CH203 Lecture 17

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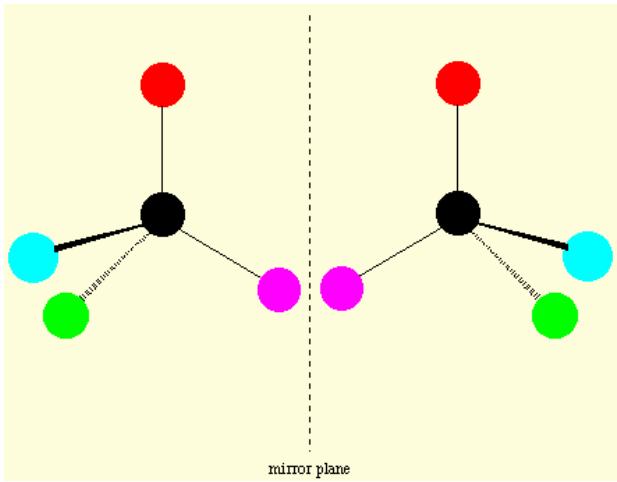
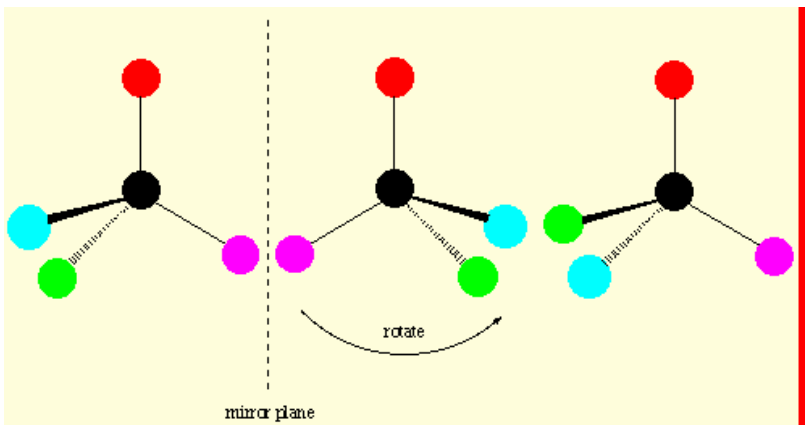
Chirality

Chirality is a special case of asymmetry. A molecule is chiral if there is no internal plane of symmetry, and the molecule and its mirror image are not superimposable.



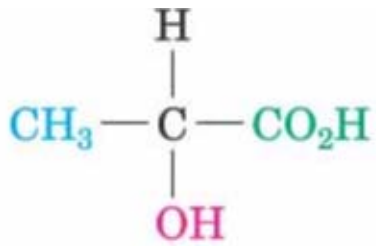
Even after rotating one of the molecules it remains different from its stereoisomer. They are not superimposable.

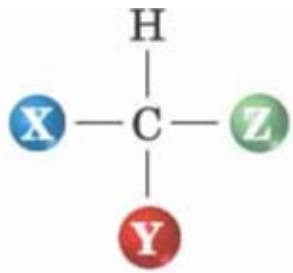


Examples of Enantiomers

- Molecules that have one carbon with 4 different substituents have a nonsuperimposable mirror image – enantiomer
- Build molecular models to see this

Mirror-image Forms of Lactic Acid

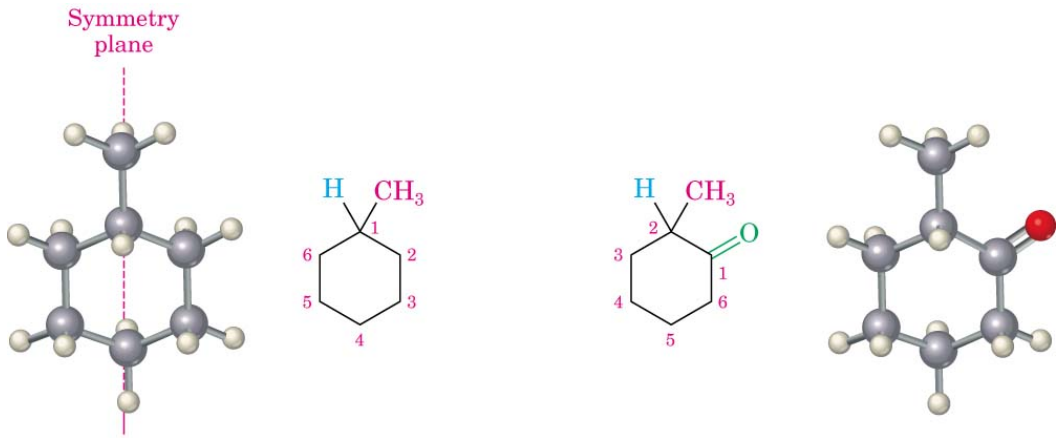




Lactic acid: a molecule of general formula CHXYZ

Chirality Centers in Chiral Molecules

- Groups are considered “different” if there is any structural variation (if the groups could not be superimposed if detached, they are different)
- In cyclic molecules, we compare by following in each direction in a ring

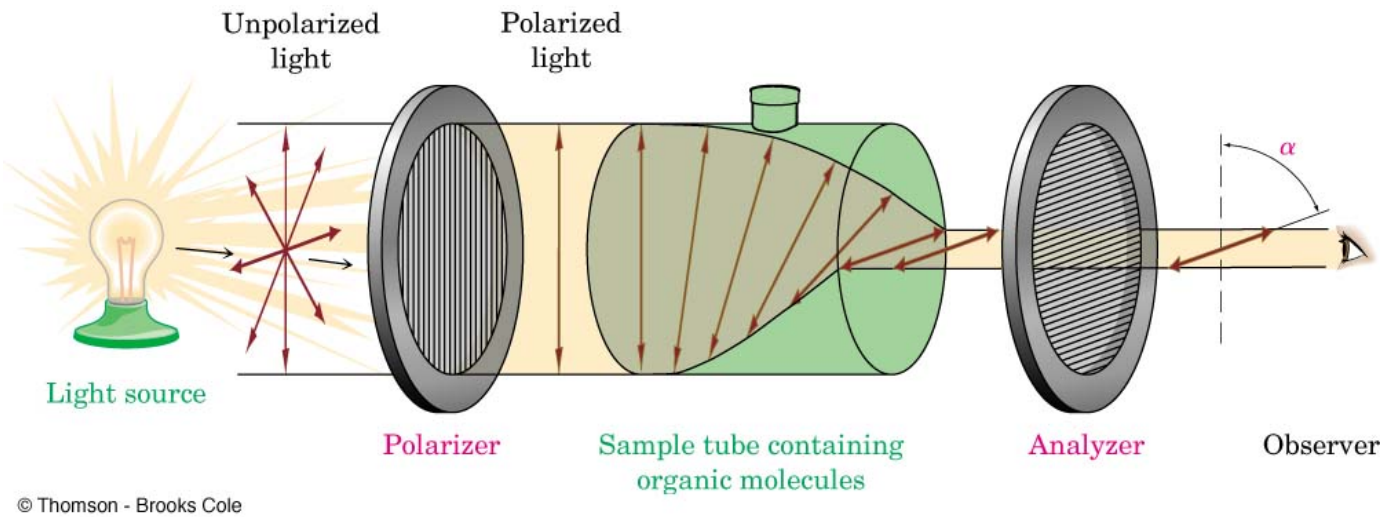


Methylcyclohexane (achiral)

2-Methylcyclohexanone (chiral)

Measurement of Optical Rotation

- A *polarimeter* measures the rotation of plane-polarized that has passed through a solution
- 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.

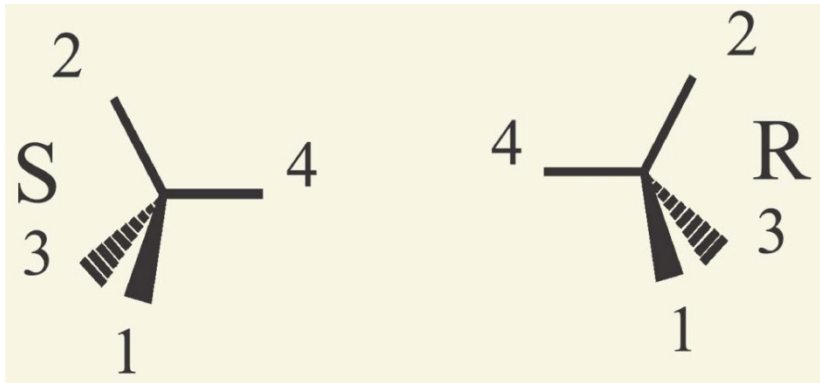


Sequence Rules for Specification of Configuration

- A general method applies to the configuration at each chirality center (instead of to the the whole molecule)
- The configuration is specified by the relative positions of all the groups with respect to each other at the chirality center
- The groups are ranked in an established priority sequence and compared
- The relationship of the groups in priority order in space determines the label applied to the configuration, according to a rule

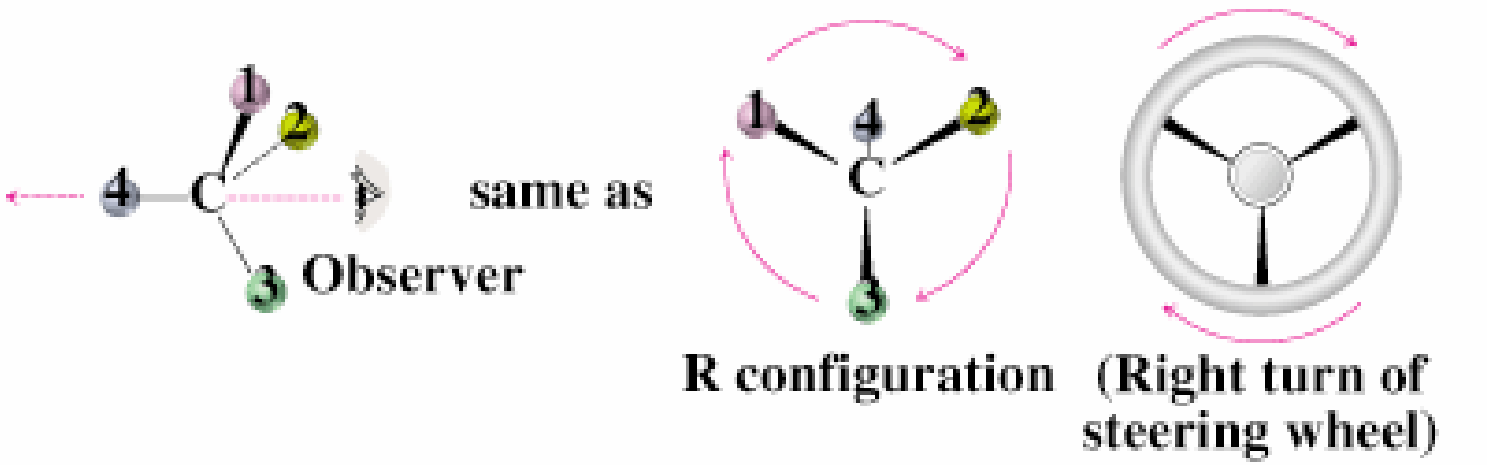
Sequence Rules (IUPAC)

- Assign each group priority according to the Cahn-Ingold-Prelog scheme With the lowest priority group pointing away, look at remaining 3 groups in a plane
- Clockwise is designated R (from Latin for “right”)
- Counterclockwise is designated S (from Latin word for “left”)

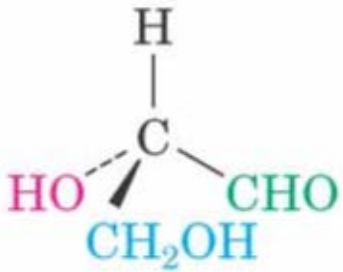


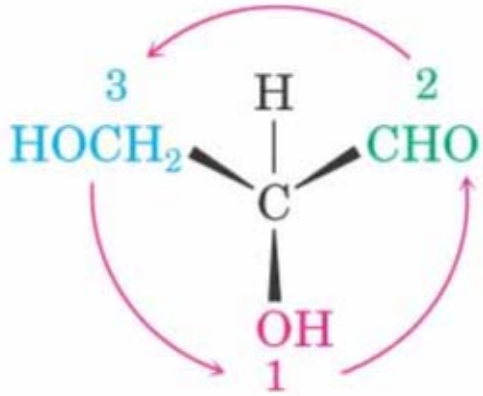
R-Configuration at Chirality Center

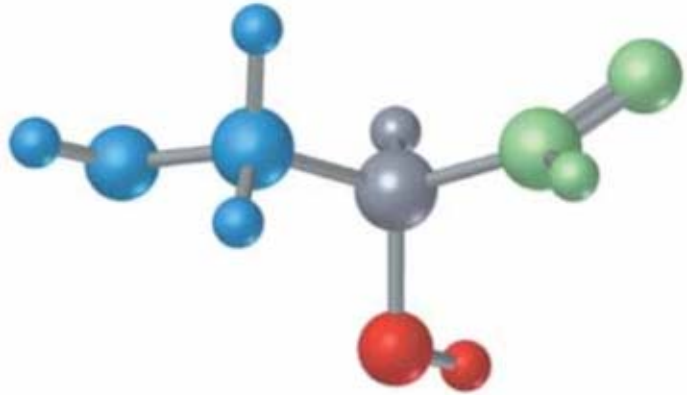
- Lowest priority group is pointed away and direction of higher 3 is clockwise, or right turn



(a)

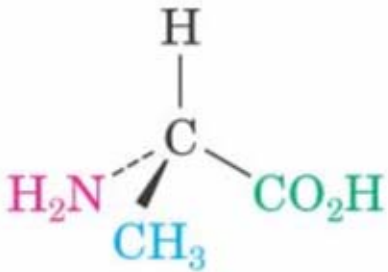


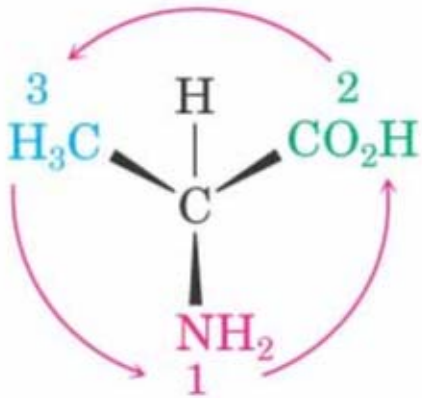


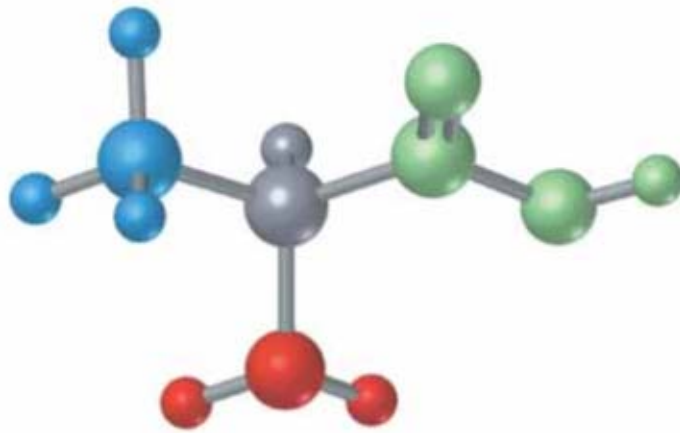


(*S*)-Glyceraldehyde
[(*S*)-(−)-2,3-Dihydroxypropanal]
$[\alpha]_D = -8.7°$

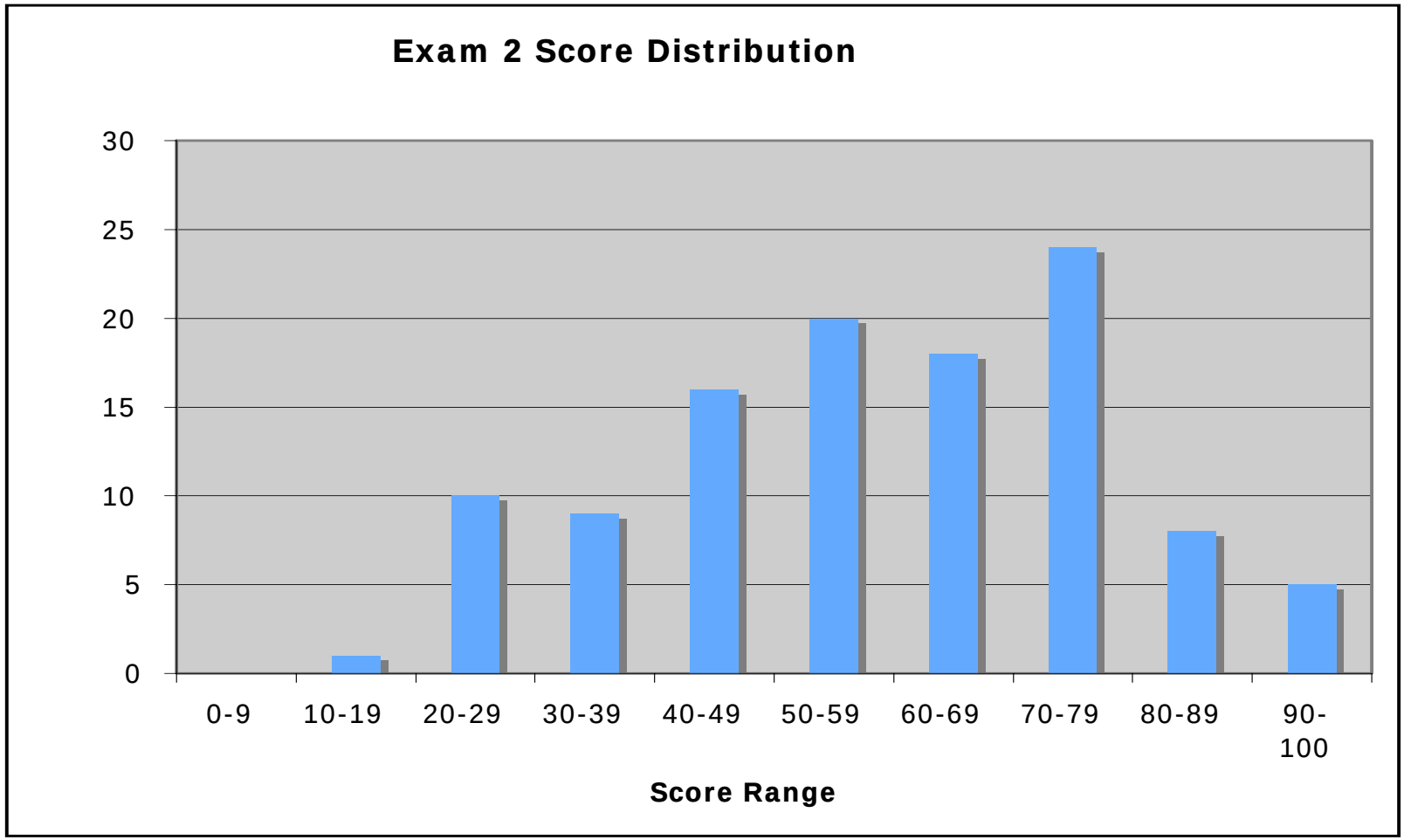
(b)







(*S*)-Alanine
[(*S*)-(+)-2-Aminopropanoic acid]
$[\alpha]_D = +8.5°$



Median: 59

High: 93

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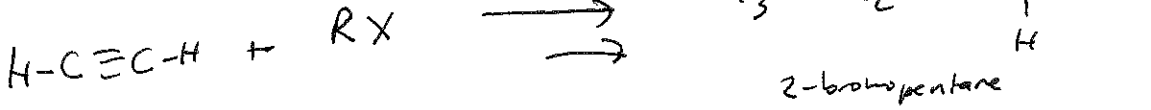
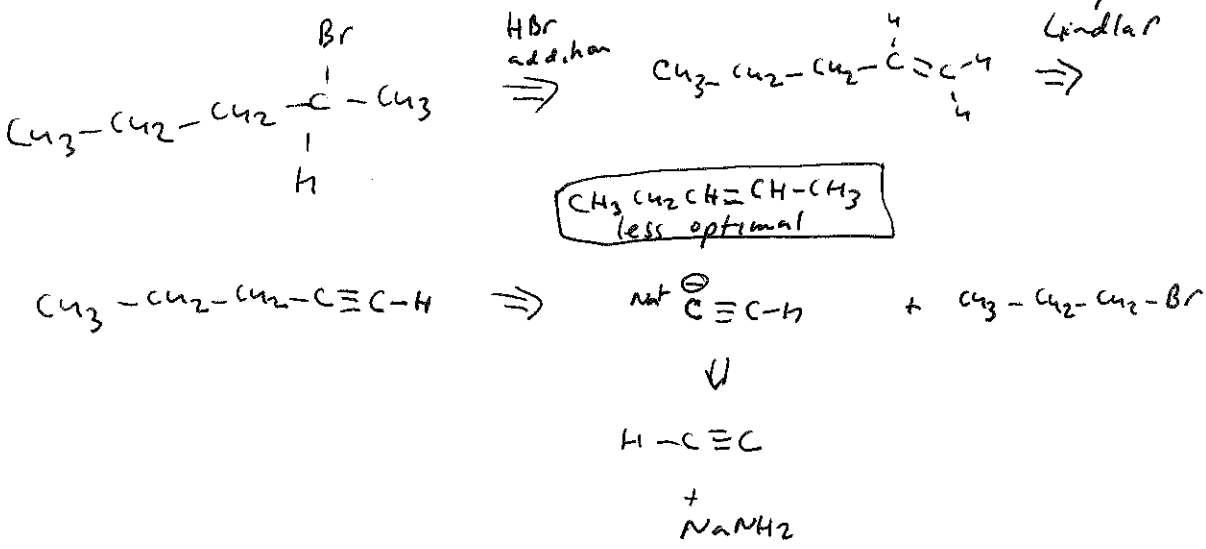
Problem # 2

Synthesize 2-bromopentane from acetylene and any alkyl halide needed. More than one step is required.

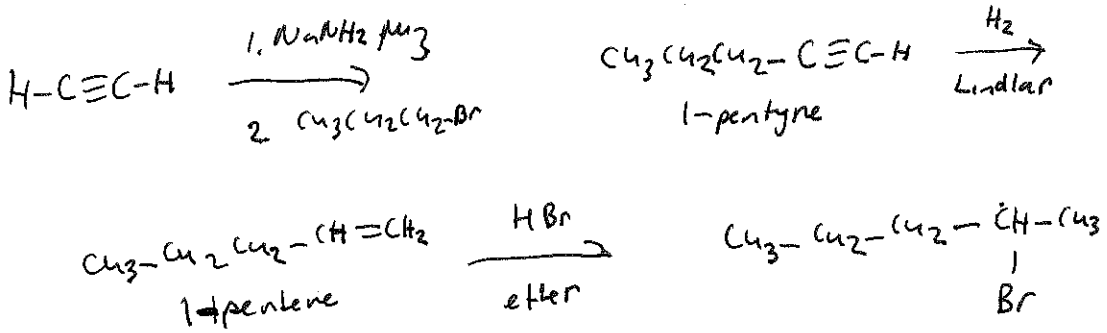
1) Draw rx:



2) Perform retrosynthetic analysis



3) Forward synthesis:

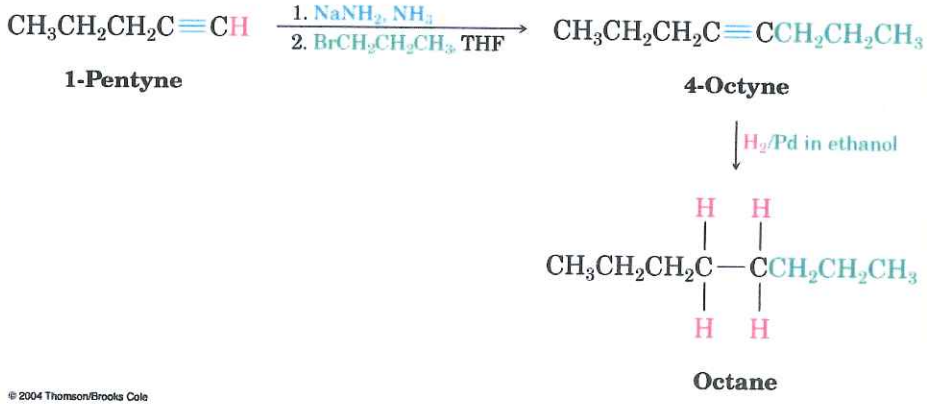


Strategies for Synthesis

- Compare the target and the starting material
- Consider reactions that efficiently produce the outcome. Look at the product and think of what can lead to it (Read the practice problems in the text)
- Example
  - Problem: prepare octane from 1-pentyne
  - Strategy: use acetylide coupling

$$CH_3CH_2CH_2C{\equiv}CH \longrightarrow CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_3$$

1-Pentyne **Octane**



Chapter 9: Stereochemistry

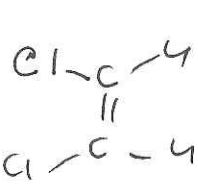
look at section 9.3 but will not discuss in lecture.

Problems: ~~2, 3, ~~4~~, 7–10, 11, 12, 14, 15, 19–22,~~ ~~28, 30, 32, 38, 41, 44, 45, 46, 47,~~ ~~49, 50, 51, 55, 59, 65, 66, 69, 71,~~ ~~81–83, 84~~

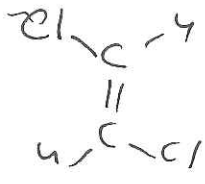
2, 3, 8–11, 13–16, 20–22, 28, 30, 31, 37, 40, 41, 43–46, 48, 50, 51, 54, 55, 59, 60, 64, 73, 74, 77–79., 81, & 82.

Stereochemistry: Chiral molecules

Stereoisomers – Isomers that have the same connectivity but differ in arrangement of atoms in space



cis-1,2 DCE



trans-1,2-DCE

Stereoisomers

Two gen. categories:

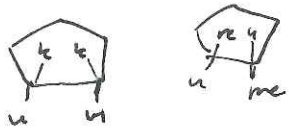
Enantiomers

stereoisomers whose molecules are nonsuperimposable mirror images

Diastereomers

stereoisomers whose molecules are not mirror images of each other

e.g.

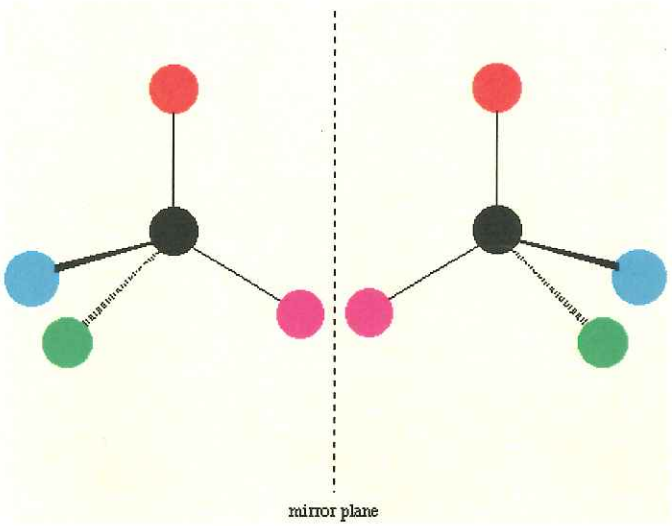


– not mirror images

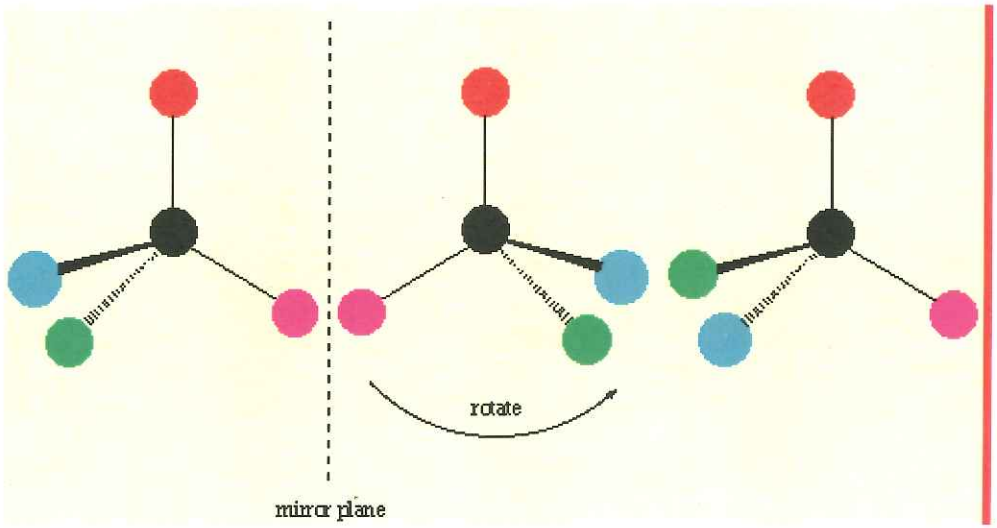
– diff. only in arrangement of their atoms in space

Chirality

Chirality is a special case of asymmetry. A molecule is **chiral** if there is no internal plane of symmetry, and the molecule and its mirror image are not superimposable.



Even after rotating one of the molecules it remains different from its stereoisomer. They are not superimposable.



Enantiomers are related to each other (as a rt hand is related to a left hand) and result whenever a tetrahedral carbon is bonded to 4 diff subst. (one need not be H).

Stereoisomers whose molecules are non-superimposable mirror images

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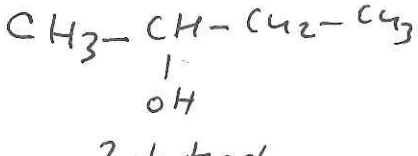
A molecule that has a plane of symmetry in any of its possible conformations must be identical to its mirror image (achiral)

Stereoisomers which are different from their mirror images are called enantiomers

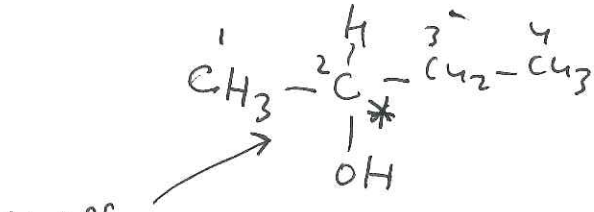
Detecting chirality of molecules:



2-butanol

~~Expect~~

A pair of enantiomers is always possible for molecules that contain one tetrahedral atom w 4 diff groups attached



4 diff groups attached to C2

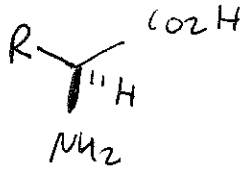
C2 * is called a stereocenter: an atom bearing groups of such nature that an interchange of any 2-groups will produce a ~~stereomer~~ stereoisomer.

(chirality center, stereogenic center, or asymmetric center)

Other exs:

Biological Importance of Chirality

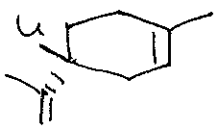
Chirality pervades the universe

1) 

20 amino acids

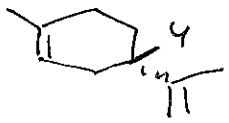
L-amino acids

(Left-handed)

2) 

(+)-limonene

odor oranges

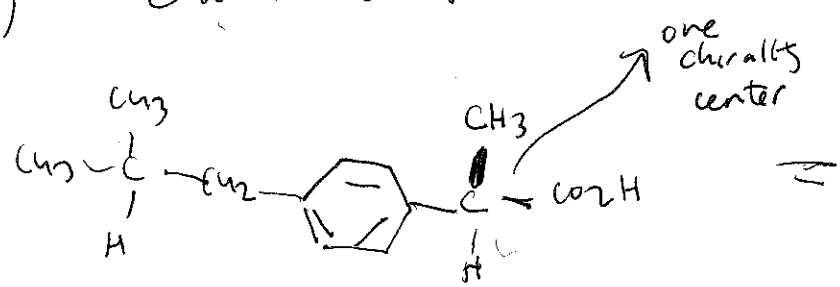


(−)-limonene

odor of lemons

Diff. enantiomers have diff. biological effects

3) Chiral drugs



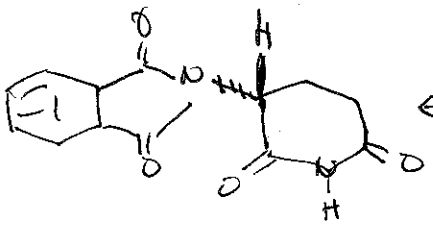
Advil

Nuprin

motrin

S-Ibuprofen

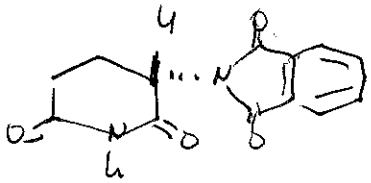
active analgesic



thalidomide (1960's) ← cures morning sickness

teratogen

used to treat morning sickness in preg. women.



(caused birth defects)

Properties of Enantiomers : optical Activity

~ sec. 9.3

Opt. Activity : ability of a chiral molecule to rotate plane polarized light using a polarimeter

ordinary light beam

oscillations of elec. field in all poss. planes ⊥ to direc. of propag.

↓ polarizer (polarizing lens)

light waves in a single plane pass through

polarimeter measures rotation of plane pol. light by chiral molecules (plane of polarization is rotated by molecules & can be measured

α = obs. rot.

$$[\alpha]_D = \frac{\alpha}{c \times l}$$

l → length of the dm

c → conc g/mL

D line Na 589 nm

Enantiomers rotate plane of polarization in exactly equal amounts (same magnitude) but in opp directions

dextrorotatory (+) - rot. pol. lt to the right

levorotatory (−) - rot. pol. lt to the left

Examples on overhead

Show no correlation exists betwn R,S config. of enantiomers and (+) or (−) direction in which they rotate plane-polarized light.

Cahn - Ingold - Prelog (R/S) rules for naming enantiomers

1. Identify stereogenic centres (most commonly sp^3 C with 4 diff groups attached.

2. Assign priority group (high = 1, low = 4) based on atomic # of atom attached to stereogenic center. If double or triple bonded grps are substituents, then are treated as equiv set of single-bonded atoms.

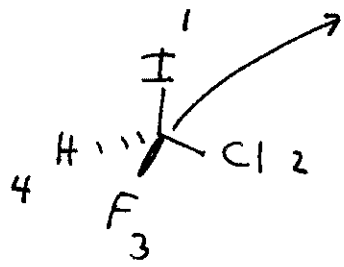
3. Position the lowest priority group away

4. For the other 3 groups, det. dir. of low to hi priority

5. IF clockwise, center is R
   Latin rectus = right

6. IF counterclockwise then S
   Latin sinister = left

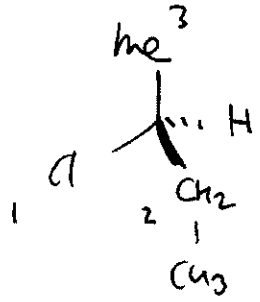
Example



stereogenic center

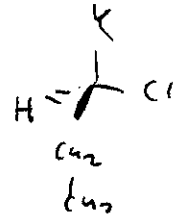
chloro fluoro iodo methane

1) clockwise (R)

2) 

counterclockwise (S)

(S)-2-chlorobutane



(R)-2-chlorobutane

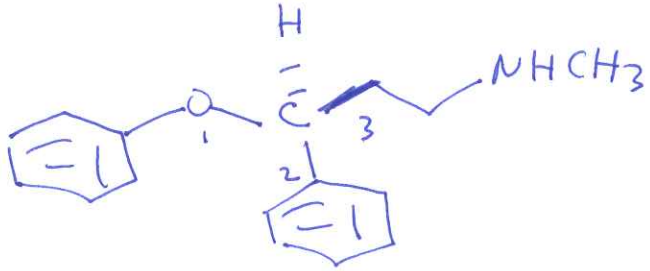
A mixture containing equal quantities of enantiomers = racemate or racemic mixture

~~9H 203 H/05~~

Enantiomers

1) Chiral molecules which are non-superimposable mirror images

one carbon, four diff. substituents



(S) - fluoxetine

active against migraine

(Prozac) antidepressant

2) Chiral centers assigned R + S configuration with lowest group pointing away

R

S

(R) - fluoxetine

non-active against migraine