Objective 7

Stereochemistry – identify chirality centers,
determine configuration (R/S),
identify enantiomers, diastereomers, and meso
compounds.

Stereochemistry is the Spatial Orientation of Atoms in a Molecule

Tetrahedral Carbon is responsible for stereochemistry

History:

http://web.fccj.org/~ethall/stereo/stereo.htm

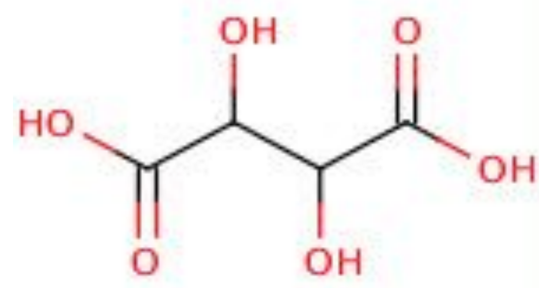
1815: Biot – optical activity

1848: Pasteur - optical activity of tartaric acid crystals in wine – mirror images

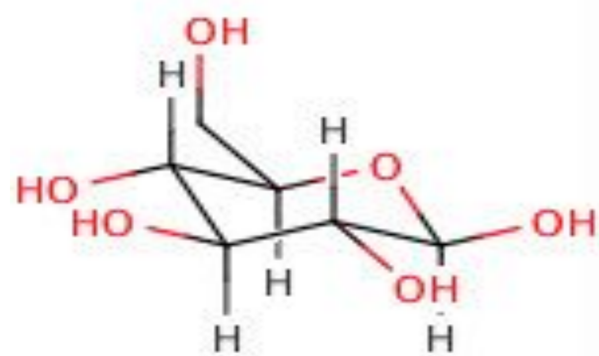
1874: LeBel and Van't Hoff – tetrahedral carbon

1894: Fisher – ID 16 stereoisomers of aldohexoses, including D-glucose

1915: John Steinbeck - sugar analysis in Spreckels Sugar Company



tartaric acid

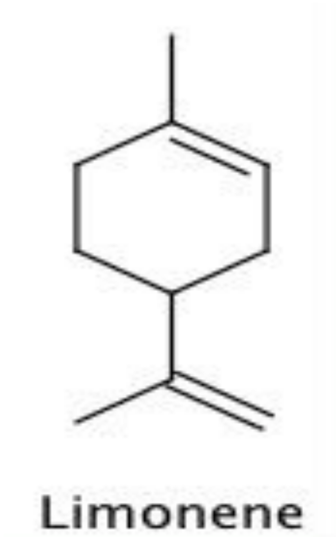


glucose

Stereoisomers May Have *Different* Properties

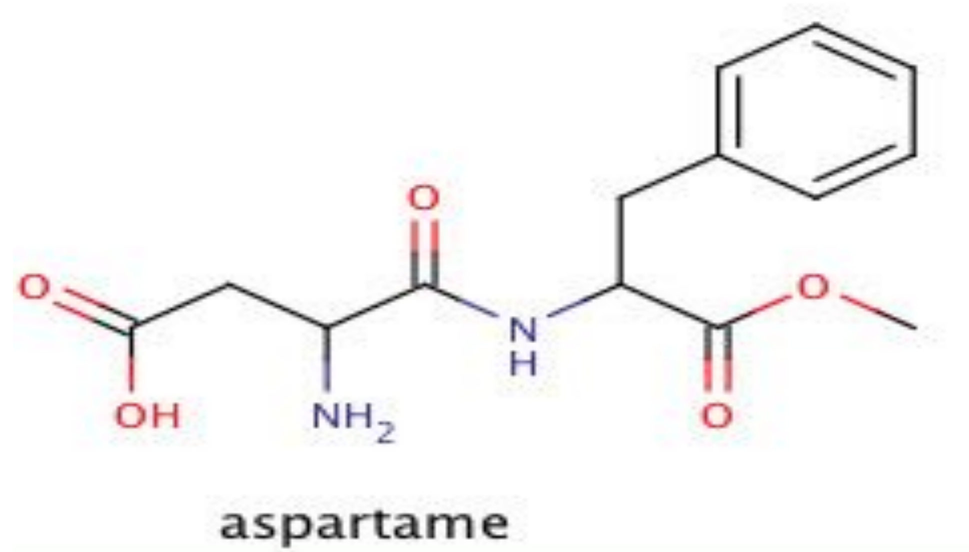
Yeast – one isomer undergoes fermentation; the other does not.

Amino acids – one isomer is predominant in nature

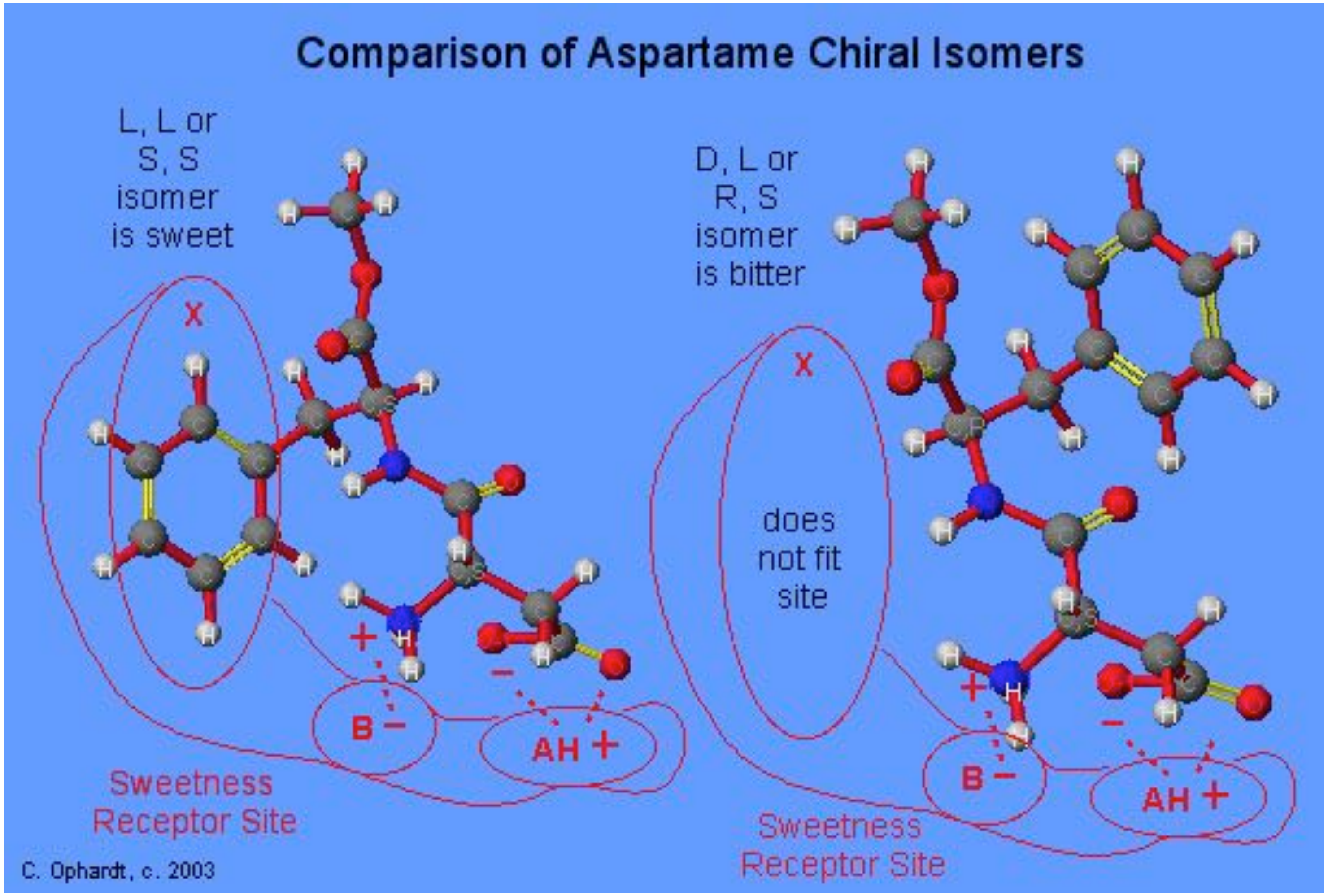


– one isomer gives lemons their flavor; the other isomer gives oranges their flavor

Aspartame – S isomer is sweet; R isomer is bitter



One Stereoisomer of Aspartame fits into the Sweetness Receptor Site; the others do not.

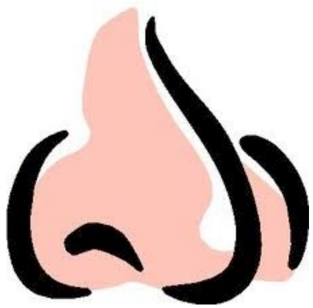


three-point attachment theory (AH-B-X)

http://www.elmhurst.edu/~chm/vchembook/549receptor.html

The Nose is capable is distinguishing between stereoisomers

thedailyblarg.com



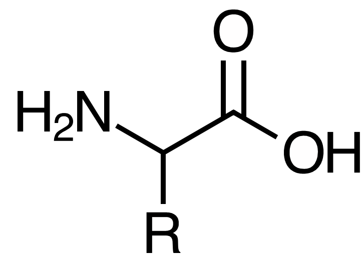
piperbasenji.blogspot.com

Receptor sites for sense of smell are *chiral*

In general, stereoisomers do not interact identically with other chiral molecules.

Many Biologically Active Molecules Are Chiral

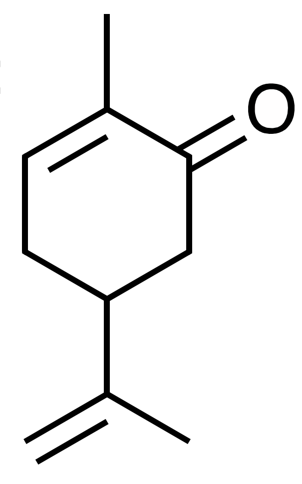
E.g., most amino acids are L
Most sugars are D



Enzymes distinguish between two enantiomers of a chiral substrate

D amino acids tend to taste sweet; L amino acids are usually tasteless.

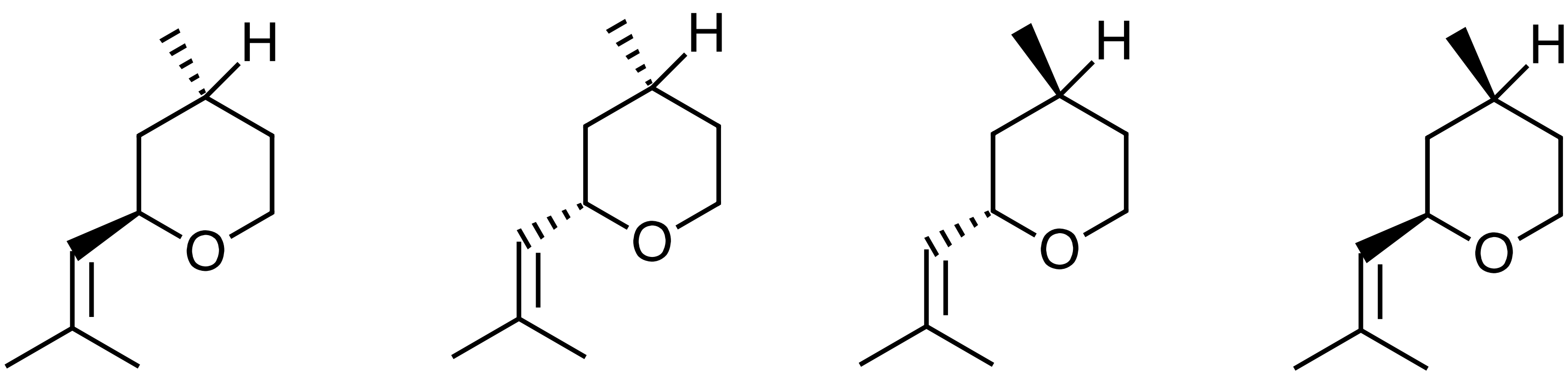
Olfactory (smell) receptors contain chiral molecules:
Spearmint leaves contain R-(-)-carvone
Caraway seeds contain S-(+)-carvone



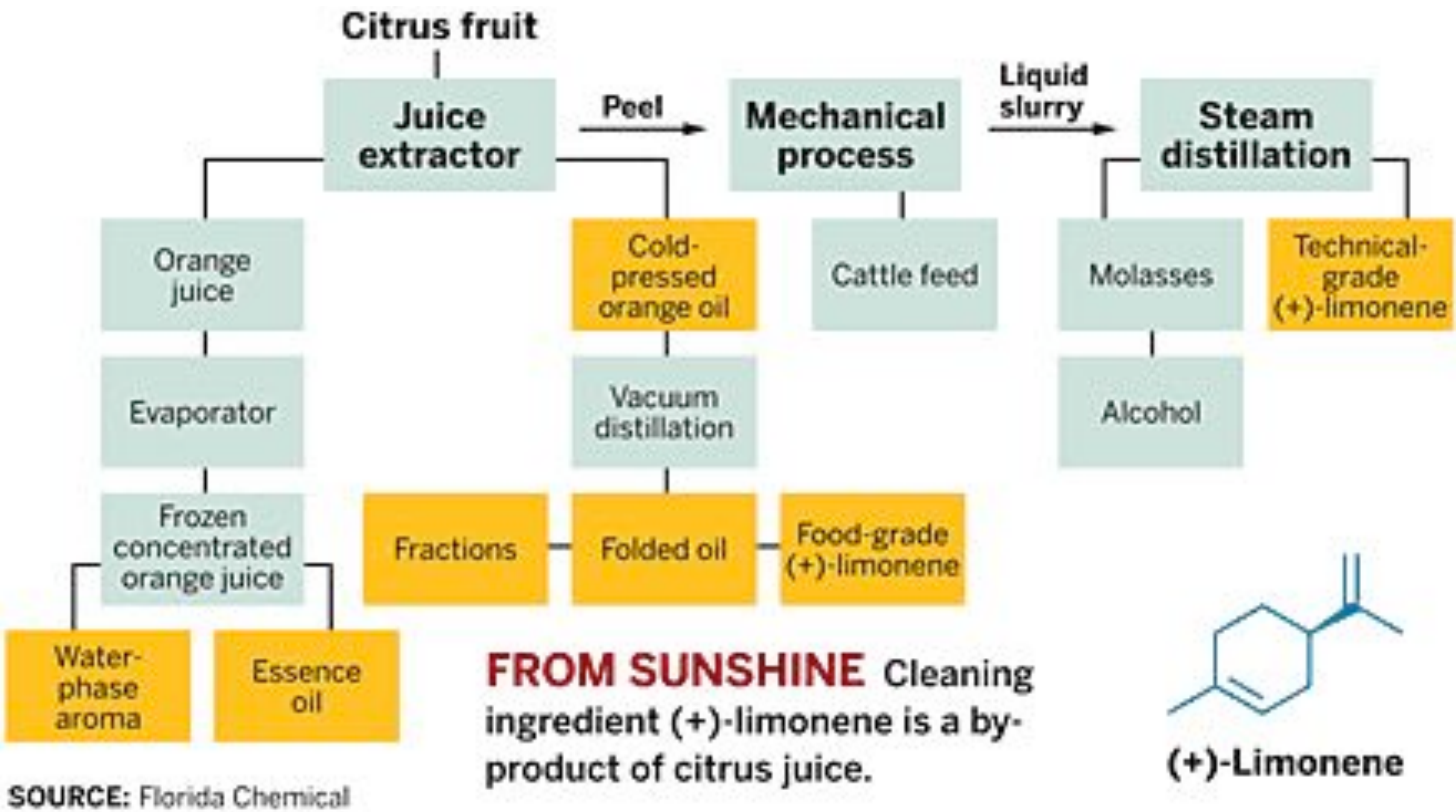
“Why Do Roses Smell So Sweet?”

(https://www.youtube.com/watch?v=dQyQns4i5hI)

Rose oxide has 4 stereoisomers ➔ 4 different smells



CEN, 4/4/11, p. 21. Limonene (from lemons) is used to make many citrus –based cleaning products:

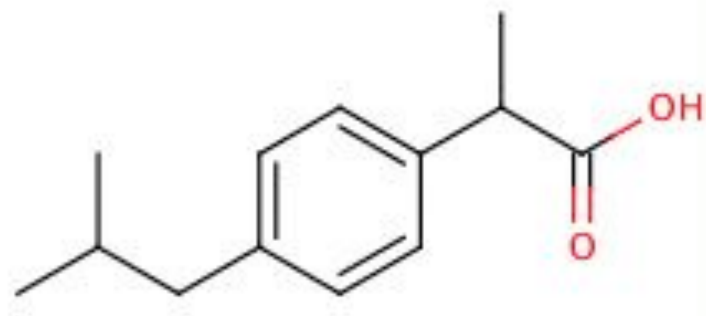


Lab: *Microwave Extraction* of Limonene

Bring Lemons or Oranges

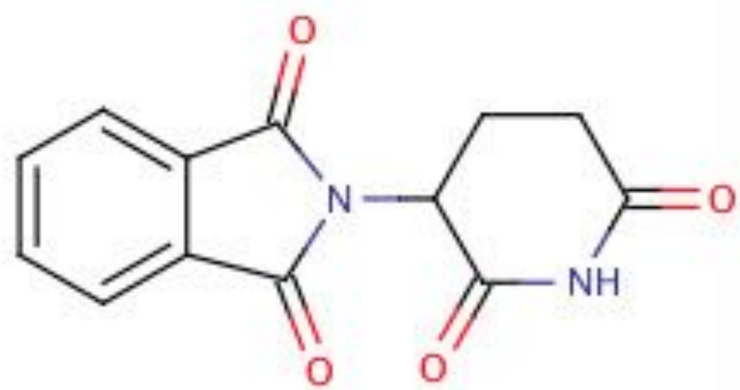
Stereoisomers Are Used in Drugs

Ibuprofen – S isomer works;
R isomer does not.



Ibuprofen

Thalidomide – one isomer is a sedative; the other causes birth defects
http://en.wikipedia.org/wiki/Stereochemistry

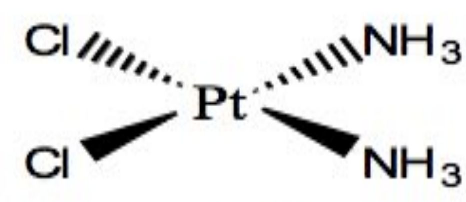


Thalidomide

cis/trans (E/Z) isomers are geometric isomers

Unsaturated fats are cis or trans

Cis-platin – cancer drug
What is the structure of trans-platin?



cis-Platin

Introduction to Stereochemistry

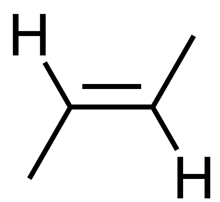
http://www.colby.edu/chemistry/OChem/DEMOS/Chirality.html

Stereoisomers are *different* from structural (constitutional) isomers.

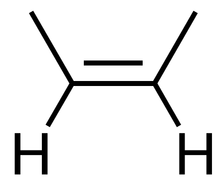
Structural Isomers have **different connectivty**

Stereoisomers Isomers have **different orientation in space**

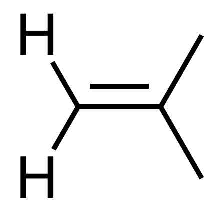
Which compounds are structural isomers?
Which compounds are stereoisomers?



A



B



C

- Stereoisomers are classified as ***enantiomers*** and ***diastereomers***.

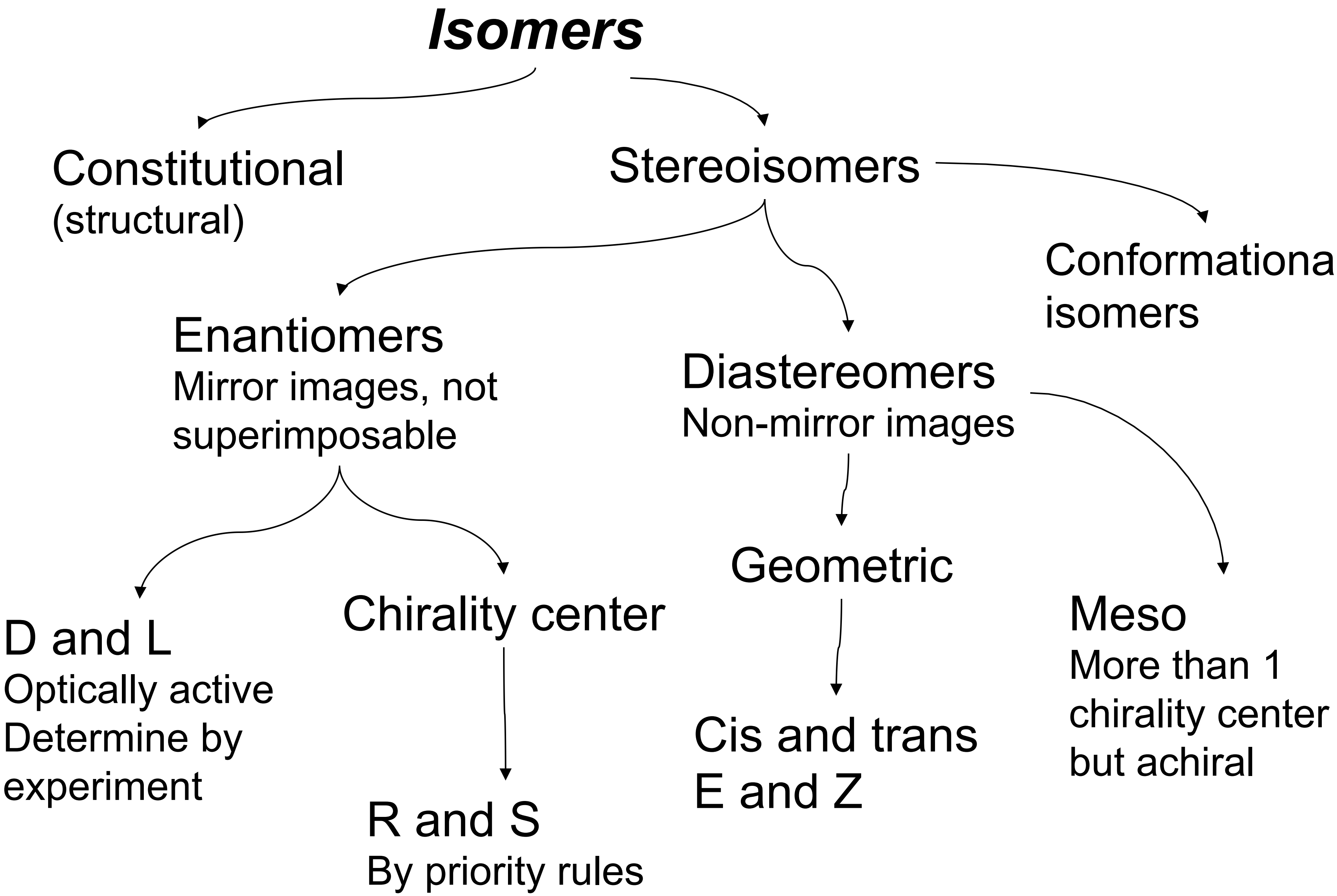
- **Enantiomers** are stereoisomers that are **mirror images** of each other and are **not superimposable** on each other.

- Diastereomers are stereoisomers that are **not** mirror images of each other. Example: cis and trans isomers

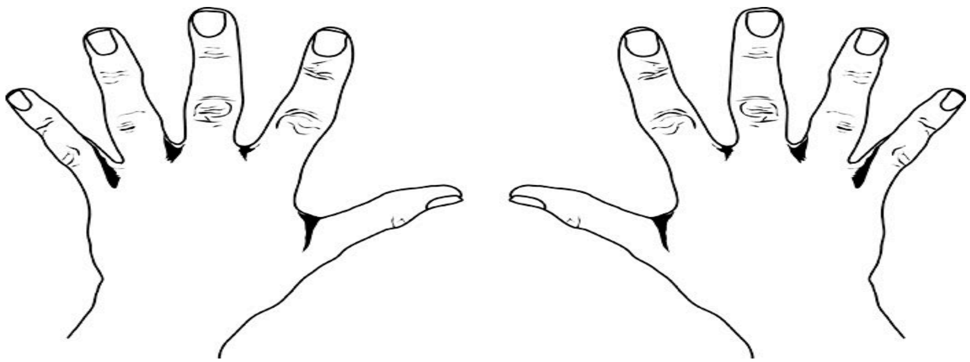
- Enantiomers have a ***chirality center***. A chirality center has four different atoms or groups bonded to it.

- If a molecule has a **plane of symmetry** or center of symmetry, then it is **achiral**.

- ***Optically active*** compounds are enantiomers that rotate a plane of polarized light


Isomers
Constitutional
(structural)
Stereoisomers
Conformational
isomers
Enantiomers
Mirror images, not
superimposable
Diastereomers
Non-mirror images
D and L
Optically active
Determine by
experiment
Chirality center
R and S
By priority rules
Geometric
Cis and trans
E and Z
Meso
More than 1
chirality center
but achiral

1. Are your two hands enantiomers or diastereomers or the same?



2. Determine whether each object is chiral. <u>Hint</u>: check for a plane of symmetry or center of symmetry.

Enantiomers have a ***<u>chirality center</u>***.

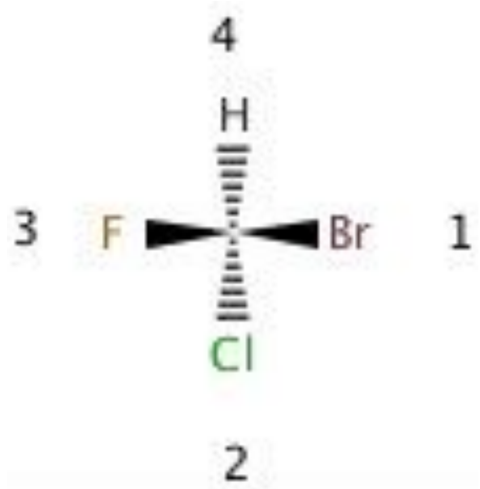
A chirality center has ***four different atoms or groups*** bonded to it.

The **<u>configuration</u>** at a chirality center is **R** or **S**.

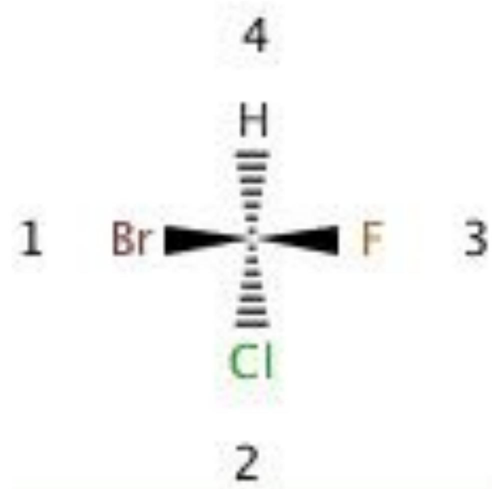
Priority rules to rank atoms/groups are based on **atomic weight**.

Point <u>lowest</u> priority group <u>away</u> from you.

1 --> 2 --> 3: **CW = R** **CCW = S**

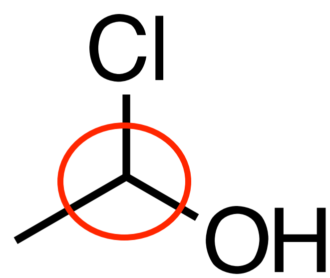


R



S

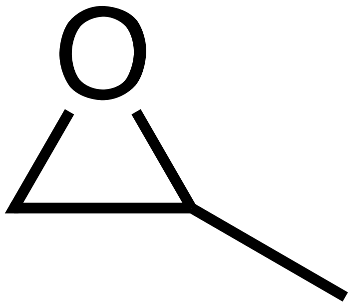
Objective: Identify the chirality center.
Determine the configuration (R or S) at each chirality center.



Carbon has 4 different atoms or groups bonded to it:
$-CH_3$, -Cl, -OH, -H

Priority: 1. −Cl, 2. -OH, 3. $-CH_3$, 4. −H
Lowest priority group points away from you.
Cl → OH → CH_3 Clockwise therefore R

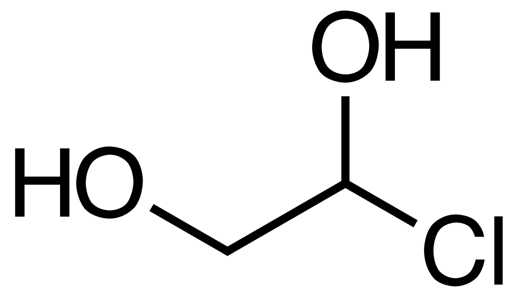
Astronomers find FIRST chiral molecule in space (C&EN, 6/20/16, p. 4)



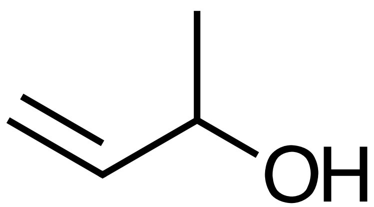
Propylene oxide (astronomers could not ID enantiomer)
Which atom is the chirality center?
Using wedges and dashes, draw the two enantiomers.

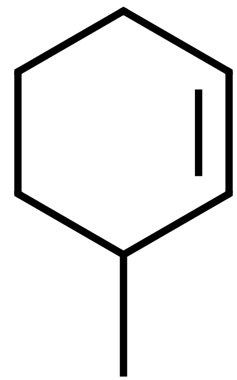
All Earth organisms have proteins built almost entirely on left-handed enantiomers of amino acids.
Discovery of propylene oxide may lead to understanding of chemical processes that led to the preference of one enantiomer over another in the formation of biomolecules on Earth.

Objective: Identify the chirality center.
Determine the configuration (R or S) at each chirality center.

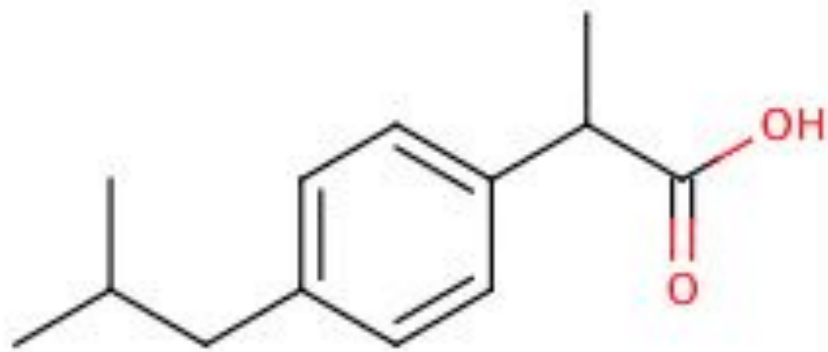


Objective: For each compound, identify the chirality center. Determine the configuration (R or S) at each chirality center.



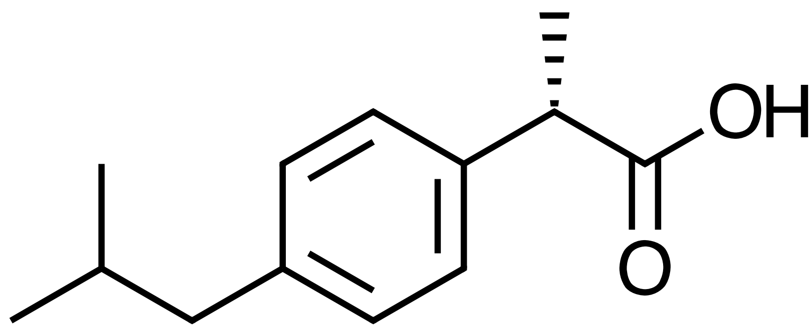


Ibuprofen is an OTC analgesic. It has one chirality center.
Mark the chirality center with a *.



Ibuprofen

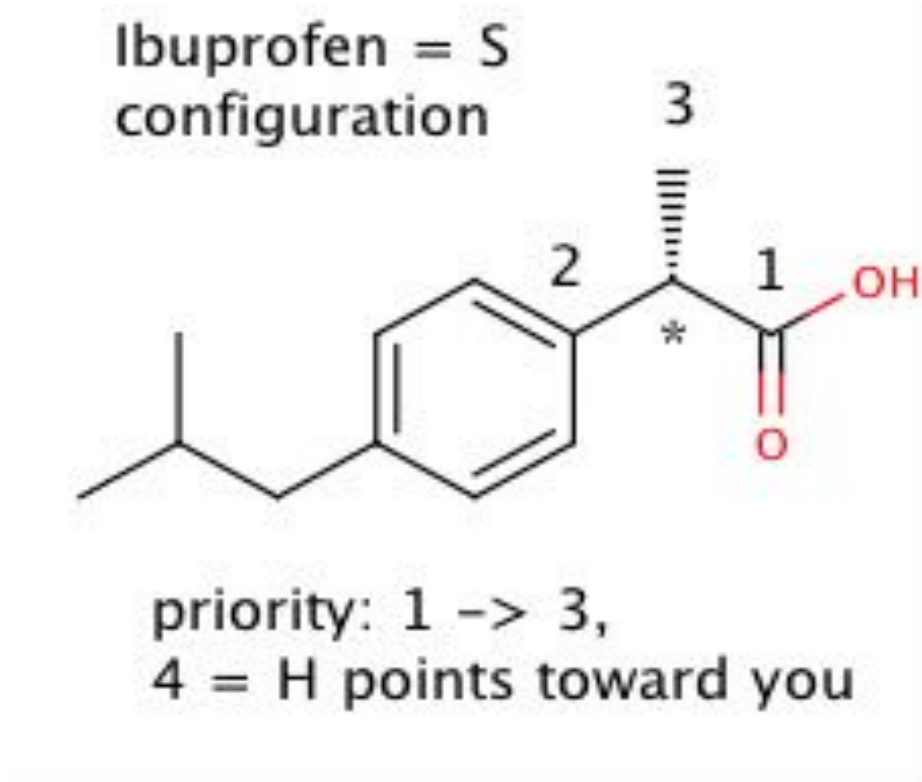
Ibuprofen is an OTC analgesic. It has one chirality center.
Mark the chirality center with a *.
Determine the configuration (R or S).



Ibuprofen

Hint: Which direction is the H pointing?

Ibuprofen is an OTC analgesic.



Draw the Fischer projection of Ibuprofen.

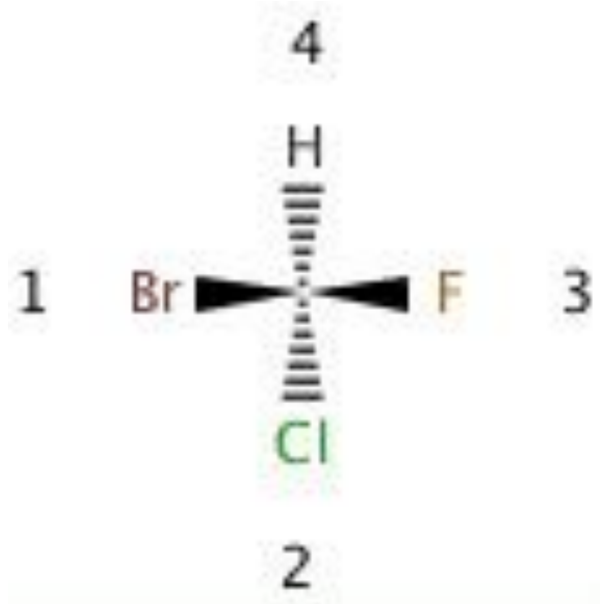
Fischer Projection

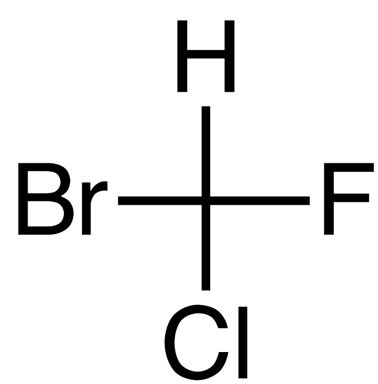
Horizontal lines: wedges

(point toward you)

Vertical lines: dashes

(point away from you)



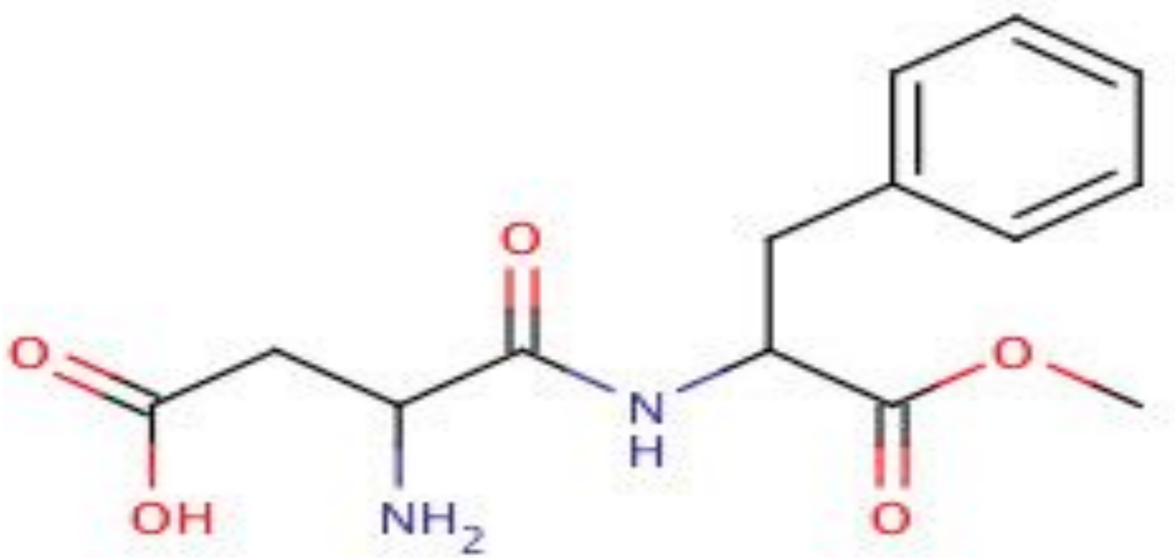


Fischer projection is a shortcut to using wedges and dashes.

Aspartame (*NutraSweet*) is an artificial sweetener

(180x sweeter than sucrose)

ID the chirality center(s).



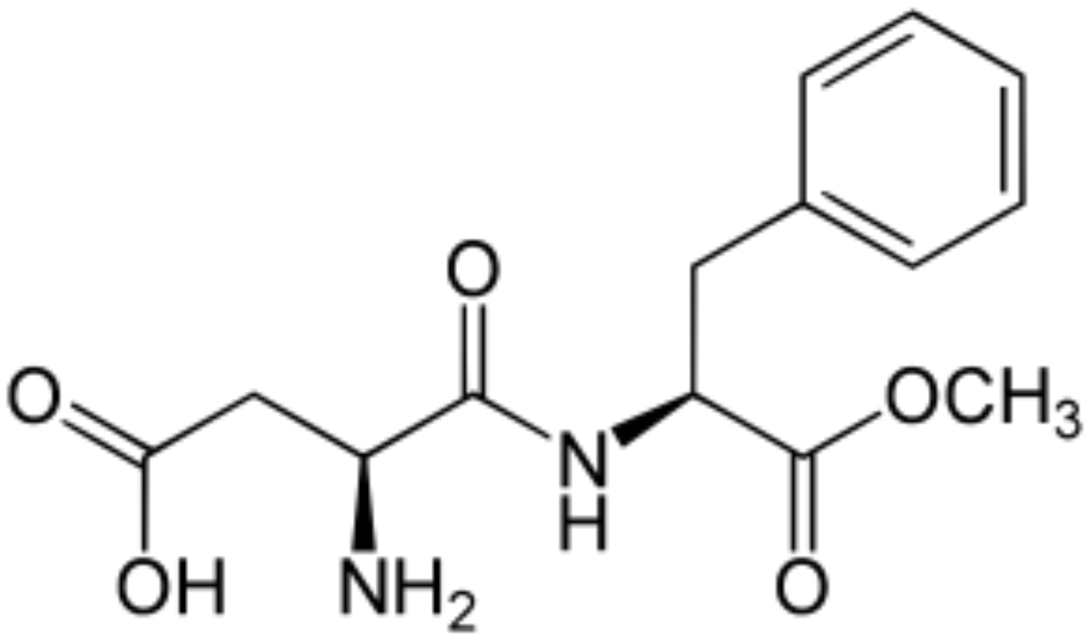
aspartame

Aspartame (*NutraSweet*) is an artificial sweetener

(180x sweeter than sucrose)

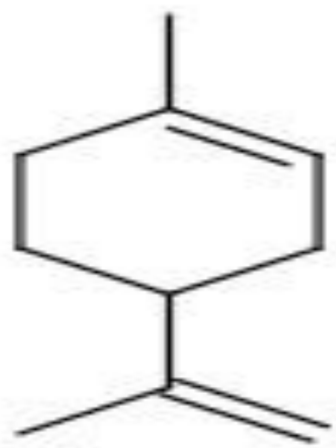
Determine the configuration at each chirality center.

Draw the Fischer projection.



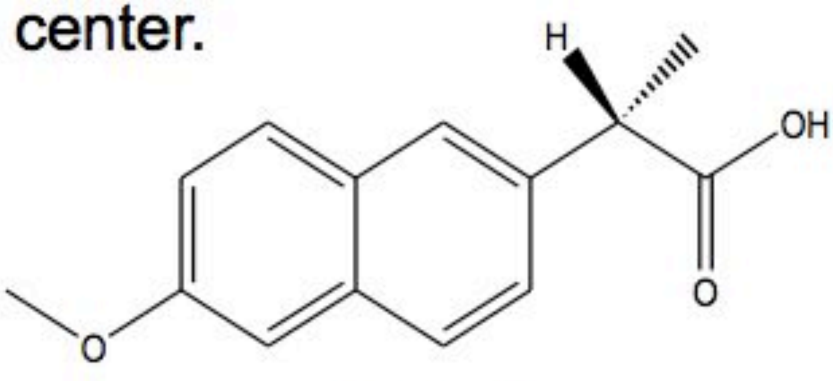
https://en.wikipedia.org/wiki/Aspartame

D-Limonene has an orange smell and is the R enantiomer.
ID the chirality center.
Draw the R isomer.
Draw the Fischer projection.

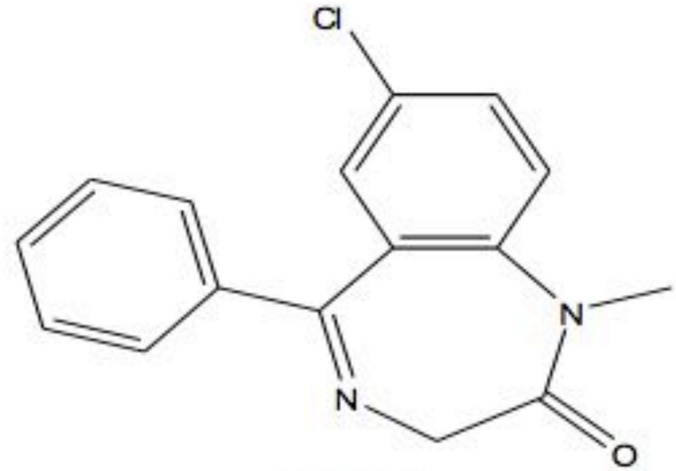


Limonene

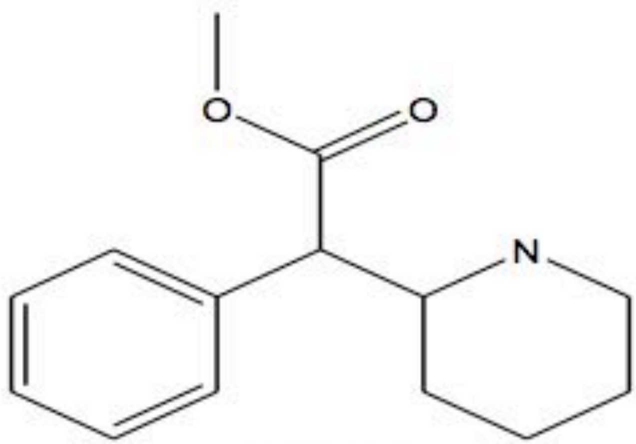
Which compounds are chiral? If chiral, identify the chirality center(s). Determine the configuration (R/S) at each chirality center.



Naproxen



Valium



Ritalin

CEN, 9/21/98, “Counting on Chiral Drugs”. Celgene develops single-isomer Ritalin.

Some Compounds Have More Than 1 Chirality Center

***2^n rule** - **compound with n chiral C can have a max of 2^n stereoisomers**.*

Chiral: no plane of symmetry.

- 0 chirality centers: usually achiral. (Find a plane of symmetry.)
- 1 chirality center: chiral ==> enantiomers
- 2 chirality centers: depends.

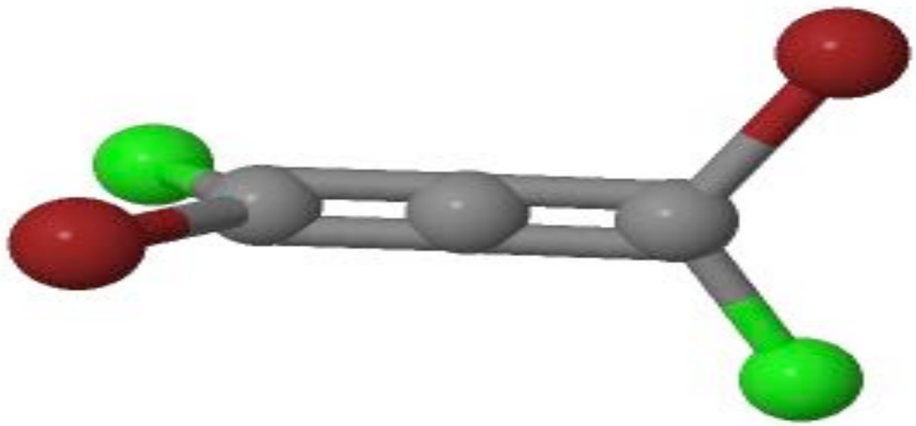
If mirror images are superimposable ==> same.
If mirror images are not superimposable ==> enantiomers and determine R/S at each chirality center.
Non-mirror images ==> Diastereomers
Meso compounds - achiral compound that contains chiral C.
Why achiral? Contains a plane of symmetry.

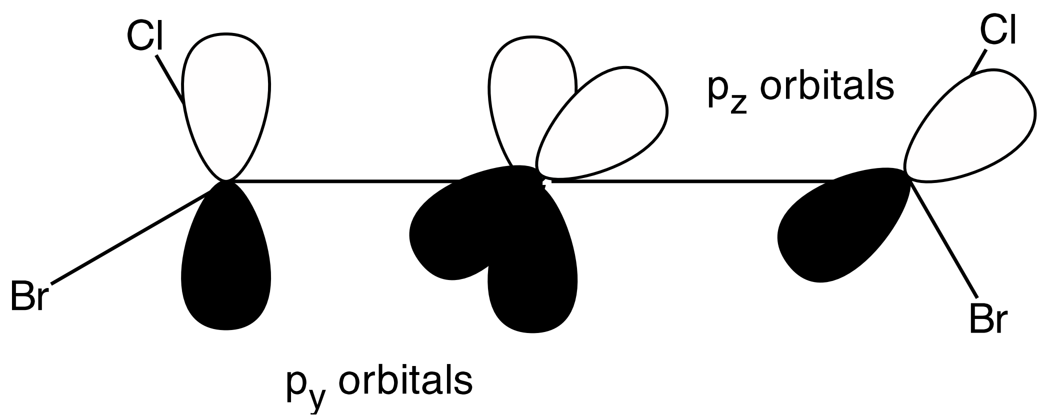
Practice Makes Perfect!

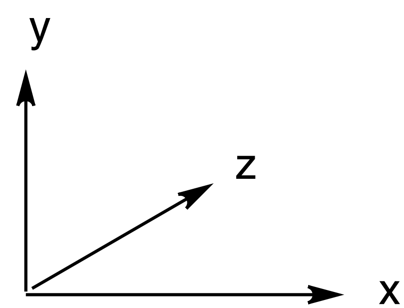
a. CH_2Cl_2 and CH_2ClBr. Find the plane of symmetry.

b. Is BrClC=C=CBrCl chiral?

C=C bond involves a σbond and π bond





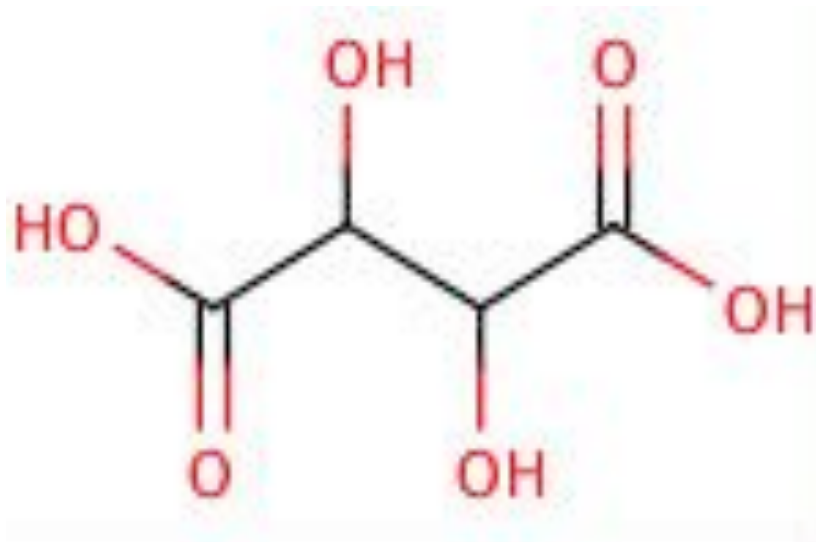


C1-C2 σbond involves sp^2 hybrid orbitals (s + p_x + p_z)
C1-C2 π bond involves p_y orbitals

C2-C3 σbond involves sp^2 hybrid orbitals (s + p__ + p__)
C2-C3 π bond involves p__ orbitals

Practice Makes Perfect!

Tartaric acid has more than 1 chirality center.
ID the chirality centers.
Determine the number of stereoisomers. Which isomers are enantiomers? Which are diastereomers?
Is there a meso compound?
Draw the Fisher projection of each isomer.

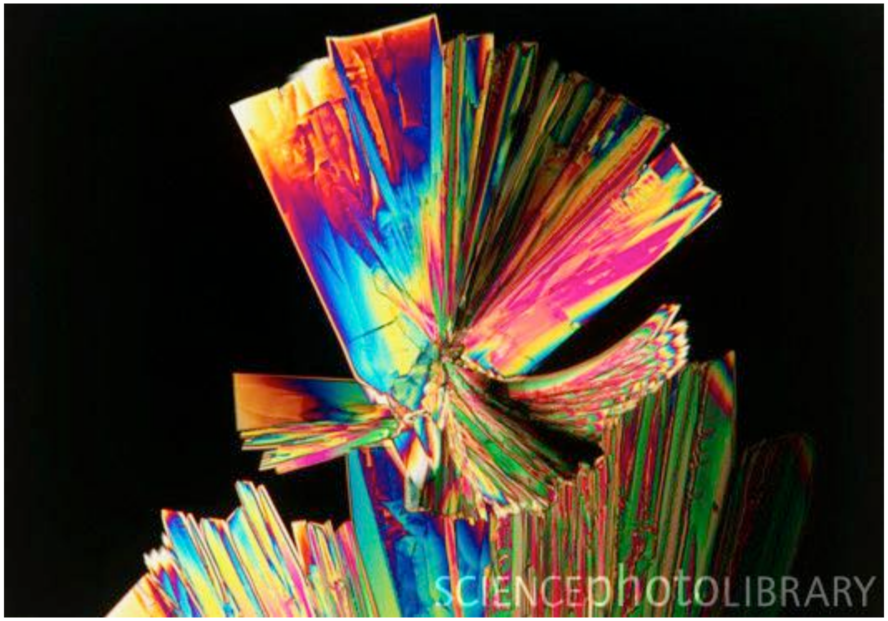


http://winesworld.com/wine-crystals/68/

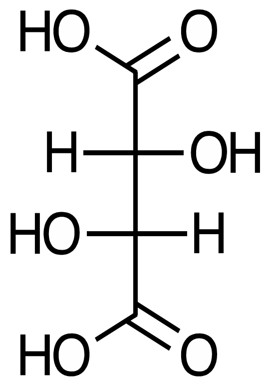
Wine crystals (“wine diamonds”) are indicative of good quality.

http://www.sciencephoto.com/media/5942/enlarge

Polarized light micrograph of tartaric acid crytals

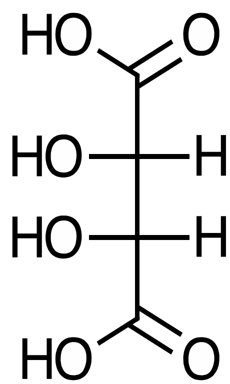


Tartaric acid has _______ stereoisomers. *(Apply 2^n rule)*



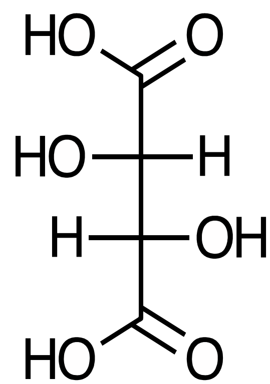
A

R, R
Naturally occurring



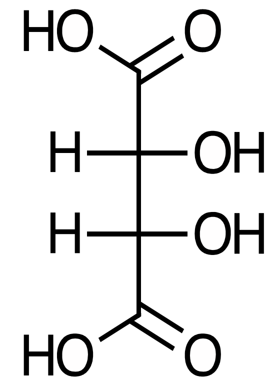
B

S, R



C

S, S

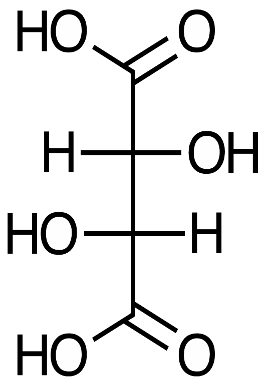


D

R, S

Which isomers are Enantiomers?
Which isomers are Diastereomers?
Is there a Meso compound?

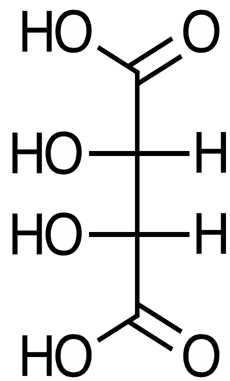
Tartaric acid has 4 stereoisomers. *(Apply 2^n rule)*



A

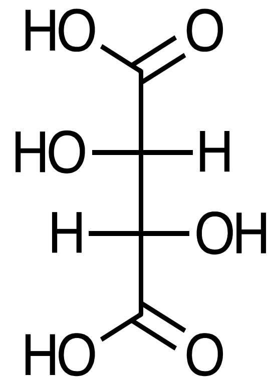
R, R

Naturally occurring



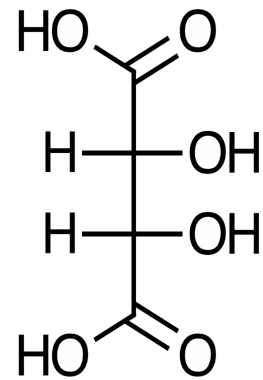
B

S, R



C

S, S



D

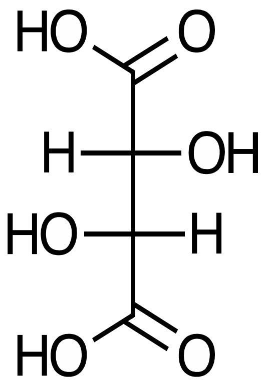
R, S

Enantiomers = A and C

Meso compound = B and D

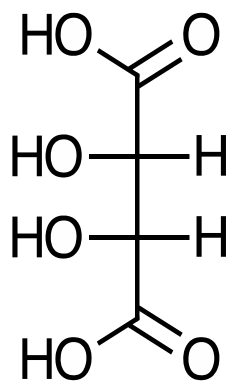
which means B and D are _____.

Tartaric acid has 3 stereoisomers. (B and D are the same - **Meso**)



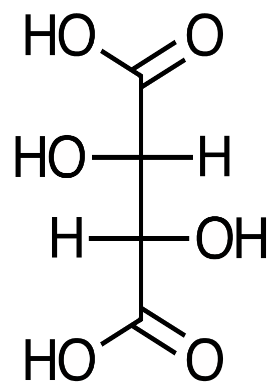
A

R, R
Naturally occurring



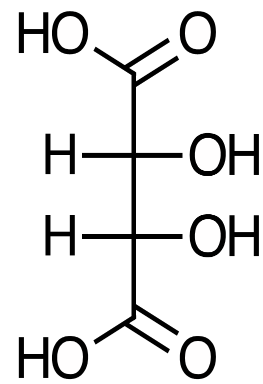
B

S, R



C

S, S

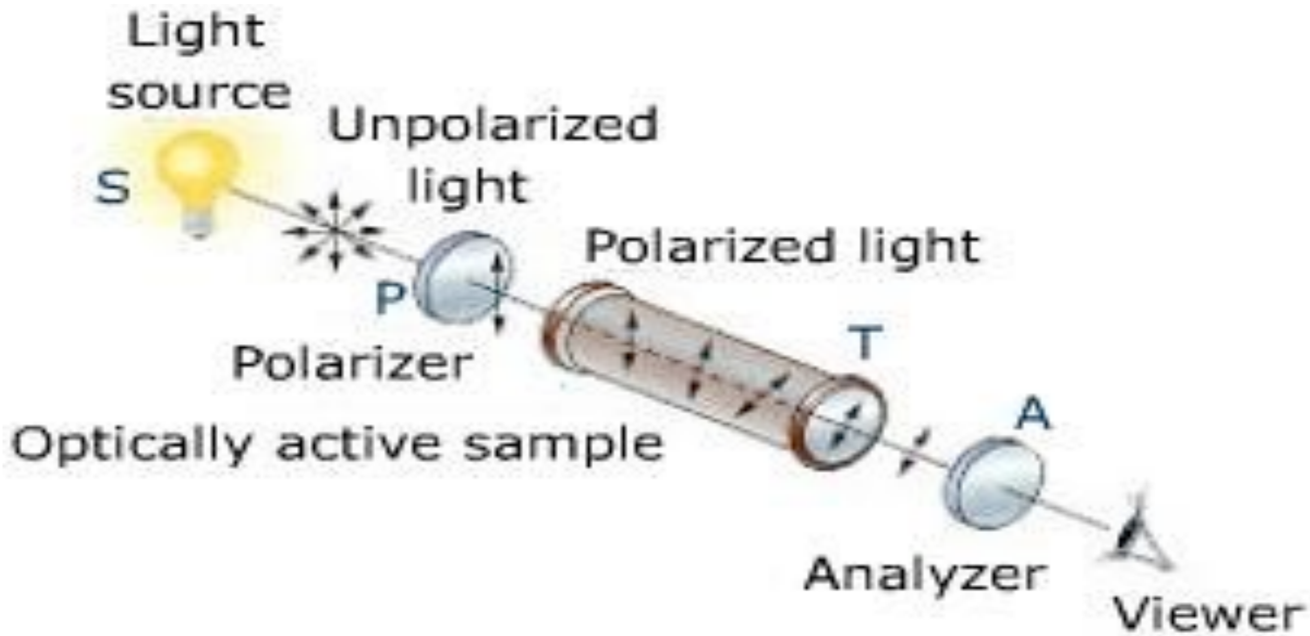


D

R, S

Change an acid group on B and D to a methyl group.
Do you still have a meso compound? If not, what type of isomer?

Optical Activity is the ability of a substance to rotate the plane of polarized light.



http://chemwiki.ucdavis.edu/Organic_Chemistry/Chirality/Optical_Activity

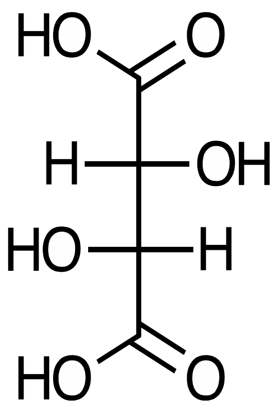
Specific Rotation = [α]
Std C = 1 g/ml and ℓ = 1 dm

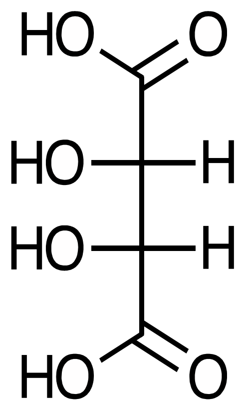
CW rotation = (+) or D
CCW rotation = (-) or L

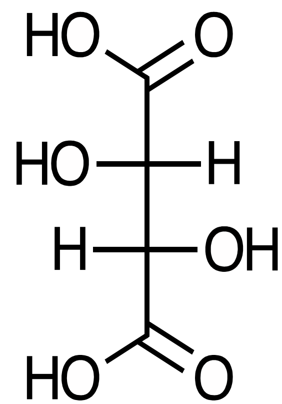
Non std conditions: $[\alpha] = \dfrac{\alpha}{c \times \ell}$

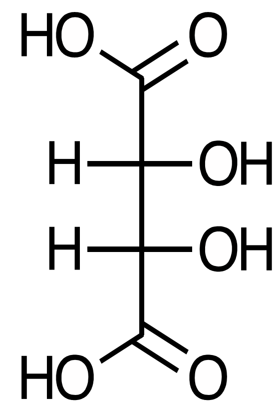
What type of substance is optically active?

Tartaric Acid is optically active. It has **3** stereoisomers.
Naturally occurring (R, R)-tartaric acid [α] = +12.4^{o}.


A
R, R
Naturally occurring

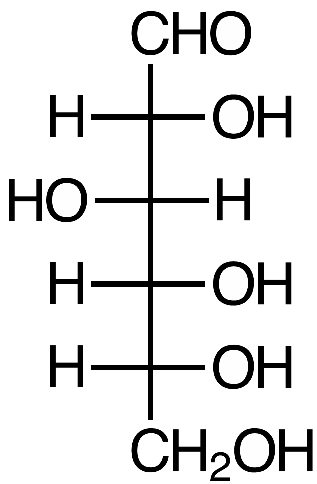

B
S, R


C
S, S

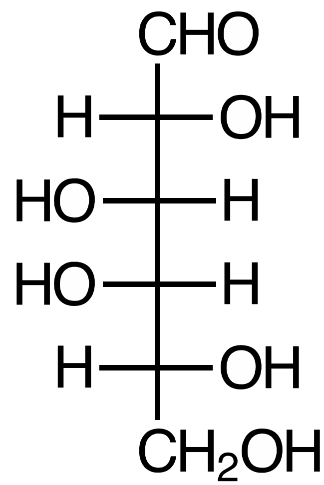

D
R, S

What is [α] of (S, S)-tartaric acid?
What is [α] of (2R, 3S)-tartaric acid?
What is [α] of a 50% (R, R):50% (S, S) mixture of tartaric acid?
What is this type of mixture called?

Glucose and Galactose are 2 examples of Aldohexoses



D-glucose



D-galacose

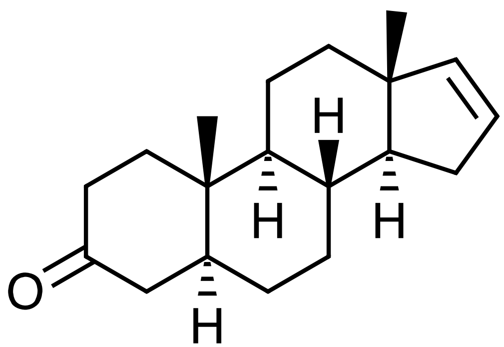
How many aldohexose stereoisomers are there?

Draw an enantiomer of D-gluose.
Draw a diastereomer of D-galactose.

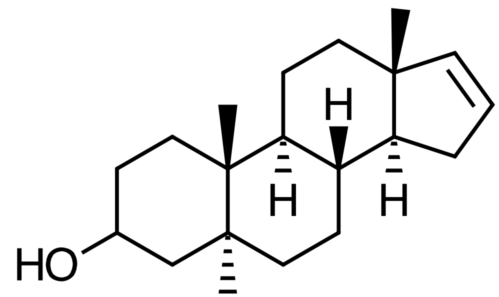
Do Human Pheromones Exist?

(https://www.youtube.com/watch?v=_aoWR1ZDUQc)

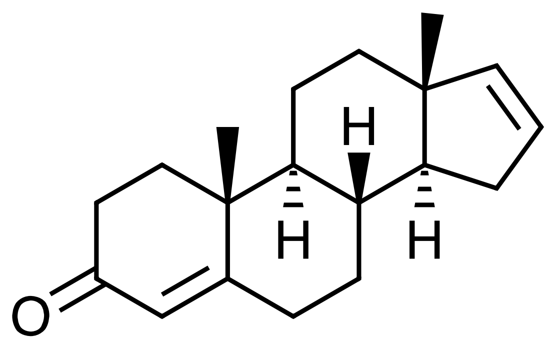
How many stereoisomers?



Androstenone



Androstenol



Anddrostadienone

Stereochemistry has its own Vocabulary

Optical purity - chiral compound in which only ***one*** enantiomer is present.

Enantiomeric excess (ee) - difference between % of major enantiomer present in a mixture and % of minor enantiomer. Optically pure = 100% ee, Racemic mixture = 0% ee.

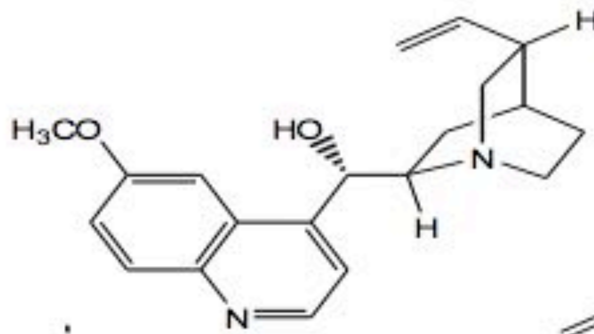
Resolution - separation of racemic mixture into its enantiomers.

Erytho and threo - Molecule with 2 or more chirality centers:
Erythro: like substituents are on the same side of a Fischer projection.
Threo: like substituents are on opposite sides of a Fischer projection.

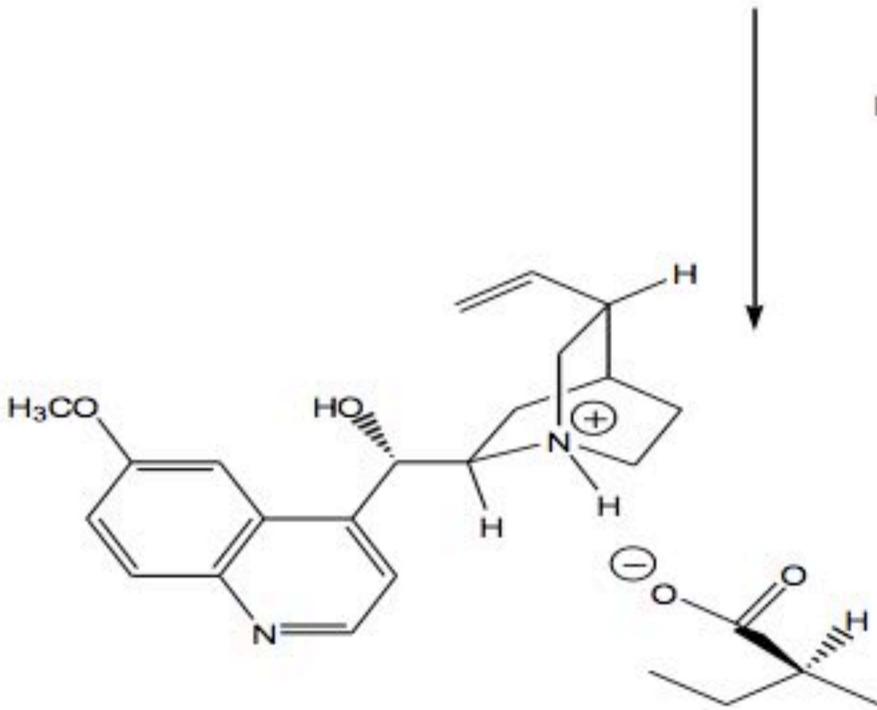
Stereospecific reaction - reaction in which stereoisomeric reactants give stereoisomeric products. E.g., S_N2
Stereoselective reaction - single reactant can form two or more stereoisomers, with one major product (syn, anti, inversion of configuration)

Resolution Using _____ Salts

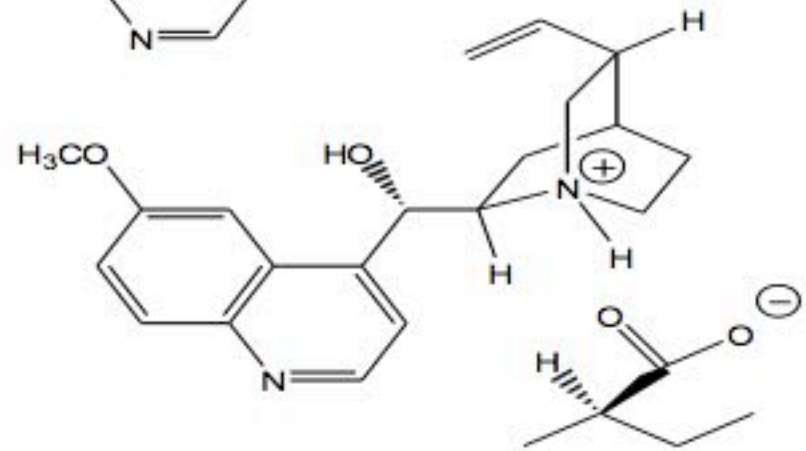
enantiomers



Quinine



(1)



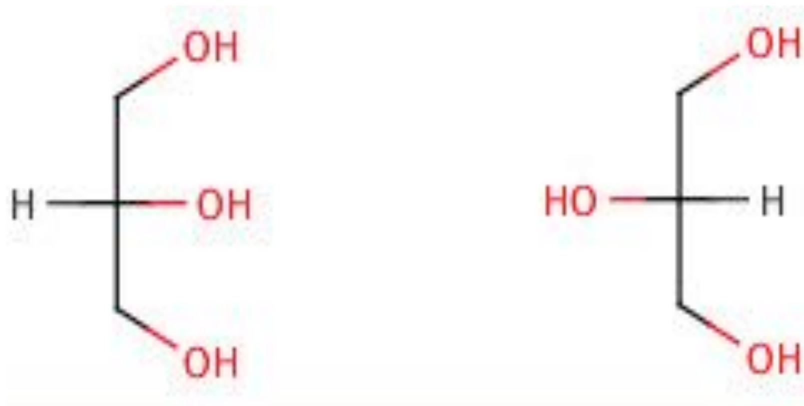
(2)

What type of stereoisomers are (1) and (2)?

Reference: I.D. Reingold,"Organic Chemistry: An Introduction Emphasizing Biological Connections", 2002, p. 427

Identify the relationship in each of the following pairs. Do the drawings represent constitutional isomers or stereoisomers, or they just different ways of drawing the same compound? If they are stereoisomers, are they enantiomers or diastereomers?

a.



b.