

CHEM 221 section 52

LECTURE #09

Thurs., March 06, 2008

ASSIGNED READINGS:

TODAY'S CLASS:

- 5.1-5.4 in Lect.07's notes actually...
- 5.21 Biological relevance of chirality
- 5.5-5.14 Drawing & naming enantiomers & diastereomers
Measuring chiral compounds in the lab
Separating enantiomers

NEXT CLASS: finish Ch.5, start Ch.9, 10

(1)

Reality check: why care about stereochemistry?

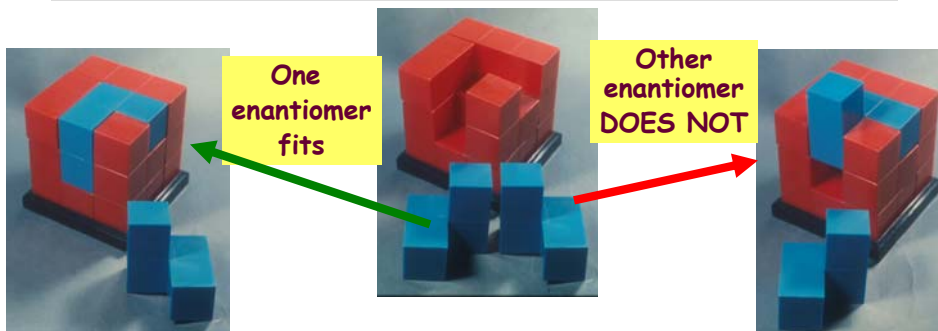
Many naturally occurring compounds are CHIRAL

- All natural amino acids have same handedness (LEVOROTATORY)
↳ proteins/enzymes CHIRAL too!

RESULT:

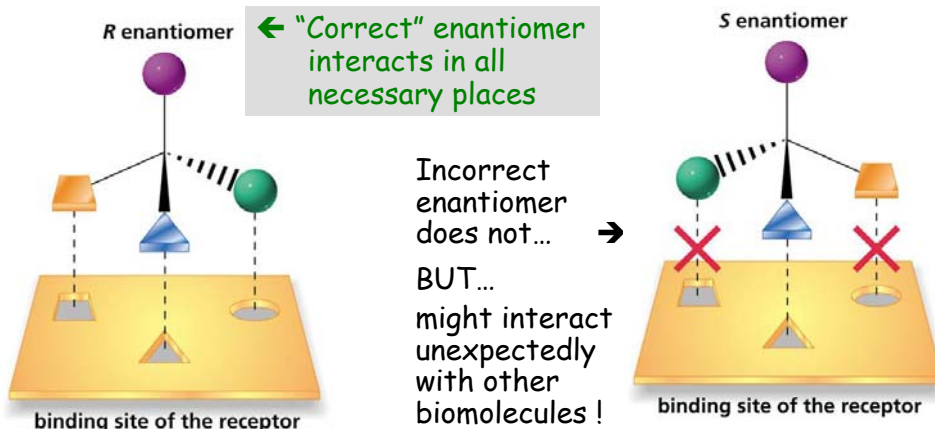
Mirror image molecules can behave quite differently in biological systems

The interaction between SUBSTRATE & ENZYME
is superficially analogous to HAND & GLOVE



(2)

5.21 Discrimination of enantiomers by biological molecules



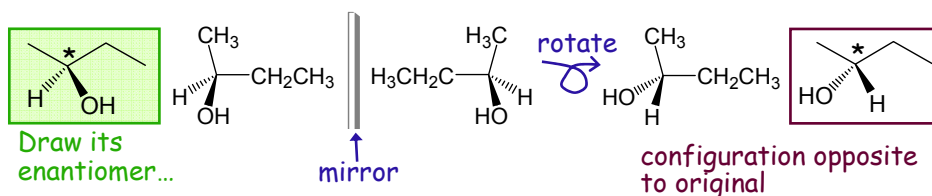
Interactions between enzyme & substrate = *stereospecific*
 ⇒ only 1 stereoisomer fits

So?! Enantiomers have SAME physical properties
 SAME reactivity with achiral substances
 (3) ONLY difference = way they interact with other chiral things!

5.4, 5.6 Drawing enantiomers

To draw a molecule's enantiomer:

1. Draw perspective drawing: show all 3D info. for *asymmetric* atoms (*)
2. Imagine reflecting molecule in a mirror
 - configuration of EVERY asymmetric atom will be inverted
3. Check: is this really a different compound?
 - original & mirror image are enantiomers only if *nonsuperimposable*



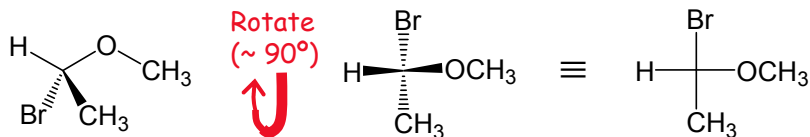
Shortcut: to draw a chiral C (*i.e.*, C*) with opposite configuration, detach any 2 groups from that C* & switch their places

(4)

Perspective drawings vs. Fisher projections

Fisher projections: a short-hand often used by biologists (will not test...)

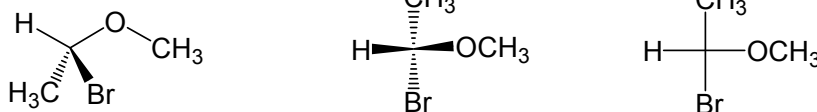
- each chiral C looks like a planar cross, but REALLY means this:
 horizontal lines: aimed towards you (out of page)
 vertical lines: aimed away from you (into page)



perspective drawing
(intuitively meaningful)

Fisher projection
(use carefully!)

This molecule's enantiomer:



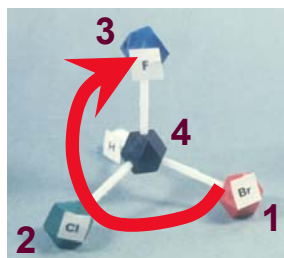
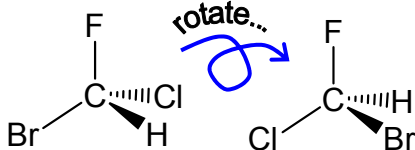
BEWARE: a Fisher projection does look flat, but it is NOT flat...
 Thus: if rotate by 180° ⇒ still represents same molecule
 if rotate by 90° ⇒ **no longer** represents the same molecule!

(5)

5.7 Assigning configuration of chiral centres: "the R,S system"

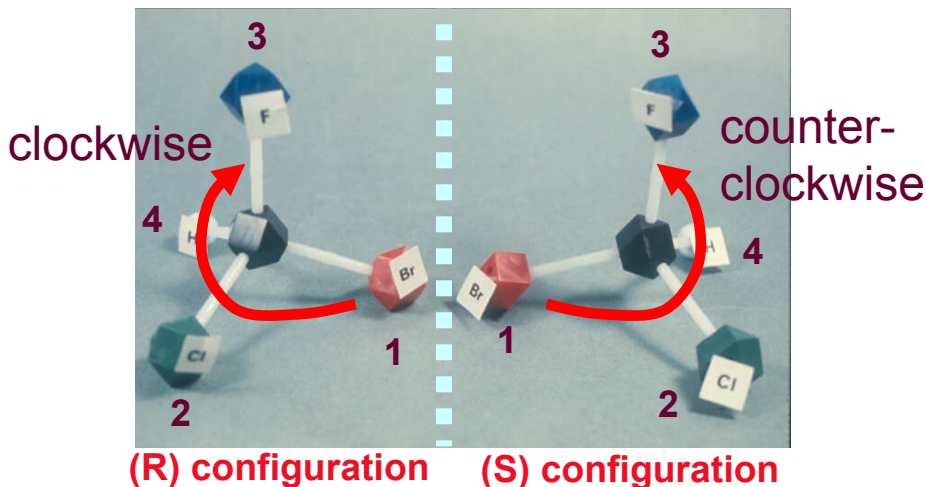
- Assign priority to 4 groups attached to asymmetric centre.
 use Cahn-Ingold-Prelog rules: **higher atomic #** ⇒ **higher priority**
 (same as for E/Z...)
- Picture molecule with **LOWEST** priority group aimed **AWAY** from you
- Trace a circle through other 3 groups from
highest → lowest priority:
 Clockwise = (R) *rectus* (Latin right)
 Counterclockwise = (S) *sinister* (Latin left)

e.g.,



Traces in a
clockwise
direction
⇒ "R"
*Like turning
right on a
steering wheel*

(6)



Rectus = right

The (R) enantiomer of bromochlorofluoromethane

Sinister = left

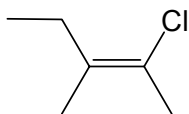
The (S) enantiomer of bromochlorofluoromethane

(7)

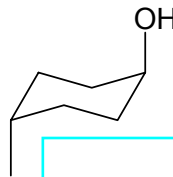
Can only invert R vs S configuration by breaking/making bonds

5.7 & 5.13: IUPAC naming of stereoisomers

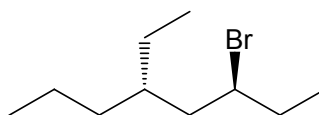
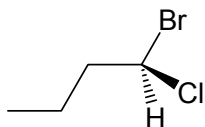
Geometric isomerism: using cis/trans (Z/E for double bonds) at front of name, followed by dash:



cis-1-chloro-3-methylpent-2-ene
or *Z*-chloro-3-methylpent-2-ene



Configuration of chiral C atoms: add R/S after position #, in brackets, followed by dash:



(3S, 5S)-3-bromo-5-ethyloctane

If more than one chiral C, use comma between #-letter combinations

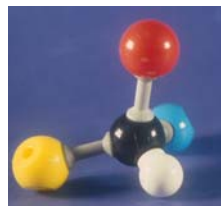
5.3, 5.5 Stereocenters & stereoisomers: terms & #s

stereogenic centre = atom that gives rise to stereoisomers
stereocentre if two groups attached to it are interchanged (via breaking & making bonds...)

ONE TYPE OF STEREOCENTRE:

asymmetric centre
chirality centre
chiral centre

} = atom bonded to 4 **different** groups (i.e., no symmetry!)



How many stereoisomers possible ?

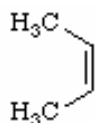
n stereocentres \Rightarrow max. **2^n** stereoisomers

(9)

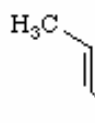
How are different stereoisomers related?

Relationship	Structural difference	Physical properties	Practical implications
Enantiomers	ALL stereocentres opposite config.	identical	Only distinguishable in chiral environments
Diastereomers	Not ALL stereoCs opposite config.	different	Separable by distillation, crystallization, chromatography...

cis / trans isomers are diastereomers



vs.



← NOT mirror images at this point (C's with same configuration)

← Mirror images at this point (C's with opposite configuration)

Total # stereoisomers?

Are any of them enantiomers?

Each has horizontal internal mirror plane & superimposable on own mirror image \Rightarrow **achiral** (neither has an enantiomer)

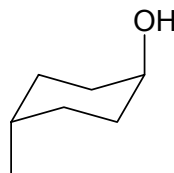
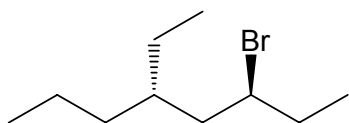
(10)

Molecules with asymmetric centres:

- if molecule is chiral: will have an enantiomer *AND*
- if >1 chiral centre: will also have diastereomers...

For each molecule below...

- How many stereocentres vs. asymmetric centres ?
- How many stereoisomers possible? How are they related?

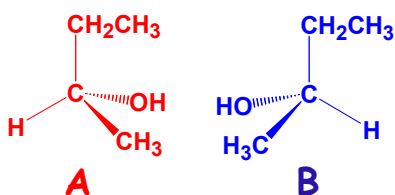


(11)

5.8-9: Chiral compounds are "optically active" *i.e.*, they rotate the plane of plane-polarized light

Enantiomers: same physical properties, different handedness

- interact differently with plane-polarized light (chiral!)
- rotate the plane of PPL to same extent, but in opposite directions (clockwise vs. counterCW)



"optical rotation"
↓

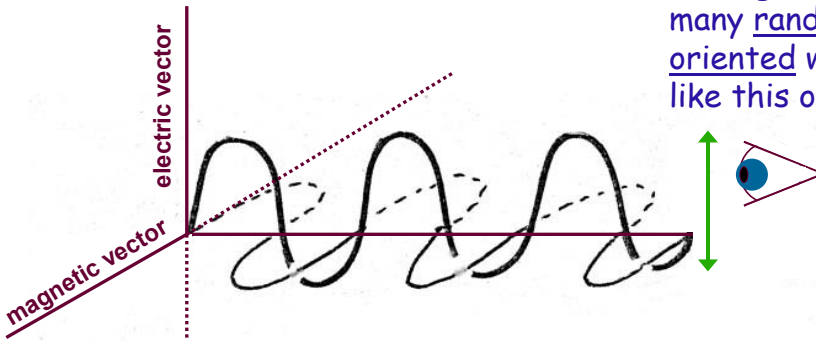
	bp °C	solubility	$[\alpha]_D$
A	99.5	12.5	+13.8°
B	99.5	12.5	-13.8°

So: What IS plane-polarized light?
and: How is it chiral?

(12)

1st: Refresher on the nature of light

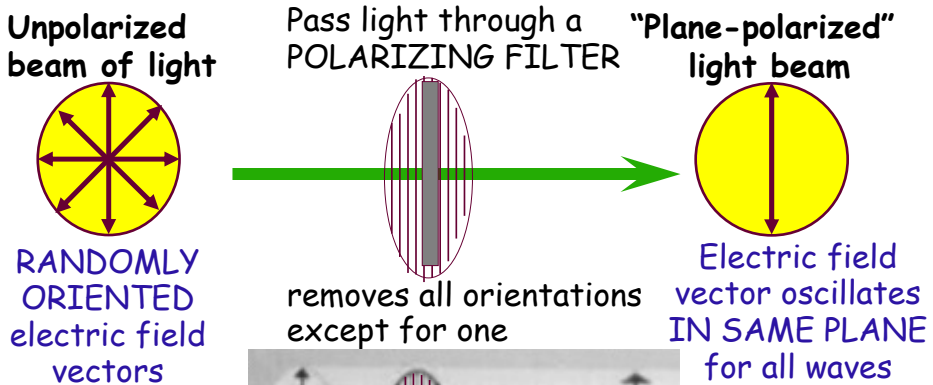
In a light beam:
many randomly oriented waves
like this one...



Light = a wave with oscillating electric & magnetic fields
that are perpendicular to each other
and the direction of propagation

PAY ATTENTION TO THE ELECTRIC VECTOR ONLY
i.e., picture an arrow \leftrightarrow that maps out the amplitude
of the electric field's oscillation

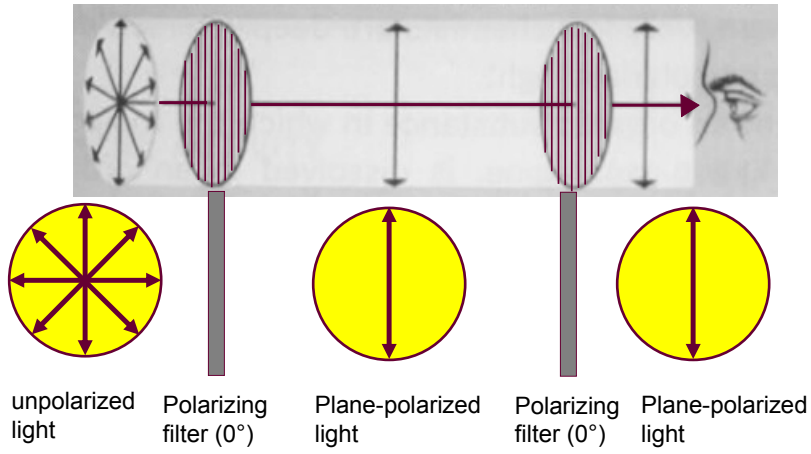
(13)



ONLY light waves with their direction of vibration aligned
PARALLEL TO THE FILTER'S SLITS can pass through!!

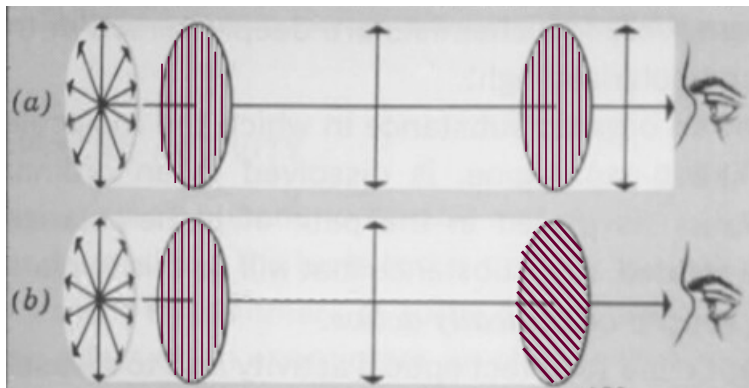
(14)

If we have two polarizers in a row...
...light passes through if they are aligned (both at 0°)



(15)

If not aligned: less light passes through...



NO LIGHT passes if polarizers are "crossed"
(oriented at 90° to each other)

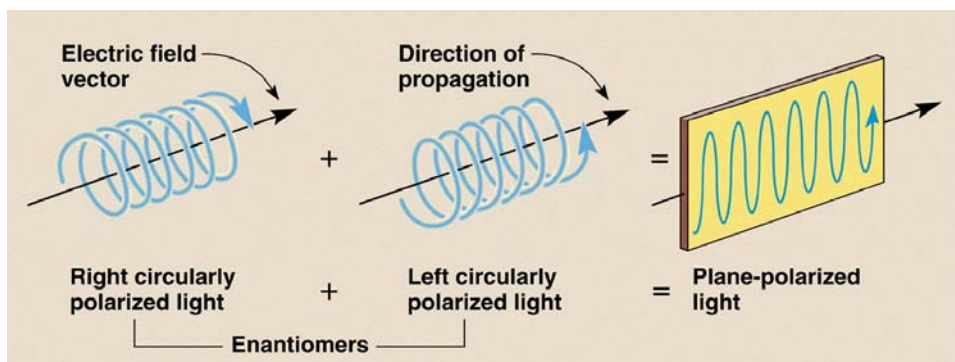
see demonstration...

(16)

So, how is PPL chiral ?

Plane-polarized light = made up of two chiral light waves!
(right CPL) + (left CPL)

Circularly polarized light (CPL) propagates through space as helices, either right-handed or left-handed
i.e., CHIRAL light beams!



Brown & Foote (on reserve) Figure 3.6

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**Remember: right hands fit better into right gloves...
i.e., interactions of chiral species are hand-specific**

When plane-polarized light interacts with chiral molecules, rotation of the plane of polarization occurs.

- right CPL & left CPL are each chiral...
- interact to different extents with chiral molecules!
- result: one CPL gets slowed down more than other
⇒ net rotation of polarization plane

Clockwise rotation: (+) "dextrorotatory" species (d or D)
e.g., (d)-methionine

Counterclockwise: (-) "levorotatory" species (l or L)
e.g., (l)-methionine

A **polarimeter**:

- used to measure rotation of polarized light
- substance of interest placed between two polarizers

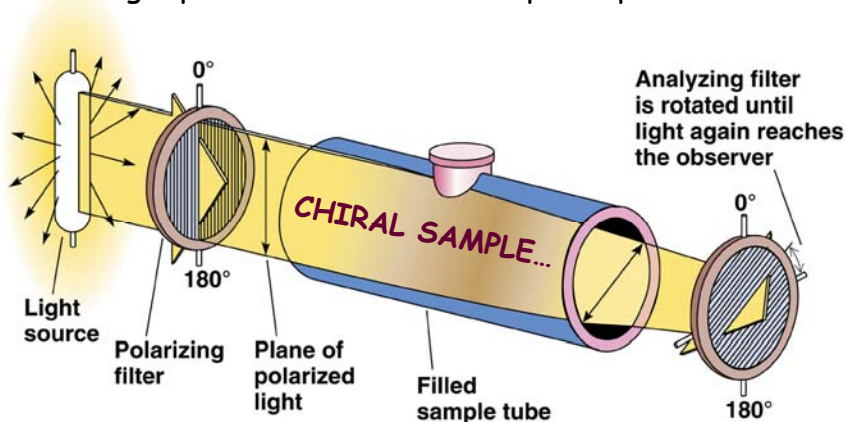
(18)

USING A POLARIMETER

chiral sample rotates plane \Rightarrow less light passes...

\rightarrow YOU turn one polarizer until appears bright again

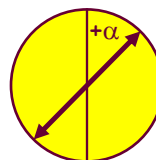
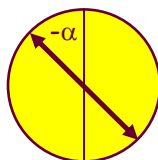
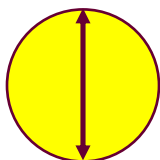
\rightarrow angle polarizer rotates = sample's optical rotation (α)



Similar: Bruice Fig.5.2

(19)

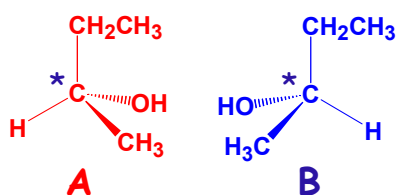
Rotation of Plane Polarized Light



Direction of the electric vector of plane-polarized light	Plane rotated counterclockwise : angle of rotation = $-\alpha$	Plane rotated clockwise : angle of rotation = $+\alpha$
	Compound is "levorotatory" (-) or <i>l</i>	Compound is "dextrorotatory" (+) or <i>d</i>

- For a pair of enantiomers: one is (+), other is (-)
magnitude of rotation is identical
- "racemic mixture" : 50/50 mixture of enantiomers
+/- rotations equal \Rightarrow no net rotation!

(20)



A and B are **chiral**

\therefore optically active

A and B are **enantiomers**

\therefore opposite optical rotation

	bp °C	solubility	$[\alpha]_D$
A	99.5	12.5	+13.8°
B	99.5	12.5	-13.8°

A racemic mixture
of A & B would have
 $\alpha = 0$ (rotations cancel)

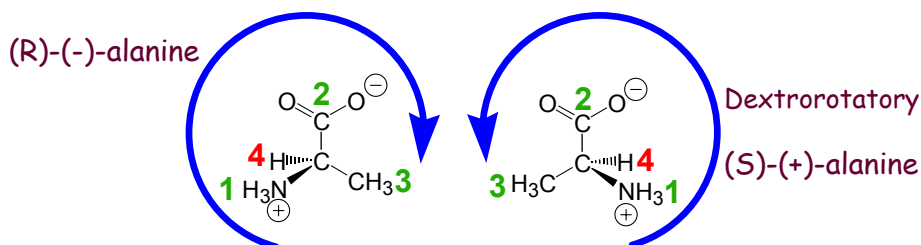
ENANTIOMERS ARE EQUAL BUT OPPOSITE:
If optical rotation for one enantiomer is known...
other enantiomer has **same degree of rotation**,
but in opposite direction.

(21)

Knowing the absolute configuration (R/S) of a compound
does NOT let us predict the sign of the optical rotation,
d(+) or l(-)

Likewise, absolute configuration CANNOT be determined
from the sign of the optical rotation.

BUT: if sign of rotation of one enantiomer IS known...
the other enantiomer will have opposite sign.



NOTE: cannot predict rotation direction, but
if known, can specify in compound's name...

(22)

Quantifying optical rotation: an extensive property...

How much the plane of polarized light is rotated depends on:

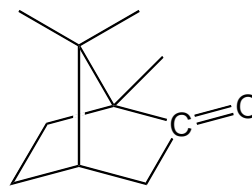
- compound's identity & its concentration
- temperature, length of sample tube, wavelength of light

$$\text{"Specific rotation"} = [\alpha]_D^T = \frac{\alpha}{lC} \text{ (concentration, solvent)}$$

Temperature °C → T
 measured rotation → α
 D line of sodium spectrum → D
 Tube length in decimeters → l
 concentration in g/mL ... & we specify the solvent → C

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EX: A solution (100 mL) of 16.5 g of (/)-camphor in ethanol has an optical rotation of -7.29° at 20°C , using a 10 cm sample tube and a sodium lamp. What is its specific rotation?



$$\begin{aligned} \text{Specific rotation} &= [\alpha]_D^{20} = \frac{\alpha}{lC} \\ &= \frac{-7.29^\circ}{1 \text{ dm} \times 16.5 \text{ g}/100 \text{ mL}} \\ [\alpha]_D^{20} &= -44.2^\circ \text{ (0.165; ethanol)} \end{aligned}$$

Conc. g/mL → 0.165
 solvent → ethanol

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5.10 Optical purity & enantiomeric excess

Enantiomers rotate PPL in opposite directions

thus: net rotation depends on how much of each is present

A racemic mixture (racemate):

- contains equal #s of molecules of two enantiomers ("optical isomers")
- shows NO optical rotation.

WHY? \Rightarrow equal concentration of molecules that rotate plane polarized light clockwise and counterclockwise.

In a non-racemic mixture of optical isomers:

- one enantiomer "A" is present in larger amount (excess)
 - rotation due to enantiomer B will be cancelled out by A's rotation
- \Rightarrow net rotation observed: due to the excess quantity of A

"Enantiomeric excess" (e.e.) or "optical purity"

$$\frac{\text{Measured specific rotation of the mixture}}{\text{Specific rotation of the pure enantiomer}} \times 100 = \% \text{ enantiomeric excess}$$

(25)

Ex: Describe the composition of an unequal mixture of enantiomers, with measured optical rotation: $[\alpha] = 10^\circ$ if optically pure (+) enantiomer has: $[\alpha] = 20^\circ$

THUS: $(10^\circ / 20^\circ) \times 100 = 50\%$ optical purity
or, 50% enantiomeric excess

measured rotation has + sign \Rightarrow means (+) enantiomer is in excess!

What is the ratio of optical isomers present in the mixture?

What is the true meaning of optical purity / enantiomeric excess?

If 50% is optically pure, then the remaining 50% is racemic (+/- or *d/l*)

$$\left. \begin{array}{l} 50\% \text{ } d/l \\ 50\% \text{ } d \end{array} \right\} \begin{array}{l} \frac{\%d}{25} \quad \frac{\%l}{25} \\ \hline 50 \\ \hline 75 \text{ total } d \end{array} \Rightarrow d:l = 75:25 = 3:1$$

(26)

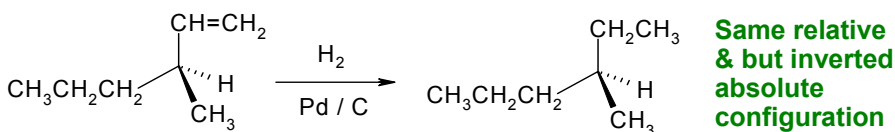
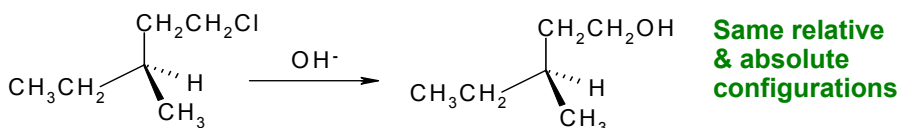
5.14: Rxns of cmpds with asymmetric carbons

Does the configuration at asymmetric centres change?

→ depends on whether or not bonds to asymmetric atom are broken during the reaction

1.) If no bonds to C* broken: relative configuration same

- *i.e.*, no change in relative positions of groups
- BUT: might have changed one of the substituents enough that priority of group changes!
i.e., absolute configuration might change



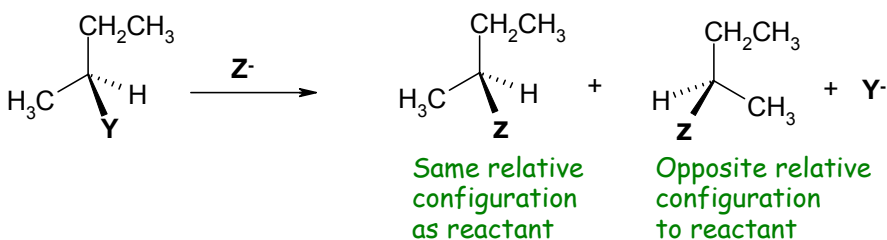
(27)

Does the configuration at asymmetric centres change?

→ depends on whether or not bonds to asymmetric atom are broken during the reaction

1.) If no bonds to C* broken: relative configuration unchanged

2.) If a bond to C* is broken: configuration MAY change
→ depends on mechanism of reaction!



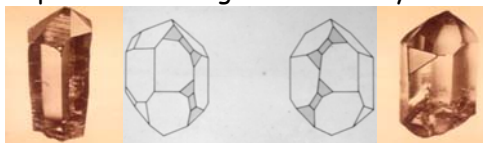
Coming soon: mechanisms of this type of reaction!

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5.16: Resolution of racemic mixtures = separating enantiomers (using clever tricks!)

1. BRUTE FORCE: Pasteur...

- resolved crystals of sodium ammonium tartrate (from wine)
- viewed crystals under microscope: left- vs. right-handed crystals
- separated them by hand...



2. BIOLOGICAL RESOLUTION: stereoselective rxn

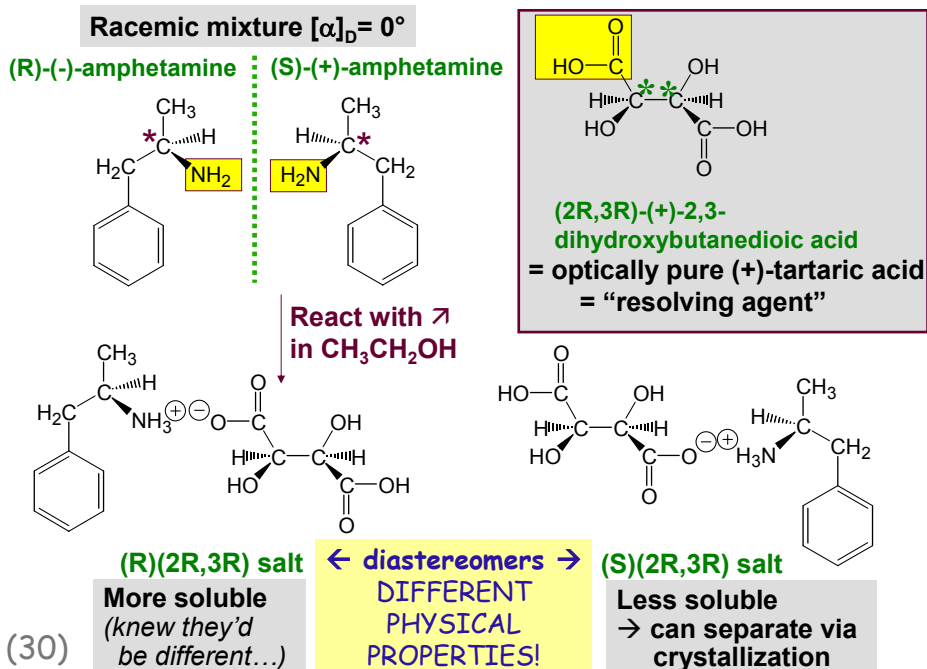
- feed a racemic mixture to a biological system
- only converts one enantiomer to another product
- leaves behind the other enantiomer unchanged (= the one you want?)

3. PREPARATION OF DIASTEREOMERS: reversible rxn

- chemical rxn: modify enantiomers so they stop being enantiomers...
- separate diastereomeric products (different physical properties!)
- undo the rxn: convert separated products back into reactants
e.g., acid-base chemistry (easily reversible)...

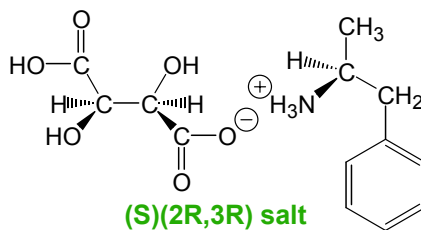
(29)

Using reversible chemistry to resolve enantiomers: step 1

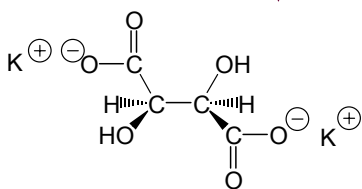


Using reversible chemistry to resolve enantiomers: step 2

Filter off crystals of the less soluble of the two diastereomeric salts
→ recrystallize to purify it!

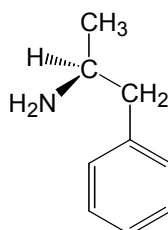


KOH/H₂O treat with base to deprotonate the ammonium ion → regenerate amine!



CHARGED!
soluble in water
(deprotonated form
of the resolving agent)

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insoluble in water
(the desired compd)

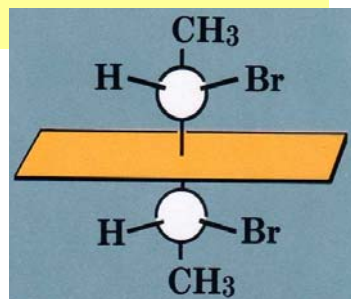
(S)-(+)-amphetamine, $[\alpha]_D = +40^\circ$

5.12: Meso Compounds

Picture a molecule with two asymmetric centres that have identical groups on them...

Depending on their configurations, the molecule overall can have an INTERNAL plane of symmetry.

→ Molecule overall is **ACHIRAL** called a "meso compound"



Brown & Foote Fig. 3.4
(textbook on reserve)
Nice pictures in Bruice too

IMPLICATION: optically inactive

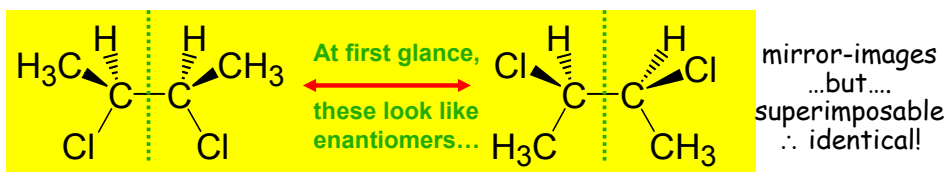
stereocentres in SAME molecule are mirror images

⇒ cancel out each other's optical rotation

⇒ like a racemic mixture inside one molecule!

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MESO COMPOUNDS: contain mirror-image stereocenters

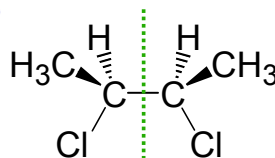


Internal plane of symmetry \Rightarrow ACHIRAL molecule

A "MESO" COMPOUND

The molecule is not chiral
 \therefore has no optical activity

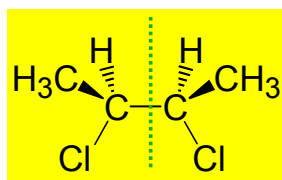
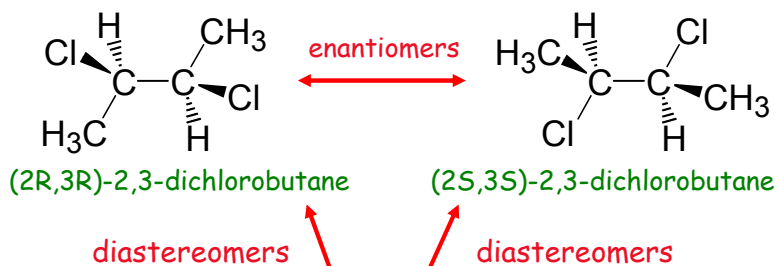
Like a racemic mixture
 within one molecule!



Aside: in 5.9, see "erythro" vs. "threo" to describe isomers with $>1 C^*$
 If can rotate to have similar groups on same side of chain: erythro
 If config. Makes similar groups remain on opposite sides: threo
BUT YOU ARE NOT STRICTLY RESPONSIBLE FOR THIS!

(33)

2,3-dichlorobutane: 2 stereocentres \Rightarrow max. 2^2 stereoisomers,
 but actually only 3 different cmpds since 1 is a meso cmpd



A meso compound

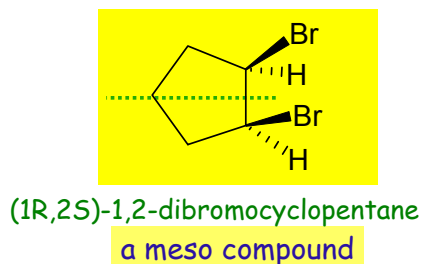
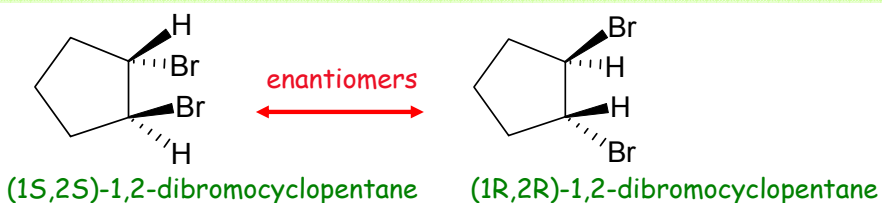
(2S,3R)-2,3-dichlorobutane ?
 (2R,3S)-2,3-dichlorobutane ?

Must have a unique name.
 Which name is correct?

For meso compounds: stereocenter with lower #
 designated as R configuration

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Disubstituted cycloalkanes: many have a meso diastereomer



NOTE: convince yourself of this:

- all symmetrically disubstituted cyclopentanes have meso isomers
→ both 1,2- and 1,3-substituted
BUT...
- not the case for all disubstitution patterns of cycloalkanes!
→ don't always have asymmetric Cs!



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ASSIGNED READINGS

BEFORE NEXT LECTURE:

Read: Ch.5 (all)

Practice: assigning R/S configuration
identifying enantiomers & diastereomers
DRAWING & NAMING stereoisomers

products/mechanisms of alkene reactions
→ try thinking about stereochemistry too...
(covered next class)

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