Stereochemistry

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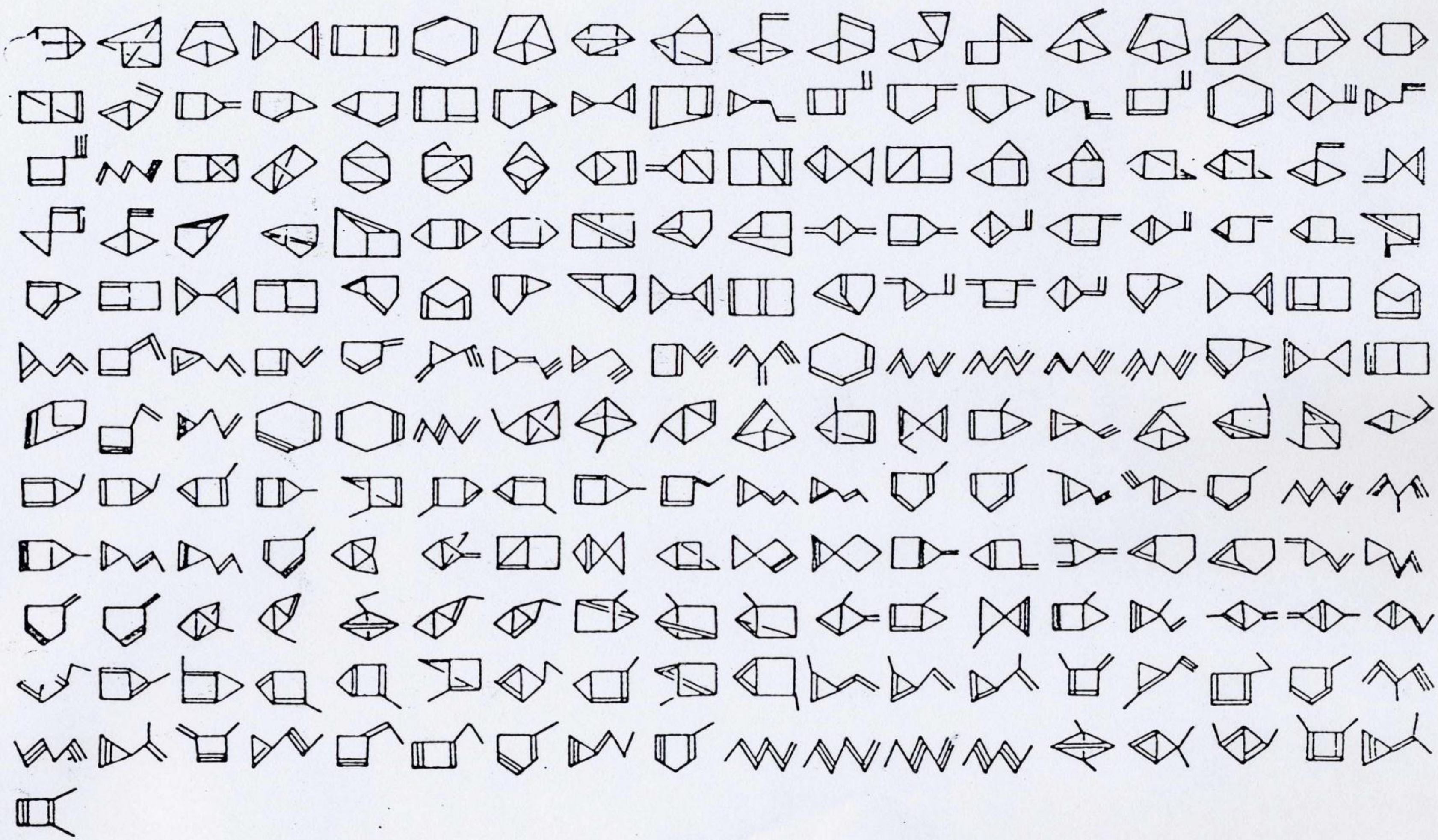
C_6H_6 Isomers: Can you imagine How many isomers with the composition C_6H_6 ?? can you draw some of them?



THE C_6H_6 ISOMERS

Isomers and their types

- Isomers:
  - Different compounds that have the same molecular formula (composition) but different connectivity. Two classes:

- Structural (constitutional) isomers:
  - same molecular formula but different bonding sequence

- Stereoisomers:
  - same molecular formula, same bonding sequence, but different arrangement in space.

Structural Isomers in Alkanes

**** The number of isomeric alkanes increases as the number of carbons increase.**

CH_4	1	C_8H_{18}	18
C_2H_6	1	C_9H_{20}	35
C_3H_8	1	$C_{10}H_{22}$	75
C_4H_{10}	2	$C_{15}H_{32}$	4,347
C_5H_{12}	3	$C_{20}H_{42}$	366,319
C_6H_{14}	5	$C_{40}H_{82}$	62,491,178,805,831
C_7H_{16}	9		

Structural Isomers in Alkanes

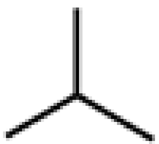
Isomers of Butane C_4H_{10}

n-Butane: $CH_3(CH_2)_2CH_3$

(B.P. - 0.4°C)

Isobutane: $(CH_3)_3CH$

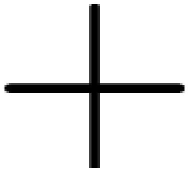
(B.P. - 10.2°C)



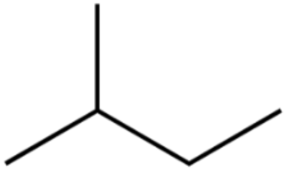
Isomers of Pentane C_5H_{12}

n-Pentane: $CH_3(CH_2)_3CH_3$

Neopentane: $(CH_3)_4C$



Isopentane: $(CH_3)_2(CH_2)_2CH_3$



Stereochemistry

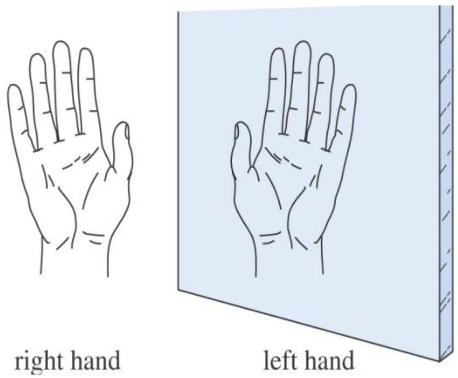
Stereochemistry refers to the 3-dimensional properties and reactions of molecules. It has its own language and terms that need to be learned in order to fully communicate and understand the concepts.

New vocabulary and concepts

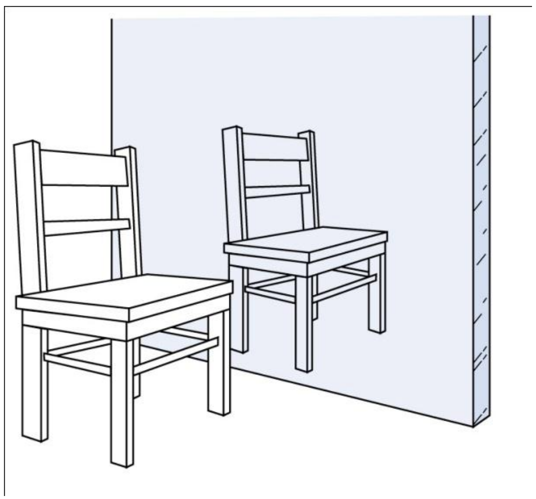
- Handedness
- Chirality
- Fischer Projections
- Depicting Asymmetric Carbons
- (R) and (S) Nomenclature
- Enantiomers
- Diastereomers
- Optical Activity

Handedness…..Chirality

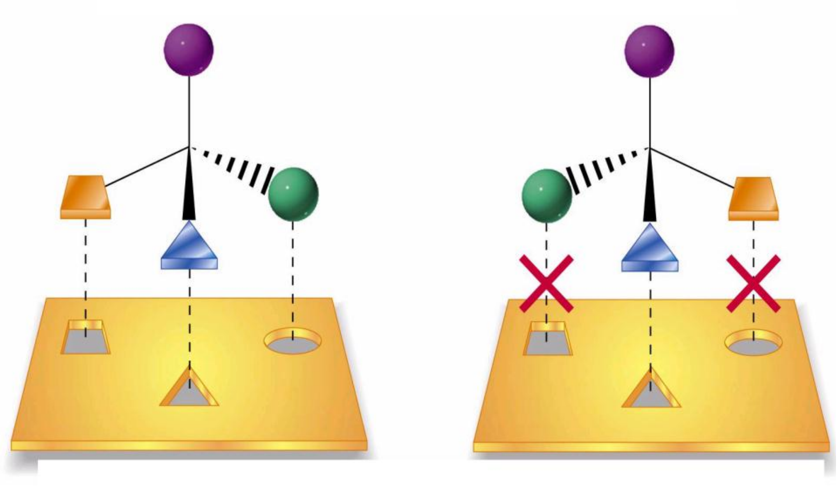
- **Handedness**" right glove doesn't fit the left hand.



Superimposable: A term that describes the ability to precisely overlap one object over another. Only identical objects are superimposable, everything else is non-superimposable



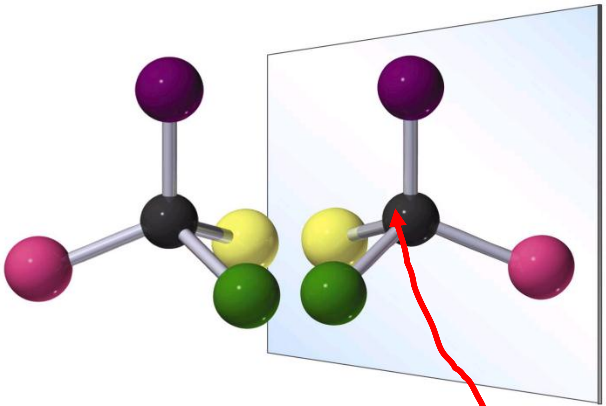
superimposable



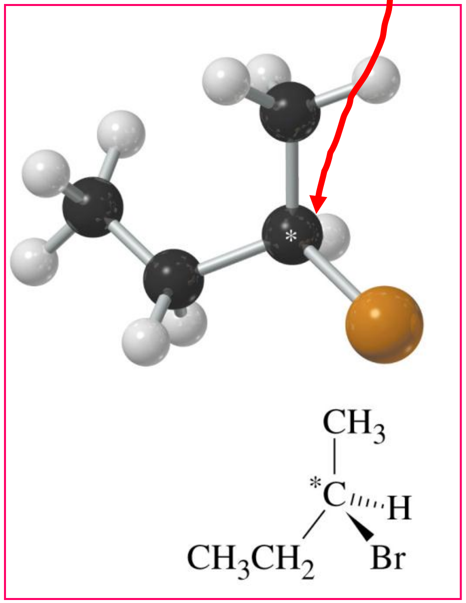
nonsuperimposable

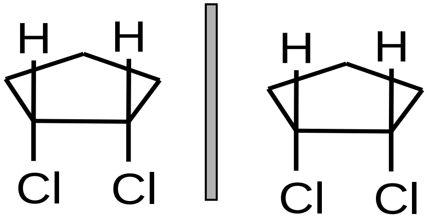
Chiral molecules & Chirality Center

- Chemical substances that can be handed are called chiral.
- Chiral Molecules: are molecules that are non-superimposable on their mirror image.
- A carbon atom that is bonded to four different groups is called chairal carbon atom or stereocenter (asymmetric carbon atom). It is sp^3 carbon and labeled with a strict (*).
- Achiral: A molecule is achiral if it is superimposable on its mirror image



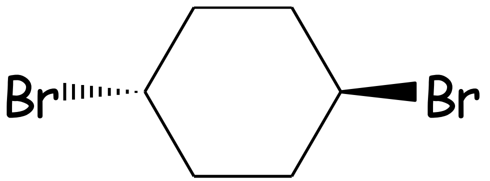
chiral carbon atom

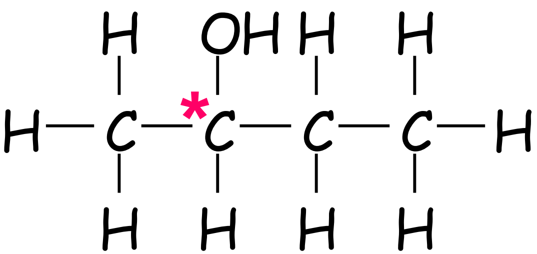


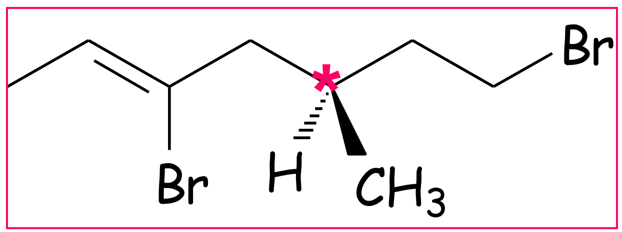


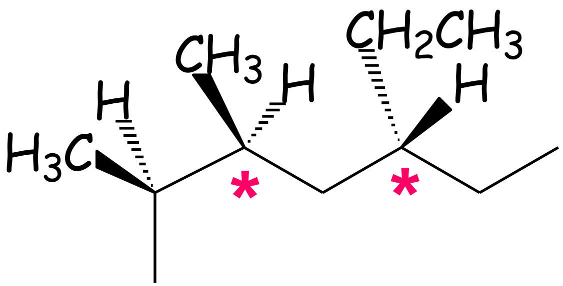
Practices on Asymmetric Carbons

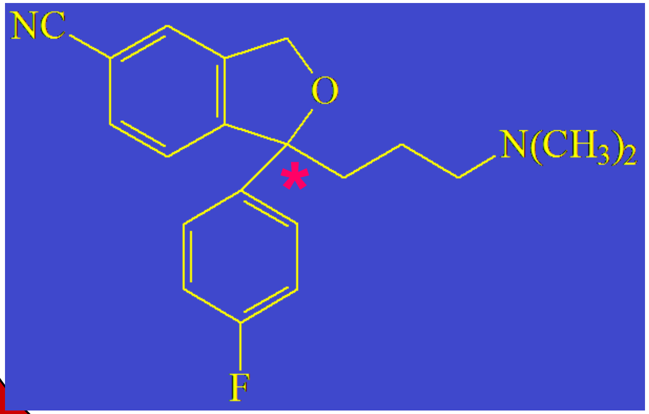
Example: Identify all asymmetric carbons present in the following compounds.

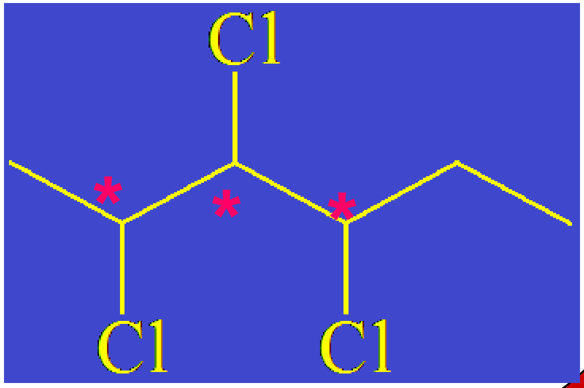












Fischer Projections:

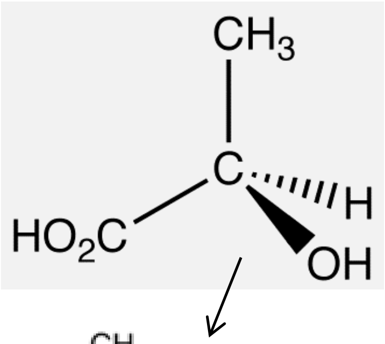
➢ It is a two-dimensional representation of a three-dimensional organic molecule by **projection**.

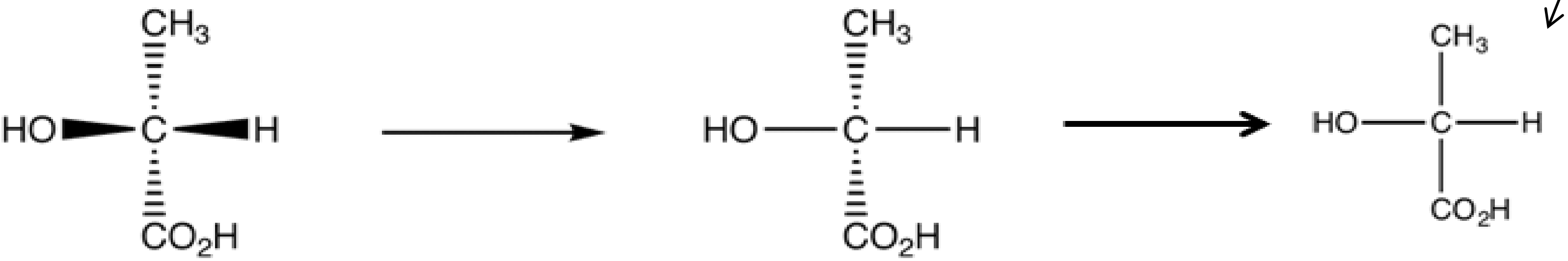
✓Carbon chain is on the vertical line.

✓Horizontal bonds pointing out of the plane of the paper.

✓Vertical bonds pointing into the plane of the paper.

Ex. Draw Lactic acid using Fischer projection

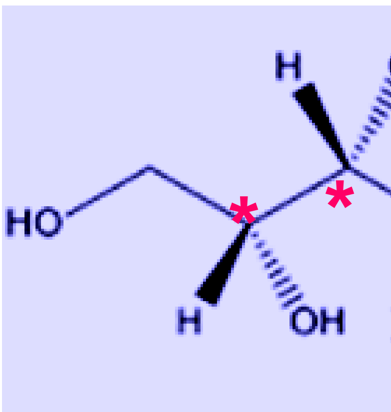




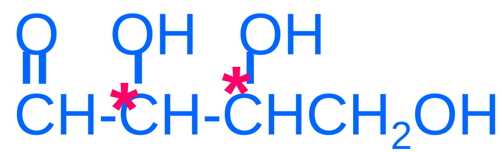
** In the original structure, wedge bonded group should be left and the dashed bonded group should be right.

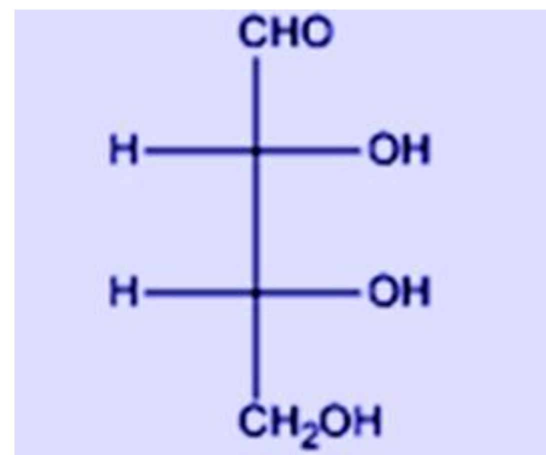
Fischer Projections:

Ex. Draw D-Threose using Fischer projection



D-threose

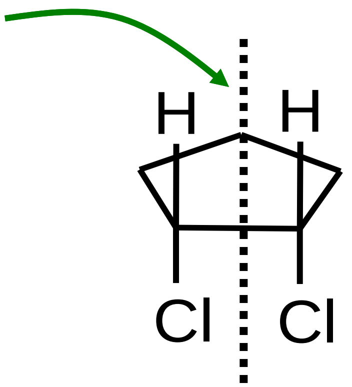




Fischer Projection

Internal Plane of Symmetry

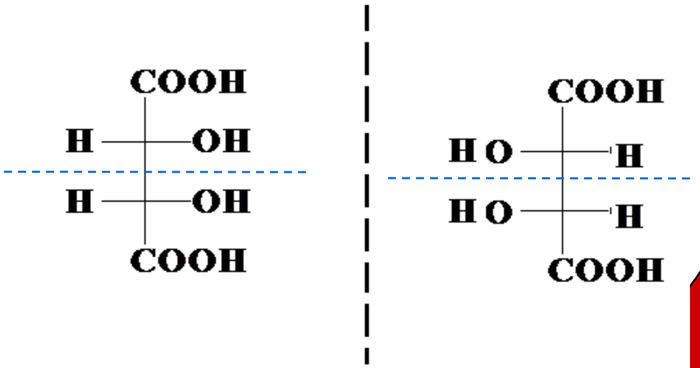
- Cis-1,2-dichlorocyclopentane contains two asymmetric carbons but is achiral because it contains an internal mirror plane of symmetry



- Any molecule that has an internal mirror plane of symmetry is achiral even if it contains asymmetric carbon atoms. It is called "meso"

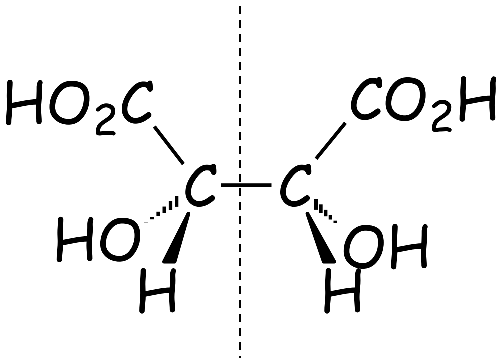
- **Meso compound**: an achiral compound that contains chiral centers often contains an internal mirror plane of symmetry

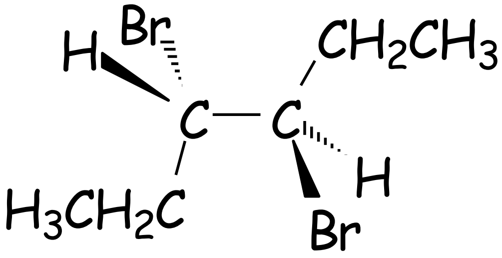
- Tartaric acid is also Meso compound because it contains 2 stereocenters and a plane of symmetry

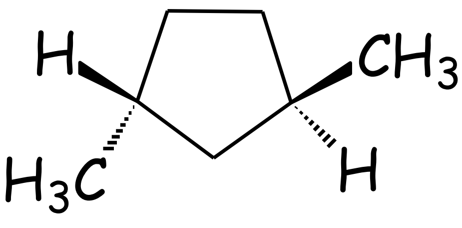


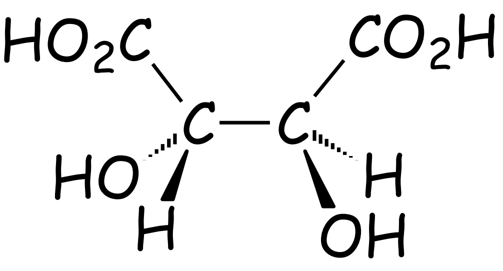
Practice on Internal Plane of Symmetry

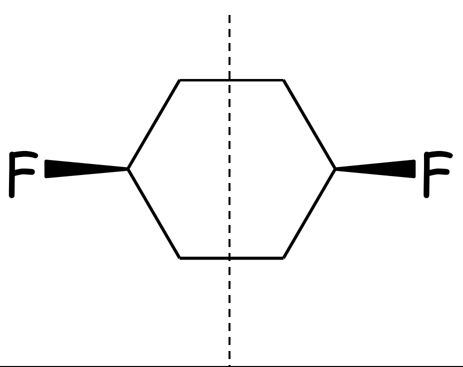
Example: Which of the following compounds contain an internal mirror plane of symmetry?

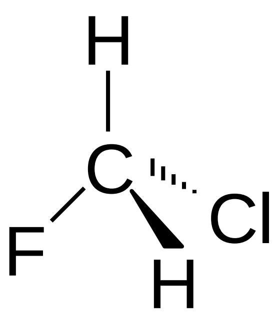










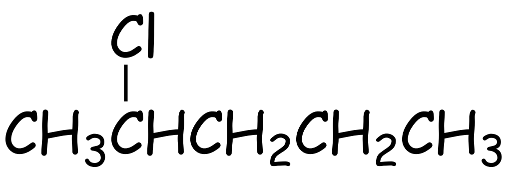


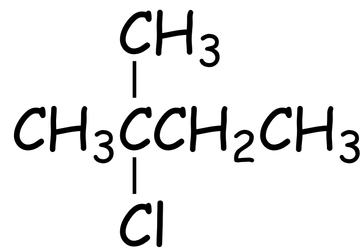
Chiral vs. Achiral

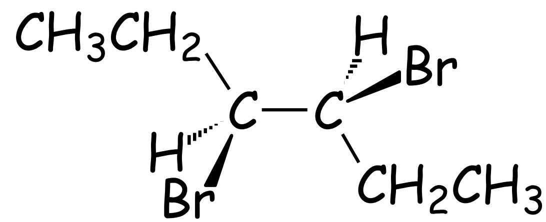
- To determine if a compound is chiral:
  - 0 asymmetric carbons: → Usually achiral
  - 1 asymmetric carbon: → Always chiral
  - 2 asymmetric carbons: → Chiral or achiral:
    - Does the compound have an internal plane of symmetry?
      - Yes: → achiral (meso)
      - No: → chiral

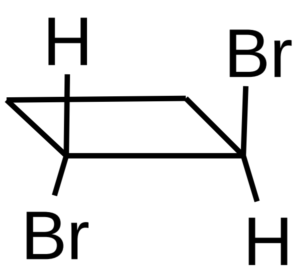
Chiral vs. Achiral

Practice: Identify the following molecules as chiral or achiral.

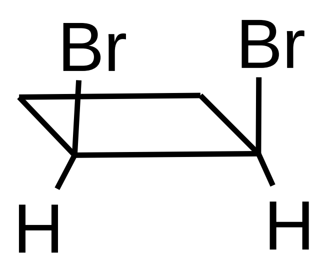








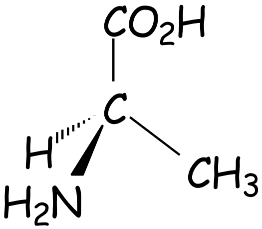
trans-1,2-dibromocyclobutane

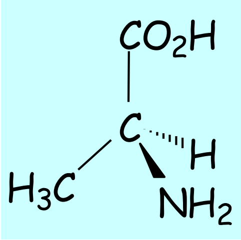


cis-1,2-dibromocyclobutane

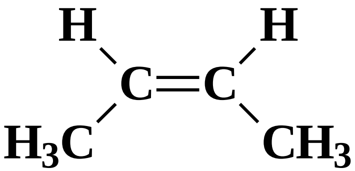
Types of Stereoisomers

- Two types of stereoisomers:
  - Enantiomers: Two compounds that are nonsuperposable mirror images of each other {(R), (S) isomers}

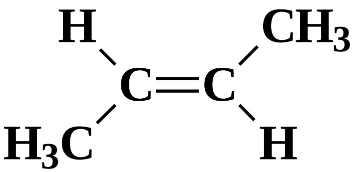




  - Diastereomers: Two stereoisomers that are not mirror images of each other.
    - Geometric isomers (cis-trans isomers) are one type of diastereomer.



cis-2-butene



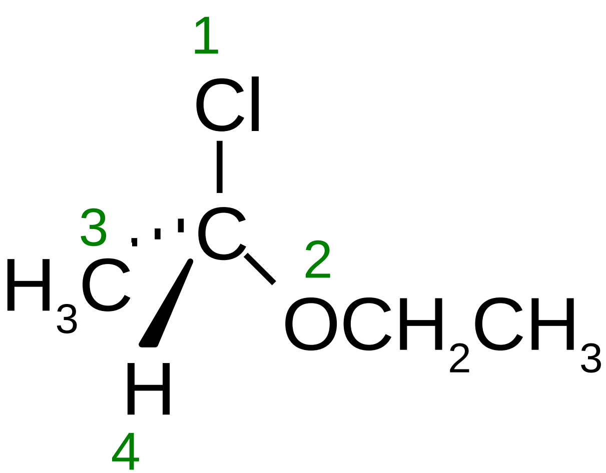
trans-2-butene

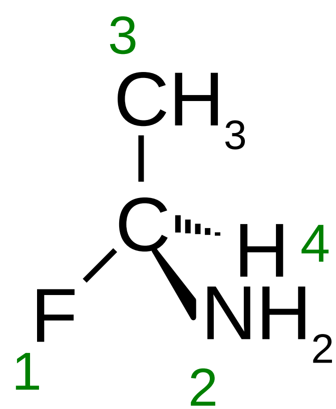
Enantiomers and (R) & (S) Nomenclature

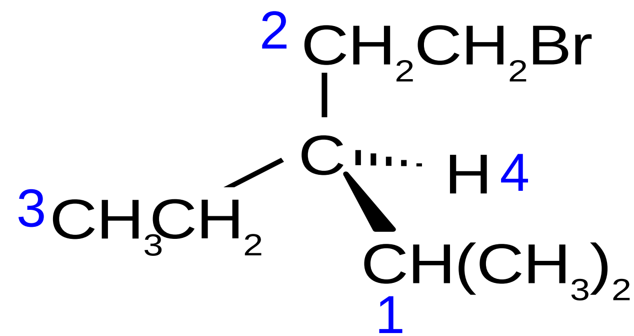
- Assign a numerical priority to each group bonded to the asymmetric carbon:
  - group 1 = highest priority (higher atomic numbers)
  - group 4 = lowest priority (lower atomic numbers)

priorities: I > Br > Cl > S > F > O > N > ^{12}C > ^{1}H

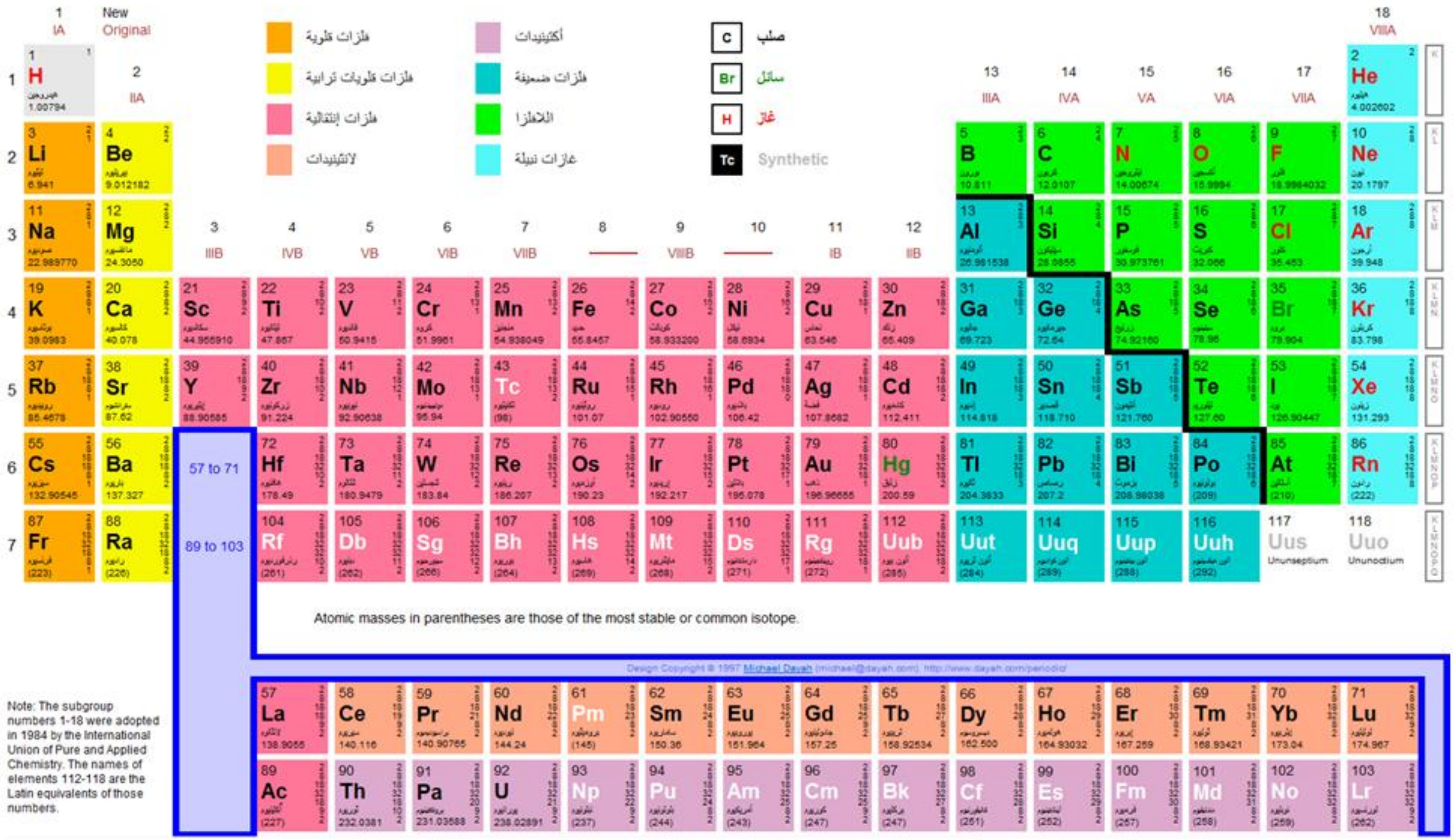
$CH(CH_3)_2$ > CH_2CH_2Br > CH_3CH_2







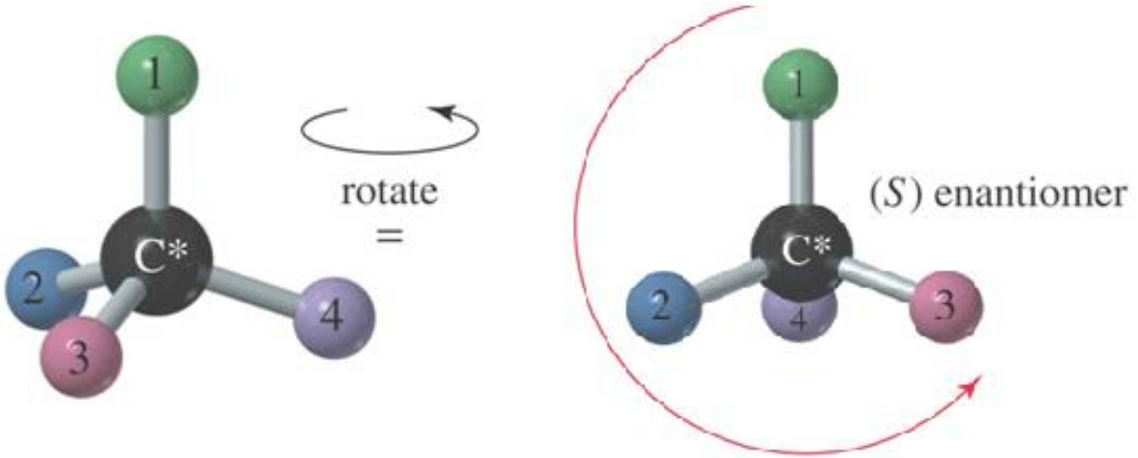
Remember the periodic table of elements



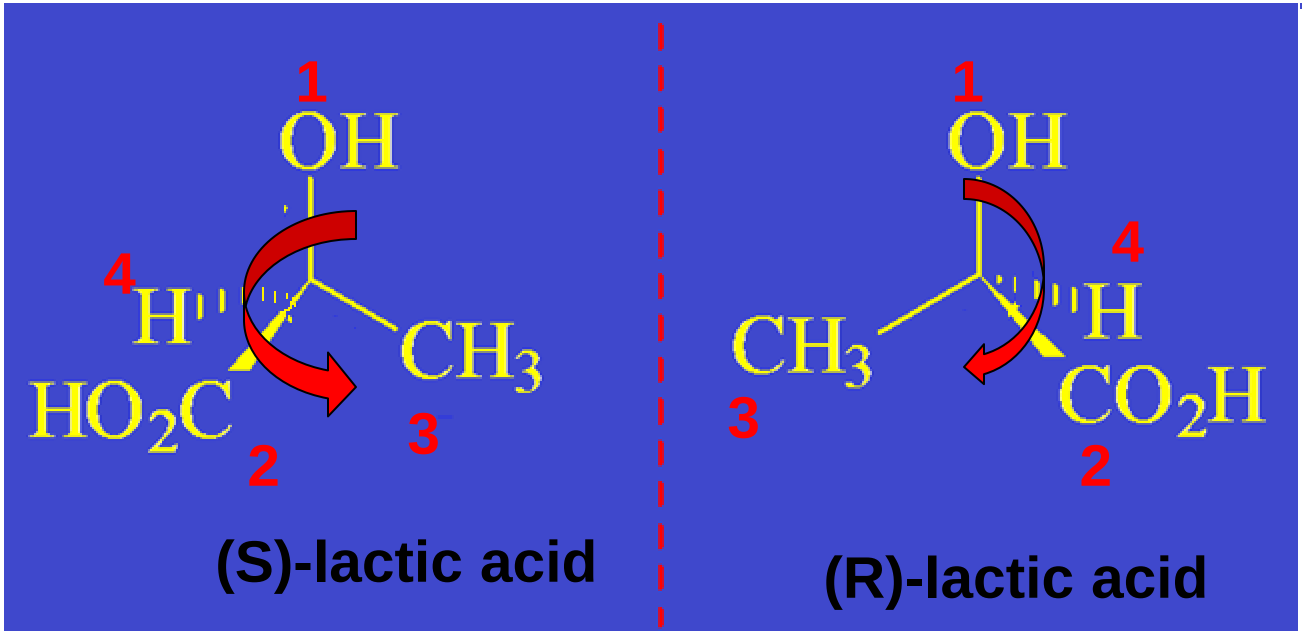
Enantiomers and (R) & (S) Nomenclature

After assigning a numerical priority to each group bonded to the asymmetric carbon,

- Use a 3-D drawing or model, put the 4th priority group in back.
- Draw an arrow from the 1st priority group to the 2nd group to the 3rd group.
  - Clockwise arrow → (R) configuration
  - Counterclockwise arrow → (S) configuration
  - If the 4th priority group is in the front, reverse the name

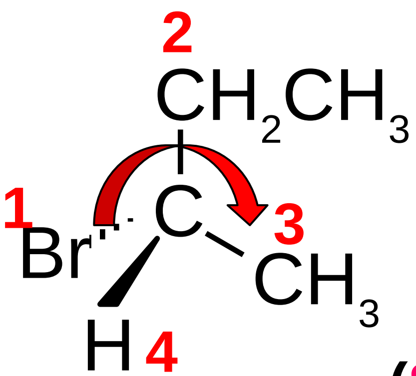


Example: Name the following compounds.



(S)-lactic acid

(R)-lactic acid

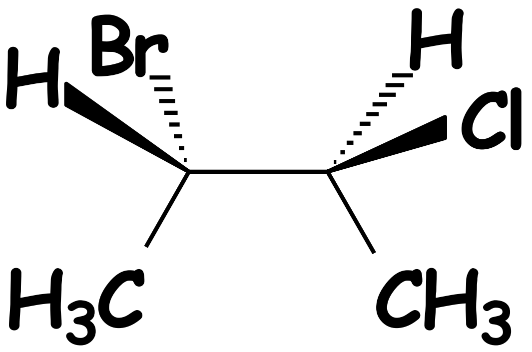


Although we have clockwise arrow, (we suppose to name it (R), but because the H is in front, so we reverse the name to (S).

(S)-2-bromobutane

Enantiomers and (R) & (S) Nomenclature

- **When naming compounds containing multiple chiral atoms, you must give the configuration around each chiral atom:**
  - **position number and configuration of each chiral atom in <u>numerical order</u>, separated by commas, all in ( ) at the start of the compound name**



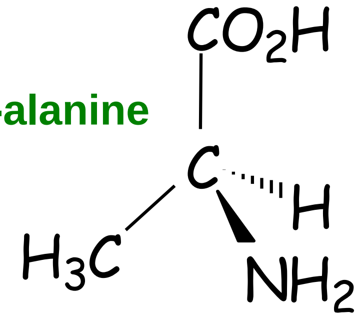
Note: in carbon #3 we see the configuration clockwise , i.e. **R**, but we reverse it to **S** because the H atom is in the front.

(2S, 3S)-2-bromo-3-chlorobutane

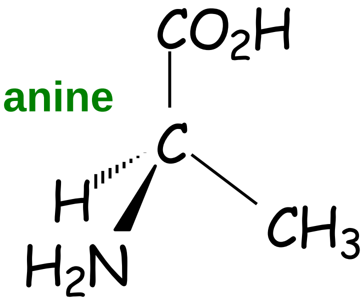
Practices on (R) and (S) Nomenclature

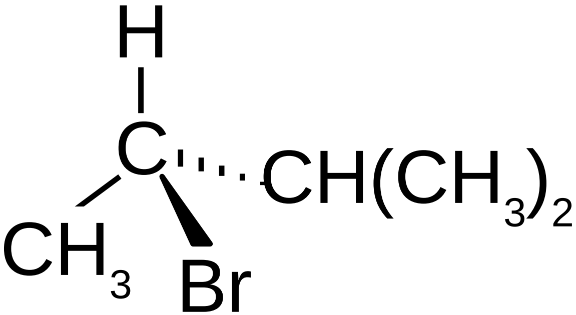
Excercies: **Identify the asymmetric carbon(s) in each of the following compounds and determine whether it has the (R) or (S) configuration.**

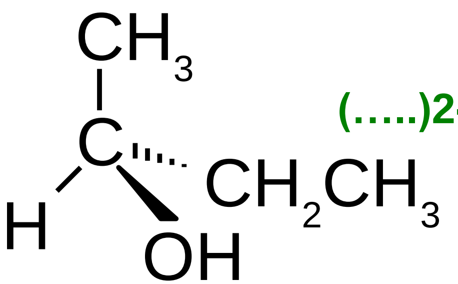
(…)-alanine



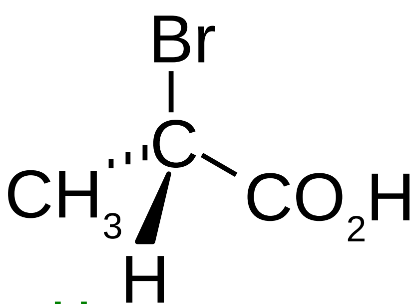
(…..)-alanine







(…..)2-butanol

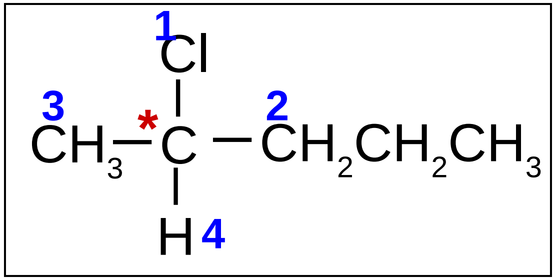


(…..)2-bromoprobionic acid

Depicting Structures with Asymmetric Carbons

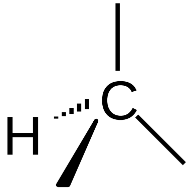
Example: Draw a 3-dimensional formula for (R)-2-chloropentane.

Step 1: Identify the asymmetric carbon.

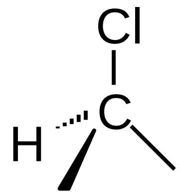


Step 2: Assign priorities to each group attached to the asymmetric carbon.

Step 3: Draw a "skeleton" with the chiral atom in the center and the lowest priority group attached to the "dashed" wedge (i.e. pointing away from you).

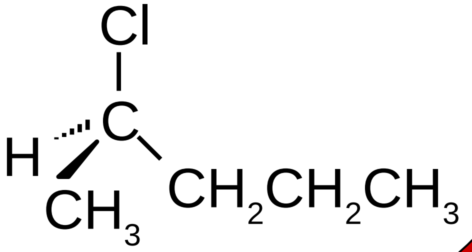


Step 4: Place the highest priority group at the top.

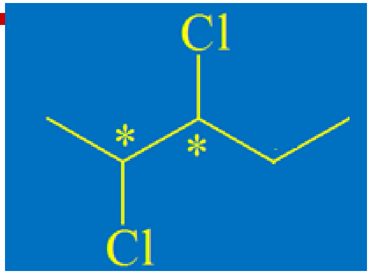


Step 5: For (R) configuration, place the 2nd and 3rd priority groups around the chiral atom in a clockwise direction.

Step 6: Double-check your structure to make sure that it has the right groups and the right configuration.



How many stereoisomers?

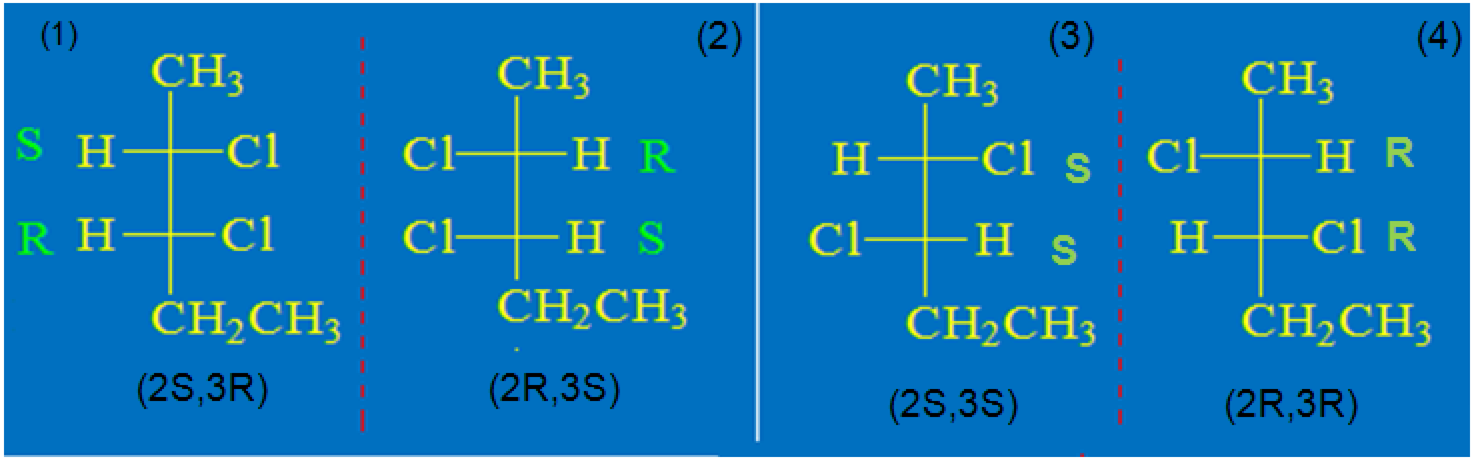


For 2,3 dichloropentane, how many stereoisomers ? ?

❖ Number of isomers = 2^n

Since “n” = the # of asymmetric centers

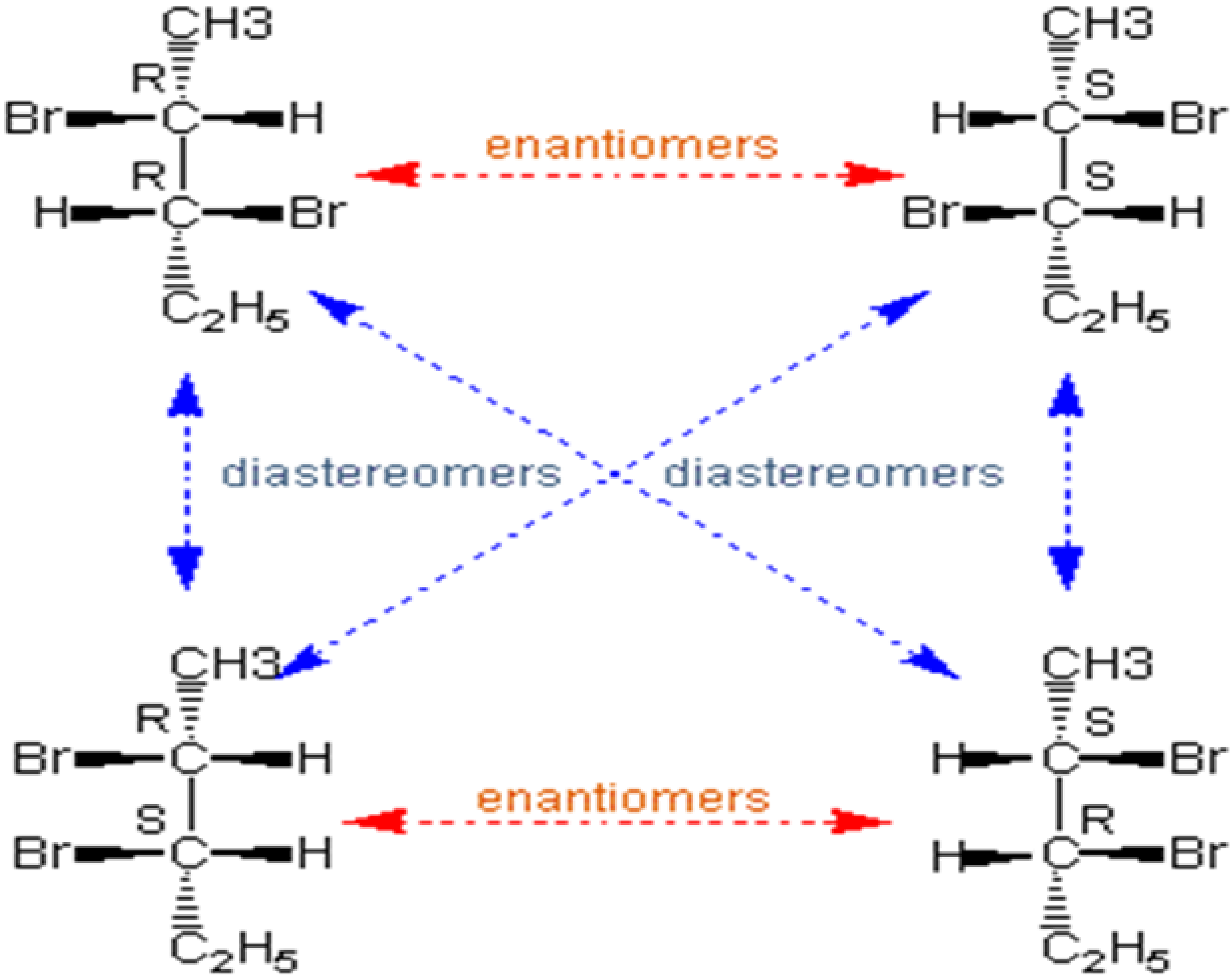
here, we have 2 asymmetric centers, So we should have 4 isomers



❖ Some of these isomers are enantiomers and some of them are diastereomers. We **may** find some of them identical !!!!!

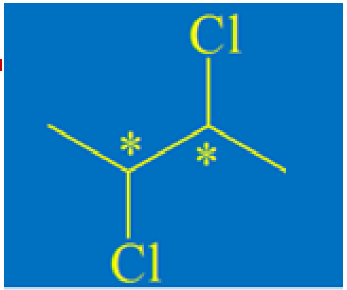
❖ Structures (1 ,2) and (3 ,4) are enantiomers (note each S became R and vice versa)

❖Structures (1, 3) ,(1,4) ,(2,3) and (2,4) are diastereomers (note one S became R, and the other dose not change)

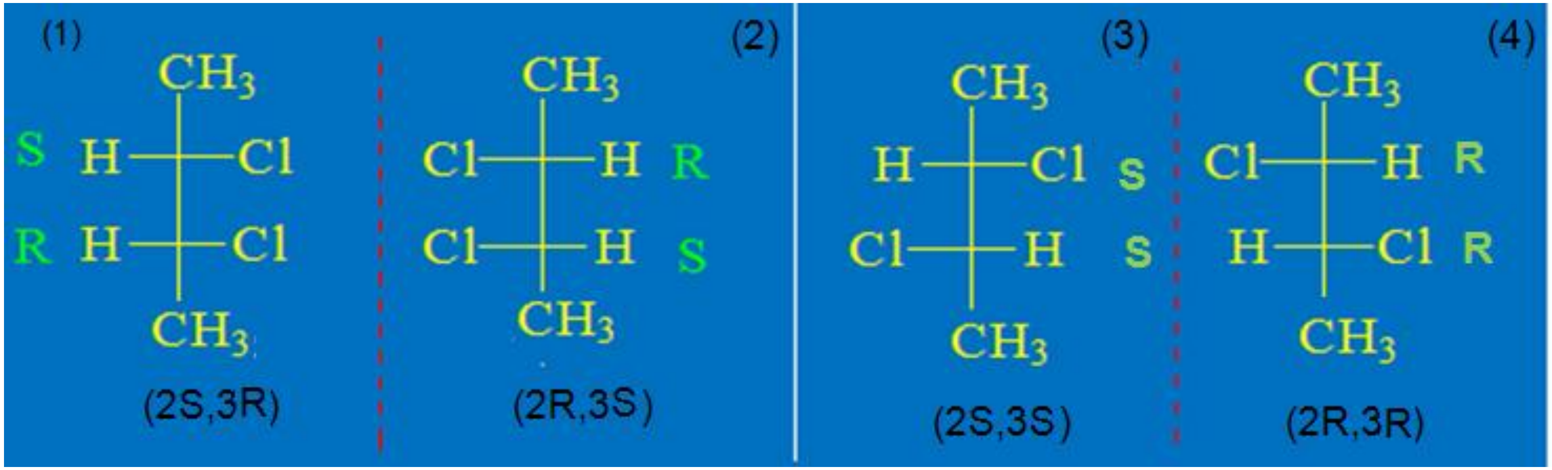


Isomeric relationship of the 2,3-dibromopentane stereoisomers.

How many stereoisomers?



For 2,3 dichlorobutane, have 2 asymmetric centers, so we should have 4 isomers. But is this true?!!!!!



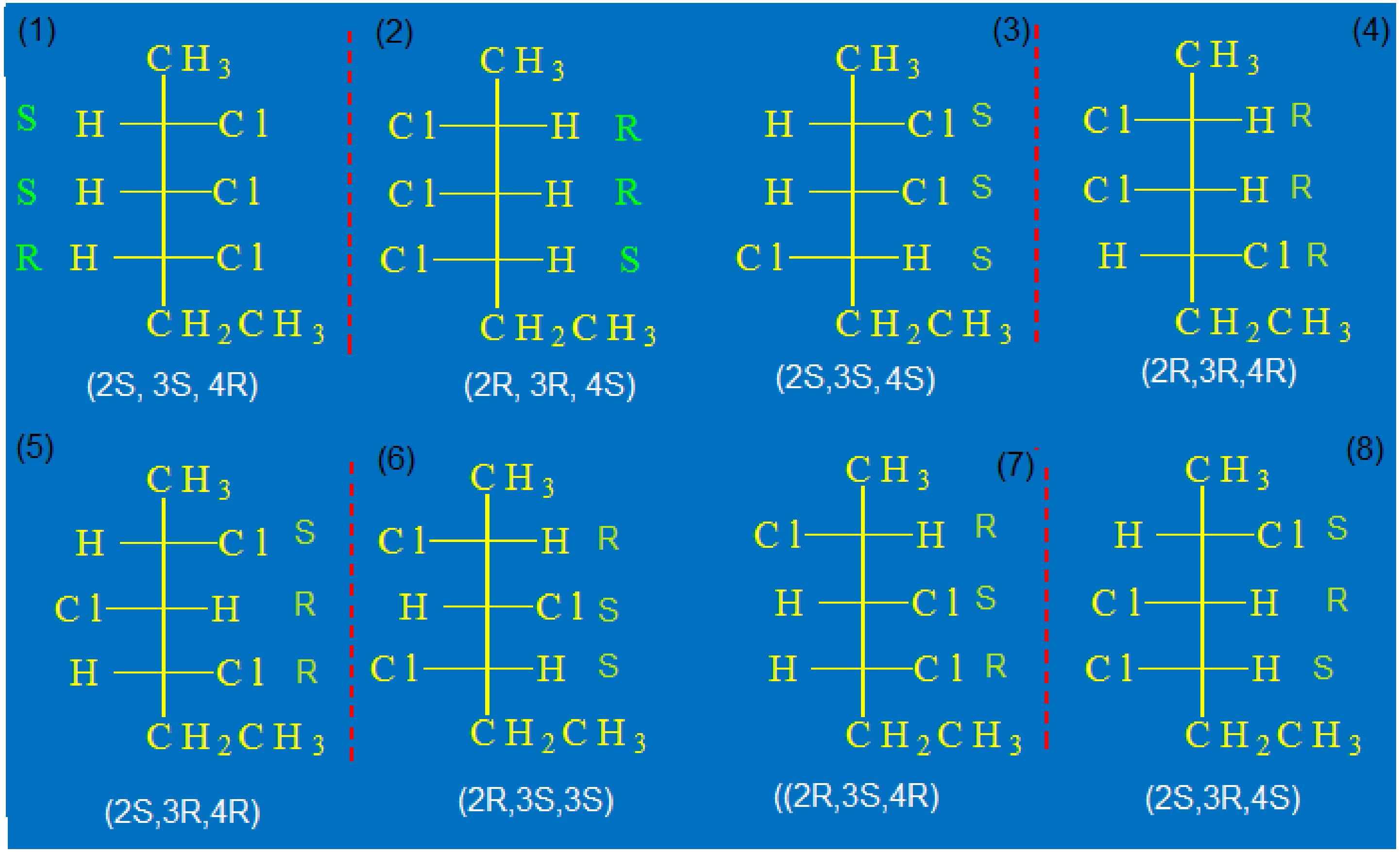
❖Structures (1,2) are identical (meso compound) because the molecule contains internal plane of symmetry. Thus we just have 3 isomers not four.

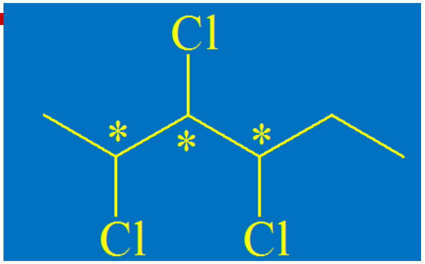
❖ Structures (3 ,4) are enantiomers.

❖Structures (1, 3) ,(1,4) and (2,4) are diastereomers.

How many stereoisomers?

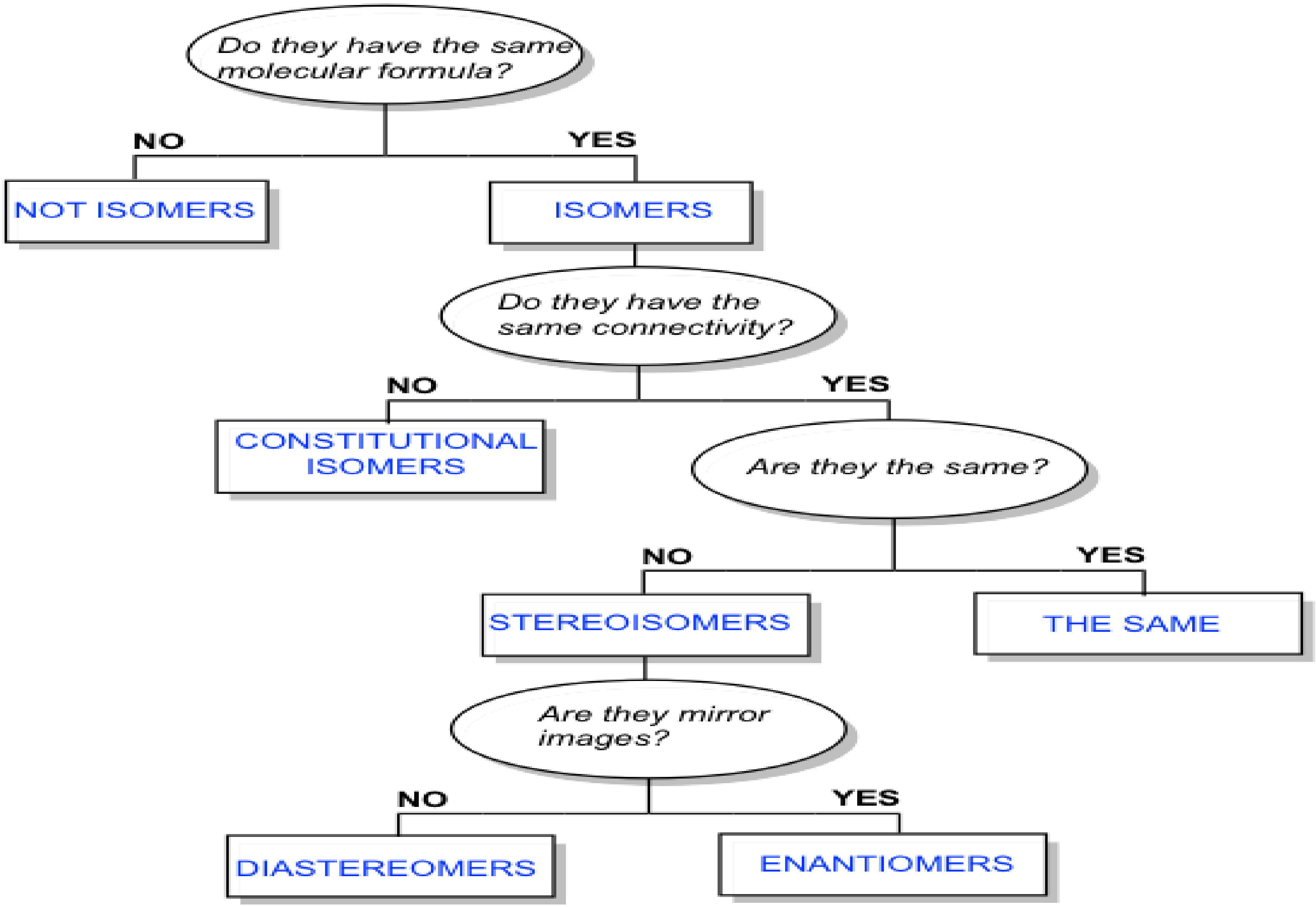
For 2,3,4-trichlorohexane, we have $2^3 = 8$ isomers ? ?





- ❖ (1 ,2) and (3 ,4), (5,6) , (7,8) are enantiomers
- ❖(1, 3) ,(1,4) ,(2,3) and (2,4) are diastereomers

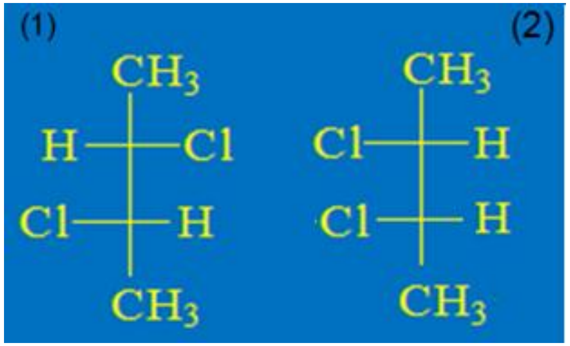
Flow chart summarizing the relationship between two molecules:



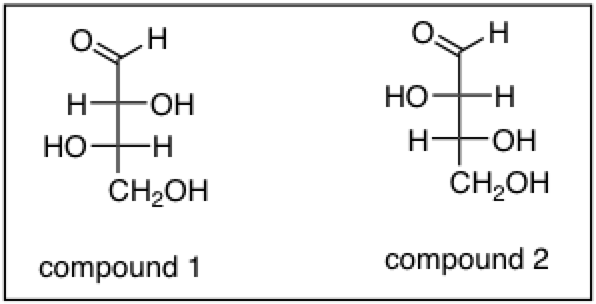
Practices

Check the relation between each pair of the following molecules:

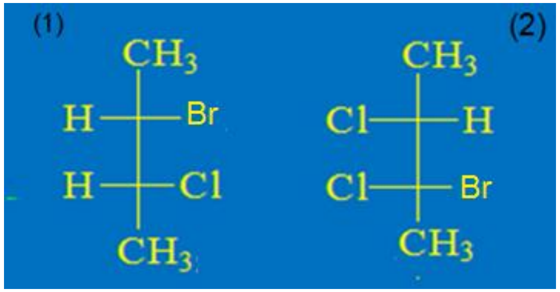
Ex$_1$



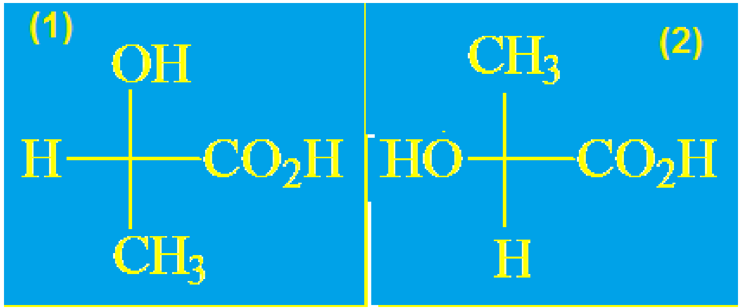
Ex$_2$



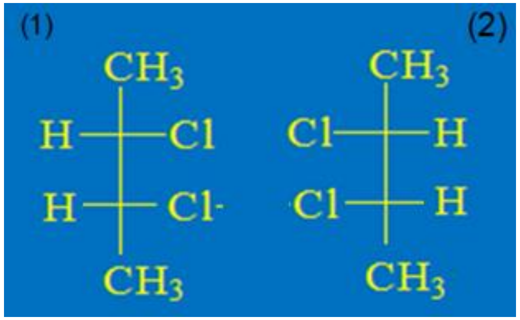
Ex$_3$



Ex$_4$

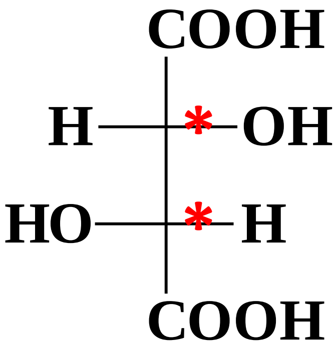


Ex$_5$



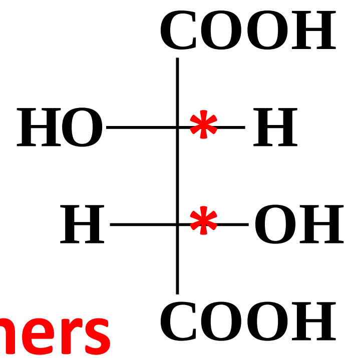
Ex$_5$

Examples

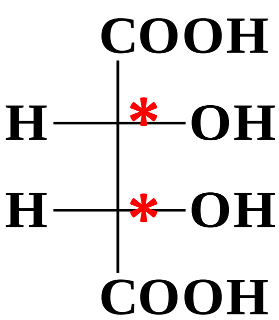


(2*R*,3*R*)-tartaric acid

enantiomers



(2*S*,3*S*)-tartaric acid

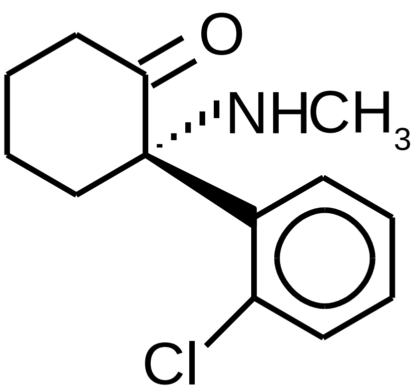


(2*R*,3*S*)-tartaric acid

A meso compound, contains 2 or more stereocenters and a plane of symmetry

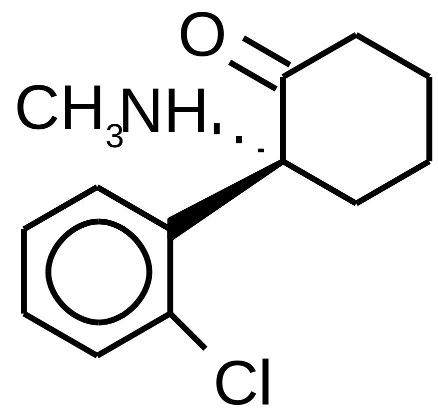
Importance of Stereochemistry

- Stereochemistry plays an important role in determining the properties and reactions of organic compounds.
- The properties of many drugs depends on their stereochemistry:



(S)-ketamine

anesthetic



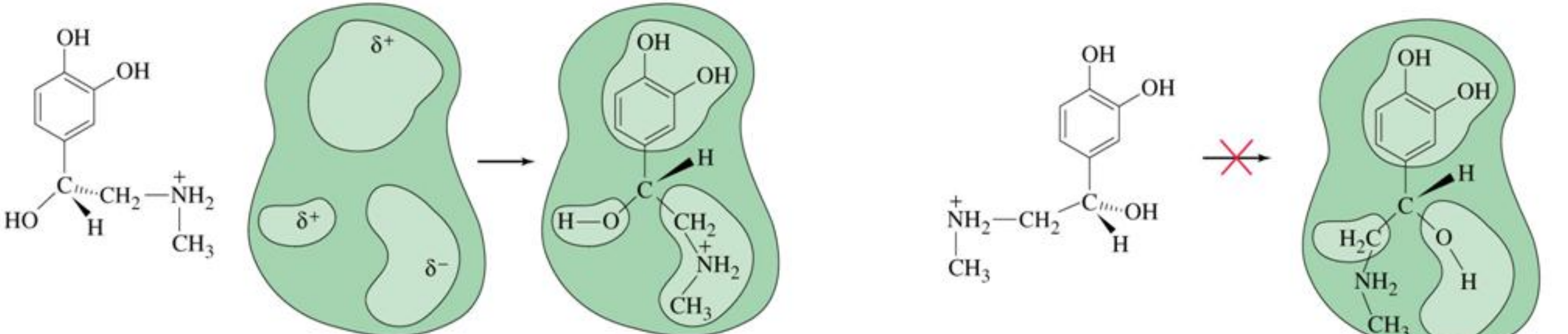
(R)-ketamine

hallucinogen

Properties of Enantiomers

1. Same boiling point, melting point, density
2. Same refractive index
3. Different interaction with other chiral molecules e.g.Enzymes

Enzymes are capable of distinguishing between stereoisomers:



(R)-(−)-epinephrine natural epinephrine

enzyme active site

enzyme–substrate complex

(S)-(+)-epinephrine unnatural epinephrine

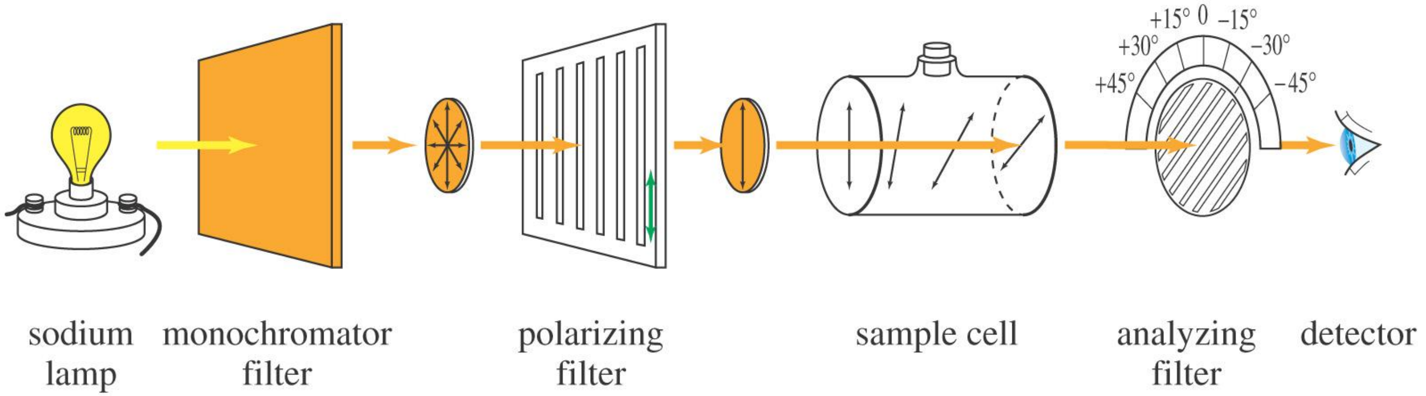
does not fit the enzyme's active site

4. Different direction of rotation in polarimeter
5. Enantiomers are difficult to separate

Polarimetry

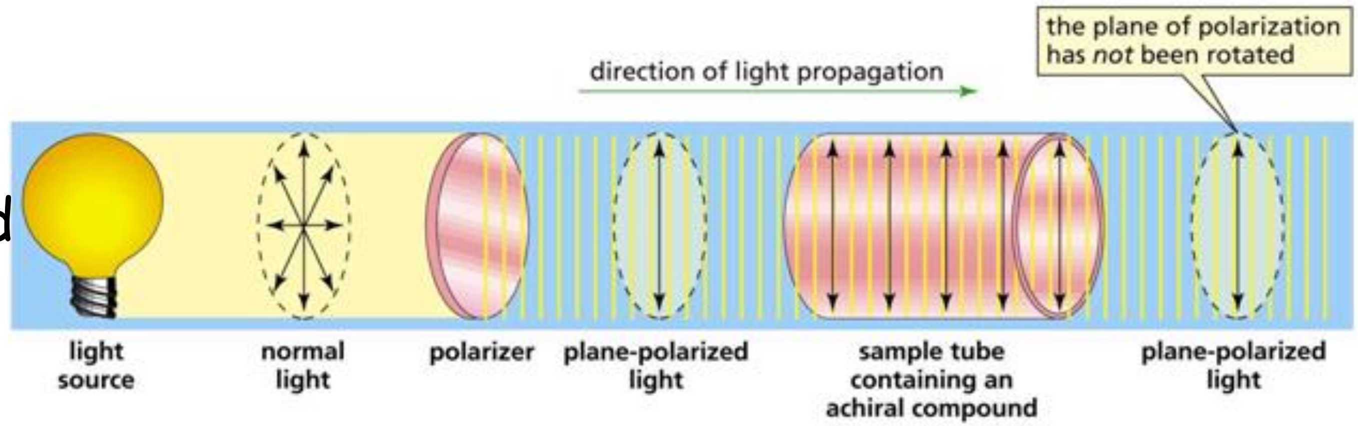
Polarimeter measures optical rotation of a compound

- **Use monochromatic light, usually sodium D**
- **Movable polarizing filter to measure angle**
- **Clockwise = (+) (R enantiomer)**
- **Counterclockwise = (-) (S enantiomer)**

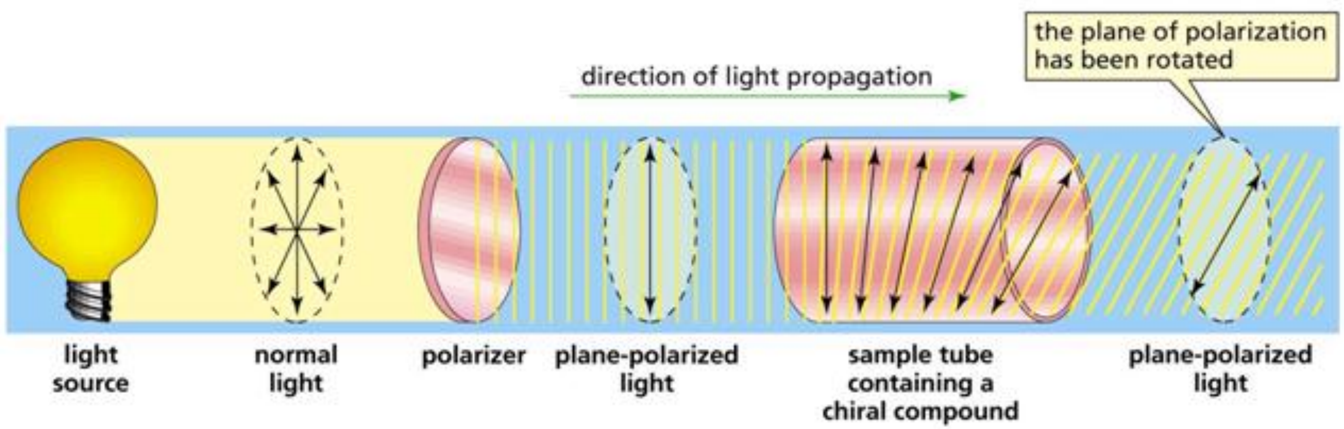


Polarimetry

Plane-Polarized Light through an Achiral Compound



Plane-Polarized Light through a chiral Compound



Specific Rotation, [α]

$$[\alpha] = \alpha / cl$$

α = observed rotation, c = concentration in g/mL

l = length of tube in dm

Dextrorotary **designated as *d* or (+), clockwise rotation**

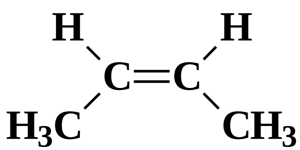
Levorotary **designated as *l* or (-), counter clockwise rotation**

Specific Rotations of some Common Organic Compounds:

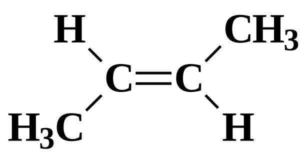
Compound	[α]	# * centers
Penicillin V	**+233.0**	**3**
Sucrose	**+66.5**	**10**
Camphor	**+44.3**	**2**
MSG	**+25.5**	**1**
Cholesterol	**-31.3**	**8**
Morphine	**-132.0**	**5**

Diastereomers

- Stereoisomers that are <u>not</u> mirror images.
- Molecules with 2 or more chiral carbons.
- Geometric isomers (cis-trans), since they are not mirror images.



cis-2-butene



trans-2-butene

Properties of Diastereomers:

- Diastereomers have different physical properties: m.p., b.p.
- They can be separated easily.