Stereochemistry
1-Introduction

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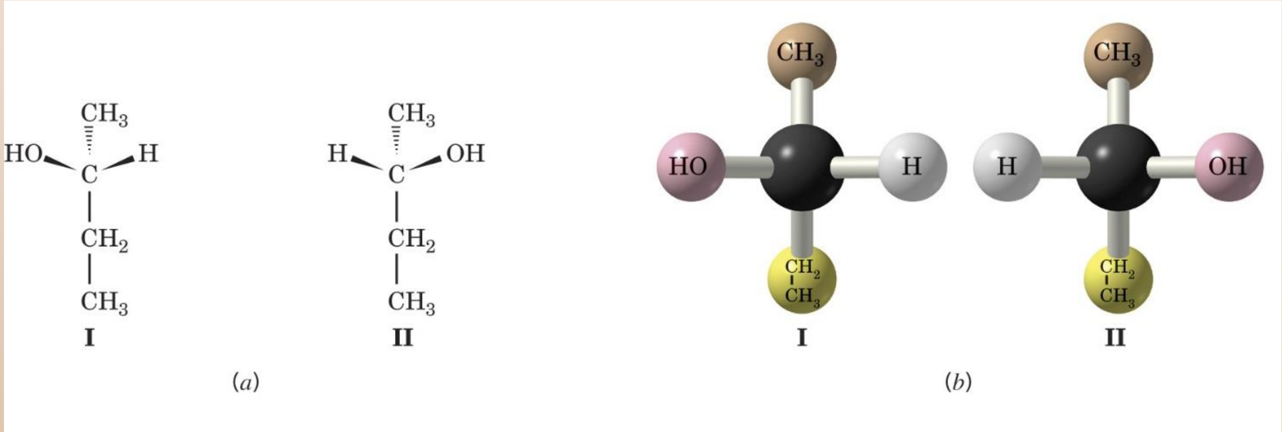
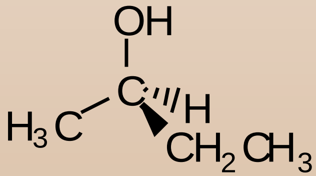
Introduction

- Stereo – left and right handedness
- Any carbon that has four different groups will show chirality.
- Chirality: the mirror image of the compound will not superimpose on the original molecule.

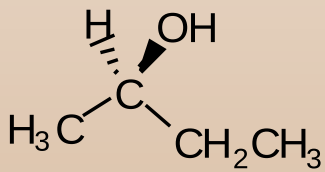


Chirality

- When two mirror images are non imposable on each other.
- When the tetrahedral carbon has four different groups it is called a chiral center.
- The mirror image pair of the compounds are called enantiomers.
- The only thing different about the two molecules is how they rotate the plane polarized light. The rotation would be in equal and opposite direction.
- Drawing chiral molecules: draw dash (behind the plane) and wedges (coming out of paper) and plane line (in the plane) for bonds.
- Here are four representations of one compound.



(1)



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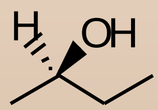

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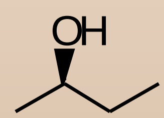
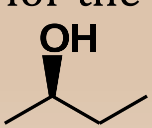
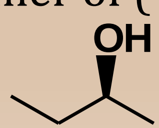


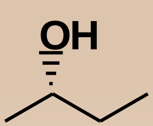
(4)

- Here are two representations for the enantiomer of (4).



(4)

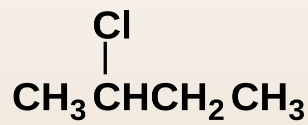




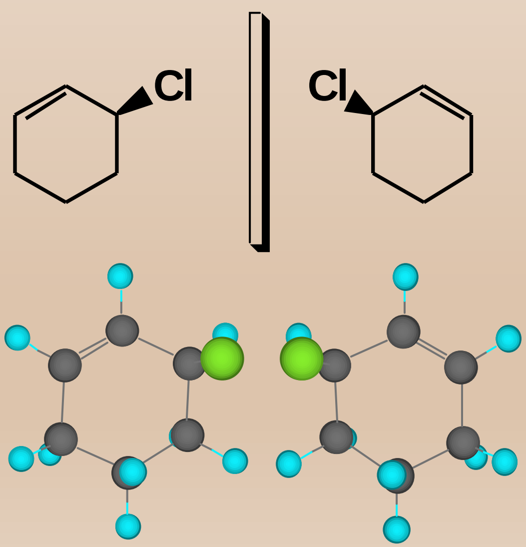
representations for the enantiomer of (4)

Some Enantiomers

- <u>2-Chlorobutane</u>

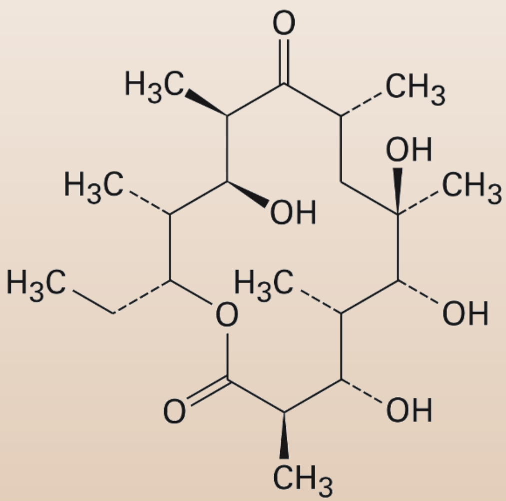


- <u>3-Chlorocyclohexene</u>

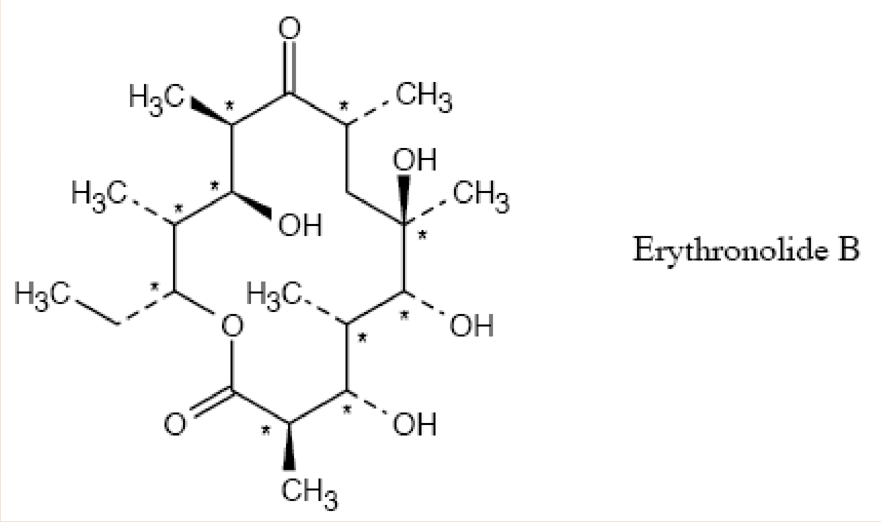


Another Example

How many chiral centers in the following compound?

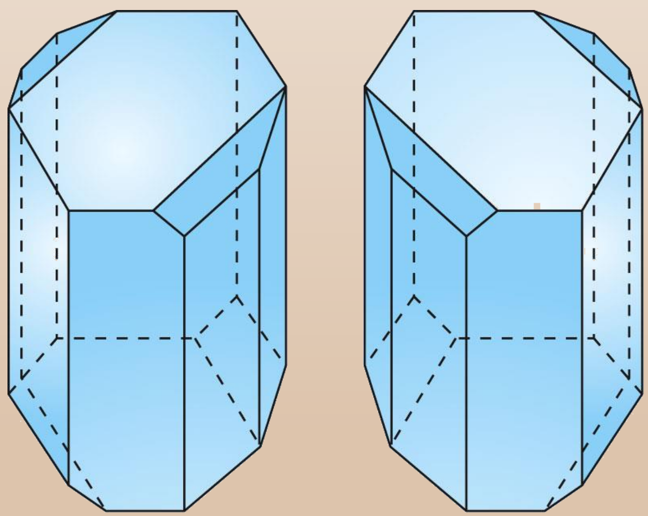


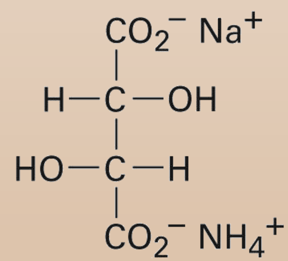
Erythronolide B



Pasteur's Discovery of Enantiomers

- Louis Pasteur discovered that sodium ammonium salts of tartaric acid crystallize into right handed and left handed forms
- The optical rotations of equal concentrations of these forms have opposite optical rotations
- The solutions contain mirror image isomers, called **enantiomers** and they crystallized in mirror image shapes – such an event is rare

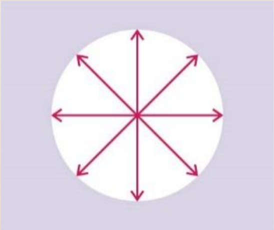


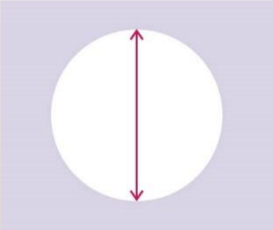


Sodium ammonium tartrate

Optical Activity

- Light restricted to pass through a plane is *plane-polarized.* Phenomenon discovered by Jean-Baptiste Biot in the early 19th century

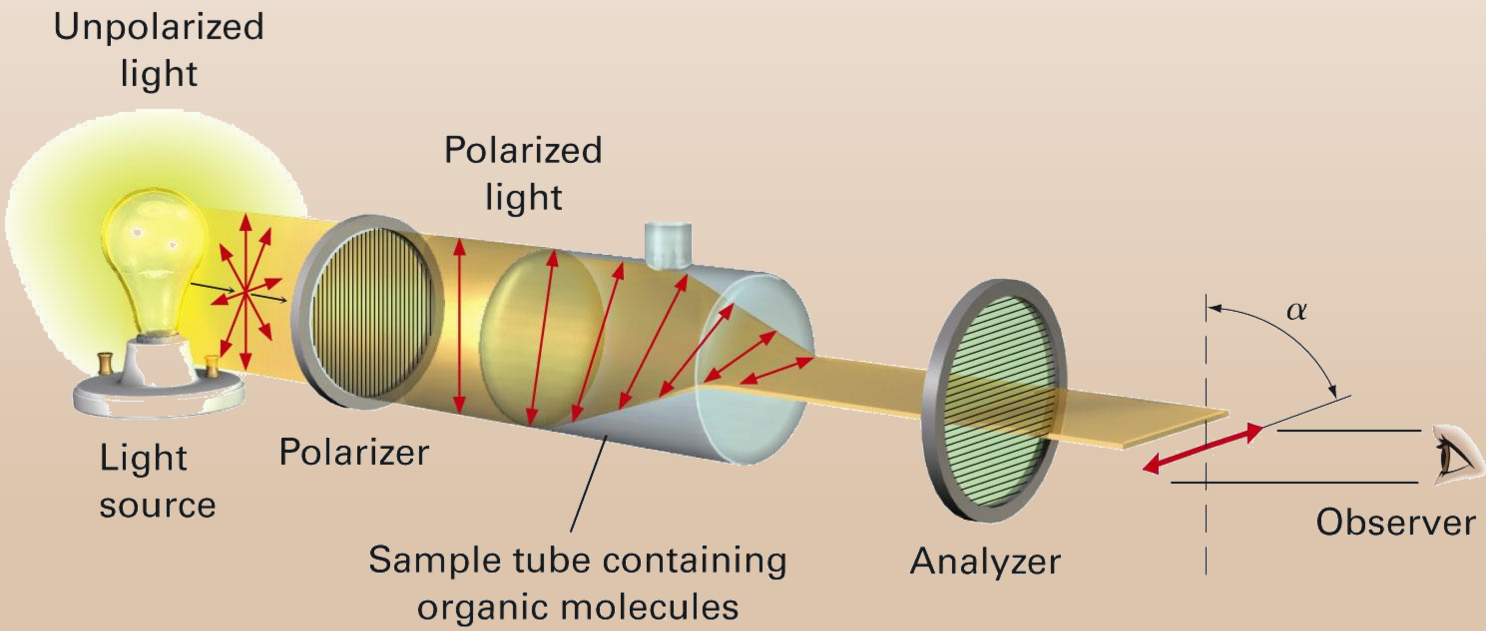




- Plane-polarized light that passes through solutions of achiral compounds retains its original plane of polarization
- Solutions of chiral compounds rotate plane-polarized light and the molecules are said to be *optically active*
- The instrument is called a polarimeter
- Rotation is measured in degrees, is $[\alpha]$
- Clockwise rotation is called **dextrorotatory (d)**
- Anti-clockwise is **levorotatory (l)**

The Polarimeter

- The source passes through a **polarizer** and then is detected at a second polarizer
- The angle between the entrance and exit planes is the optical rotation.



Specific Rotation

- To have a basis for comparison, define **specific rotation, $[\alpha]_D$** for an optically active compound
- Specific rotation is that observed for 1 g/mL in solution in cell with a 10 cm path using light from sodium metal vapor (589 nm)

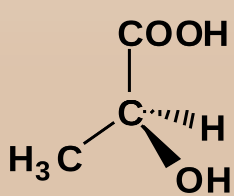
$$[\alpha] = \frac{\alpha}{c \cdot l}$$

where $[\alpha]$ = the specific rotation

α = the observed rotation

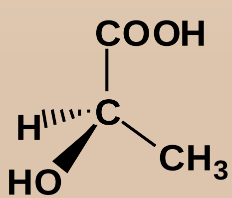
c = the concentration of the solution in grams per milliliter of solution (or density in g mL^{-1} for neat liquids)

l = the length of the tube in decimeters (1 dm = 10 cm)



(*S*)-(+)-Lactic acid

$[\alpha]_D^{21} = +2.6°$



(*R*)-(-)-Lactic acid

$[\alpha]_D^{21} = -2.6°$

Specific Rotation and Molecules

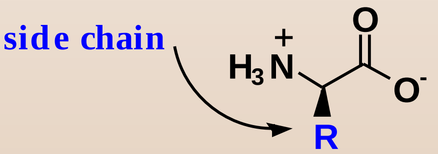
- A compound must be chiral for it to be optically active.
- The specific rotation of the enantiomer pair is equal in magnitude but opposite in sign
- There is **no correlation** between the ***R,S*** designation of an enantiomer and the direction **[(+) or (-)]** in which it rotates plane polarized light
- ([+ = d] and [– = l])
- Racemic mixture
  - A 1:1 mixture of enantiomers
  - No net optical rotation
  - Often designated as (±)

Table 5.1 Specific Rotation of Some Organic Molecules

Compound	$[\alpha]_D$	Compound	$[\alpha]_D$
Penicillin V	+233	Cholesterol	−31.5
Sucrose	+66.47	Morphine	−132
Camphor	+44.26	Cocaine	−16
Chloroform	0	Acetic acid	0

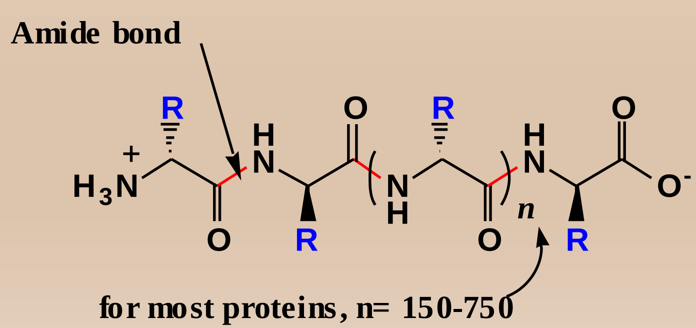
Amino Acids and Proteins

- The 20 most common amino acids have a central carbon, called an α-carbon, bonded to an NH_2 group and a COOH group.
- In 19 of the 20, the α-carbon is a chiral center.
- 18 of the 19 α-carbons have the *R* configuration, one has the *S* configuration.
- At neutral pH, an amino acid exists as an internal salt.
- The symbol R = a side chain.



Ionized or zwitterion form of an amino acid

- Proteins: Long chains of amino acids connected by amide bonds (here shown in red) formed between the carboxyl group of one amino acid and the amino group of another amino acid

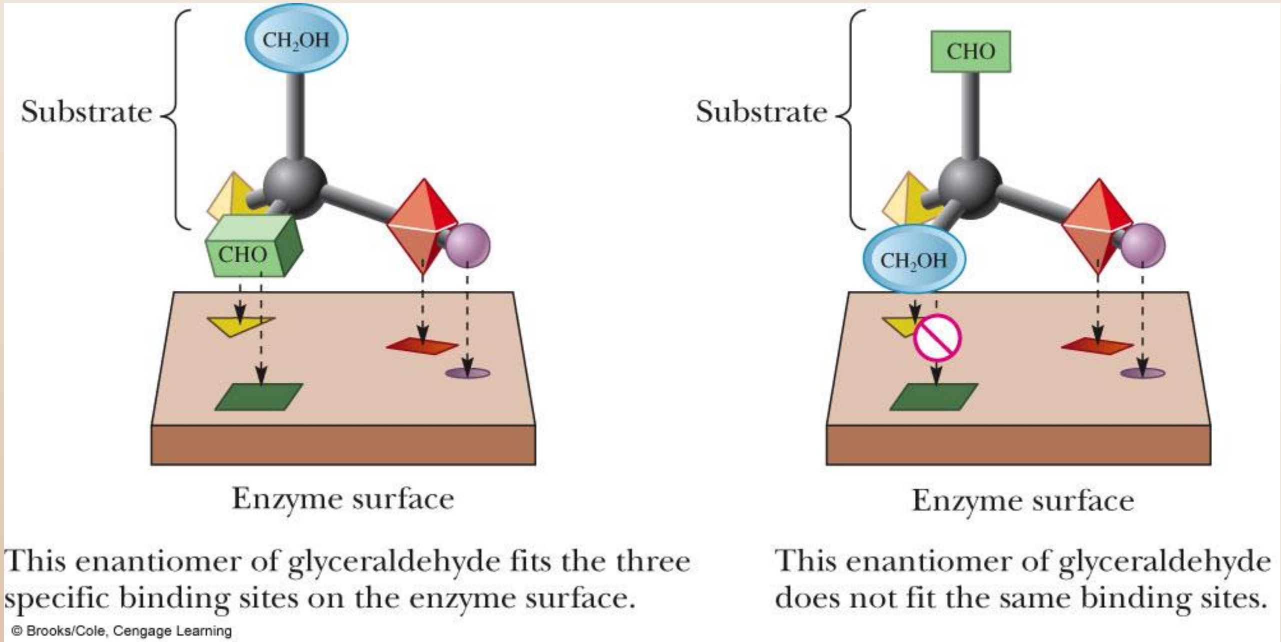


Chirality in the Biological World

- Except for inorganic salts and a few low-molecular-weight organic substances, the majority of molecules of living systems are chiral.
- Although these molecules can exist as a number of stereoisomers, generally only one is produced and used in a given biological system.
- Consider chymotrypsin, a protein-digesting enzyme in the digestive system of animals.
  - chymotrypsin contains 251 chiral centers.
  - the maximum number of stereoisomers possible is 2^{251}
  - there are only 2^{38} stars in our galaxy!
- Enzymes are like hands in a handshake.
  - The substrate fits into a binding site on the enzyme surface.
  - A left-handed molecule, like hands in gloves, will only fit into a left-handed binding site and
  - a right-handed molecule will only fit into a right-handed binding site.
  - Because of the differences in their interactions with other chiral molecules in living systems, enantiomers have different physiological properties.

Chirality in the Biological World…..

A schematic diagram of an enzyme surface capable of binding with (*R*)-glyceraldehyde but not with (*S*)-glyceraldehyde.



Key Words/Concepts

- Stereoisomers
- Chiral Center
- Chirality
- Enantiomer
- Plane polarized light
- Dextrorotatory (d)
- Laevorotatory (l)