Announcements:

- Lecture starts 9:35 am

- Before lecture please use your model kit to build a model of:

i.e.

(2-butanol)

be sure to include this H

- Remember: Lab today for Monday folks.

- This week "Friday Review" will be on Thursday (July 3) 3–5 pm Hall B.

identical to mirror image

Symmetry, Chirality, and Enantiomers

Ethanol is ACHIRAL

OH

(2 identical substituents)

H, H
OH, Me

4 different groups
– H
– OH
– Me
– Et

2-Butanol is CHIRAL

not identical to its mirror image

stereoisomers

N.B. Many of these slides have been borrowed from Prof. Garry Procter. *Reading*: Section 6.1

Same constitution, different arrangement in space.

look identical after rotate as needed around single bonds.

a pair

Some Important Vocabulary Words

- **Enantiomers**: stereoisomers that are non-superimposable mirror images
- **Chirality**: the property of having a non-superimposable mirror image

one molecule

How can I tell if a molecule is chiral?

1. Does it have a stereogenic center? ("stereocenter")

Tetrahedral C bonded to 4 distinct substituents

ex:

stereogenic center

Generalizations:

- If a molecule has 0 stereogenic centers, it is ***achiral***. → usually. (exceptions exotic)
- If a molecule has a single stereogenic center, it is ***chiral***. → always.
- If a molecule has >1 stereogenic centers, we must consider another property.

(not always 100% true)

achiral

0 stereocenters.

chiral

1 stereocenter

2 stereocenters... but achiral (!)

2. Is there an internal plane of symmetry in the molecule?

- Any molecule that has a plane of symmetry will be ***achiral***. → always
- Any molecule that *lacks* a plane of symmetry will be ***chiral***. → (exceptions exotic)

(can rotate around single bonds if needed)

• For each of the following molecules, determine whether it is chiral or achiral. If it is chiral, draw its enantiomer.

chiral

Chiral

Achiral

Reading: Section 6.1

internal symmetry plane

"Absolute configuration"

Build models

Naming Enantiomers: The *R*, *S* System

- Here are the rules for naming enantiomers: 0. Find stereocenters.

1 = top priority

4 = lowest priority.

1. Rank the groups attached to the **stereocenter** in priority order - as for *E* & *Z* nomenclature of alkenes. The greater the atomic number, the greater the priority. Use the *first point of difference* where necessary.

rotate

Re-draw

No change

2. Orient the molecule (re-draw if necessary) so that it is viewed with the **lowest priority group** is directed **away** from viewer (i.e. the bond to **4** is dashed).

Bond to #4 must be dashed.

3. Now trace the path **1 → 2 → 3**

clockwise - (turning **R**ight) - (***R***)-enantiomer

(*R*)-2-butanol

counterclockwise - (turning **L**eft) - (***S***)-enantiomer

(*S*)-2-butanol

Opposite Day!

- Assign *R* or *S* configurations to each of the following compounds:

(S)

(R)

(S)

Reading: Section 6.2

Are Enantiomers Different?

- Roald Hoffmann (who shared the Nobel Prize for frontier molecular orbitals) wrote a wonderful book about chemistry titled *The Same and Not The Same*. His point was that much of chemistry involves substances that are the same in some respects, and not the same in others. Enantiomers are an excellent example:

  A pair of enantiomers will generally have **identical physical properties**: same
  - color, boiling point, melting point, solubility, etc.

  A pair of enantiomers will generally have **different biological properties:** Life is chiral.
  - taste, smell, toxicity, therapeutic action, etc.

  A pair of enantiomers can exhibit the **same chemical reactivity OR different chemical reactivity**, depending on what they are reacting with (more on this later).

For instance:

Replacing wedges/dashes

… this enantiomer of penicillin can save your life…

… this enantiomer of penicillin cannot save your life…

R-carvone
spearmint

S-carvone
caraway ("rye")

Confirm (R), (S) on your own...

- As an excercise, can you assign the *R* and *S* designations to these enantiomers of carvone? Do you remember the rule for multiple bonds?

If you rotate light optically active.

Optical Activity of Enantiomers

sample of chiral compound

- Enantiomers rotate the plane of polarized light **equally in opposite directions**

One physical experiment where enantiomers are different

Electric field vector only oscillates in a single plane

rotated plane of polarization

If the plane has **rotated clockwise**, the compound is **dextrorotatory or (+)**
If the plane has **rotated counterclockwise**, the compound is **levorotatory or (–)**
… and we can incorporate this into the name: **(*S*)-(+)-2-butanol**

No connection with R/S

> **Note :** (+) and (–) are physical properties and CANNOT be determined by the structure or by correlation with R/S. They are properties of the entire molecule.

- What would happen to the polarized light if it passed through a solution of (*R*)-2-butanol? (R)(–) 2-butanol.

rotate counterclockwise.

- What about a *mixture* composed of equal amounts of *both* (*S*)-2-butanol and (*R*)-2-butanol?

Such a 50-50 mixture of enantiomers is called **racemic mixture** or a **racemate**

No overall rotation. ⟹ Optically inactive racemic mixture

- Standard form for reporting optical rotation:

temp

$$[\alpha]_D^{20} = \pm(\quad)^\circ$$

degrees

(+ = clockwise)

number

Sodium D-line.

Reading: Sections 6.3, 6.4

Mixtures of Enantiomers: Racemates and Purity

- What would happen to polarized light if it passed through a *mixture* composed of equal amounts of *both* enantiomers of a compound? Such a 50-50 mixture of enantiomers is called a **racemic mixture** or a **racemate**.

won't rotate

- For any other mixture of enantiomers, we can characterize the mixture by measuring its optical rotation. We define the *optical purity* or *enantiomeric excess (e.e.)* as:

$$\text{optical purity} = \text{e.e.} = \frac{\text{observed specific rotation}}{\text{specific rotation of pure enantiomer}} =$$

$$= (\%\ \text{major enantiomer}) - (\%\ \text{minor enantiomer})$$

Example:

A sample of (*S*)-(+)-monosodium glutamate (MSG) has an observed specific rotation of + 19.2°. → only rotates 19.2°. not pure.

(*S*)-(+)-monosodium glutamate

$[\alpha]_D^{20} = +24$ ← known specific rotation of pure enantiomer

What is the optical purity of the sample? What is the composition of the mixture?

$$\frac{[\alpha]_{obs}}{[\alpha]_{pure}} \equiv \text{e.e.} = \frac{19.2^\circ}{24^\circ} = 0.8 = \boxed{80\%} = \underbrace{90\%}_{\text{major}} - \underbrace{10\%}_{\text{minor}}$$

90% (S)-MSG (+)
10% (R)-MSG (−)

Let x = % of major
e.e. = (x) − (100 − x)
e.e. = 2x − 100
so if x = 100, e.e. = 100%
x = 50, e.e. = 0%

Reading: Sections 6.3, 6.4

n stereocenters, up to 2^n isomers.

Suppose more than one stereocenter

Enantiomers and Diastereomers

Each could be R/S

In a molecule with 2 or more stereocenters, **Diastereoisomers** are possible

Diastereoisomers: Stereoisomers which are ***not*** enantiomers

Example: 2,3-pentanediol

Change only one

switch some but not all of R/S

- What do we notice about enantiomers and diastereomers when we look at their *R*, *S*-designations?

Enantiomers: switch every R with S

Diastereomers
- Same constitution.
- different arrangement in space
- Not enantiomers.

- How can we determine the relationship between two molecules: "the same and not the same"

different → Constitutional isomers

isomers → connectivity?

same molec. formula

same → Stereoisomers

mirror? → enantiomers

not mirror → diastereomers

Reading: Section 6.6

two stereocenters

Physical Properties of Enantiomers and Diastereomers

		optical rotation	melting point
	(2*S*, 3*S*)	$[\alpha]_D^{25} = +15$	m.pt. = 150–151
		enantiomers	opposite	same
	(2*R*, 3*R*)	$[\alpha]_D^{25} = -15$	m.pt. = 150–151
		diastereomers	different
	(2*S*, 3*R*)	$[\alpha]_D^{25} = +21$	m.pt. = 155–156
		enantiom.	opposite	same.
	(2*R*, 3*S*)	$[\alpha]_D^{25} = -21$	m.pt. = 155–6
	***racemate of* (2*S*, 3*S*) & (2*R*, 3*R*)**	$[\alpha]_D^{25} = 0$	m.pt. = 117–123
	***racemate of* (2*S*, 3*R*) & (2*R*, 3*S*)**	$[\alpha]_D^{25} = 0$	m.pt. = 165–166

(unrelated)

Reading: Section 6.6

Watch out!

Achiral Molecules with Asymmetric Carbons

- Usually, an asymmetric carbon is a sure sign that a compound is chiral. However, consider the various stereoisomers of 2,3-butanediol:

example

2 stereocenters but achiral

because of internal plane of symmetry

distinct enantiomers

actually identical so achiral

identical!!!

BUT if we simply rotate this mirror image 180°...

internal

Carbons 2,3 are related by symmetry

MesO

The meso-stereoisomer has a plane of symmetry

rotate this "end" around 2–3 bond... *...to give an eclipsed conformation...* *...which has a plane of symmetry and so cannot be chiral*

How can we identify these *meso* compounds?

Contains stereocenters but overall achiral

(Look for even # stereocenters, with symmetry)

Reading: Section 6.7

Separation of Enantiomers: Resolution of Racemates

Enantiomers - same solubilities, melting points, boiling points, etc.

separation poses a special problem!

If we convert a mixture of ***enantiomers*** to a mixture of ***diastereoisomers***...

...then diastereoisomers can be separated (recall they have different properties).

Overall plan for resolution of a racemate

racemate —*convert*→ diastereoisomers

diastereoisomers —*separate*→ diastereoisomer A, diastereoisomer B

diastereoisomer A —*convert*→ (+)-enantiomer

diastereoisomer B —*convert*→ (–)-enantiomer

add chiral thing

remove chiral thing.

Example:

one enantiomer

RRR

SRR

Reading: Section 6.8

isolate original cation