomers
mirror images
Diastereomers
not mirror images

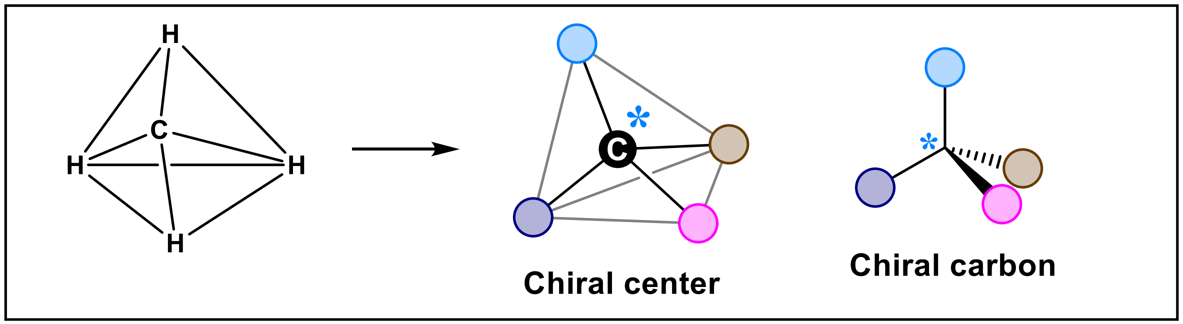
Constitutional Isomers

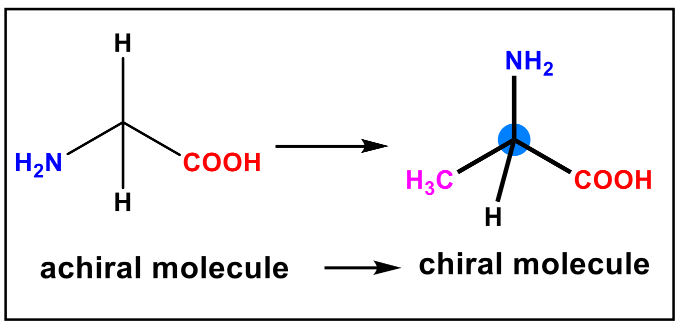
- Isomers that differ in how their atoms are arranged in chains are called **constitutional isomers**
- They must have the same molecular formula to be isomers

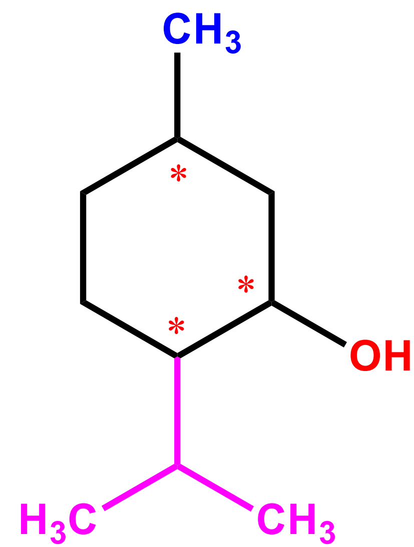
Different carbon skeletons C_4H_{10}	$\begin{array}{c} \quad CH_3 \\ \, \vert \\ CH_3CHCH_3 \end{array}$ **2-Methylpropane (Isobutane)**	and	$CH_3CH_2CH_2CH_3$ **Butane**
Different functional groups C_2H_6O	CH_3CH_2OH **Ethyl alcohol**	and	CH_3OCH_3 **Dimethyl ether**
Different position of functional groups C_3H_9N	$\begin{array}{c} \quad NH_2 \\ \, \vert \\ CH_3CHCH_3 \end{array}$ **Isopropylamine**	and	$CH_3CH_2CH_2NH_2$ **Propylamine**

Chiral Carbons

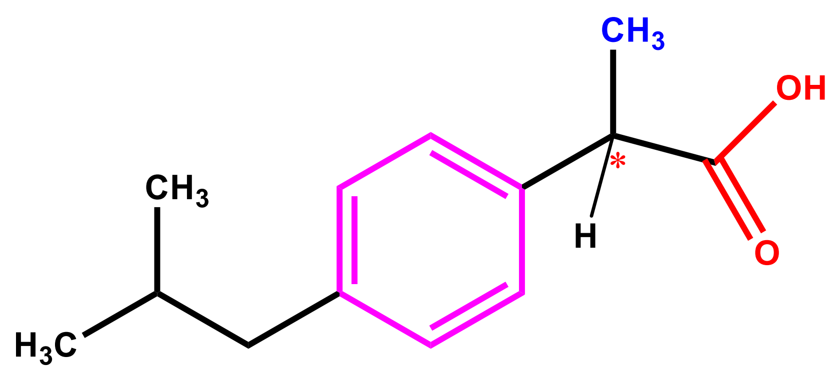
- A point in a molecule where four different groups (or atoms) are attached to carbon is called the **chiral carbon**
- A chiral molecule usually has at least one chiral carbon







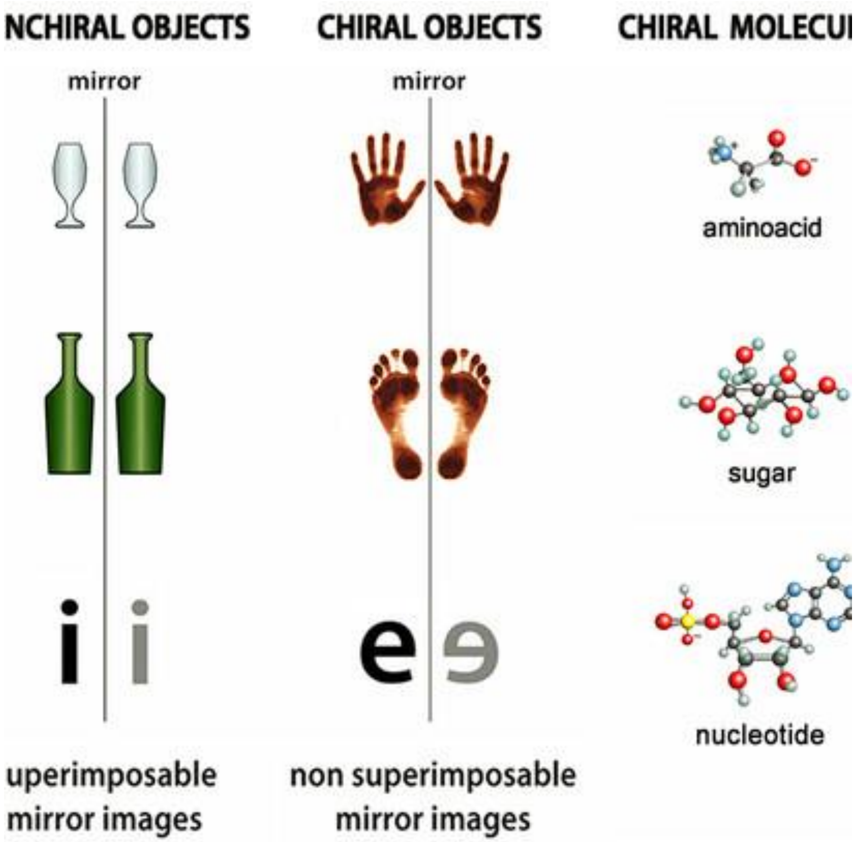
Menthol

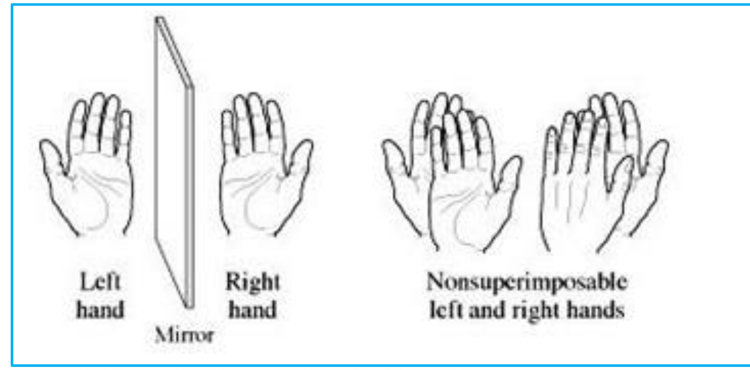


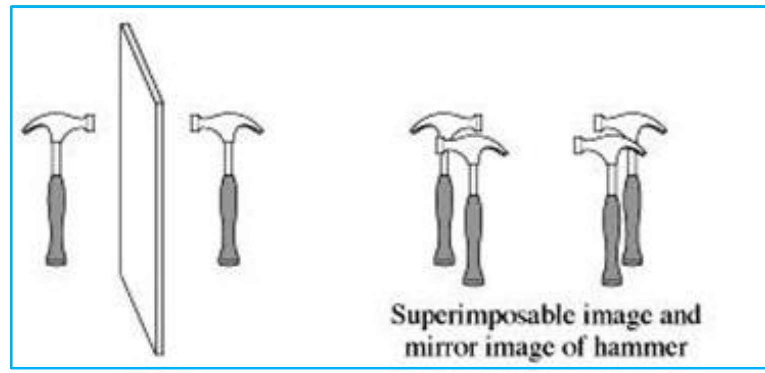
Ibuprofen

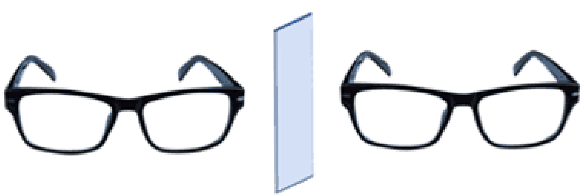
Stereoisomers:

Superimposable Image

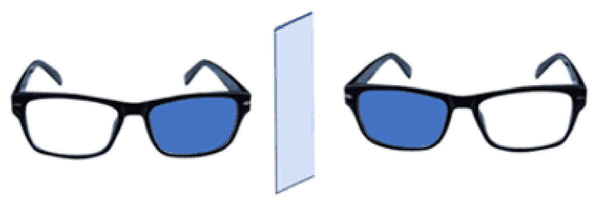




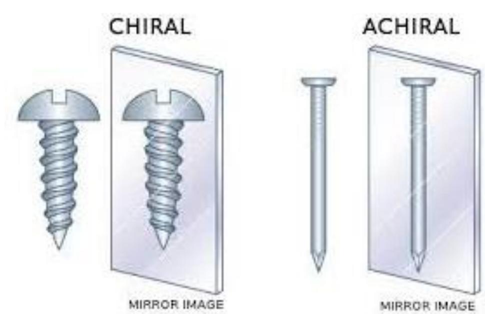




achiral - superimposable

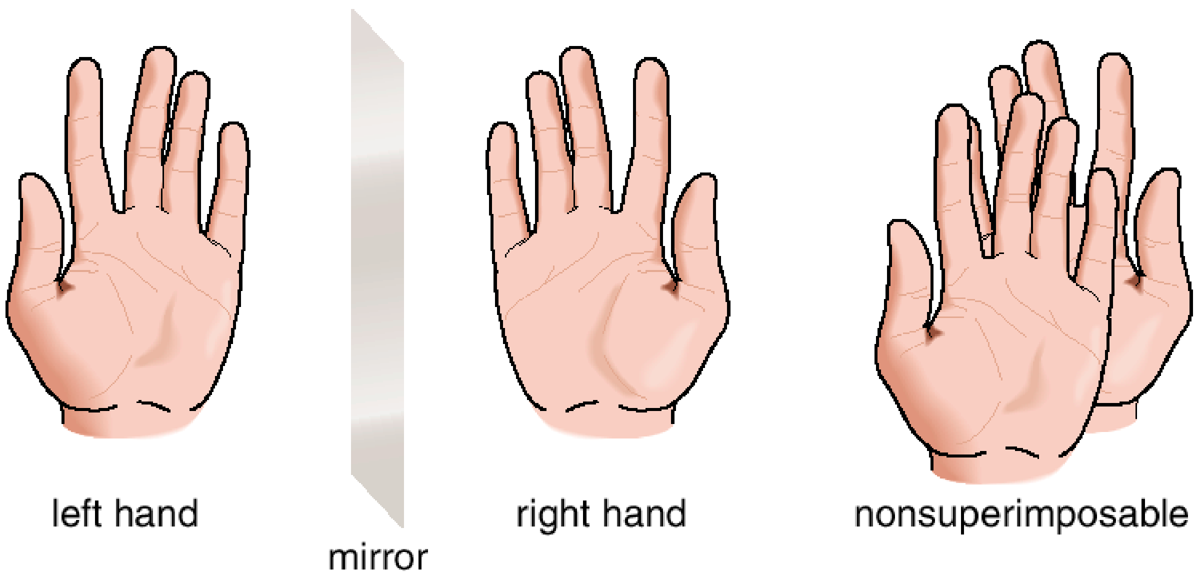


chiral - nonsuperimposable

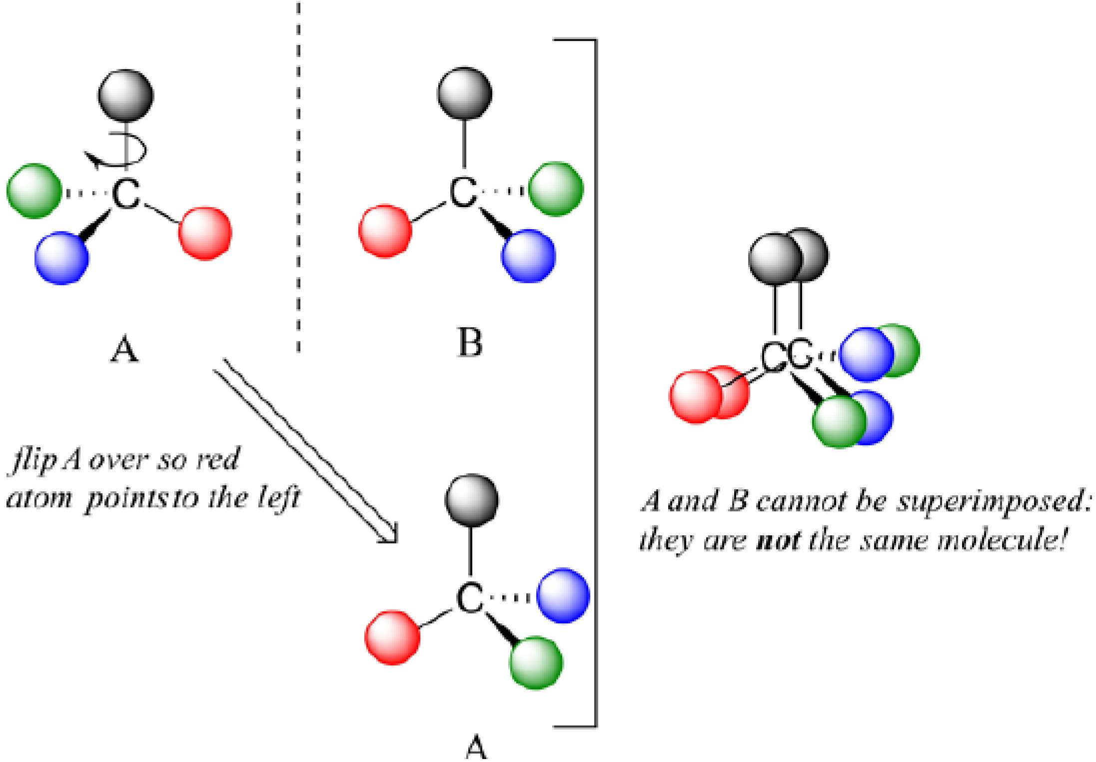


Chiral and Achiral Molecules

- **Although everything has a mirror image, mirror images may or may not be superimposable.**
- **Some molecules are like hands. Left and right hands are mirror images, but they are not identical, or superimposable.**

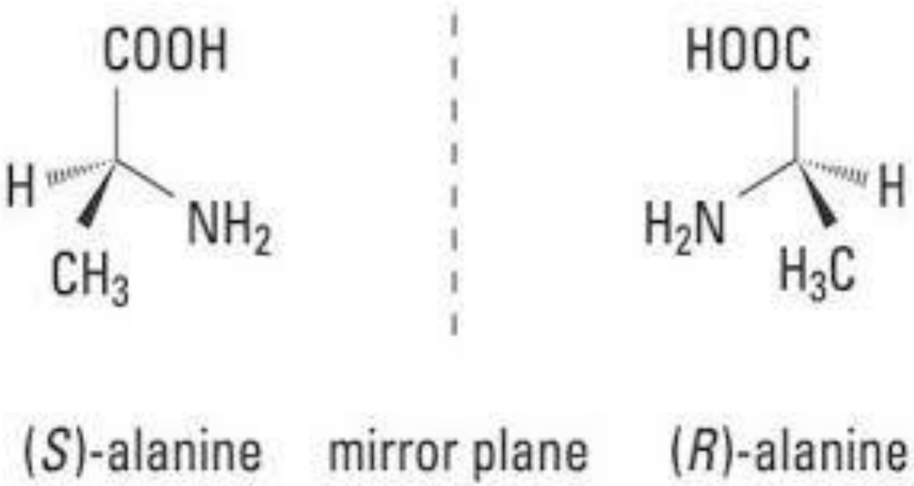


- A molecule (or object) that is *not* superimposable on its mirror image is said to be *chiral.*

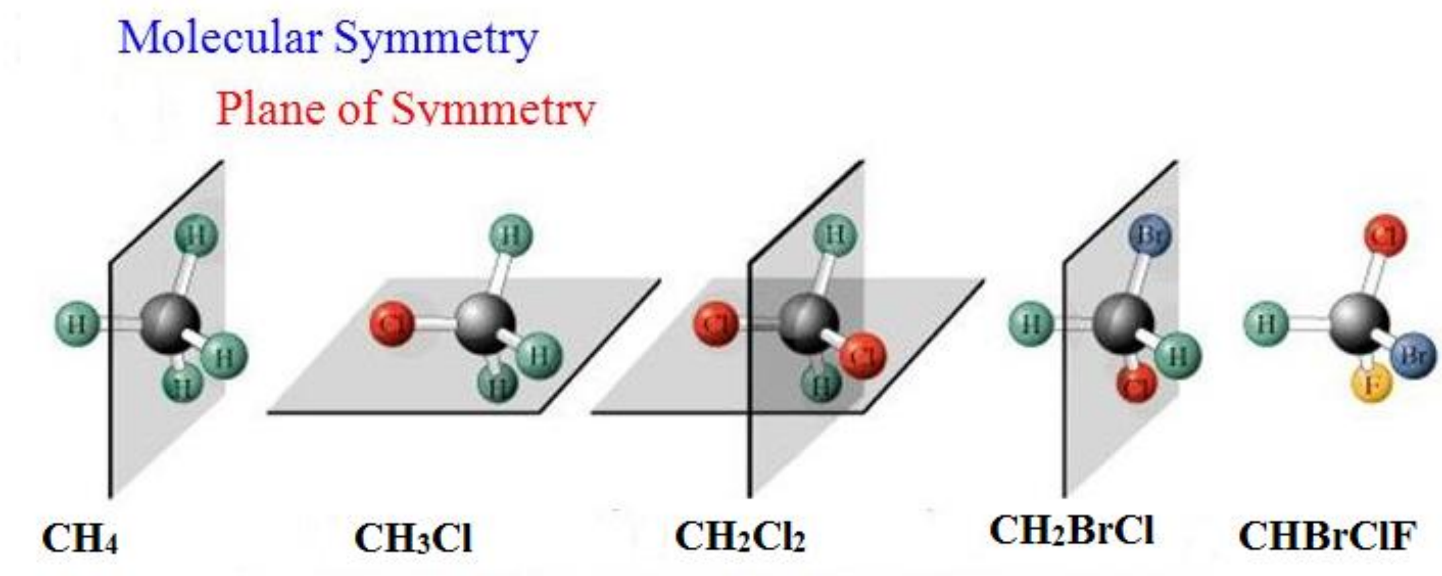


CHIRALITY:

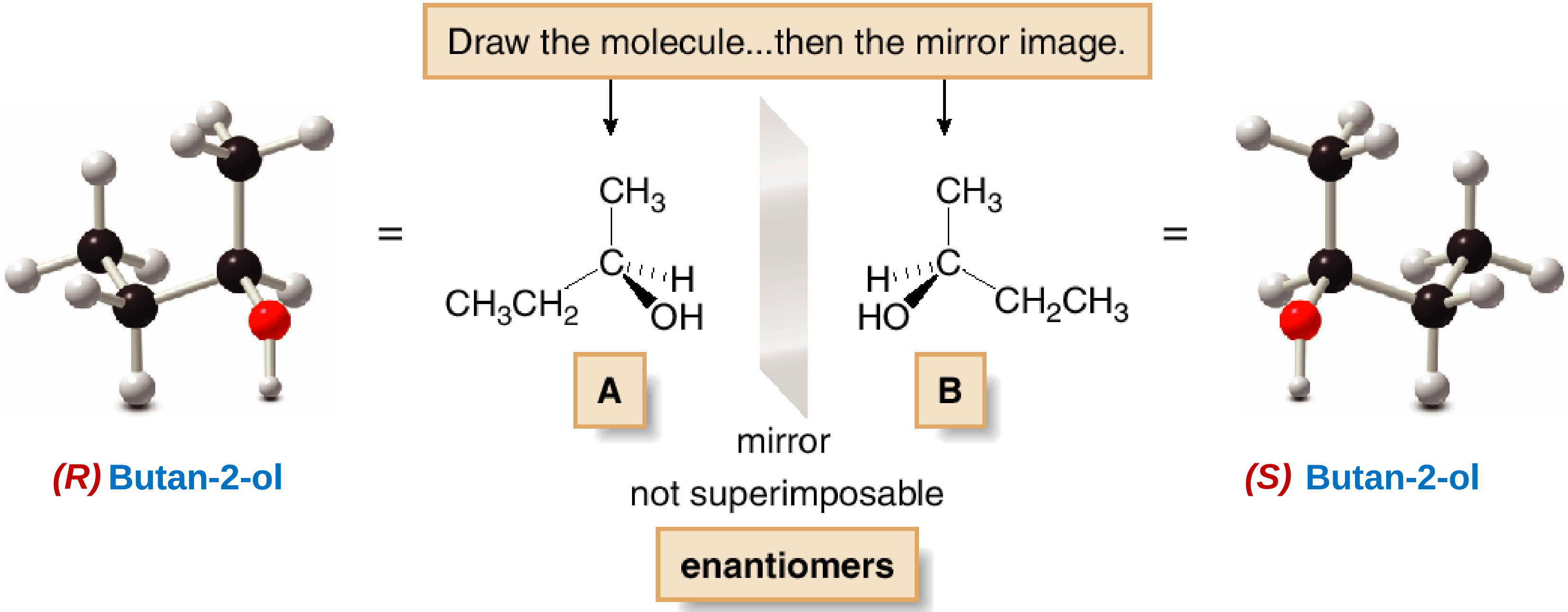
Describes objects not superimposable with their mirror image



Chirality and Plane of Symmetry



- **The molecule labeled A and its mirror image labeled B are not superimposable. No matter how you rotate A and B, all the atoms never align.**
- **A and B are stereoisomers—specifically, they are enantiomers.**
- **A carbon atom with four different groups is a tetrahedral stereogenic center.**

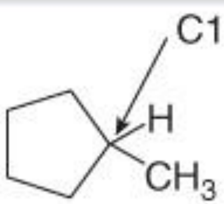


(R) Butan-2-ol

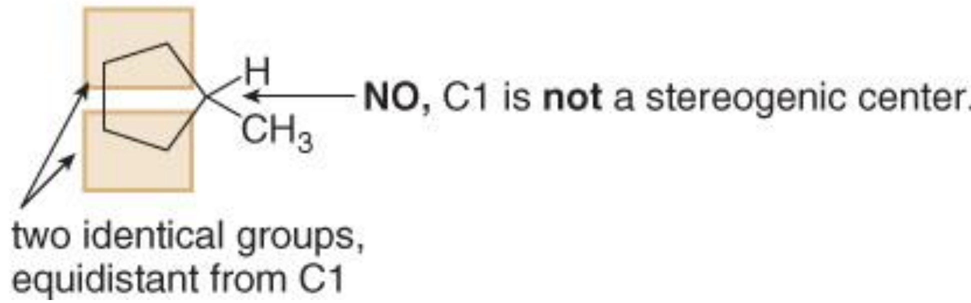
(S) Butan-2-ol

- **Stereogenic centers may also occur at carbon atoms that are part of a ring.**
- **To find stereogenic centers on ring carbons, always draw the rings as flat polygons, and look for tetrahedral carbons that are bonded to four different groups.**

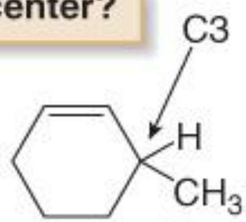
Is C1 a stereogenic center?



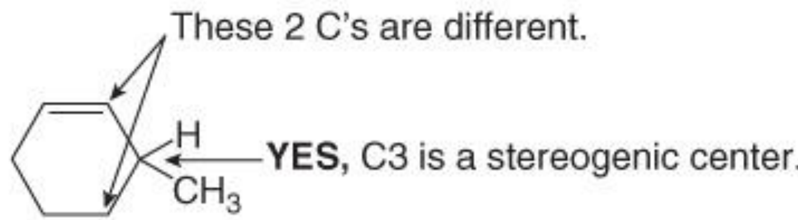
methylcyclopentane



Is C3 a stereogenic center?

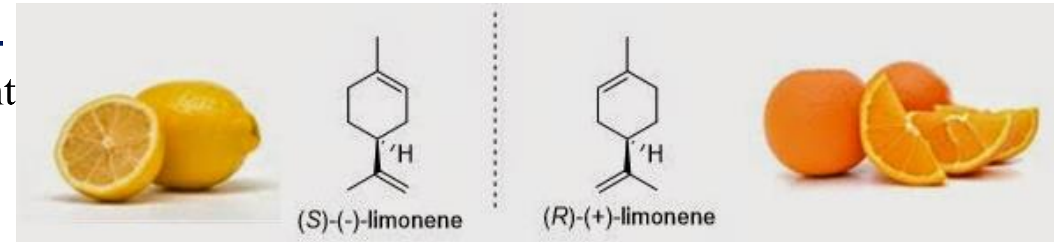


3-methylcyclohexene



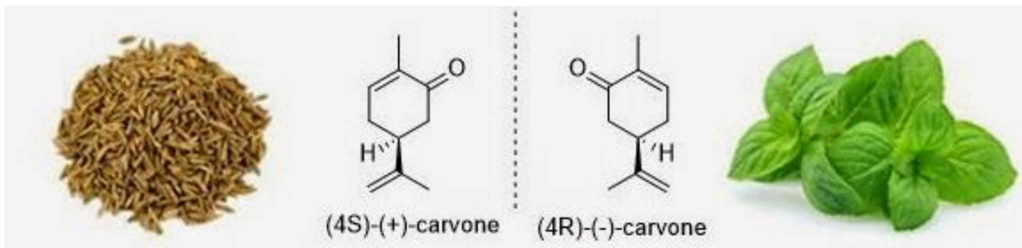
Enantiomers in NATURE !

The less common ***S*(-)-isomer** is found in mint oils and has a **piny, turpentine-like odor.**

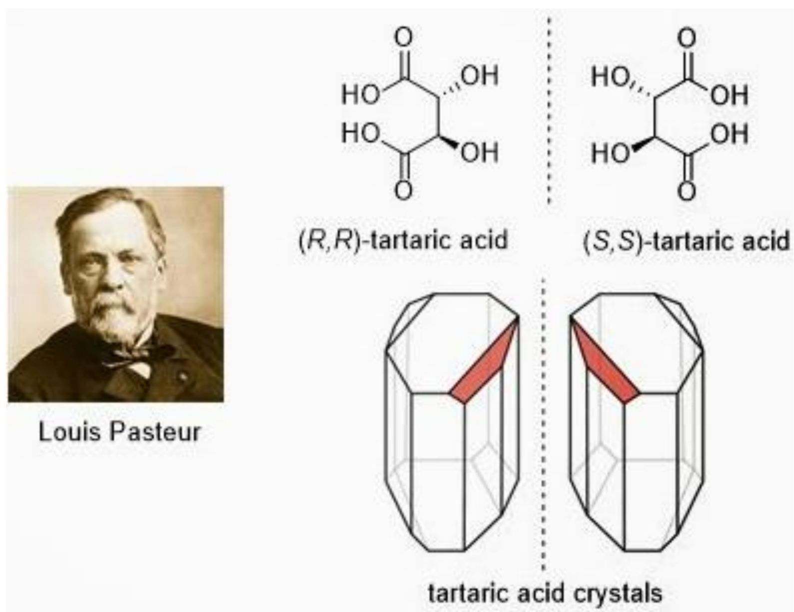


The ***R*(+)-isomer**, occurring more commonly in nature as the **fragrance of oranges**, is a flavoring agent in food manufacturing.

***S*-(+)-carvone**, has a spicy aroma.



***R*-(–)-carvone**, has a **sweetish minty smell**, like spearmint leaves.



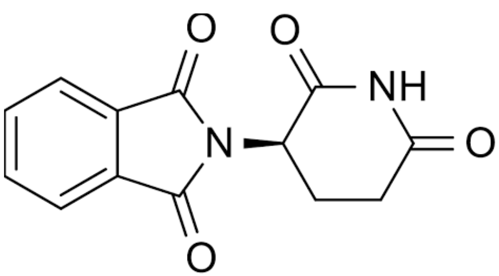
Chemical Properties of Enantiomers

- **Many drugs are chiral and often must react with a chiral receptor or chiral enzyme to be effective. One enantiomer of a drug may effectively treat a disease whereas its mirror image may be ineffective or toxic.**

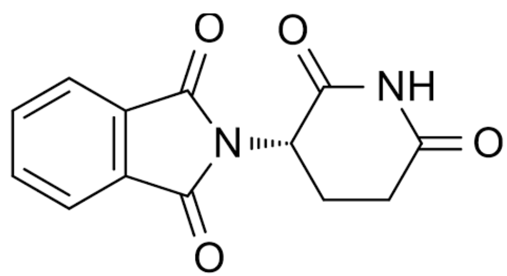
Naproxen

(*S*)-naproxen
anti-inflammatory agent

(*R*)-naproxen
liver toxin



(R)-thalidomide

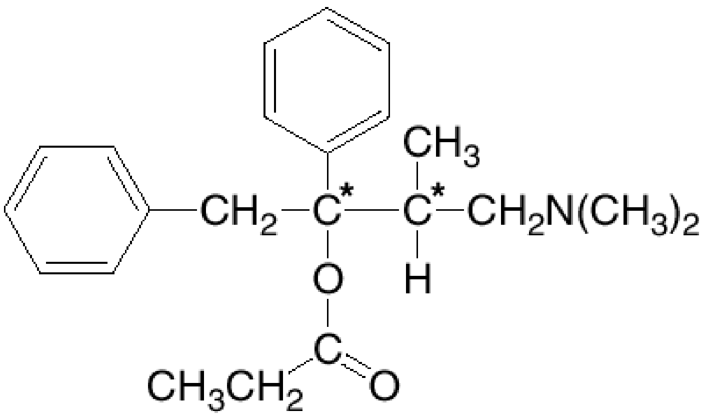


(S)-thalidomide

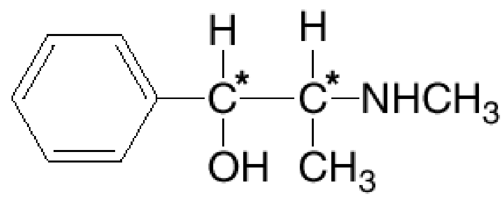
Thalidomide exists in two mirror-image forms: it is a racemic mixture of (R)- and (S)-enantiomers. The **(R)-enantiomer, shown, has sedative effects,** whereas the **(S)-isomer is teratogenic.**

Thalidomide: 1957

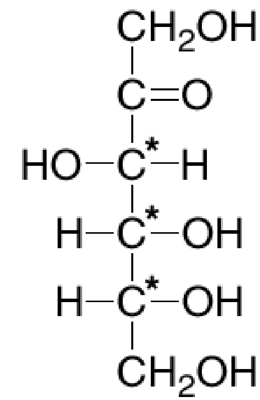
- **Larger organic molecules can have two, three or even more stereogenic centers.**



propoxyphene
Trade name: Darvon
(analgesic)



ephedrine
(bronchodilator, decongestant)

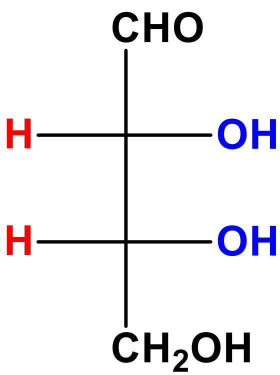


fructose
(a simple sugar)

[* = stereogenic center]

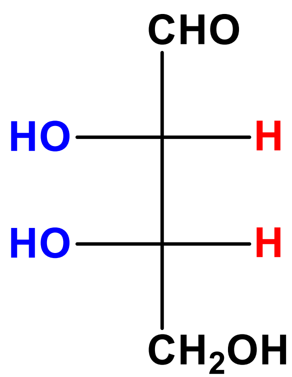
Diastereomer

$$CH_2OH\overset{*}{C}H(OH)\overset{*}{C}H(OH)CHO$$



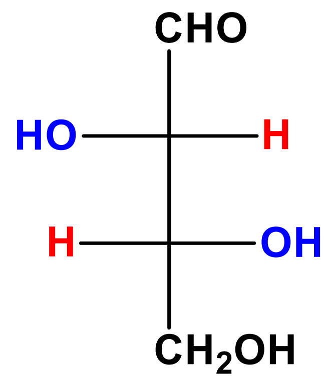
(-)Erythrose

A



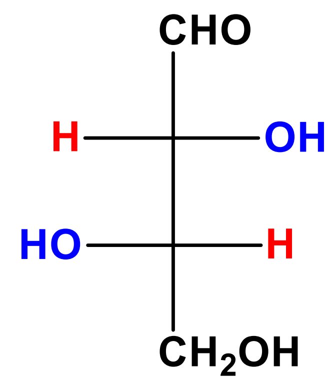
(+) Erythrose

B



(-) Threose

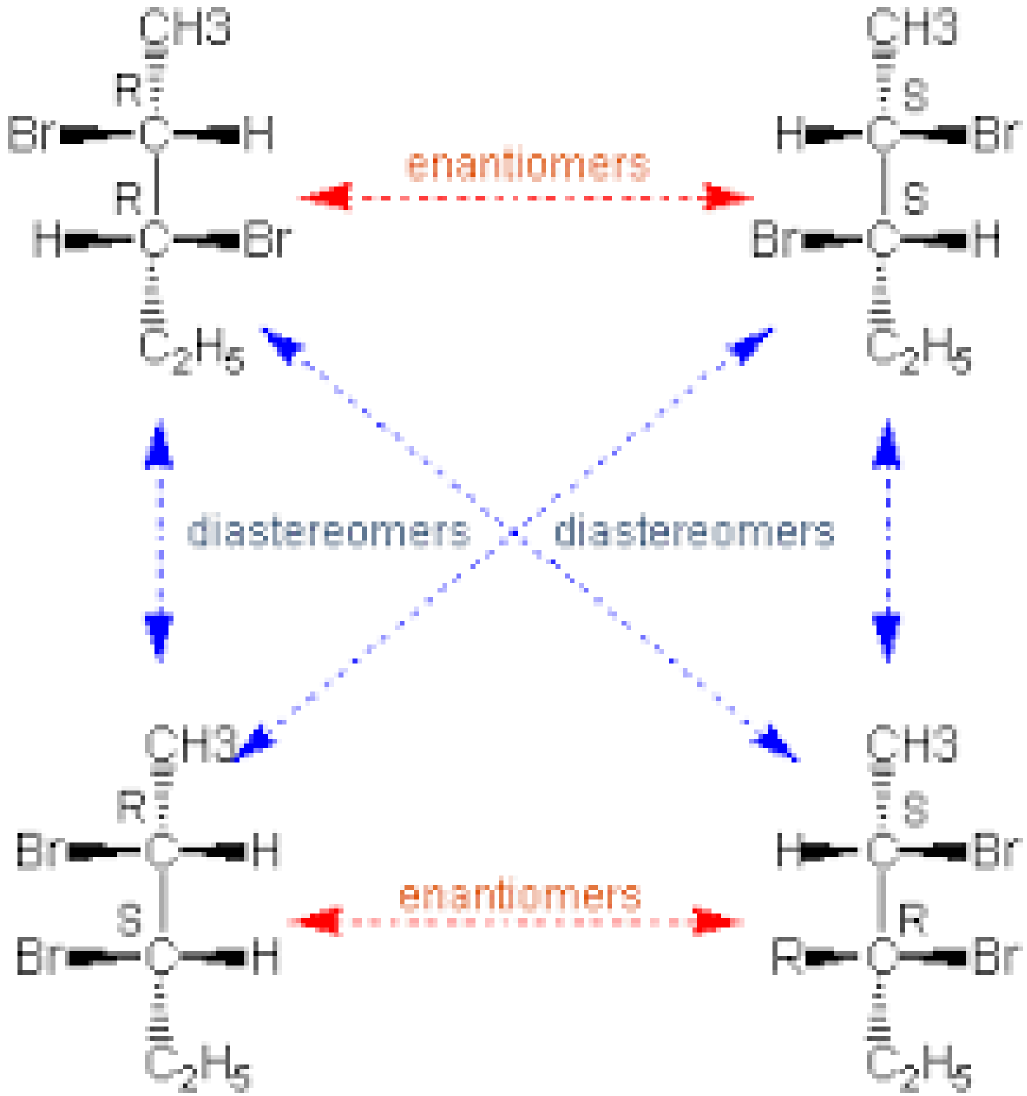
C



(+) Threose

D

- Pairs of enantiomers: **A** and **B; C** and **D.**
- Pairs of diastereomers: **A** and **C; A** and **D; B** and **C; B** and **D.**



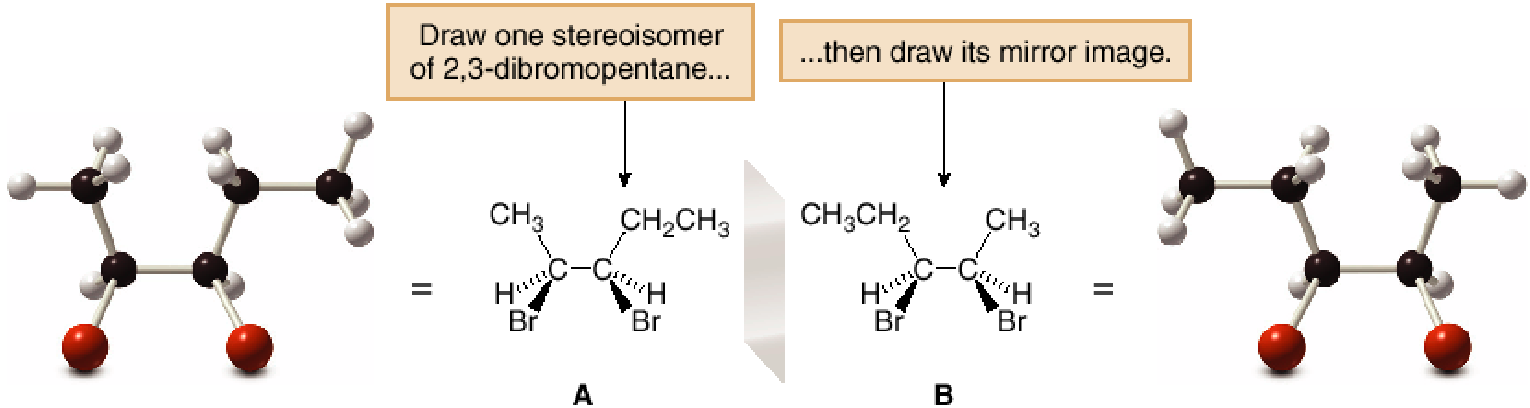
CH3
R
Br C H
R
H C Br
C2H5
enantiomers
CH3
S
H C Br
S
Br C H
C2H5
diastereomers
diastereomers
CH3
R
Br C H
S
Br C H
C2H5
enantiomers
CH3
S
H C Br
R
R C Br
C2H5

Diastereomer

- **For a molecule with *n* stereogenic centers, the maximum number of stereoisomers is 2^n. Let us consider the stepwise procedure for finding all the possible stereoisomers of 2,3-dibromopentane.**

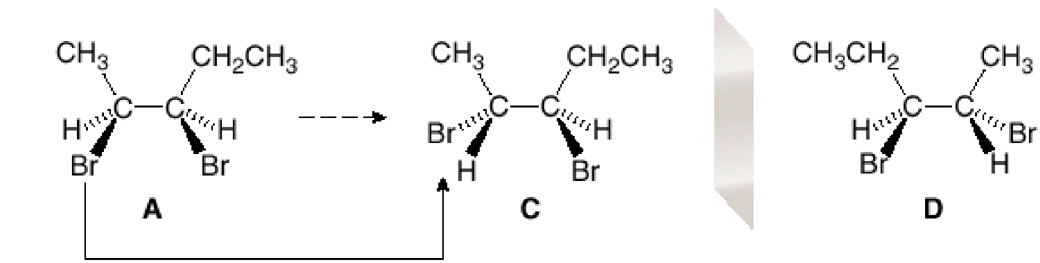
❑ **Find and draw all possible stereoisomers for a compound with two stereogenic centers**

Step [1] : Draw one stereoisomer by arbitrarily arranging substituents around the stereogenic centers. Then draw its mirror image.



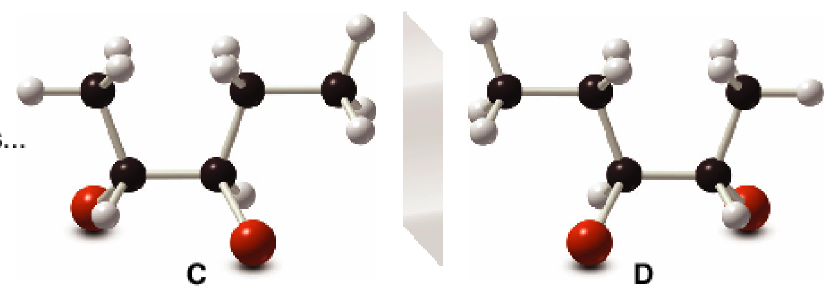
- **Switching the positions of H and Br (or any two groups) on one stereogenic center of either A or B forms a new stereoisomer (labeled C in this example), which is different from A and B. The mirror image of C is labeled D. C and D are enantiomers.**

How to, Continued…

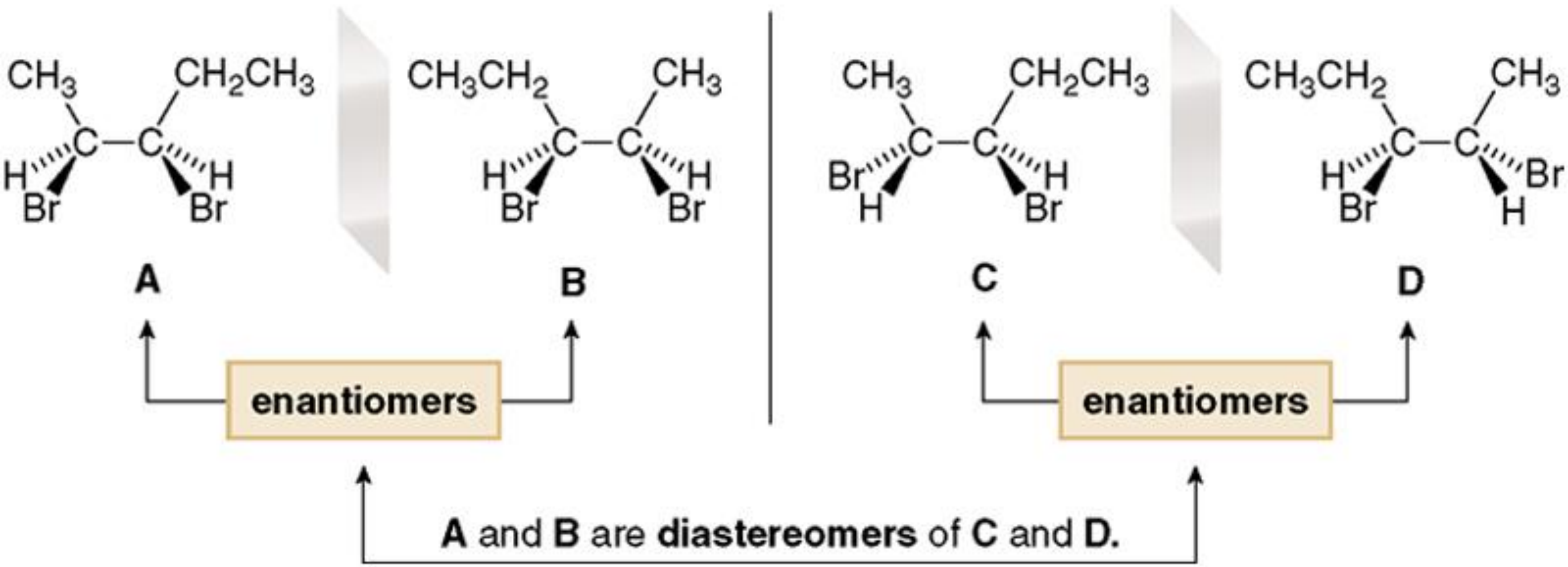


Switch H and Br on one stereogenic center.

With models...



- **Stereoisomers that are not mirror images of one another are called diastereomers. For example, A and C are diastereomers.**

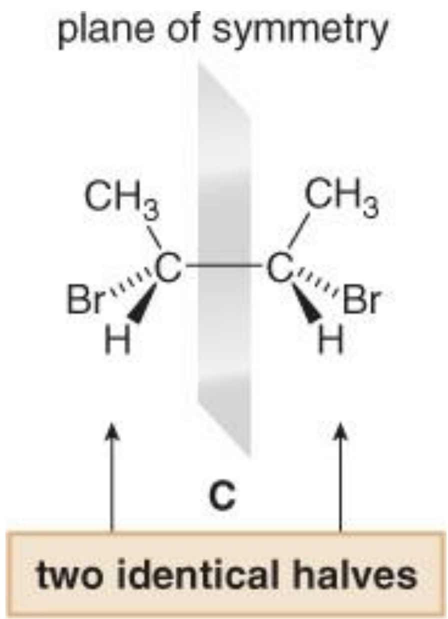


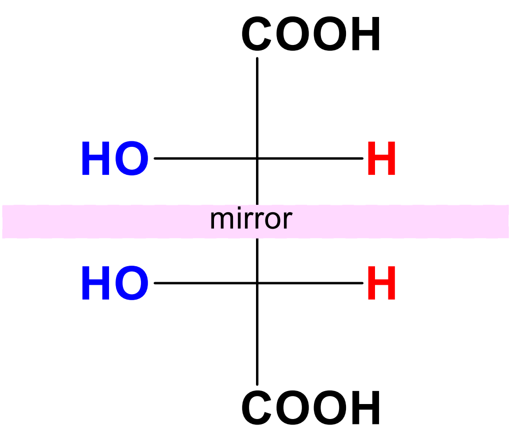
- Pairs of enantiomers: **A** and **B; C** and **D.**
- Pairs of diastereomers: **A** and **C; A** and **D; B** and **C; B** and **D.**

Enantomers *vs* Diastereomer

Enantiomers	Diastereomers
They are mirror images of each other and are non-superimposable	They are not mirror images of each other and are non-superimposable
They always have a different R, S-configuration	They have the same R,S-configuration at least on one stereocenter
They have one or more stereocenters	They have at least two stereocenters
They have the same chemical and physical properties	They have different chemical and physical properties
They all possess optical activity although they rotate light in opposite directions	Not all diastereomers possess optical activity

- Compound C contains a plane of symmetry, and is achiral.
- Meso compounds generally contain a plane of symmetry so that they possess two identical halves.

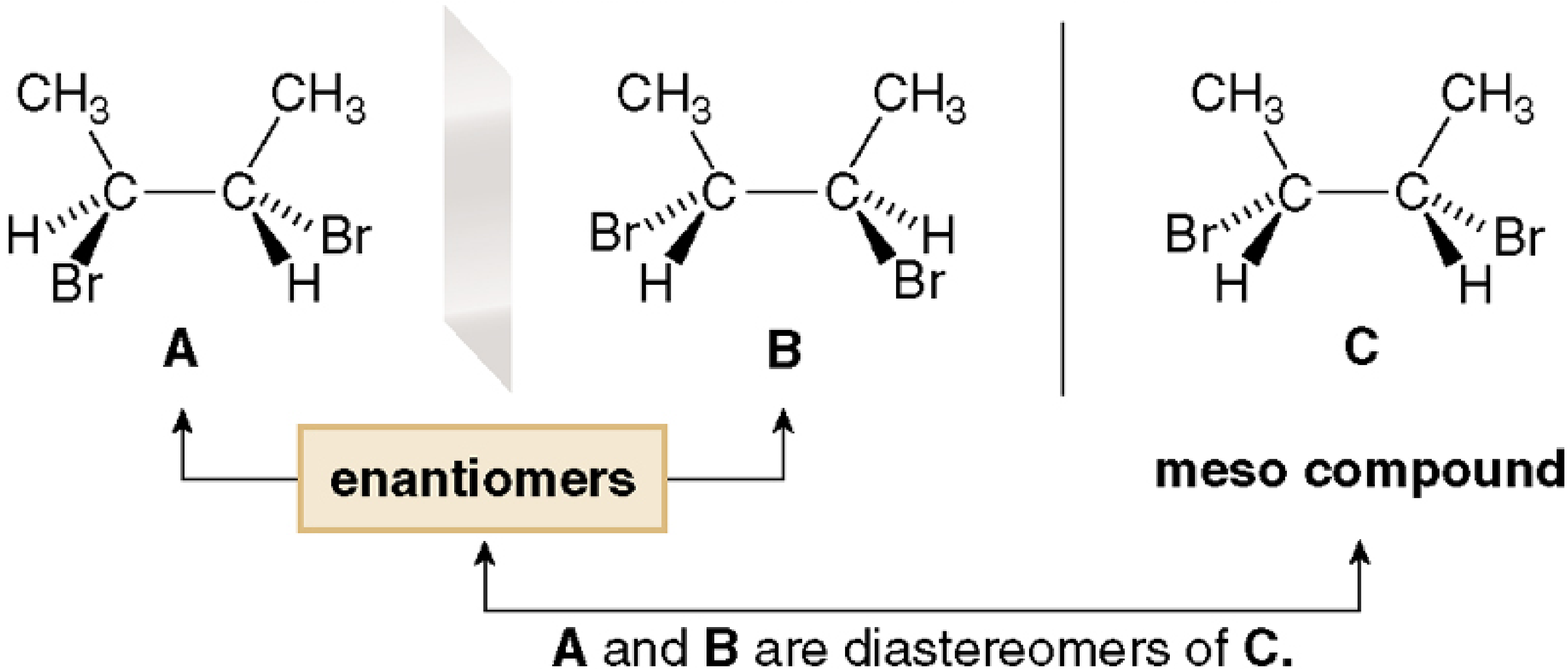




Meso-Tataric acid

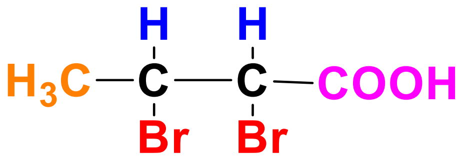
- Because one stereoisomer of 2,3-dibromobutane is superimposable on its mirror image, there are only three stereoisomers, not four.

Meso Compounds



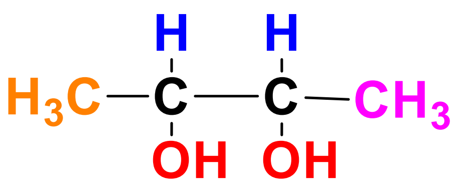
Active/Inactive Isomer

Case I



Active compounds= $2^n = 2^2 = 4$

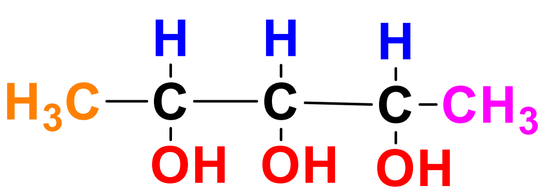
Case II



Active compounds= $2^{n-1} = 2^{2-1} = 2$

Inactive = $2^{n-2/2} = 2^{2-2/2} = 1$

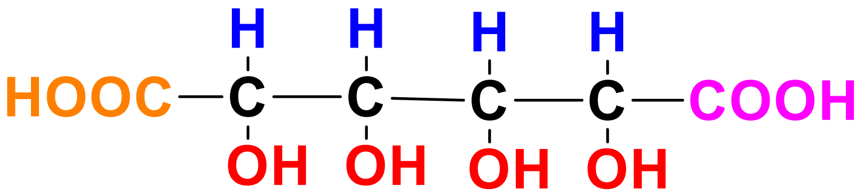
Case III



Active compounds= $2^{3-1}-2^{3-1/2} = 2^2-2^1 = 4-2=2$

Inactive = $2^{3-1/2} = 2^1 = 2$

Case IV



Active compounds= $2^{4-1} = 2^{3} = 8$

Inactive = $2^{4-2/2} = 2^{1} = 2$

General formulae

If 'n' is even (here n is the number of chiral centres):

Number of Optically active isomers 2^{n-1}

Number of Meso Compounds $2^{n-2/2}$

If 'n' is odd (here n is the number of chiral centres):

Number of Optically active isomers $2^{n-1}-2^{n-1/2}$

Number of Meso Compounds $2^{n-1/2}$