Semester-I (Hons)

Organic chemistry Notes

STEREOCHEMISTRY

by

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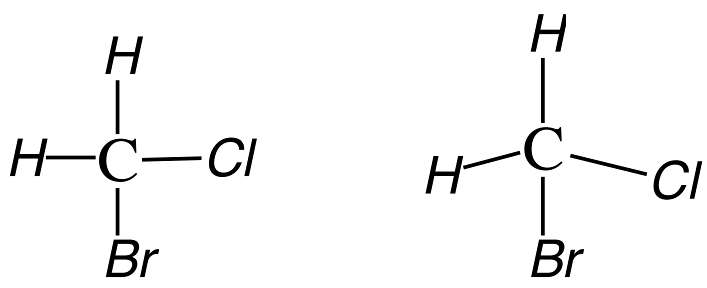
Stereochemistry of Tetrahedral Carbons

We need:

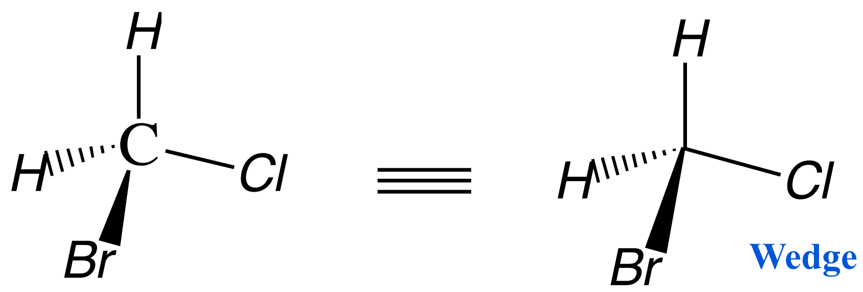
- ***one Carbon sp^3-hybridized, at least***
- ***to represent molecules as 3D objects***

For example:



2D drawing

Not appropriate for Stereochem

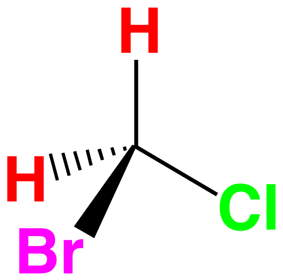


3D drawing

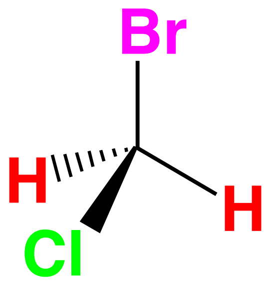
Appropriate for Stereochem

Let’s consider some molecules……

First pair



A

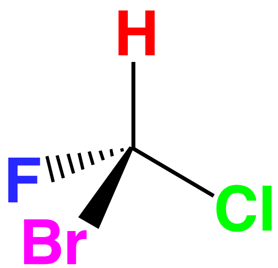


B

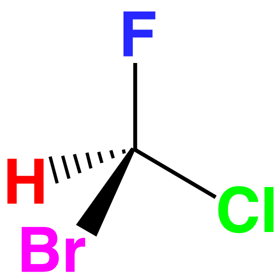
- same molecular formula (CH_2BrCl)
- same atom connectivity
- superposable

⇒ **identical (same compound)**

Second pair



C



D

- same molecular formula (CHFBrCl)
- same atom connectivity
- nonsuperposable

⇒ **stereoisomers (two different compounds)**

Thus, we can define………

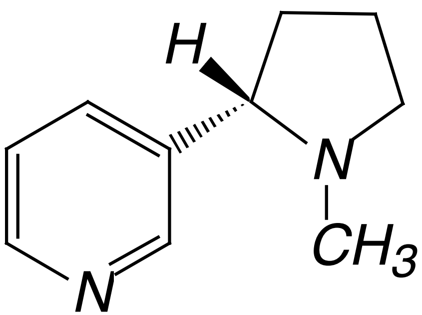
- ***Stereoisomers**: isomers that have same formula and connectivity <u>but</u> differ in the position of the atoms in space*

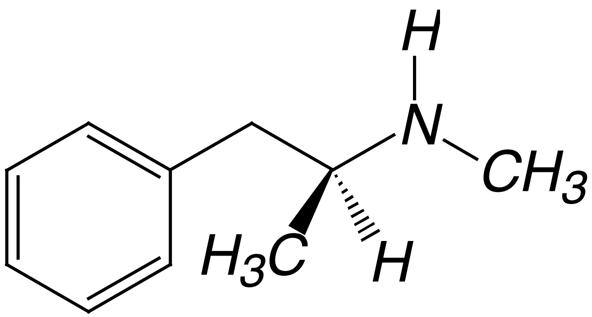
- ***Stereochemistry**: chemistry that studies the properties of stereoisomers*

Definitions

- **Optically Active**: *the ability of some compounds to rotate plane polarized light.*
- **Dextrorotatory (+)**: *an optically active compound that rotates plane polarized light in a clockwise direction.*
- **Levorotatory (-)**: *an optically active compound that rotates plane polarized light in a counterclockwise direction.*

(-)-Nicotine

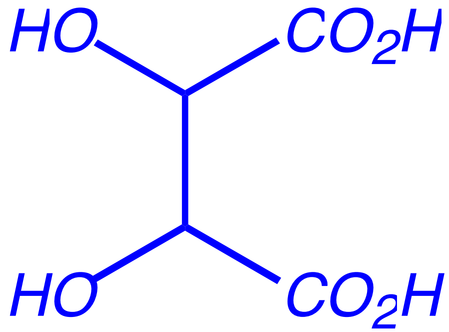




(+)-Methamphetamine

Historical perspective

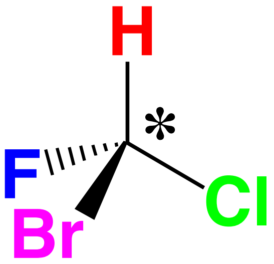
In 1853, Pasteur studies Mesotartaric Acid (same formula as Racemic and Tartaric Acid) but fails to separate into (+) and (-) crystals.



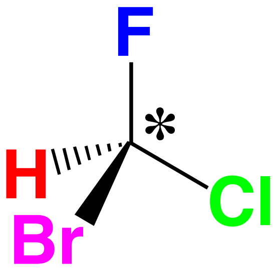
In 1854, he notes that certain plant mold metabolizes (+)-tartaric acid but not (-)-tartaric acid.

Therefore…..

- ***Stereoisomers**: isomers that differ only in the position of atoms in space, and that <u>cannot</u> be interconverted by rotation around a single bond.*
- ***Stereocenter**: a carbon atom bearing 4 different atoms or group of atoms.*



C

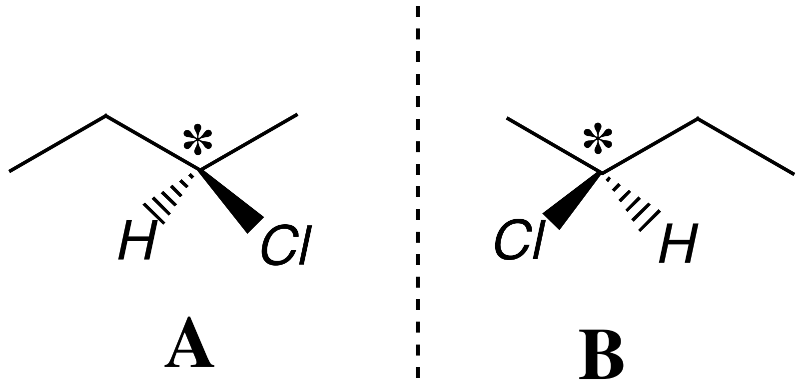


D

C,D are a pair of stereoisomers
Carbon * is a stereocenter

.....another example

Stereoisomers of 2-chlorobutane



A B

A,B are stereoisomers
Carbons * are stereocenters
A,B are nonsuperposable mirror images

↓

Enantiomers

Enantiomers: stereoisomers that are nonsuperposable mirror images.

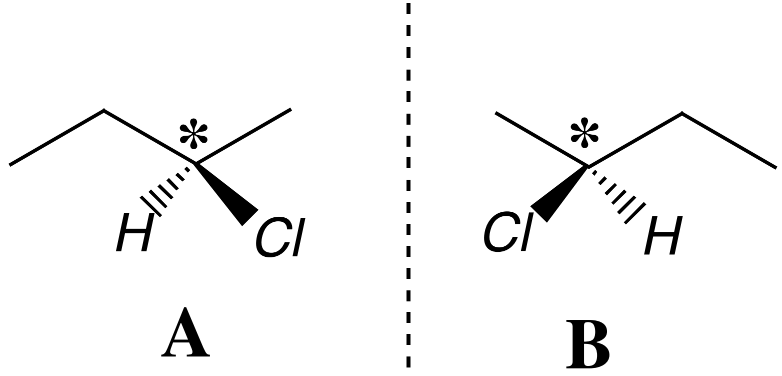
Chiral: any molecule that is nonsuperposable with its mirror image (i.e. A and B are chiral).

Achiral: any molecule that is not chiral.

Racemic mixture: a 1:1 (equimolar) mixture of two enantiomers.

Take-home problem

Stereoisomers of 2-chlorobutane



Enantiomers

Remember:

Enantiomers: stereoisomers that are nonsuperposable mirror images.

Racemic mixture: a 1:1 (equimolar) mixture of two enantiomers.

Explain why:

- **A and B cannot be physically separated.**
- **a racemic mixture of A and B has no optical activity (no rotation of plane polarized light).**

Summary

Stereoisomers: *isomers that have same formula and connectivity but differ in the position of the atoms in space. They possess one or more stereocenters.*

Stereocenter: *a carbon atom bearing 4 different atoms or group of atoms.*

Chiral: *any molecule that is nonsuperposable with its mirror image.*

Enantiomers: *stereoisomers that are non superposable mirror images.*

Racemic mixture: *a 1:1 (equimolar) mixture of two enantiomers.*

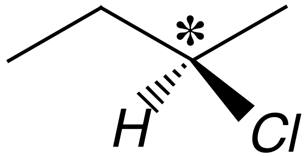
Optically Active: *the ability of some compounds to rotate plane polarized light.*

Questions

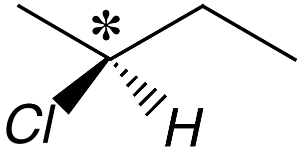
- ✓ Distinguish between diasteromer and enantiomer.
- ✓ Distinguish between dextrorotatory and levorotatory compunds.
- ✓ Explain the term “meso-compound” with suitable example.
- ✓ All optically active molecules are chiral but all chiral molecules are not optically active-Explain.

Configuration of Stereocenters

Enantiomers of 2-chlorobutane:



A

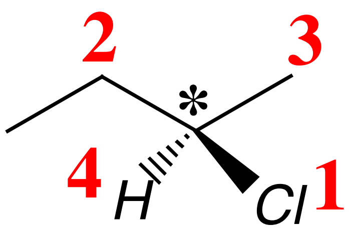


B

The Cahn-Ingold-Prelog (CIP) rule assigns R or S configuration to the two enantiomers.

1) Assign the priorities to the groups attached to the stereocenter. Priority is based on the atomic number, i.e. H has lower priority than Cl. But methyl and ethyl both are attached to the stereocenter through carbon! In these cases, priority assignments proceed outward, to the next atoms. The Methyl carbon has 3 Hs attached while the Ethyl carbon has 2Hs and and a carbon (the terminal methyl group). Therefore, the latter gets higher priority.

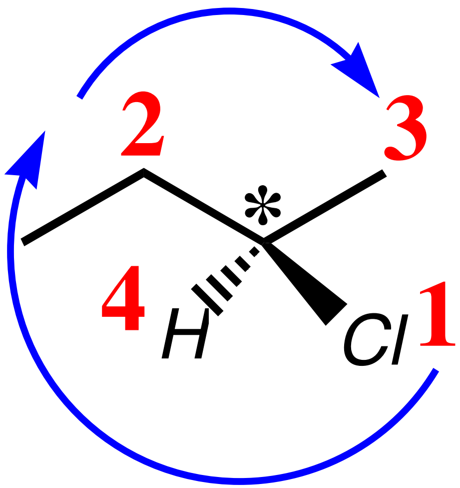
Configuration of Stereocenters



A

2) Orient the molecule so that the group of priority four (lowest priority) points away from the observer.

R- Rectus
S- Sinister

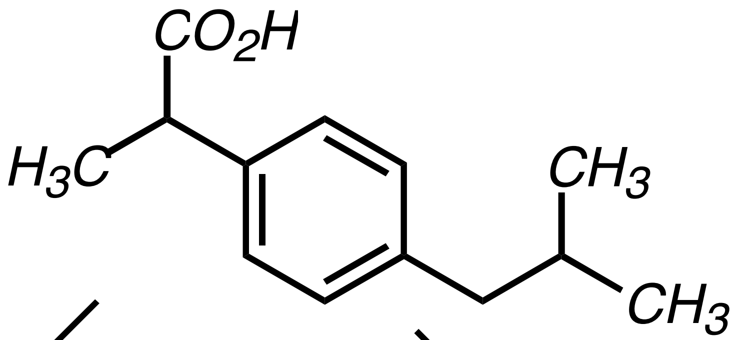


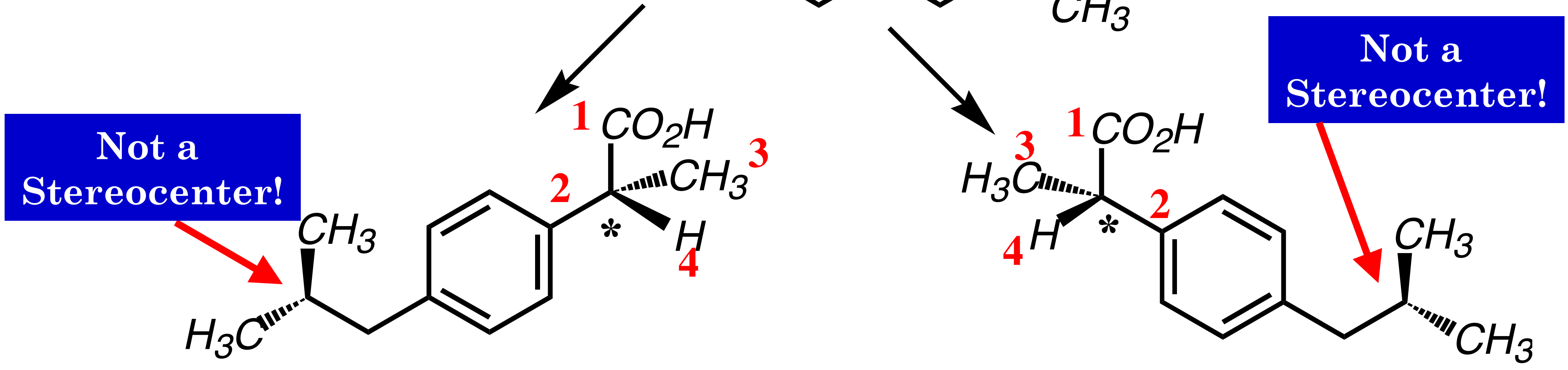
3) Draw a circular arrow from the group of first priority to the group of second priority.

4) If this circular motion is clockwise, the enantiomer is the R enantiomer. If it is counterclockwise, it is the S enantiomer. Thus, A is the <u>R enantiomer</u> of 2-chlorobutane.

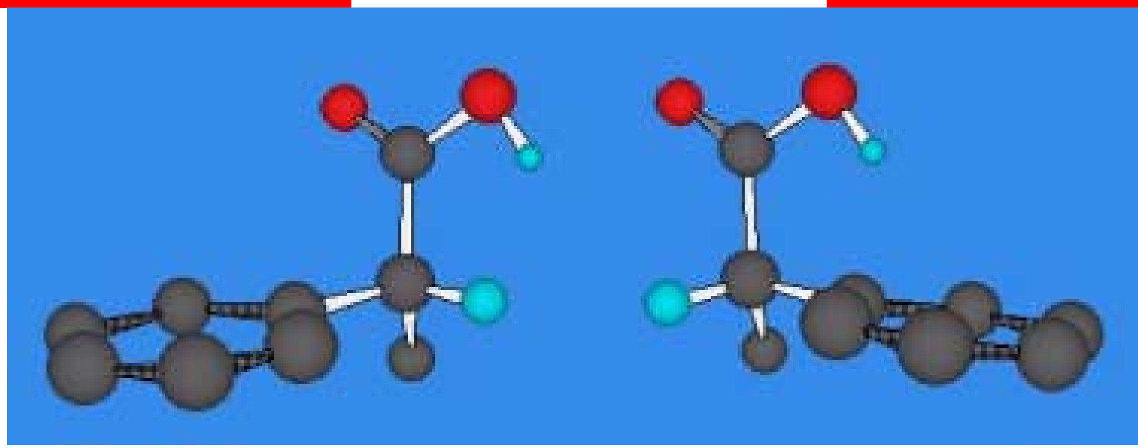
Configuration of Stereocenters

Ibuprofen, an antiinflammatory agent





R enantiomer **S enantiomer**

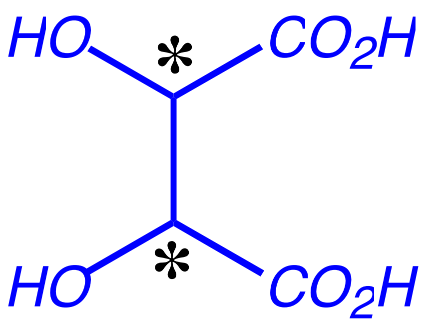


Molecules with multiple stereocenters

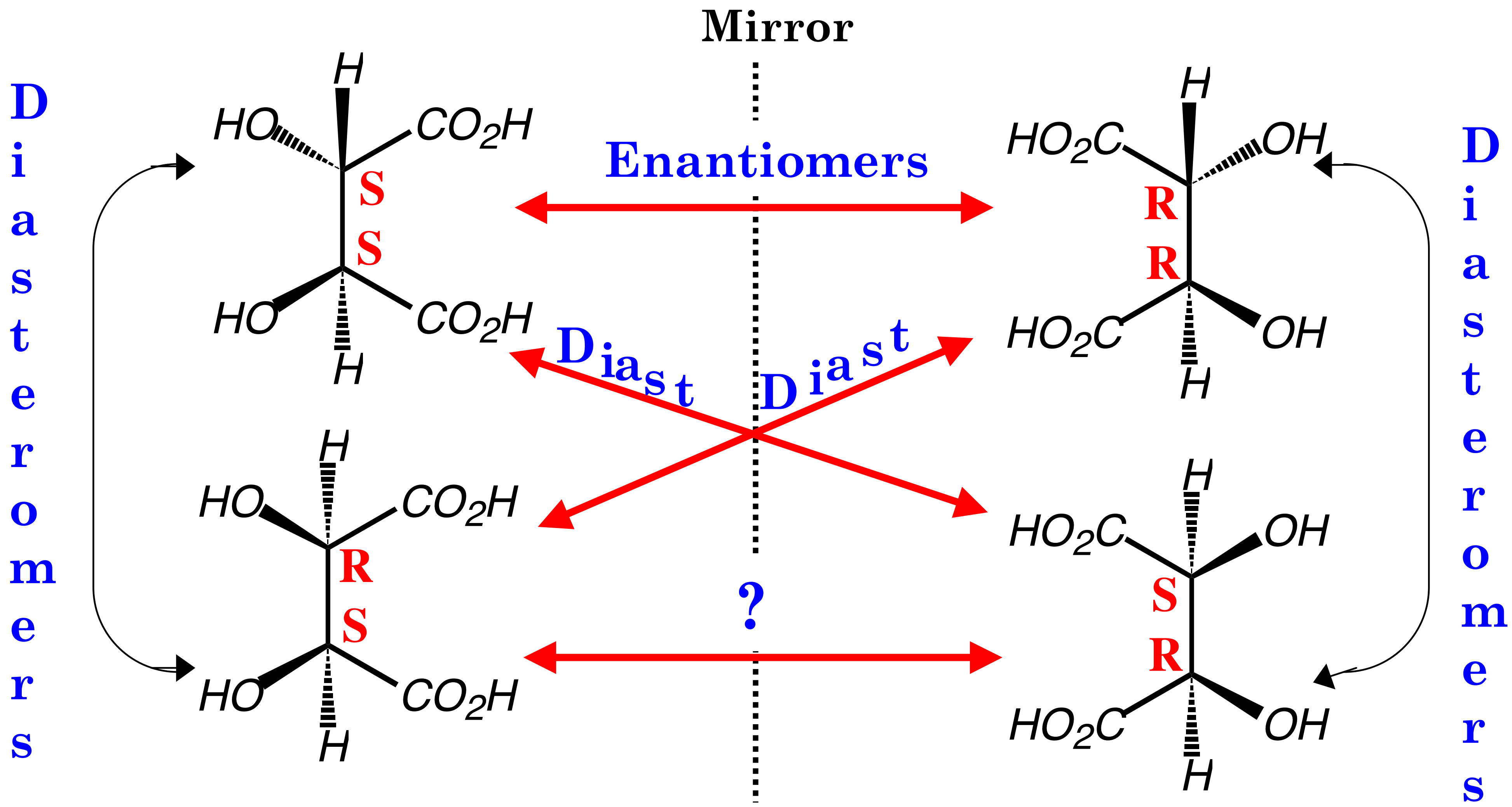
Molecules with 1 stereocenter can be R or S → **2 possible stereoisomers**

Molecules with *n* stereocenters can have all the possible combinations of R and S for each stereocenter → **2^n possible stereoisomers**

Tartaric Acid



2 stereocenters ➔ 4 possible stereoisomers

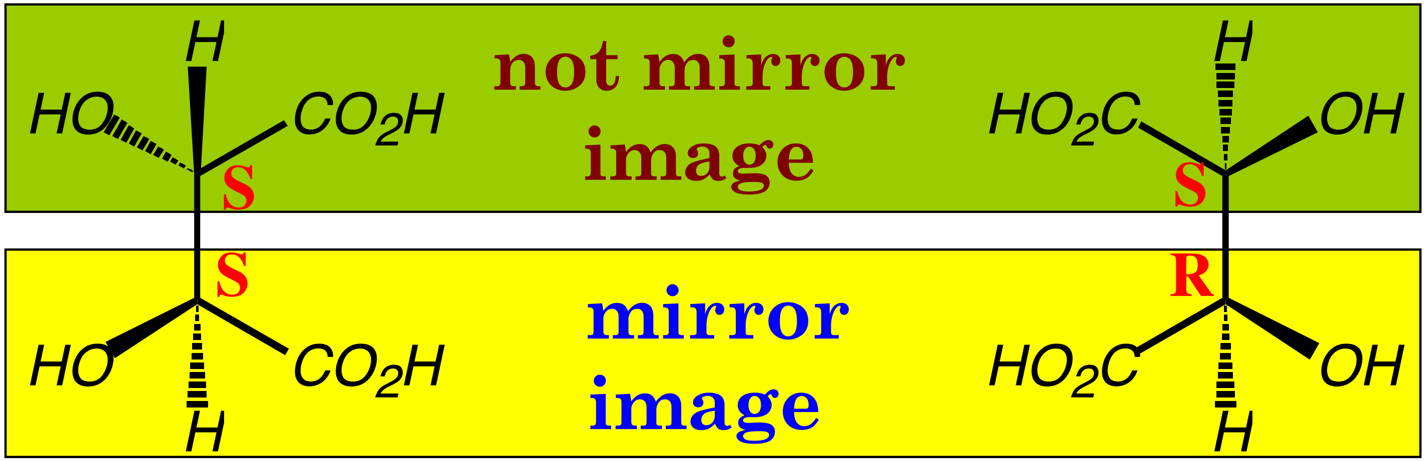


Remember

Enantiomers: stereoisomers that are non superposable mirror images.

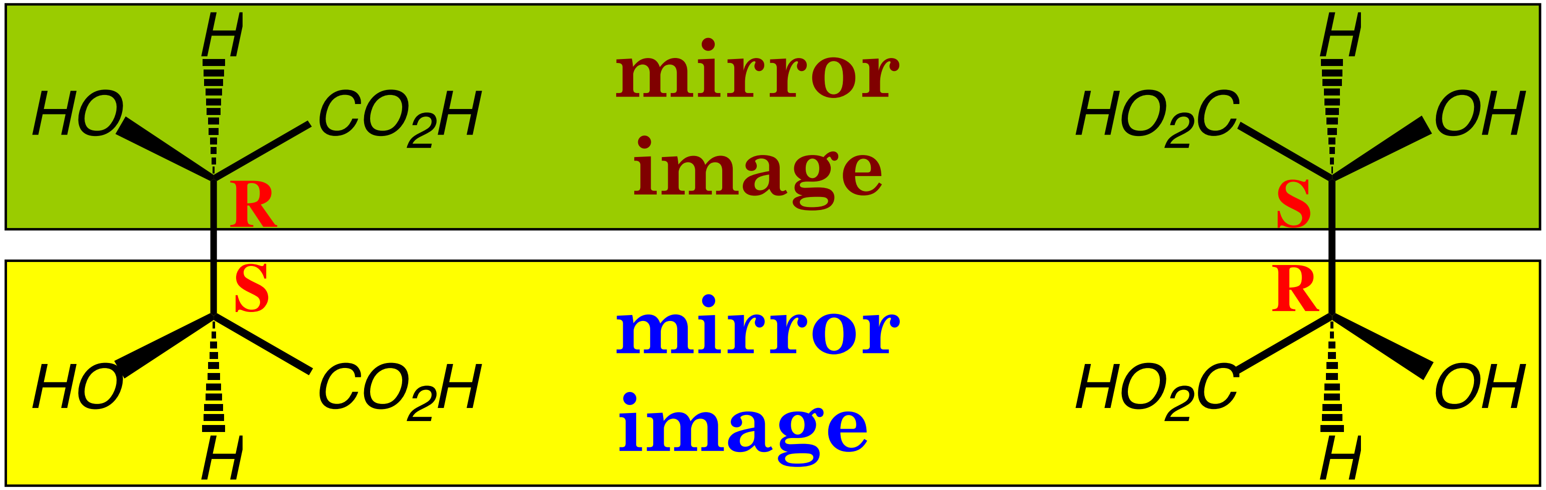
Diastereomers: stereoisomers that are not mirror images.

For example:



(S, S)-Tartaric acid **(S, R)-Tartaric acid**

DIASTEREOMERS

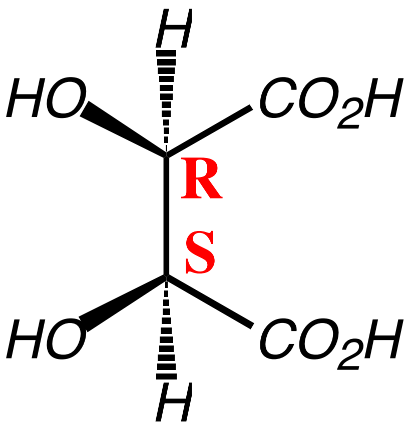


(R, S)-Tartaric acid **(S, R)-Tartaric acid**

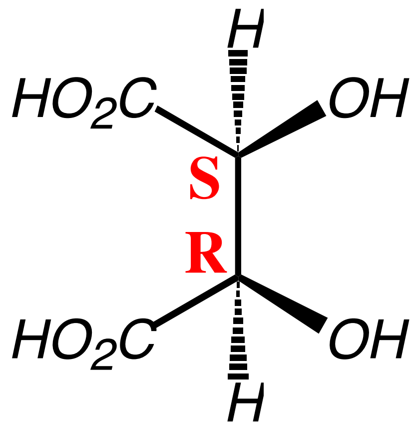
Enantiomers

?

Why not Enantiomers?



Same compound!!!!



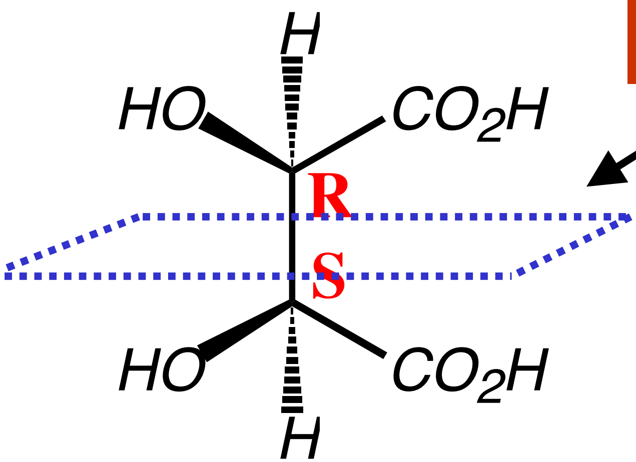
Enantiomers:

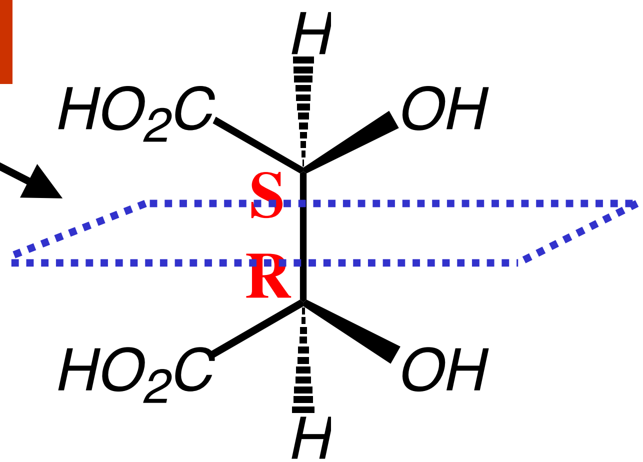
- √ **same molecular formula**
- √ **same connectivity**
- √ **mirror images**
- X **nonsuperposable** → **Superposable**

Achiral compound

Why not Enantiomers?

plane of symmetry





Same compound!!!!

Meso compound

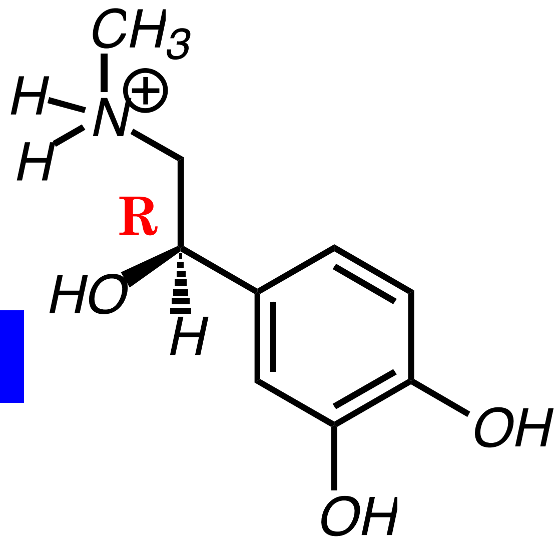
A compound with at least 2 stereocenters that is achiral due to the presence of a plane of symmetry

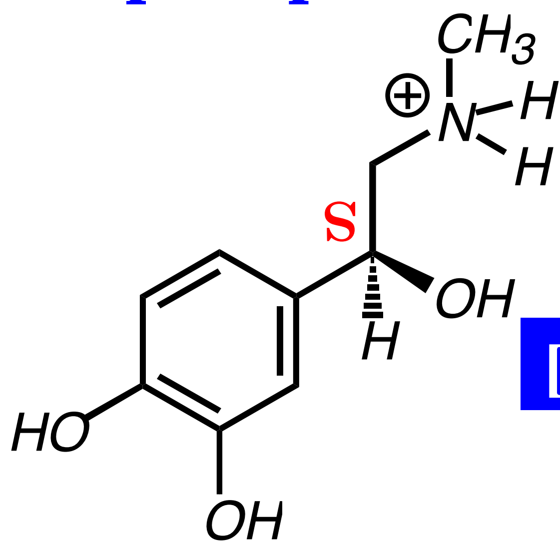
Properties of Stereoisomers

Enantiomers: have same chemical and physical properties in an achiral environment <u>but</u> they differ on the sign of rotation of plane polarized light.

For example: Enantiomers of Epinephrine (Adrenaline)

$[\alpha]_D = + 53.3^o$



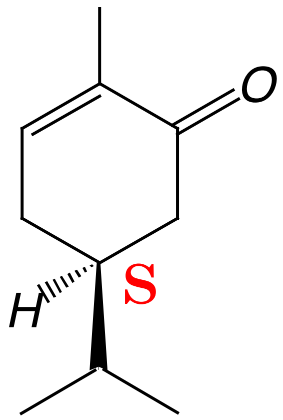


$[\alpha]_D = - 53.3^o$

Same melting/boiling point, same rate of reaction with achiral reagents, same degree of rotation of plane polarized light.........thus difficult to separate!

Properties of Stereoisomers

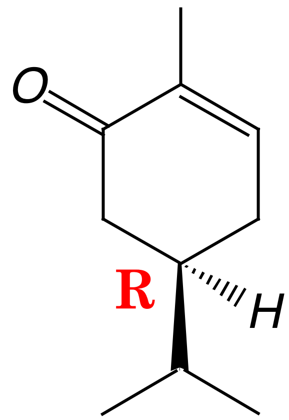
Carvone exists as a pair of enantiomers:



(+)-carvone

smells like caraway

$[\alpha]_D = + 62.5$



(-)-carvone

smells like spearmint

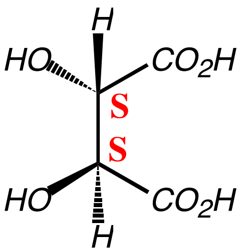
$[\alpha]_D = - 62.5$

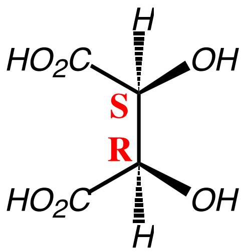
Note:

- **No relationship exists between the S/R configuration and the sign or the magnitude of rotation of plane polarized light.**
- **A 1:1 mixture of enantiomers (racemic mixture) has always no optical activity (rotation equal to zero) because the rotation of 50% of one enantiomer is cancelled out by the rotation (equal but opposite) of 50% of the other enantiomer.**

Properties of Stereoisomers

Diastereomers: have different chemical and physical properties in any type of environment.





	(S,S)-Tartaric Acid	Mesotartaric Acid
$[\alpha]_D$	- 12.7	0 (achiral)
Melting p. (^{o}C)	171-174	146-148
Density (g/cm^3)	1.7598	1.660
Solubility in H_2O	139	125

Biological Significance of Chirality

Since most of the natural (biological) environment consists of enantiomeric molecules (amino acids, nucleosides, carbohydrates and phospholipids are chiral molecules), then enantiomers will display different properties. Then, in our body: