Chirality
Lecture Outline
Chem 306
Roper

I. Overview

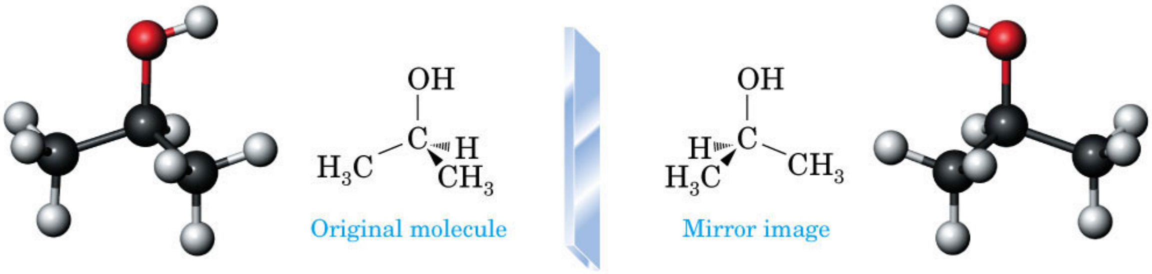
II. Chirality

A. Some objects are chiral or “handed”.

B. Some molecules are chiral.

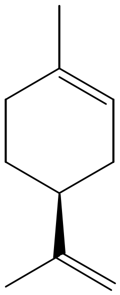
How do we know if a molecule is chiral?

1. Chiral molecules have non-superimposable (non-superposable) mirror images.

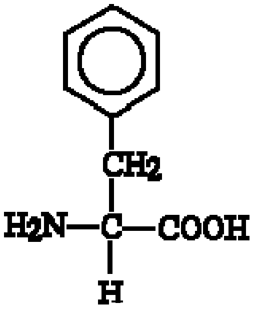


2. Most chiral molecules contain tetrahedral carbons with 4 different groups bonded to it (a stereocenter).

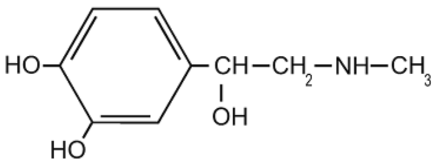
Where are the stereocenters in the molecules below?



Limonene



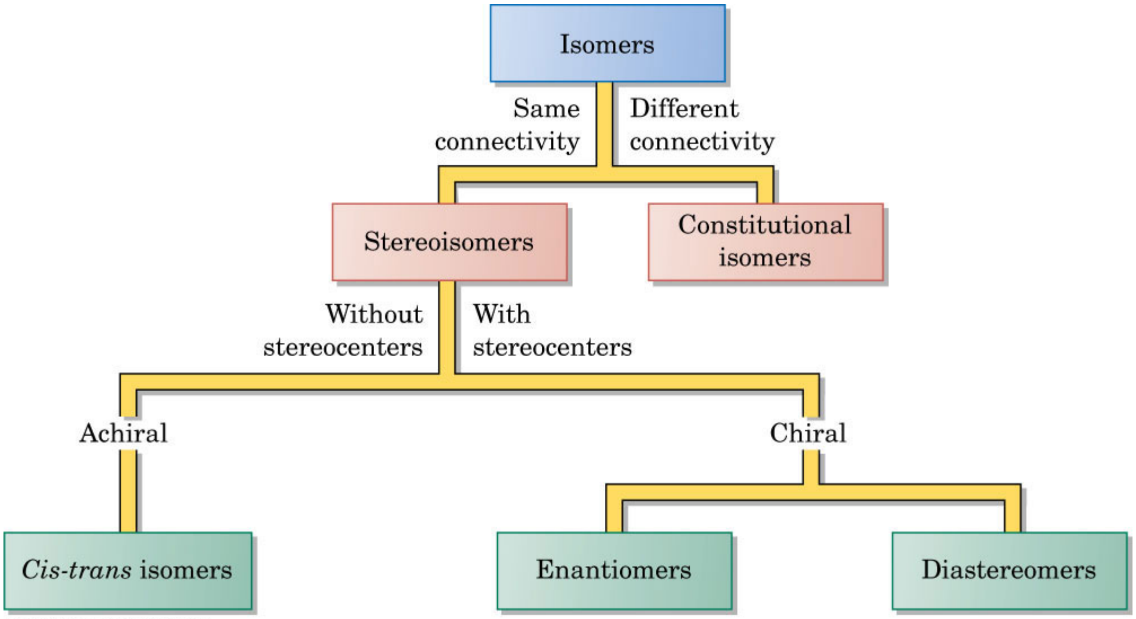
Phenylalanine



Epinephrine

Cetyl Alcohol

III. Enantiomers



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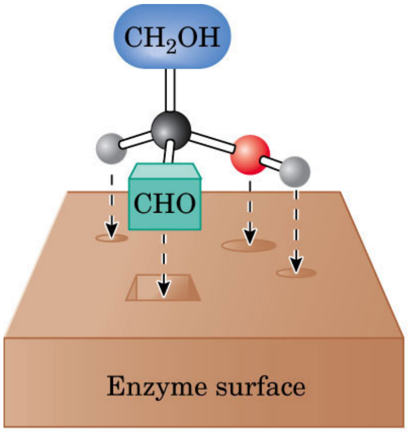
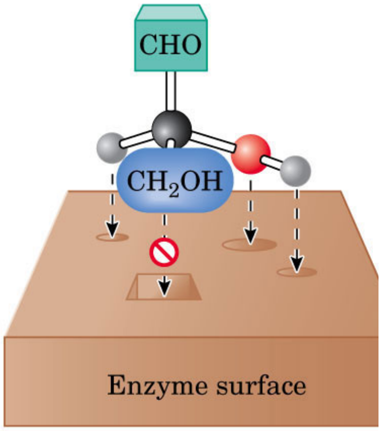
A. Pairs of enantiomers share the same properties except for

1. the interaction/reaction with other chiral systems/compounds

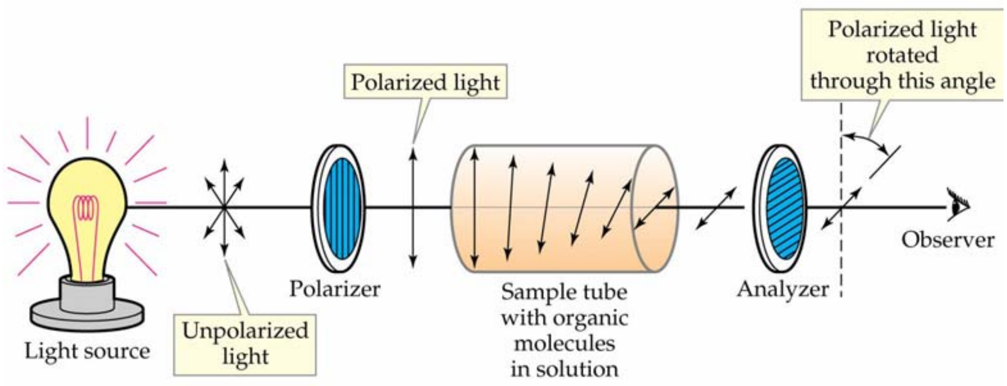


(R)-Glyceraldehyde fits the three binding sites on surface



(S)-Glyceraldehyde fits only two of the three binding sites

2. rotation of plane polarized light.



(Early attempts to understand and characterize the structure of enantiomers were based on the rotation of plane polarized light. Sometimes enantiomers are called "optical isomers".)

IV. How do we distinguish between two enantiomers?

a. Assigning R or S configuration to a stereocenter.

1. *Assign a priority to each group bonded to the stereocenter.*
2. *Orient the molecule so that the lowest group points away from you.*
3. *Read the three groups facing toward you in order from highest to lowest noting in which direction you read the groups.*
4. *If the bonded groups are oriented (priority-wise) in a clockwise direction = R configuration.*
5. *If the bonded groups are oriented (priority – wise) in a counter-clockwise direction = S configuration.*

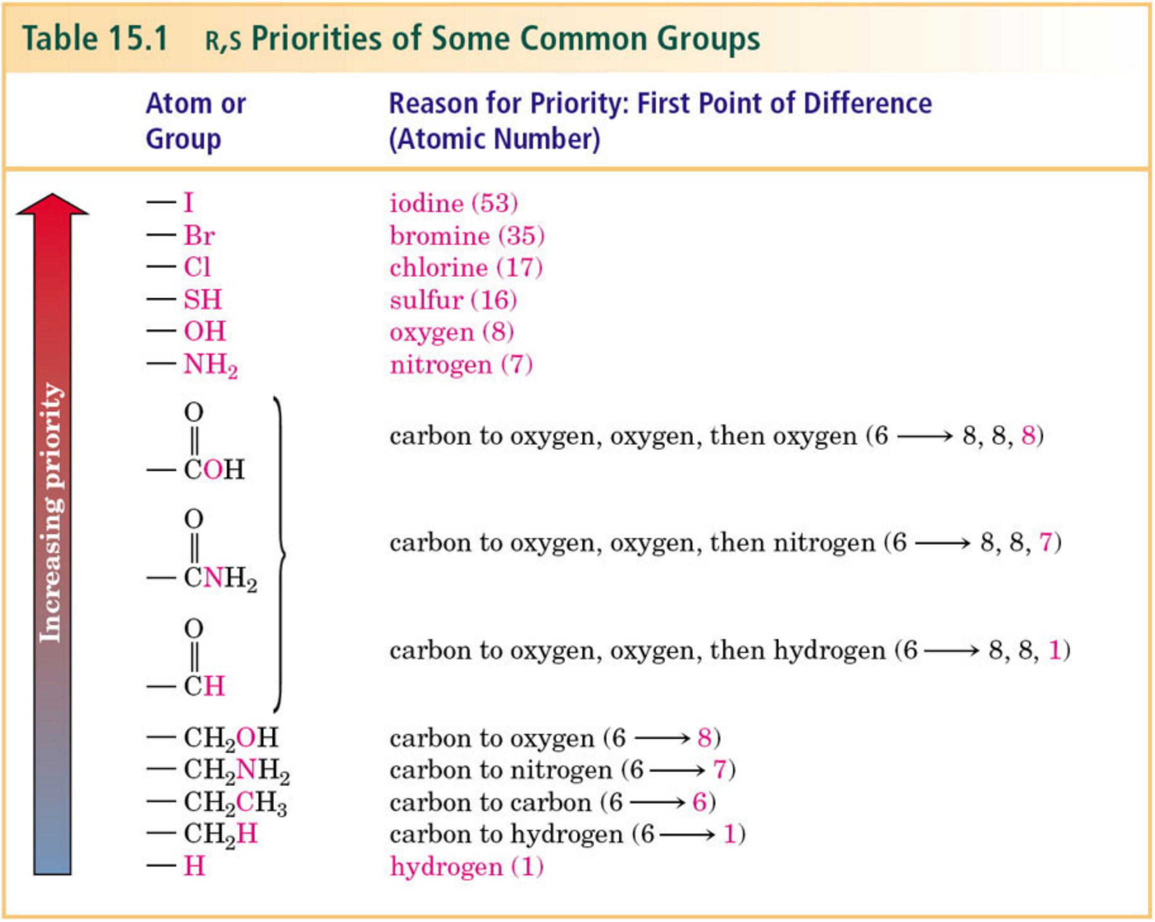
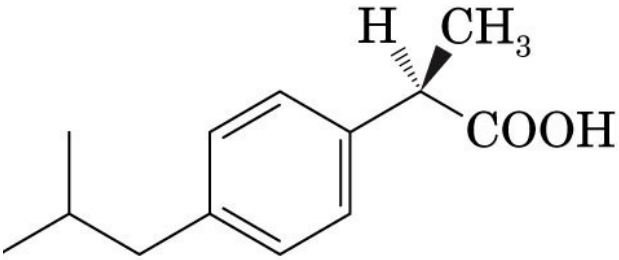


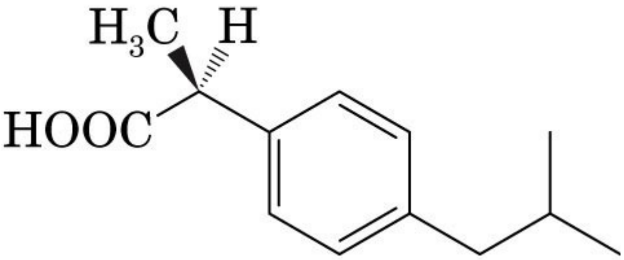
Table 15.1 R,S Priorities of Some Common Groups

Atom or Group	Reason for Priority: First Point of Difference (Atomic Number)
$-\mathrm{I}$	iodine (53)
$-\mathrm{Br}$	bromine (35)
$-\mathrm{Cl}$	chlorine (17)
$-\mathrm{SH}$	sulfur (16)
$-\mathrm{OH}$	oxygen (8)
$-\mathrm{NH_2}$	nitrogen (7)
$-\overset{\underset{\|}{\mathrm{O}}}{\mathrm{C}}\mathrm{OH}$	carbon to oxygen, oxygen, then oxygen ($6 \longrightarrow 8, 8, 8$)
$-\overset{\underset{\|}{\mathrm{O}}}{\mathrm{C}}\mathrm{NH_2}$	carbon to oxygen, oxygen, then nitrogen ($6 \longrightarrow 8, 8, 7$)
$-\overset{\underset{\|}{\mathrm{O}}}{\mathrm{C}}\mathrm{H}$	carbon to oxygen, oxygen, then hydrogen ($6 \longrightarrow 8, 8, 1$)
$-\mathrm{CH_2OH}$	carbon to oxygen ($6 \longrightarrow 8$)
$-\mathrm{CH_2NH_2}$	carbon to nitrogen ($6 \longrightarrow 7$)
$-\mathrm{CH_2CH_3}$	carbon to carbon ($6 \longrightarrow 6$)
$-\mathrm{CH_2H}$	carbon to hydrogen ($6 \longrightarrow 1$)
$-\mathrm{H}$	hydrogen (1)

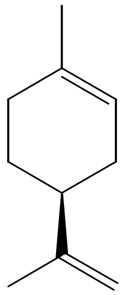
b. Practice! Determine the absolute configuration (R or S) of the chiral center in each of the following molecules.

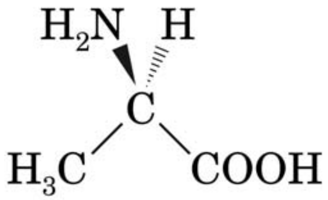


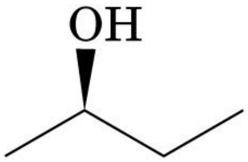
The inactive enantiomer of ibuprofen



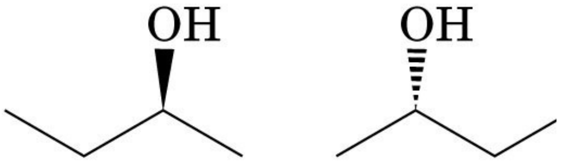
The active enantiomer of ibuprofen







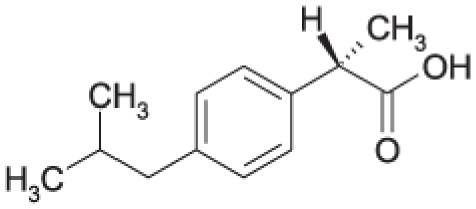
One enantiomer
of 2-butanol



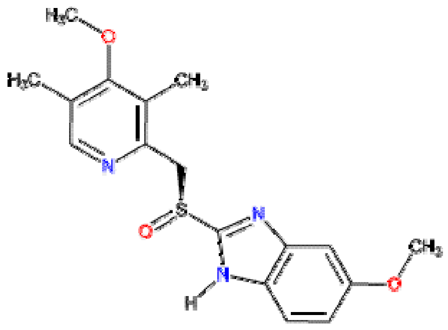
Alternative representations of
its mirror image

c. R and S designations are commonly used in pharmaceuticals and organic chemistry. Why is this important?

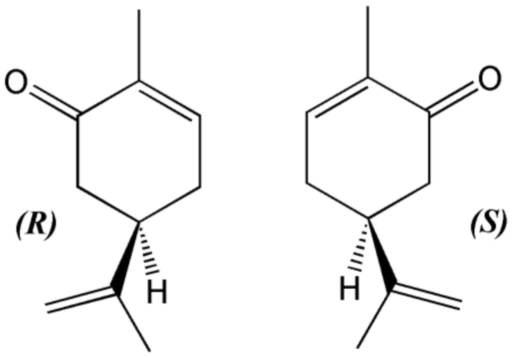
- **Motrin** tablets contain the active ingredient ibuprofen as a racemic mixture, which is (±) - 2 - (*p* - isobutylphenyl) propionic acid. The (S) -(+) - ibuprofen is the therapeutic enantiomer.



- The active ingredient in **Nexium** (esomoeprazole) is the S enantiomer of the active ingredient in **Prilosec** (omeprazole), a racemic mixture (R and S).



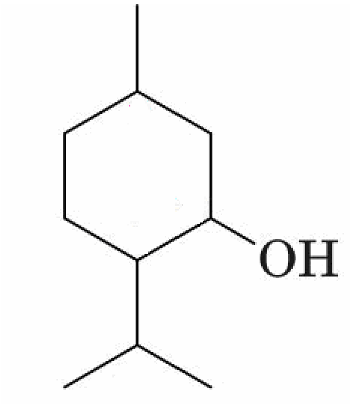
- The R and S enantiomers of **carvone** have different odors.



V. Molecules with More Than Two Stereocenters

A. An increase in the number of stereocenters in a molecule translates to an increase in the number of possible stereoisomers!

B. Menthol – a pleasant smelling alcohol used as a topical analgesic and a flavoring is found in peppermint and other mint essential oils. It exists naturally as one enantiomer. How many enantiomers are there for the menthol structure?



Menthol

(1R,2S,5R – 2 – isopropyl – 5 – methylcyclohexanol)

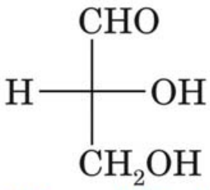
VI. D and L Designations

A. Chiral biological molecules such as sugars and amino acids are often designated as D or L.

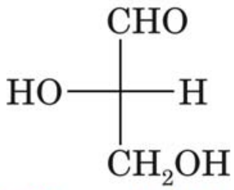
B. There is a bit of history related to why this is so. The D/L system of assigning configuration was proposed by Emil Fischer in 1891 after he studied optical characteristics of simple carbohydroates (sugars).

At that time it was known that each enantiomer of glyceraldehyde rotated plane polarized light the same number of degrees but in opposite directions.

At that time, there was no way to associate this property with molecular structure. An arbitrary assignment of D and L was made.

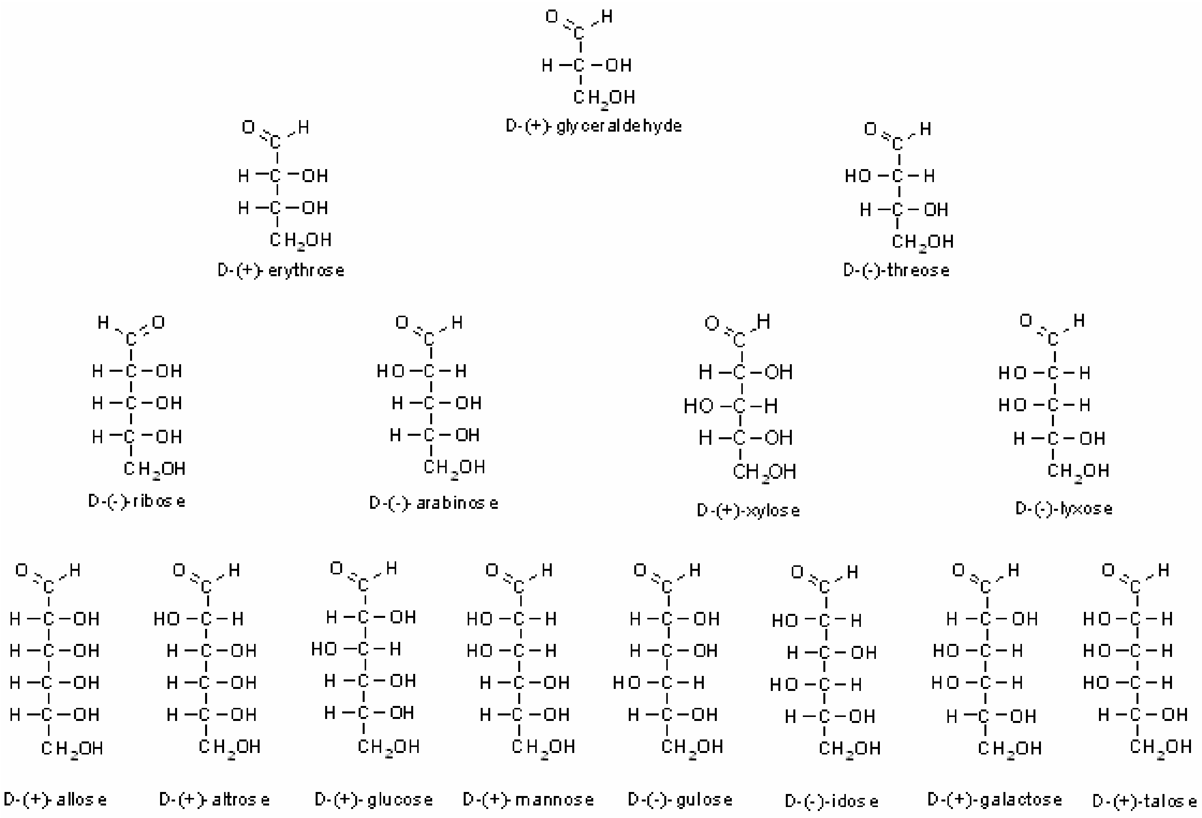


D-Glyceraldehyde
$[\alpha]_D^{25} = +13.5°$



L-Glyceraldehyde
$[\alpha]_D^{25} = -13.5°$

C. Naturally occurring sugars are D enantiomers.



D. Naturally occurring amino acids are L enantiomers.