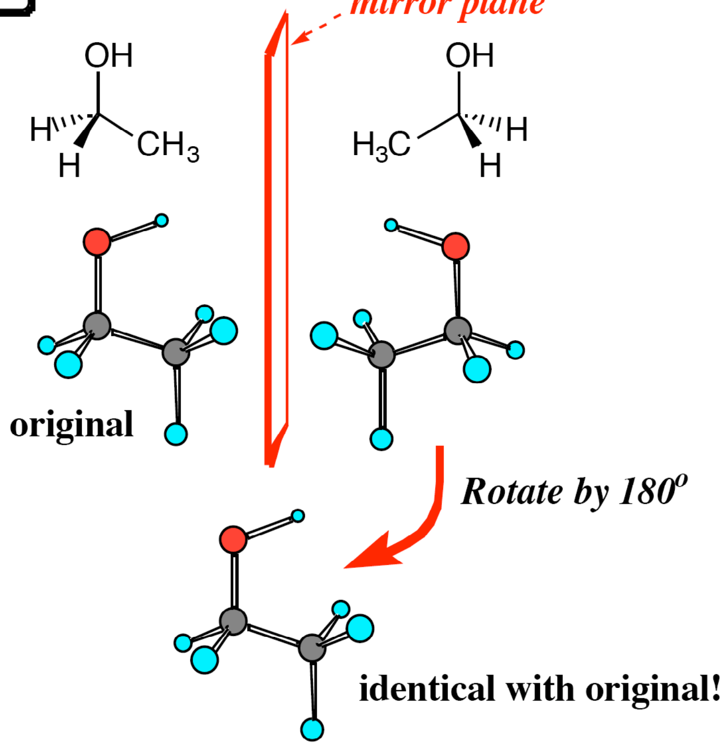
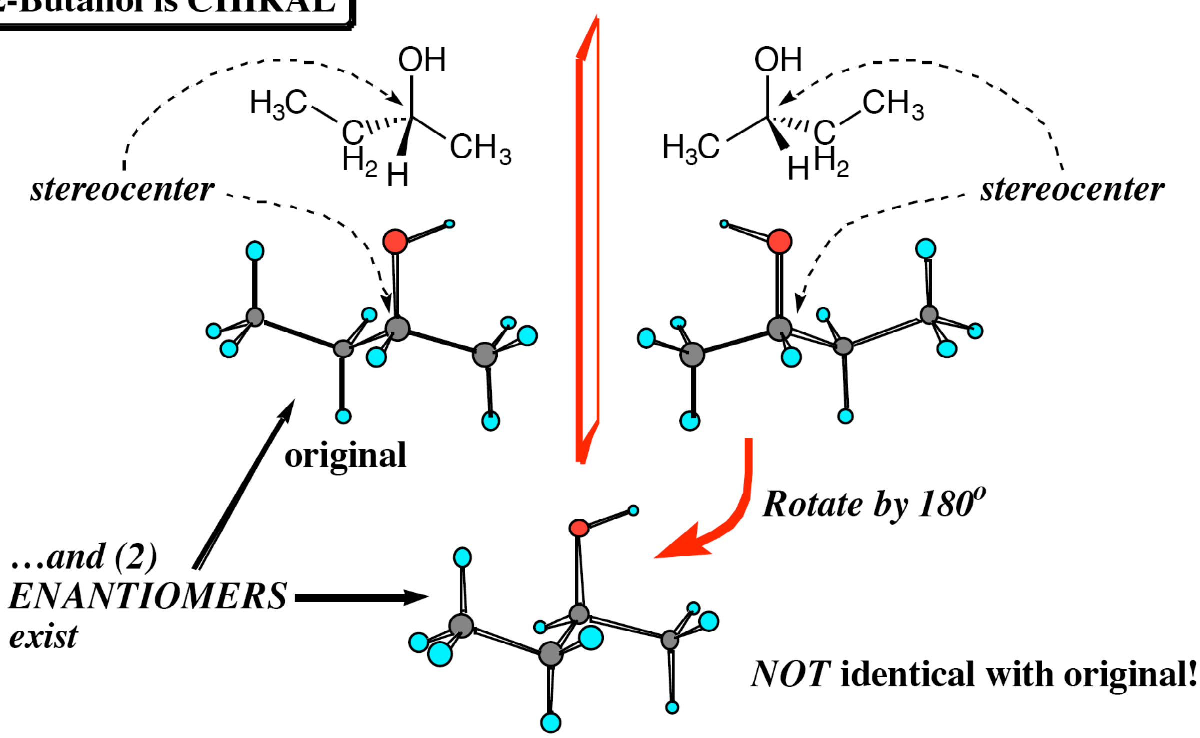
Symmetry, Chirality, and Enantiomers

Ethanol is ACHIRAL



2-Butanol is CHIRAL



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

Some Important Vocabulary Words

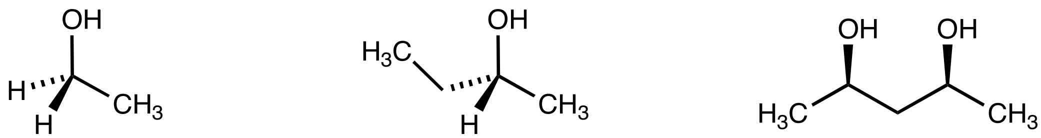
- **Enantiomers**: stereoisomers that are non-superimposable mirror images
- **Chirality**: the property of having a non-superimposable mirror image

How can I tell if a molecule is chiral?

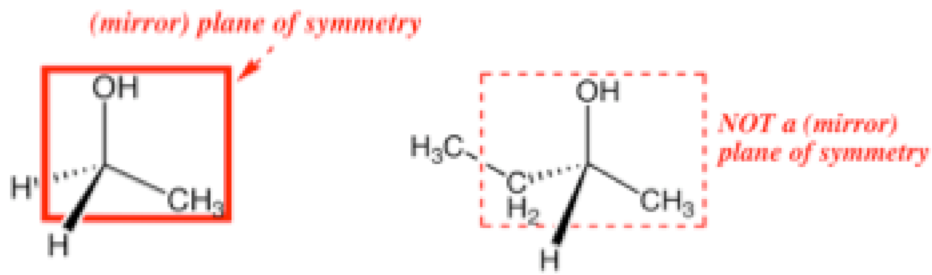
1. Does it have a stereogenic center?

Generalizations:

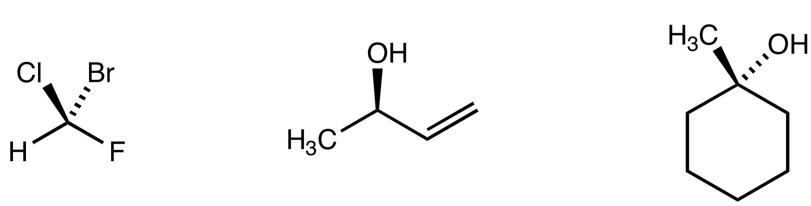
- If a molecule has 0 stereogenic centers, it is ***achiral***.
- If a molecule has a single stereogenic center, it is ***chiral***.
- If a molecule has >1 stereogenic centers, we must consider another property.



2. Is there an internal plane of symmetry in the molecule?
   - Any molecule that has a plane of symmetry will be ***achiral.***
   - Any molecule that *lacks* a plane of symmetrty will be ***chiral***.



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

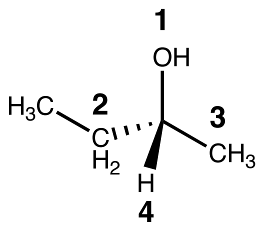


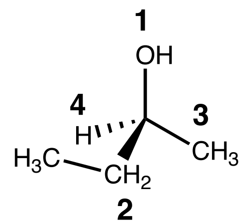
Reading: Section 6.1

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

- Here are the rules for naming enantiomers:

    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.

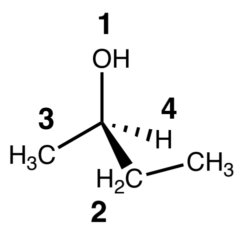


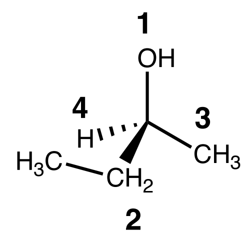


Re-draw

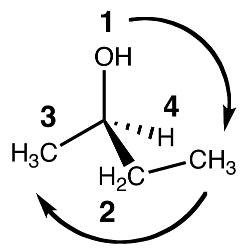
No change

    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).



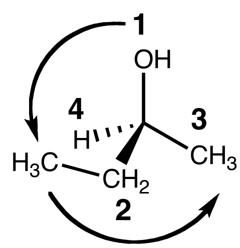


    3. Now trace the path **1** → **2** → **3**



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

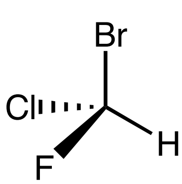
(*R*)-2-butanol

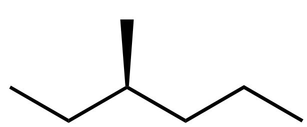


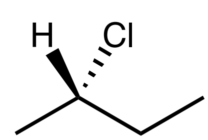
counterclockwise - (turning **L**eft) -
(*S*)-enantiomer

(*S*)-2-butanol

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







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:

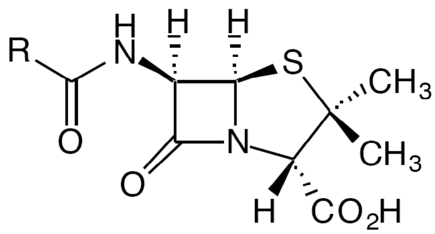
  A pair of enantiomers will generally have **identical physical properties**:
  - color, boiling point, melting point, solubility, etc.

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

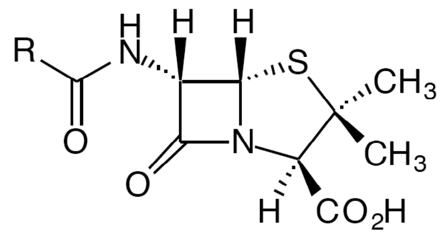
  A pair of enantiomers can exhibit the **same chemical reactivity OR different chemical reactivity**, depending on what they are reacting with (more on this later).

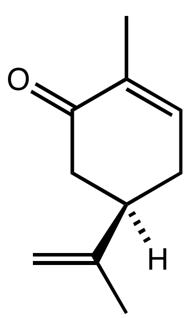
For instance:

… this enantiomer of penicillin can save your life...

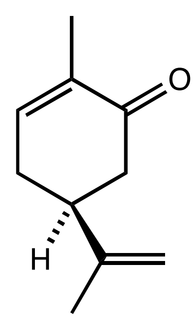


… this enantiomer of penicillin cannot save your life...





R-carvone
spearmint

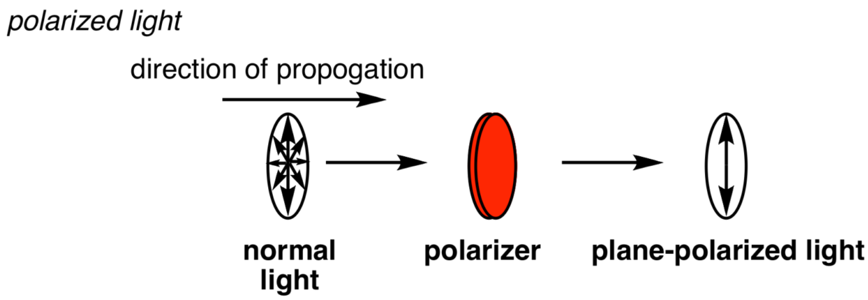


S-carvone
caraway ("rye")

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

Optical Activity of Enantiomers

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



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**

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?

- 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**

- Standard form for reporting optical rotation:

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**.

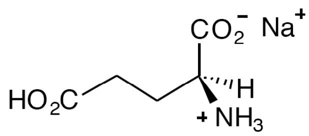
- For any other mixture of enantiomers, we can characterize the mixture by measuring its optical rotation. We define the *optical purity* or *enantiomeric excess (e.e.)* as:

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

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

Example:

A sample of (*S*)-(+)-monosodium glutamate (MSG) has an observed specific rotation of + 19.2°.



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

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

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

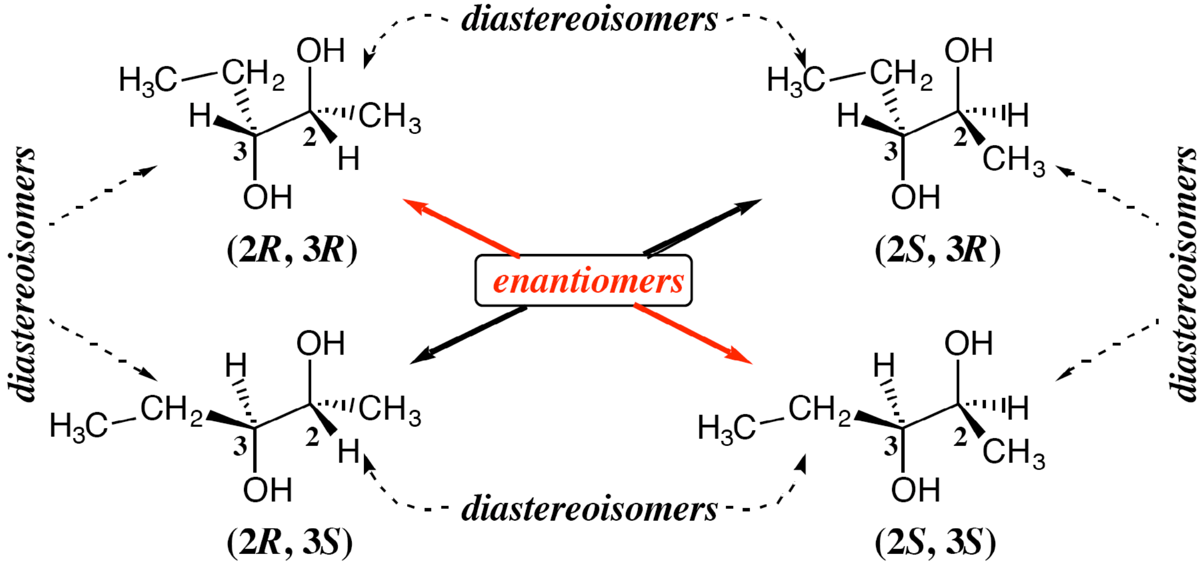
Reading: Sections 6.3, 6.4

Enantiomers and Diastereomers

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

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

Example: 2,3-pentanediol

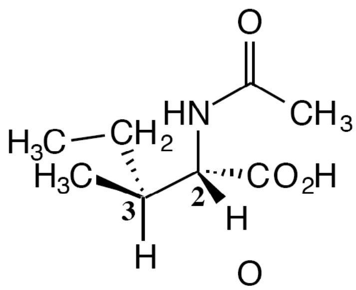


- What do we notice about enantiomers and diastereomers when we look at their *R*, *S*-designations?

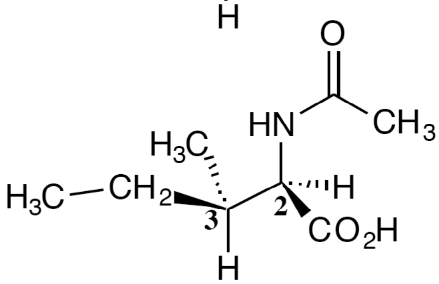
- How can we determine the relationship between two molecules: "the same and not the same"

Reading: Section 6.6

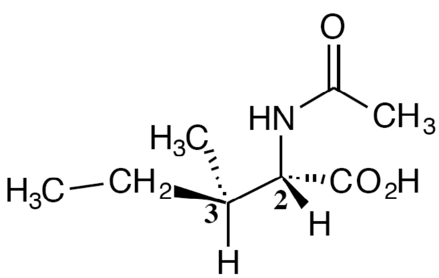
Physical Properties of Enantiomers and Diastereomers



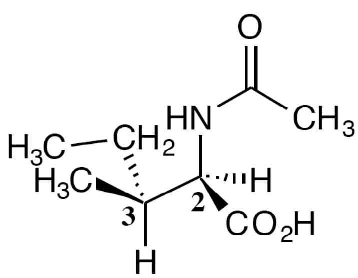
(2*S*, 3*S*) $[\alpha]^{25}_{D} = +15$ m.pt. = 150–151



(2*R*, 3*R*) $[\alpha]^{25}_{D} = -15$ m.pt. = 150–151



(2*S*, 3*R*) $[\alpha]^{25}_{D} = +21$ m.pt. = 155–156



(2*R*, 3*S*) $[\alpha]^{25}_{D} = -21$ m.pt. = 155–6

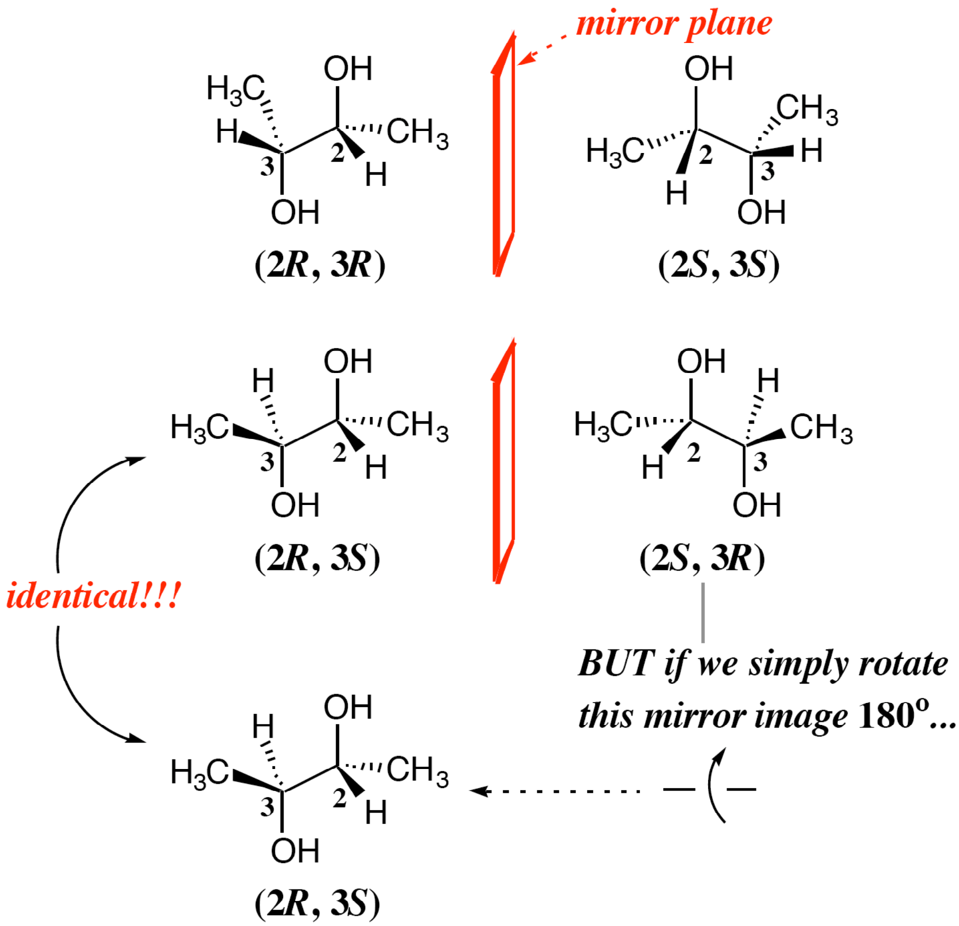
***racemate of* (2*S*, 3*S*) & (2*R*, 3*R*)** $[\alpha]^{25}_{D} = 0$ m.pt. = 117–123

***racemate of* (2*S*, 3*R*) & (2*R*, 3*S*)** $[\alpha]^{25}_{D} = 0$ m.pt. = 165–166

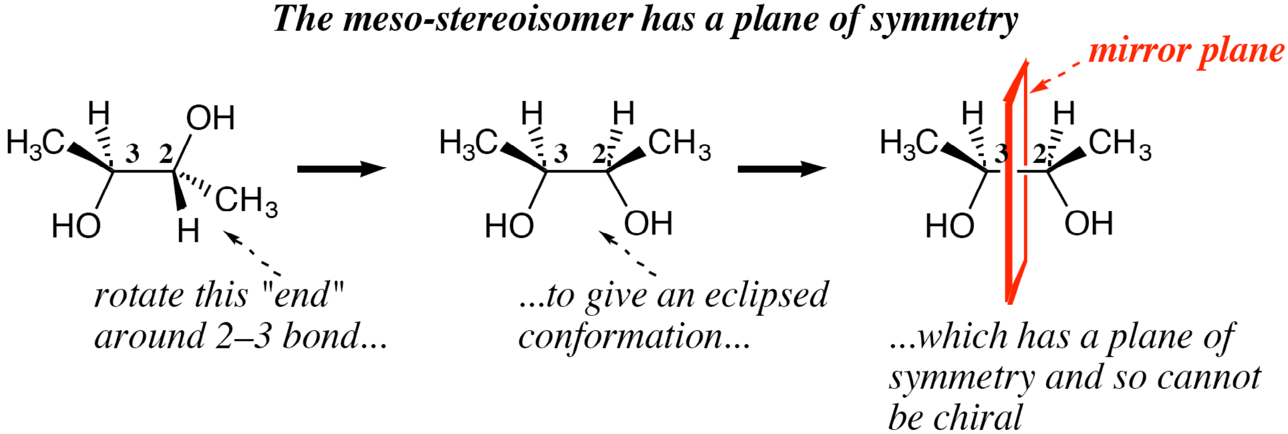
Reading: Section 6.6

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:



The meso-stereoisomer has a plane of symmetry



How can we identify these *meso* compounds?

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

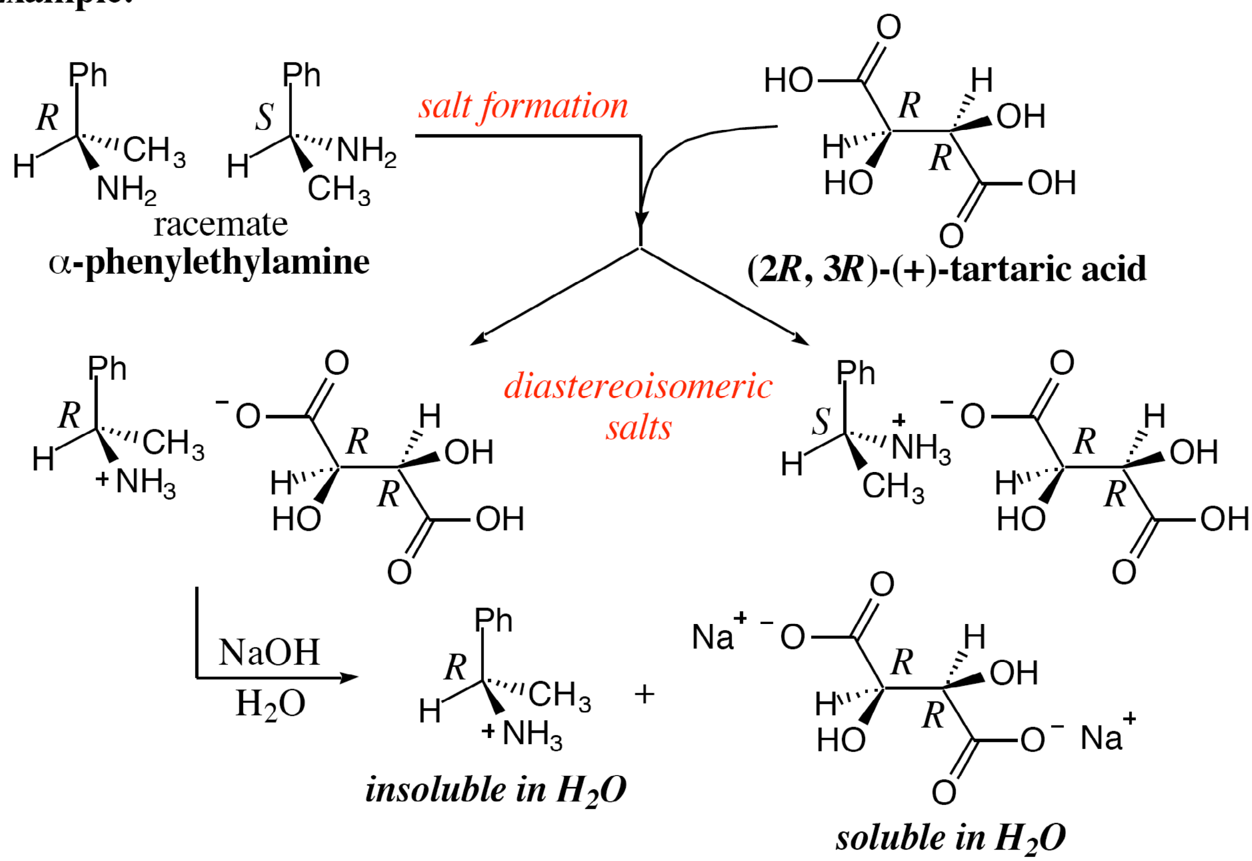
racemate $\xrightarrow{\text{convert}}$ diastereoisomers

separate

diastereoisomer A $\xrightarrow{\text{convert}}$ (+)-enantiomer

diastereoisomer B $\xrightarrow{\text{convert}}$ (–)-enantiomer

Example:



Reading: Section 6.8