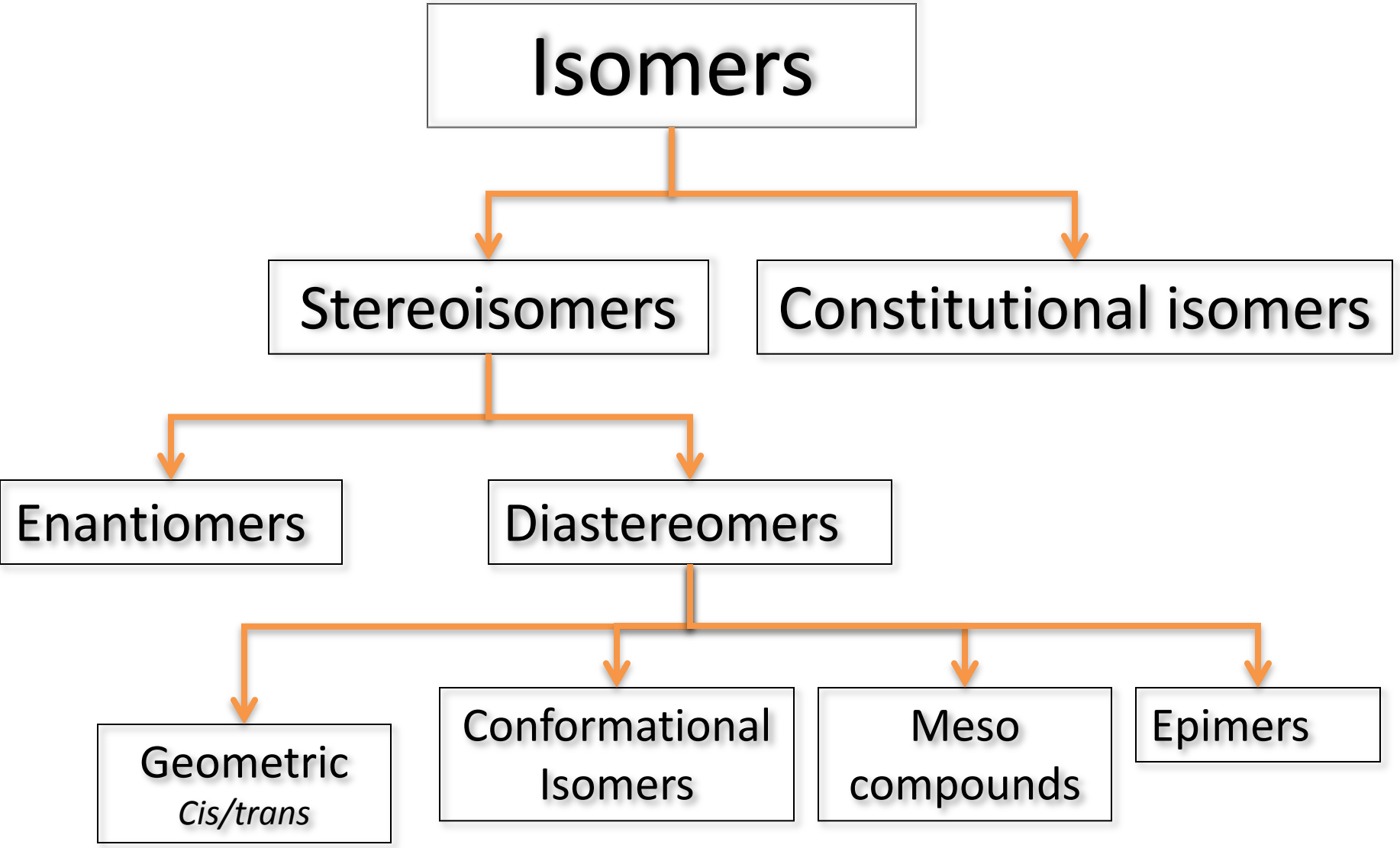
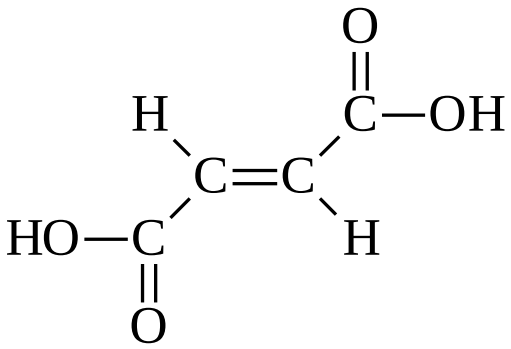
Stereochemistry

Isomer Organization

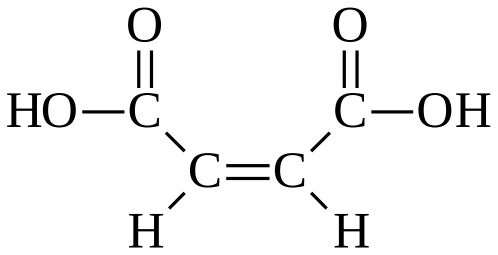


Stereoisomers

- Same bonding sequence.
- Different arrangement in space.
- Example: HOOC-CH=CH-COOH
  has two geometric (cis-trans) isomers



fumaric acid, mp 287° C
essential metabolite



maleic acid, mp 138 °C
toxic irritant

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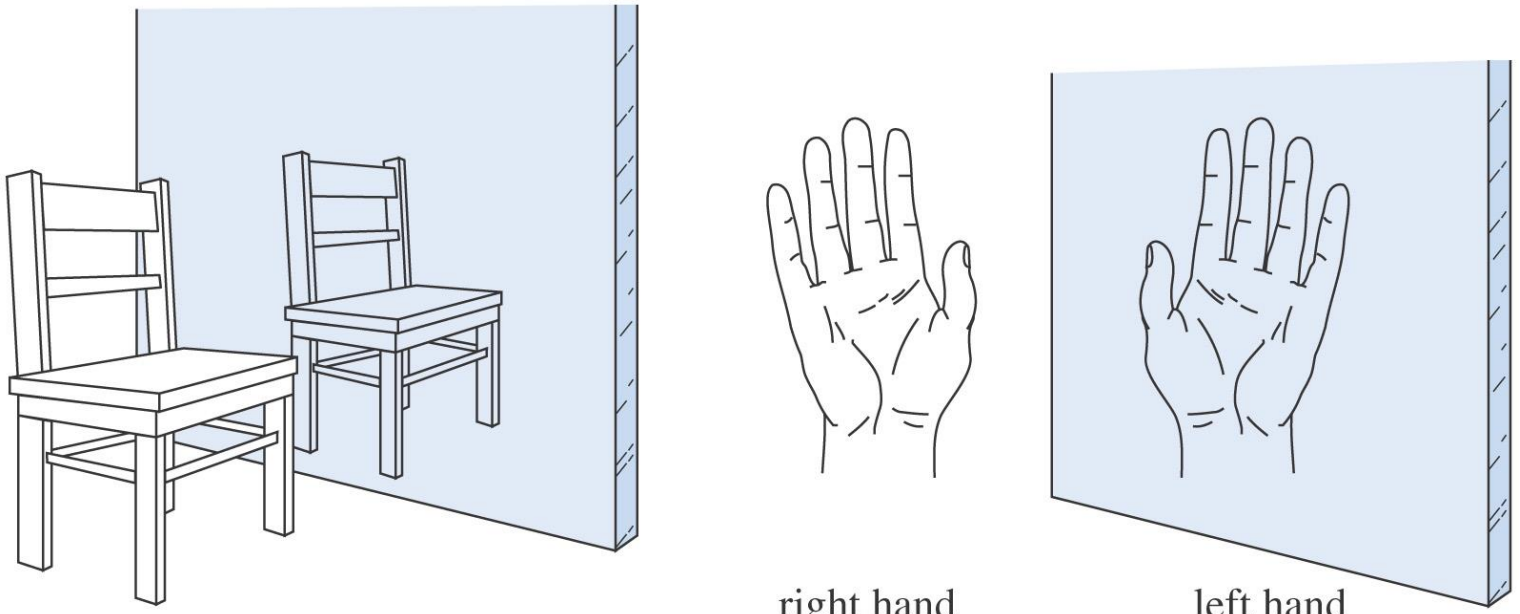
Chirality

- "**Handedness**": right glove doesn't fit the left hand.
- Mirror-image object is different from the original object

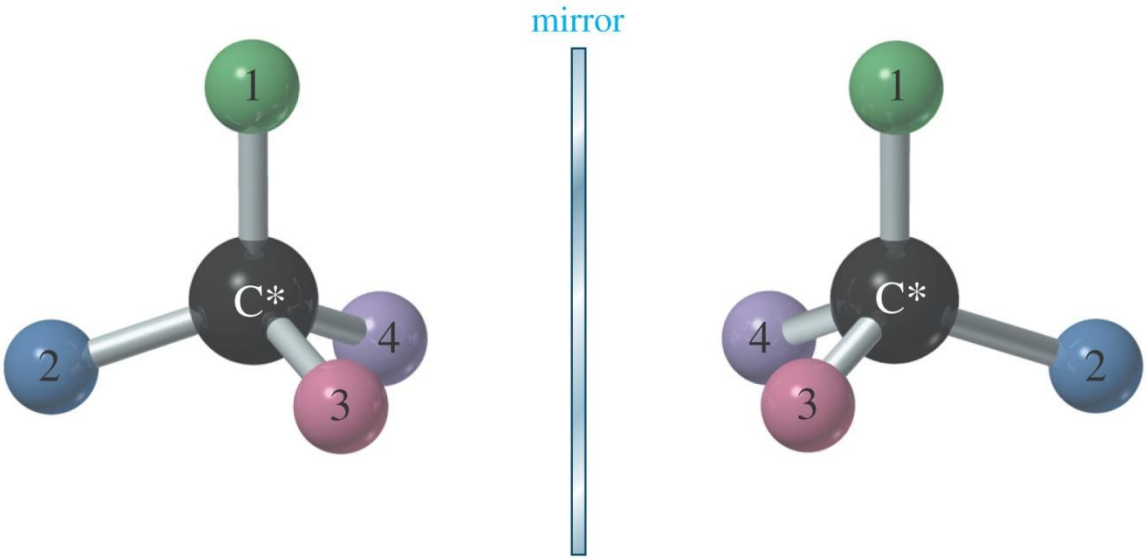


Examples of Handed Objects

- Your hands, from the previous slide
- Gloves
- Scissors
- Screws
- Golf clubs

How about molecules?

- Chemical substances can be **handed**
- Handed substances are said to be **chiral**
- Molecules, that are **chiral** are nonsuperimposable on their mirror image



Chirality in Molecules

- *cis* isomers are **achiral** (not chiral).

Chirality in Molecules

- The *cis* isomer is **achiral**.
- The *trans* isomer is **chiral**.

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- The one **enantiome**r of carvone is the essence of caraway, and the other, the essence of spearmint.
- Most molecules in the plant and animal world are **chiral** and usually only one form of then enantiomer is found.

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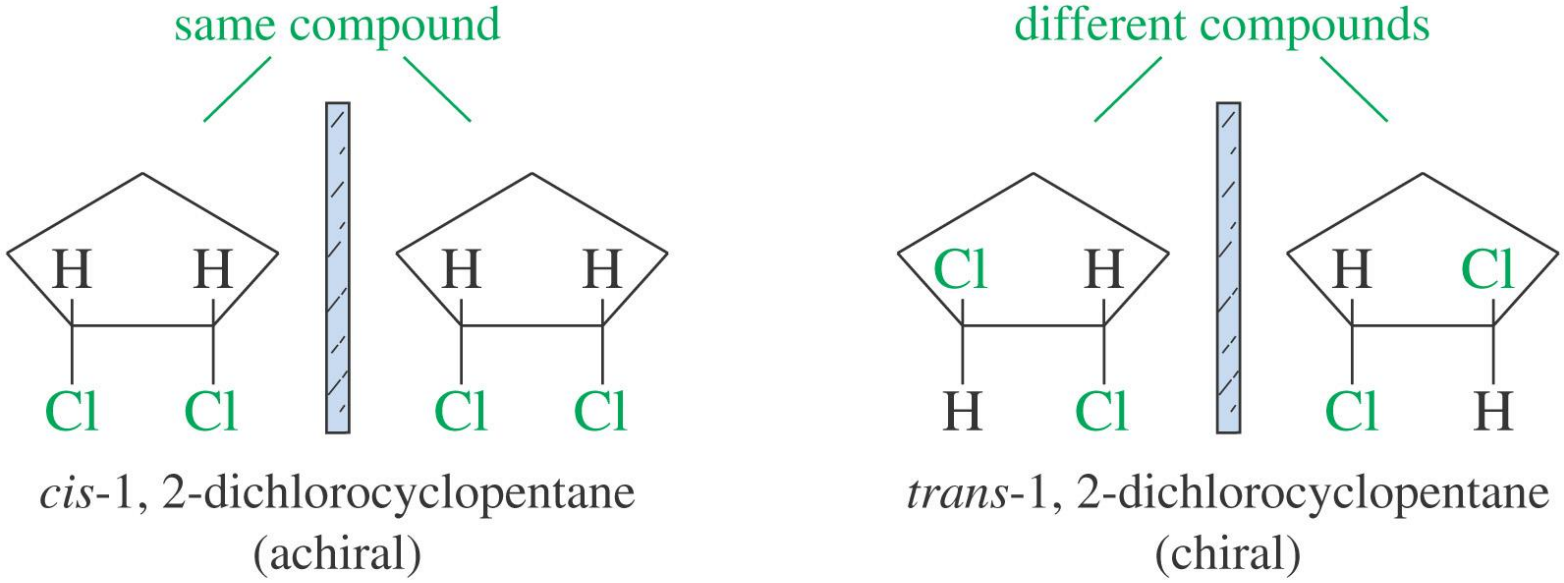
- Nineteen of the twenty known amino acids are **chiral**, and all of them are classified as left handed.

Chirality in Molecules

- The *cis* isomer is **achiral**.
- The *trans* isomer is chiral.
- **Enantiomers:** nonsuperimposable mirror images, different molecules.

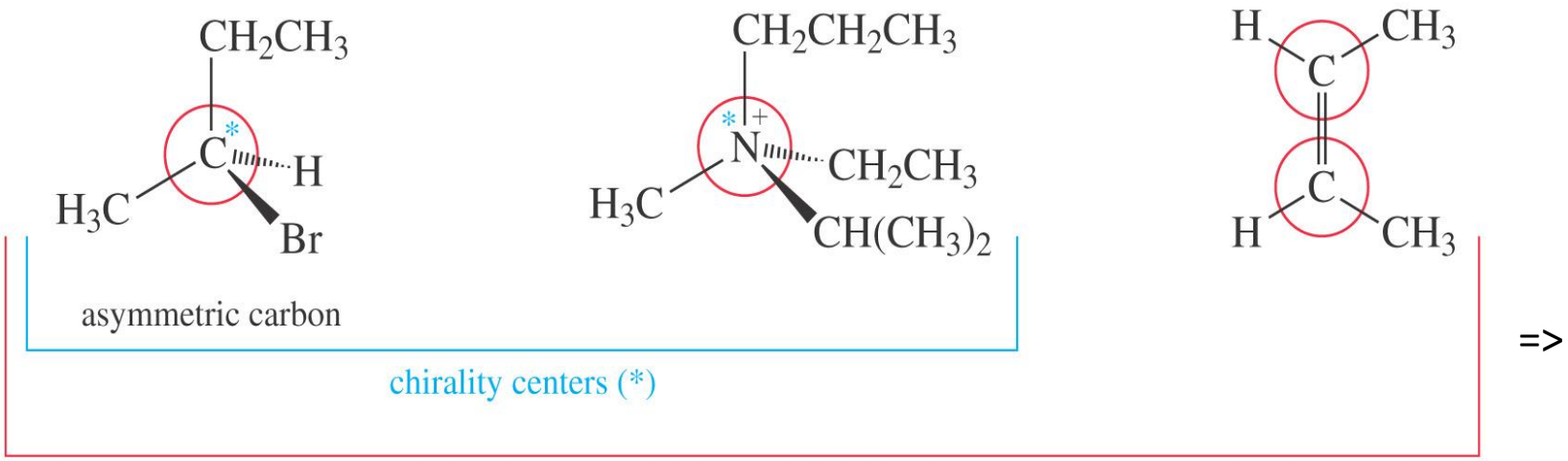


cis-1, 2-dichlorocyclopentane (achiral)

trans-1, 2-dichlorocyclopentane (chiral)

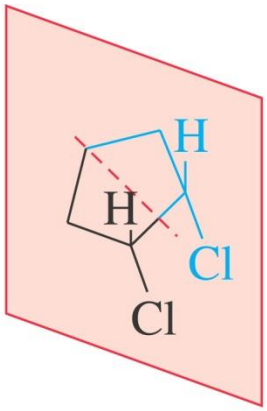
Stereocenters

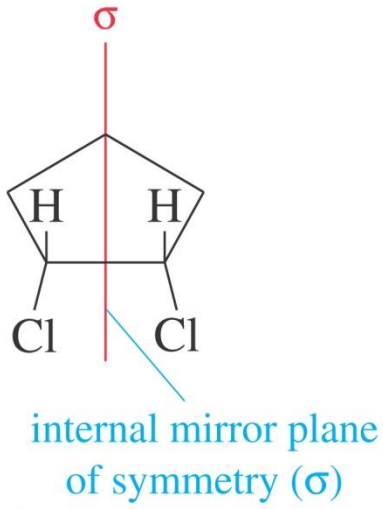
- Any atom at which the exchange of two groups yields a **stereoisomer**.
- Examples:
  - Asymmetric carbons
  - Double-bonded carbons in cis-trans isomers



Mirror Planes of Symmetry

- **If two groups are the same, carbon is achiral. (animation)**
- **A molecule with an internal mirror plane cannot be chiral.***





Caution! If there is no plane of symmetry, molecule may be chiral or achiral. See if mirror image can be superimposed.

Absolute Configuration

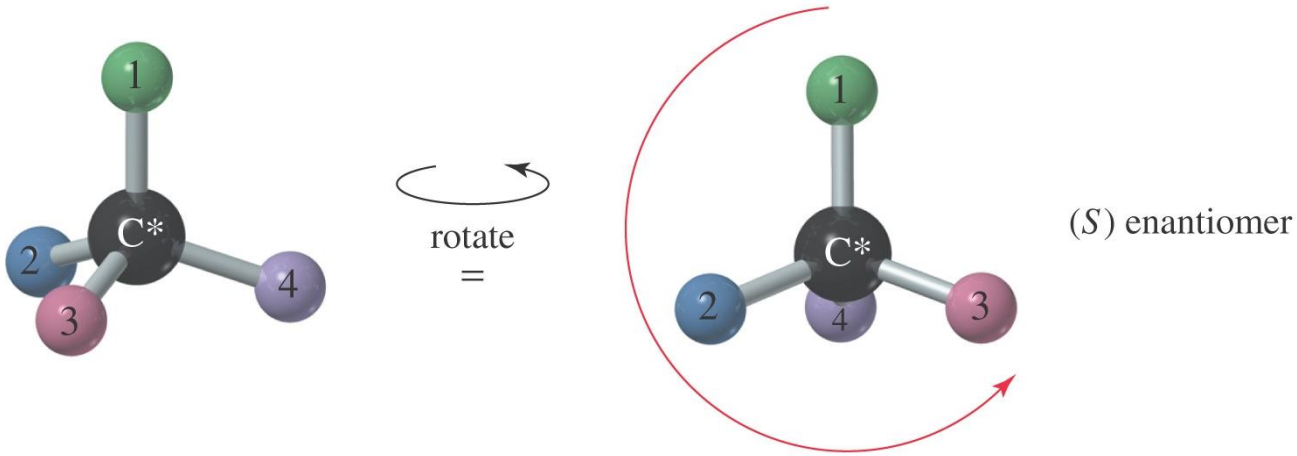
- Called the **Cahn-Ingold-Prelog** convention
- Different molecules (**enantiomers**) must have different
- names.
- Usually only one **enantiomer** will be biologically active.
- Configuration around the chiral carbon is specified
  with (*R*) and (*S*).

Cahn-Ingold-Prelog Rules

- Assign a priority number to each group attached to
- the **chiral** carbon.
- Atom with highest atomic number assigned the
- highest priority #1.
- In case of ties, look at the next atoms along the
- chain.
- Double and triple bonds are treated like bonds to
- duplicate atoms.

Assign (*R*) or (*S*)

- Working in 3D, rotate molecule so that lowest priority group is in back.
- Draw an arrow from highest to lowest priority group.
- Clockwise = (*R*), Counterclockwise = (*S*)

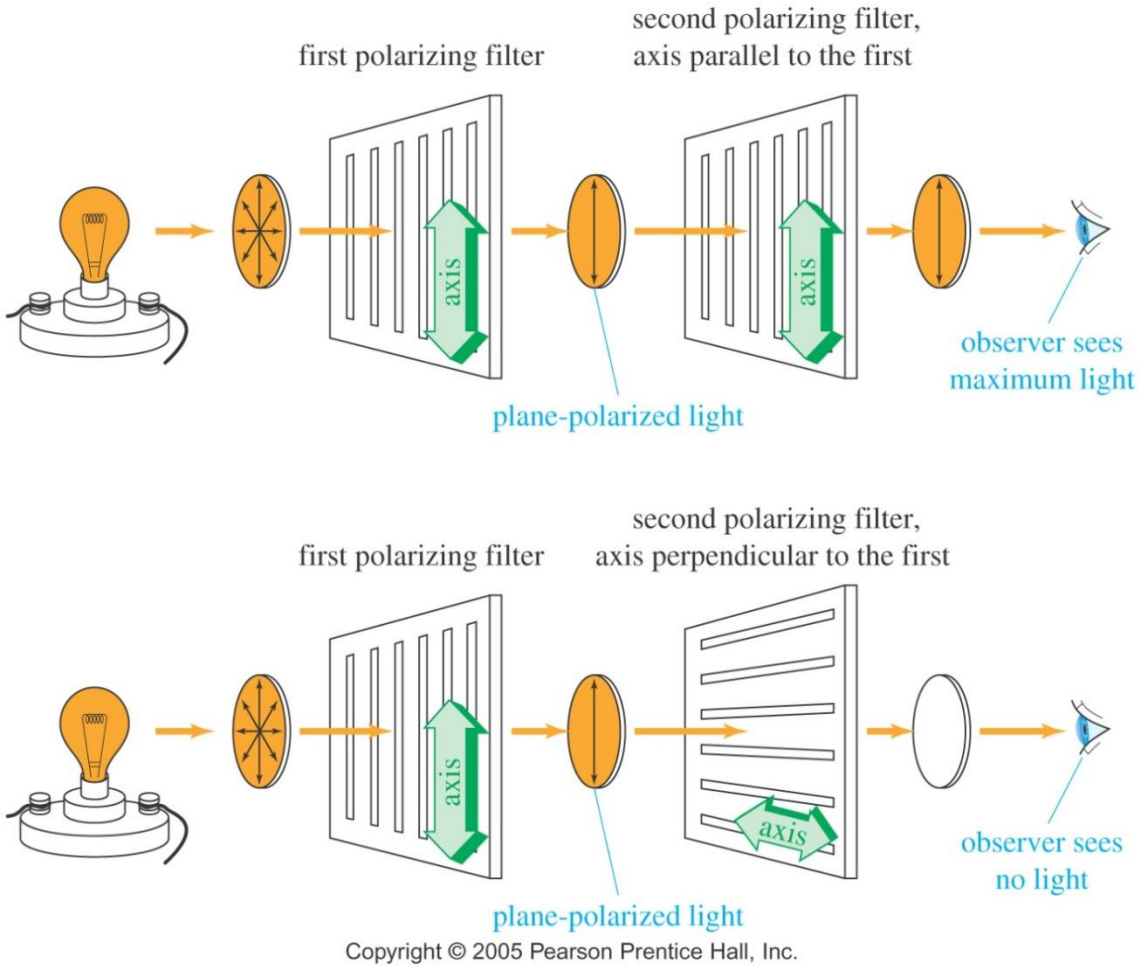


Properties of Enantiomers

- Same boiling point, melting point, density
- Same refractive index
- Different direction of rotation in polarimeter
- Different interaction with other chiral molecules
  - Enzymes
  - Taste buds, scent

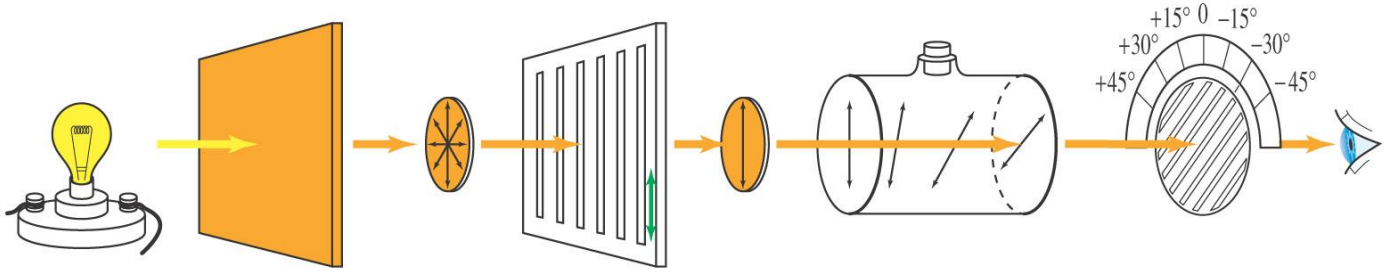
Plane-Polarized Light

- Polarizing filter – calcite crystals or plastic sheet.
- When two filters are used, the amount of light transmitted depends on the angle of the axes.

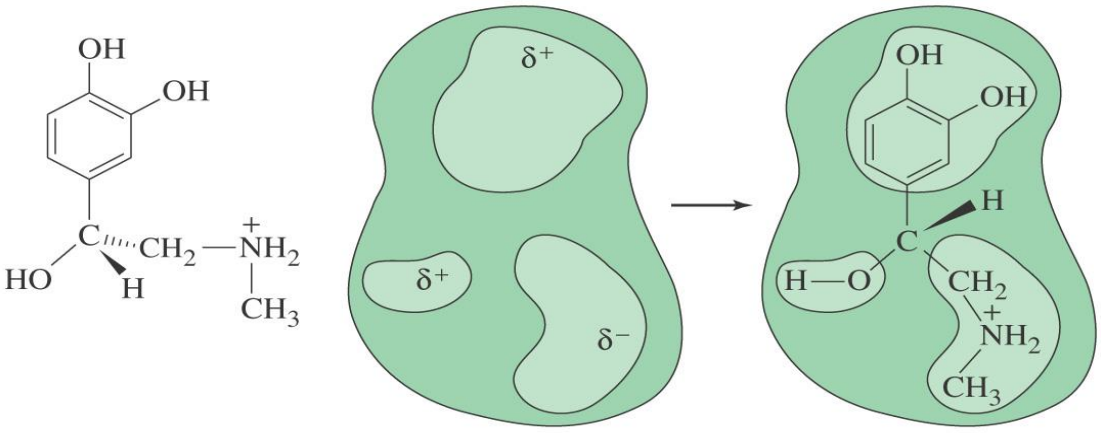


Polarimetry

- Use monochromatic light, usually sodium D
- Movable polarizing filter to measure angle
- Clockwise = dextrorotatory = *d* or (+)
- Counterclockwise = levorotatory = *l* or (-)
- Not related to (*R*) and (*S*)



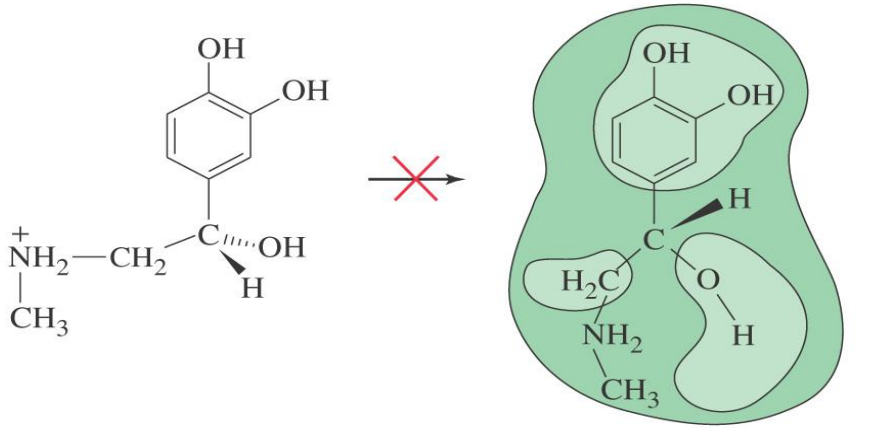
Biological Discrimination



(*R*)-(−)-epinephrine
natural epinephrine

enzyme active site

enzyme–substrate complex



(*S*)-(+)-epinephrine
unnatural epinephrine

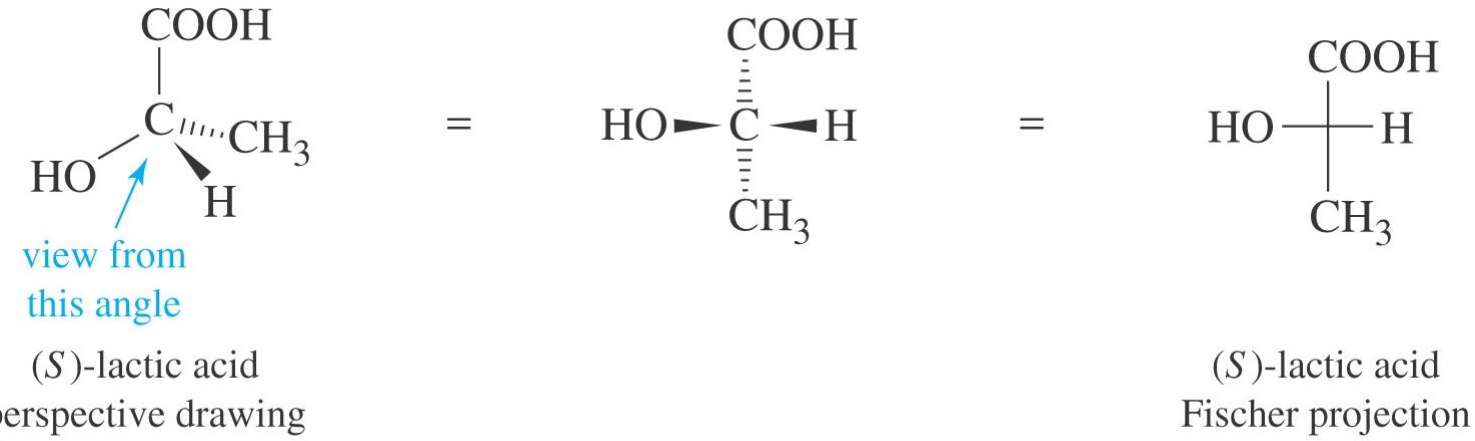
does not fit the enzyme's active site

Racemic Mixtures

- Equal quantities of *d*- and *l*- enantiomers a 50/50 mixture.
- Notation: (*d,l*) or (±)
- No optical activity.
- The mixture may have different b.p. and m.p. from the enantiomers!

Fischer Projections

- Flat drawing that represents a 3D molecule.
- A chiral carbon is at the intersection of horizontal and vertical lines.
- Horizontal lines are forward, out-of-plane.
- Vertical lines are behind the plane.



(*S*)-lactic acid
perspective drawing

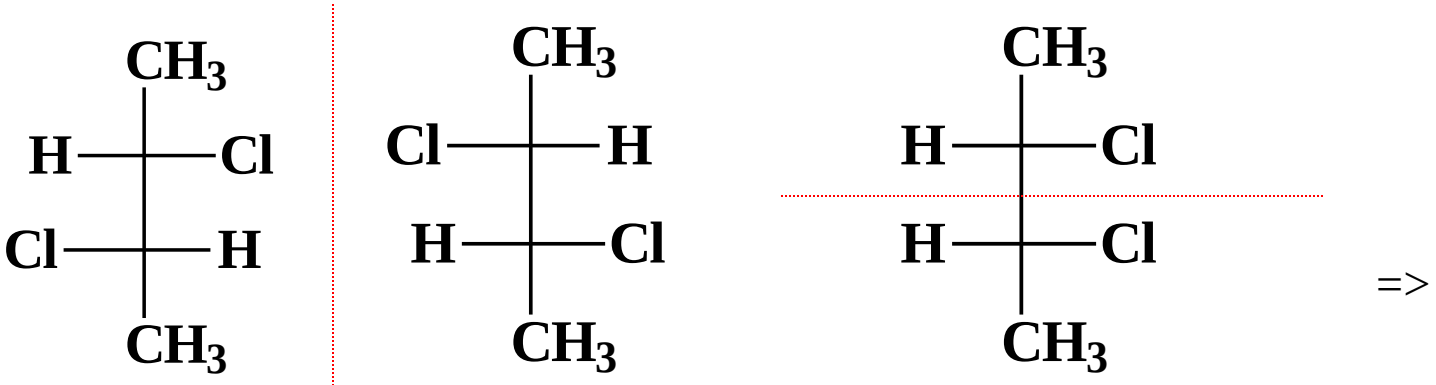
(*S*)-lactic acid
Fischer projection

Fischer Rules

- Carbon chain is on the vertical line.
- Horizontal bonds pointing up with respect to the plane of the paper.
- Vertical bonds pointing down with respect to the plane of the paper.
- Highest oxidized carbon at top.
- Rotation of 180° in plane doesn't change molecule.
- Do not rotate 90°!
- Do not turn over out of plane!

Fischer Structures

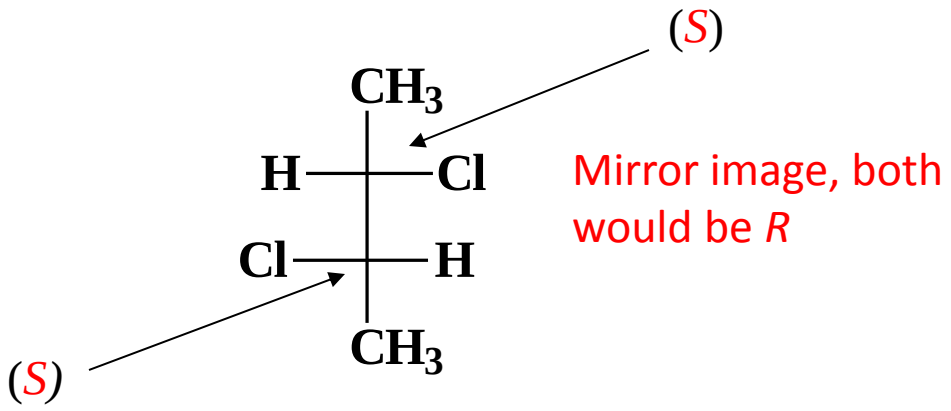
- Easy to draw, easy to find enantiomers, easy to find internal mirror planes.
- Examples:



A meso compound

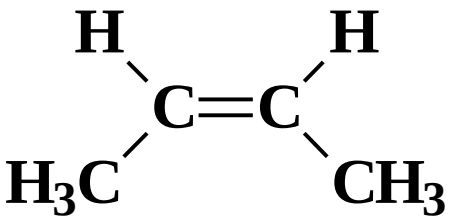
Fischer (*R*) and (*S*)

- Lowest priority (usually H) comes forward, so assignment rules are backwards!
- Clockwise 1-2-3 is (*S*) and counterclockwise 1-2-3 is (*R*).
- Example:

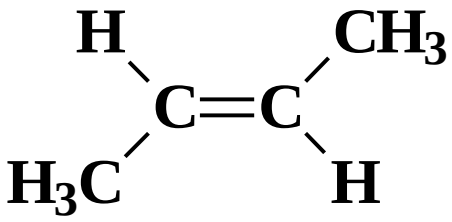


Diastereomers

- Stereoisomers that are not mirror images.
- Molecules with 2 or more chiral carbons.
- Geometric isomers (cis-trans), since they are not mirror images.



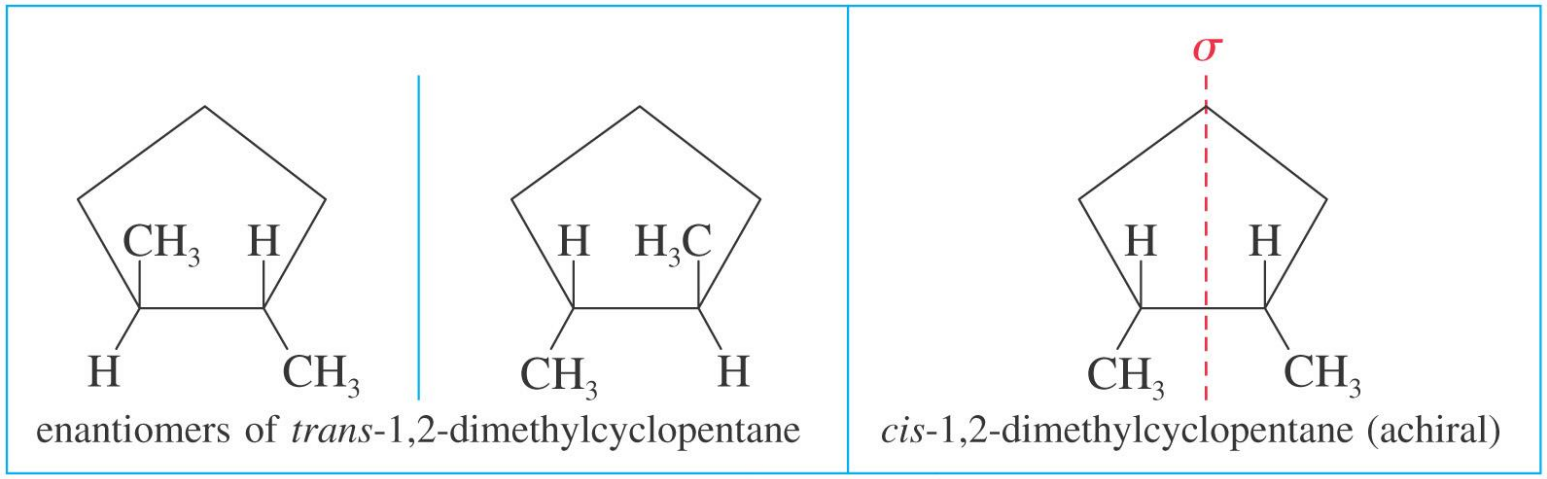
***cis*-2-butene**



***trans*-2-butene**

Ring Compounds

- Cis-trans isomers possible.
- May also have enantiomers.
- Example: *trans*-1,2-dimethylcyclopentane



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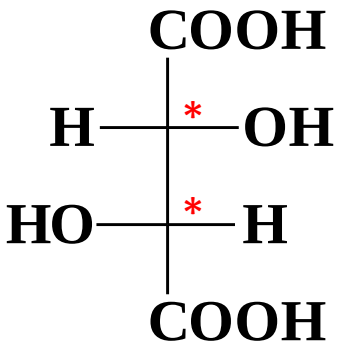
Two or More Chiral Carbons

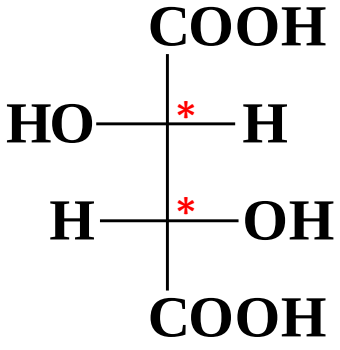
- Enantiomer? Diastereomer? Meso? Assign (*R*) or (*S*) to each chiral carbon.
- Enantiomers have opposite configurations at each corresponding chiral carbon.
- Diastereomers have some matching, some opposite configurations.
- Meso compounds have internal mirror plane.
- Maximum number is 2^n, where n = the number of chiral carbons.

Examples

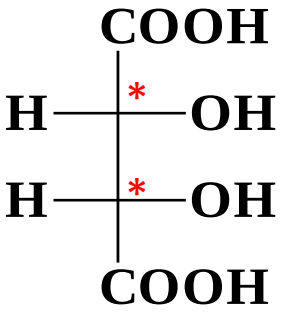


(2*R*,3*R*)-tartaric acid

enantiomers



(2*S*,3*S*)-tartaric acid



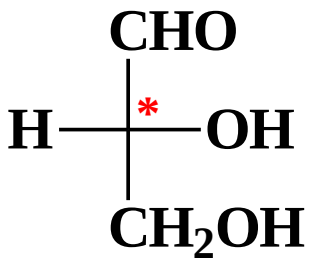
(2*R*,3*S*)-tartaric acid

A meso compound, contains 2 or more stereocenters and a plane of symmetry

Fischer-Rosanoff Convention

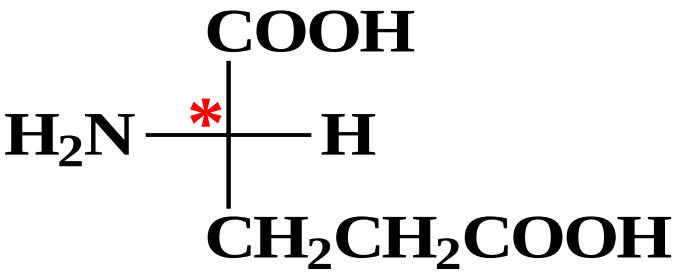
- Before 1951, only relative configurations could be known.
- Sugars and amino acids with same relative configuration as (+)-glyceraldehyde were assigned D and same as (-)-glyceraldehyde were assigned L.
- With X-ray crystallography, we now know absolute configurations: D is (*R*) and L is (*S*).
- No relationship to dextro- or levorotatory, meaning that some D enantiomers are *(R*) and some are *(S*).
- Anyone who can look at a structure and determine which way it will rotate polarized light receives an automatic Noble Prize! There is a lot we do not know!

D and L Assignments

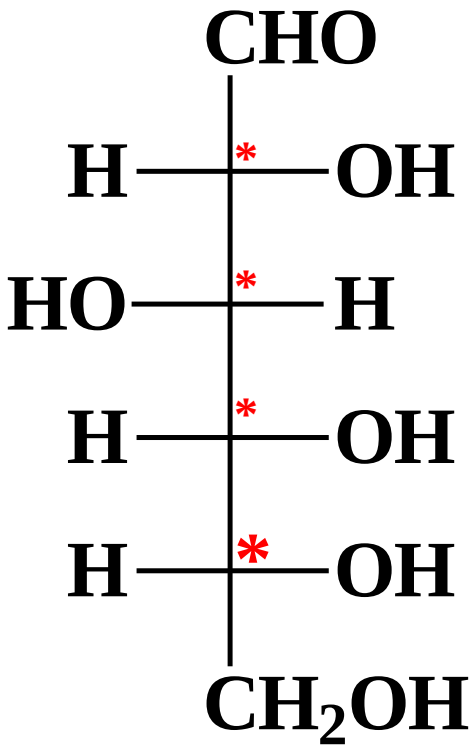


D-(+)-glyceraldehyde

Penultimate carbon is the stereocenter farthest away from the carbonyl group. If the higher priority group is on the left, then (L), if on the right then (D) sugar.



L-(+)-glutamic acid



D-(+)-glucose

Properties of Diastereomers

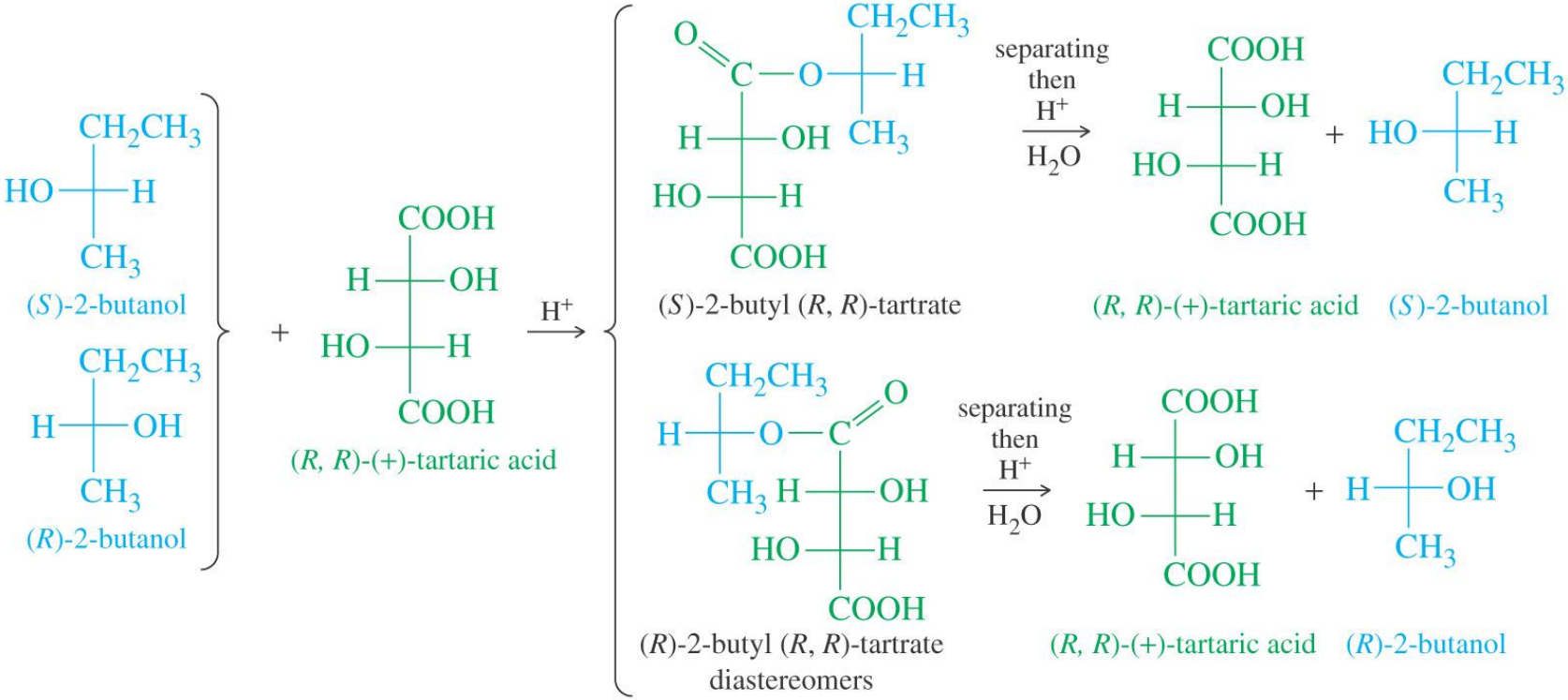
- Diastereomers have different physical properties: m.p., b.p.
- They can be separated easily.
- Enantiomers differ only in reaction with other chiral molecules and the direction in which polarized light is rotated.
- Enantiomers are difficult to separate

Resolution of Enantiomers

- Pasteur was the first to resolve an enatiomeric mixture, using a magnifying glass and tweezers.
- Animals can consume a racemate and metabolize on of the tow enantiomers, while the other is recovered in their waste products.
- Chemical means, described on the next slide

Chemical Resolution of Racemate

- React a racemic mixture with a chiral compound to form diastereomers, which can




Thank You.