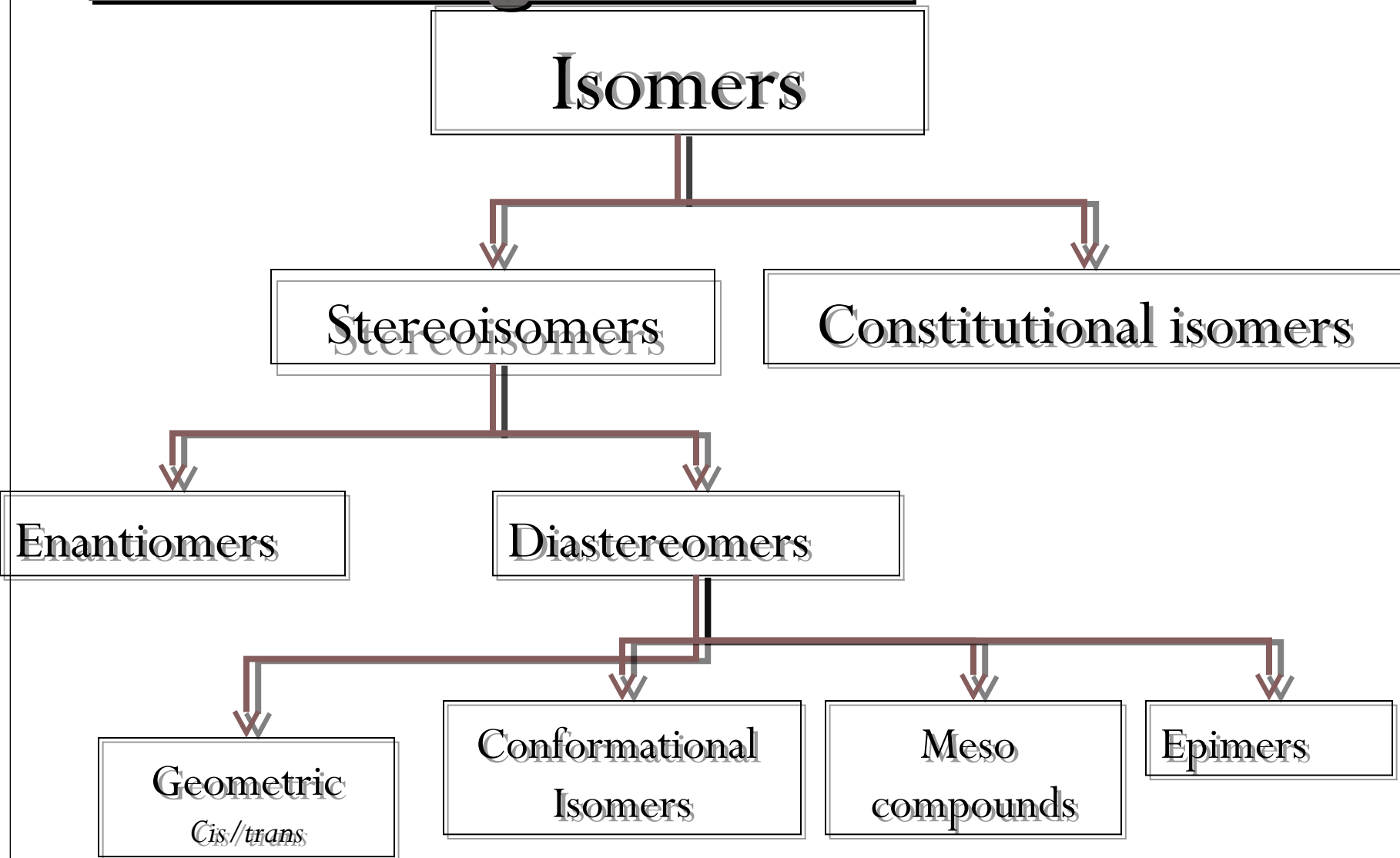


STEREOCHEMISTRY

Presented by :

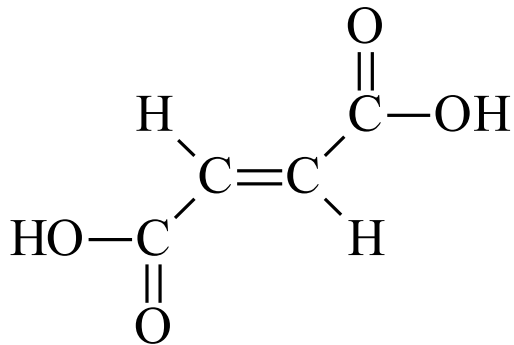
Arvind Singh Heer
(M.Sc -Analytical Chemistry)

Isomer Organization

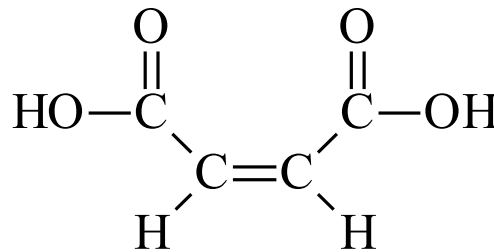


Stereoisomer's

- 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

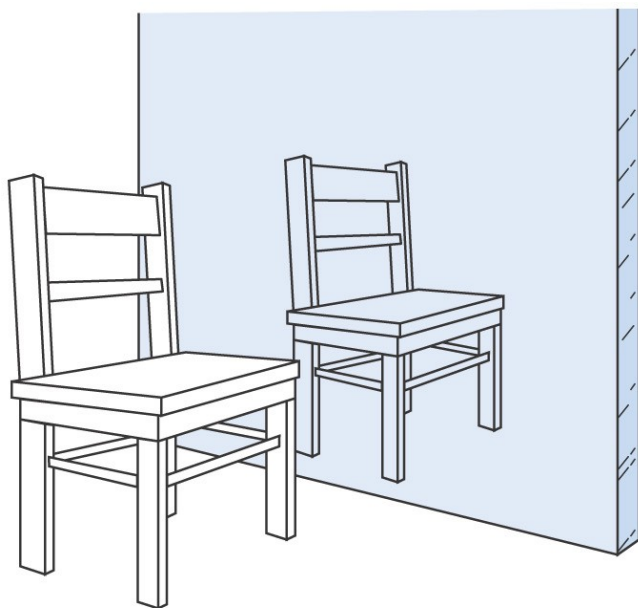


maleic acid, mp 138°C
toxic irritant

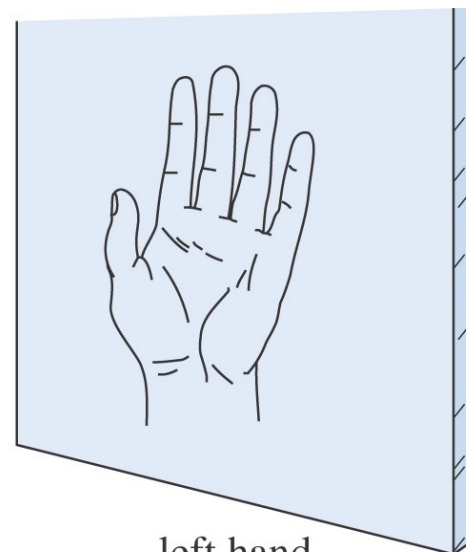
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Chirality

- “Handedness”: right glove doesn’t fit the left hand.
- Mirror-image object is different from the original object



right hand



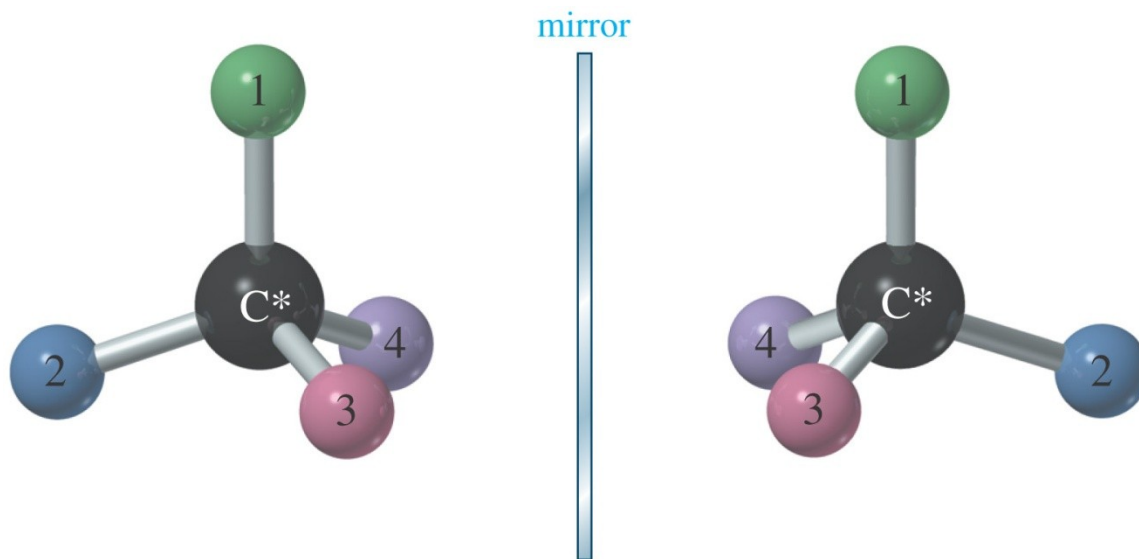
left hand

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

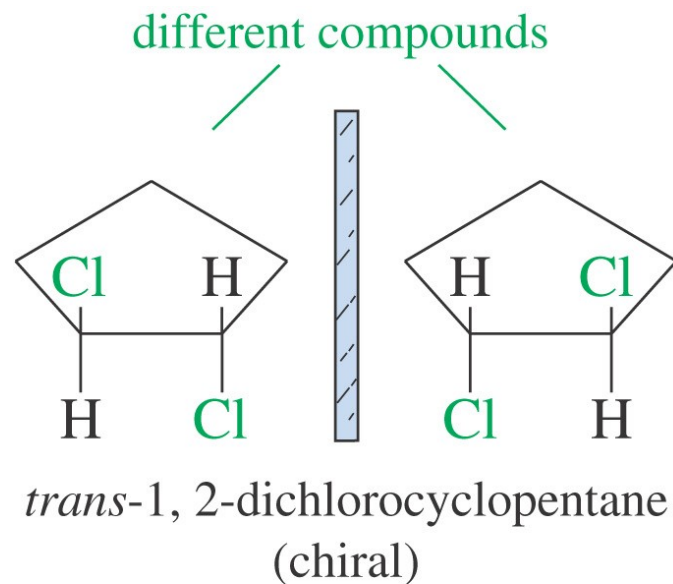
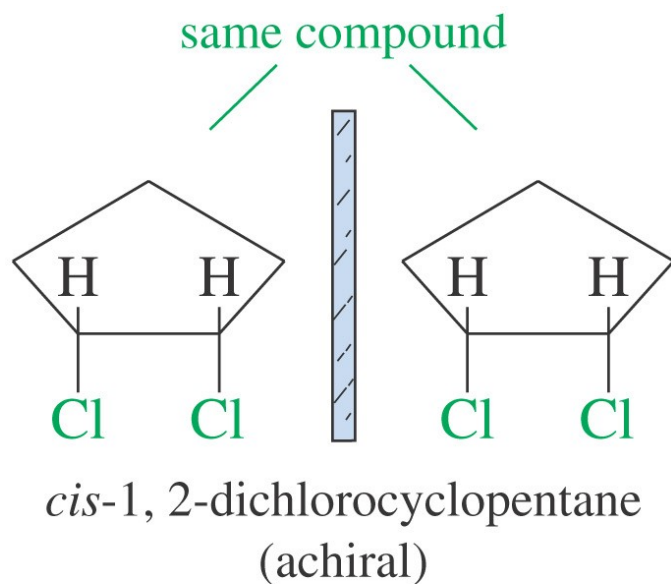


Chirality in Molecules

- The *cis* isomer is **achiral**.
- The *trans* isomer is **chiral**.
- Enantiomers: nonsuperimposable mirror images, **different** molecules.
- One enantiomeric form of limonene smells like oranges, while its mirror image smells like lemons.
- The one **enantiomer** 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.
- Nineteen of the twenty known amino acids are **chiral**, and all of them are classified as left handed.

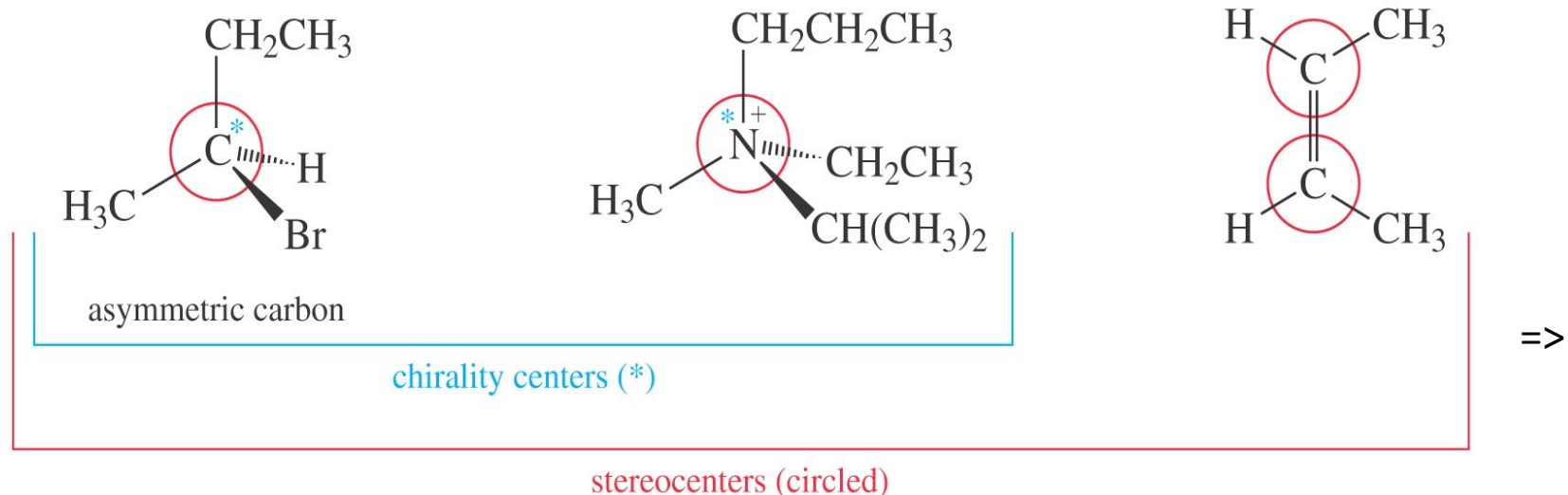
Chirality in Molecules

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



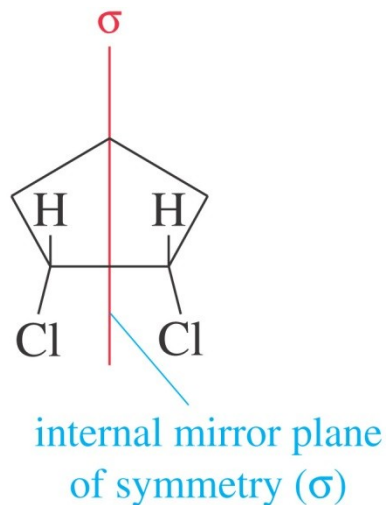
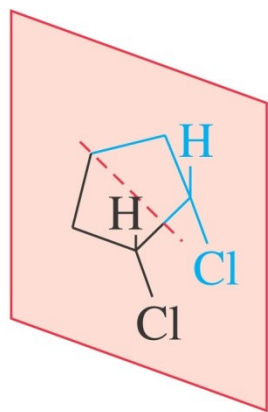
Stereocenters

- 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.*



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

Absolute Configuration

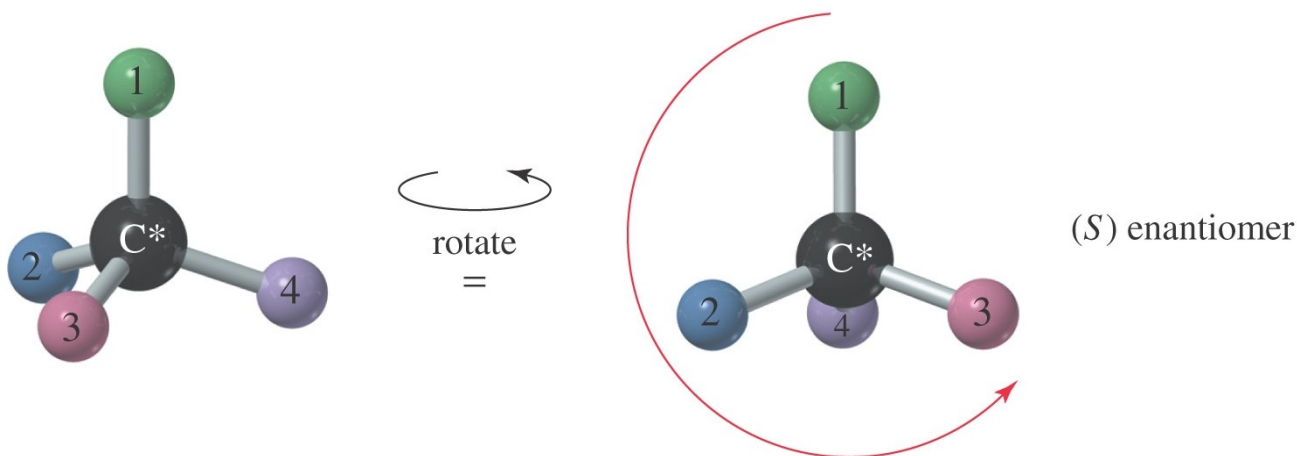
- Called the Cahn-Ingold-Prelog convention
- Different molecules (enantiomers) must have different
 - names.
- Usually only one enantiomer will be biologically active.
- Configuration around the chiral carbon is specified with (*R*) and (*S*).

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)

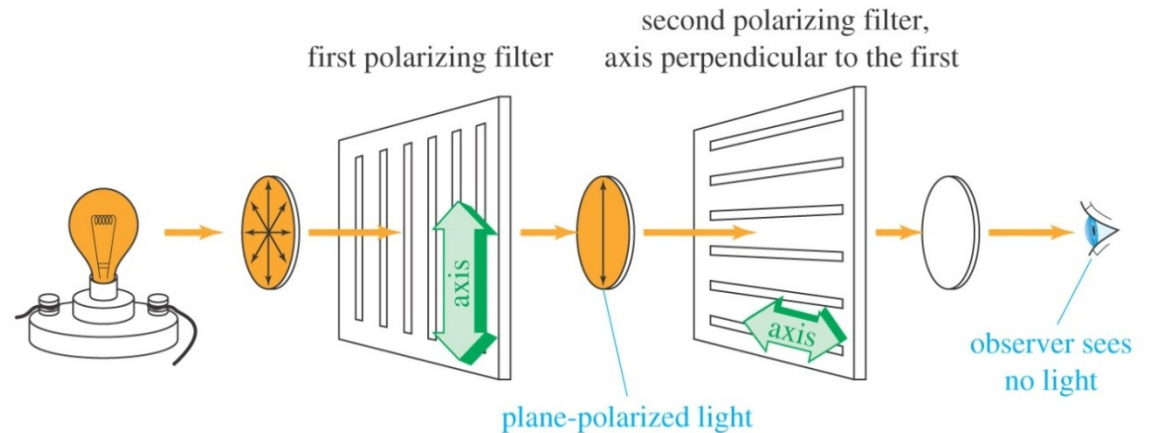
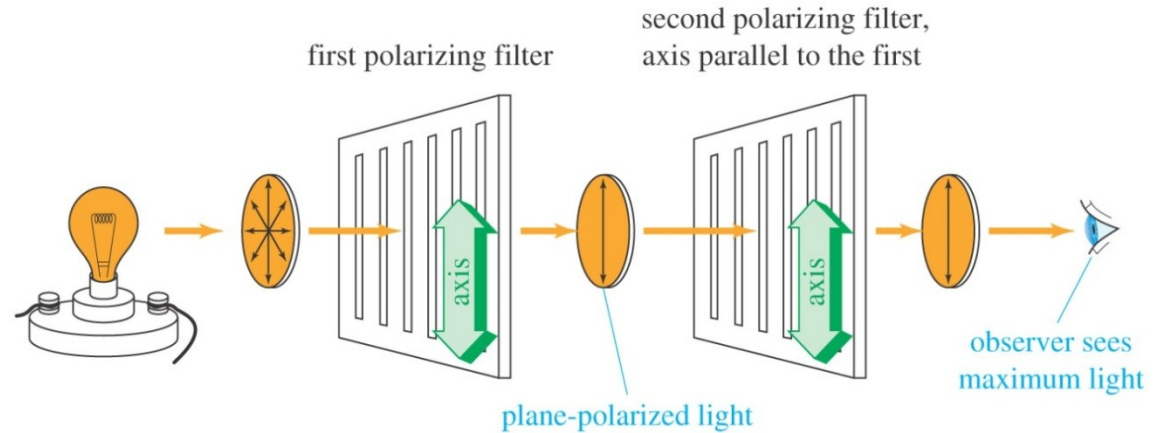


Properties of Enantiomers

- 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

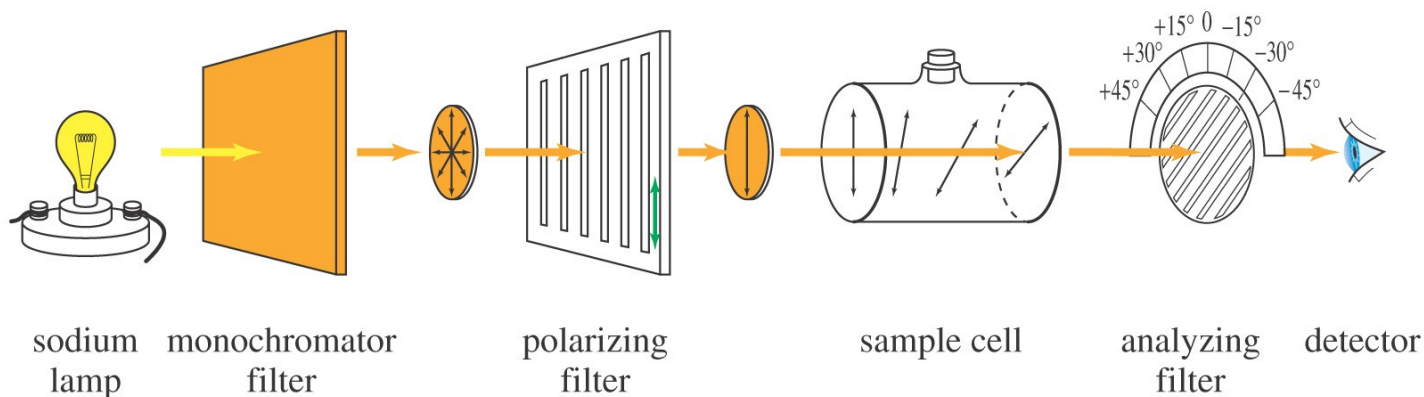
Plane-Polarized Light

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

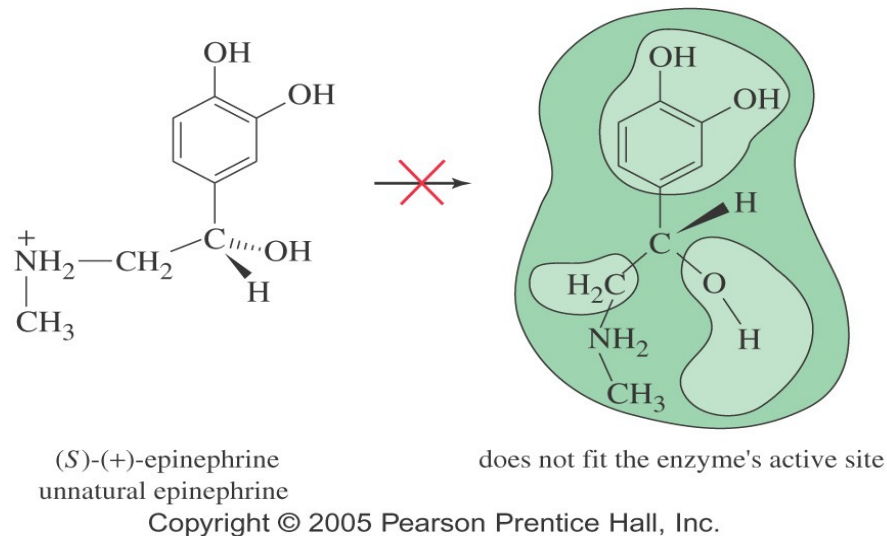
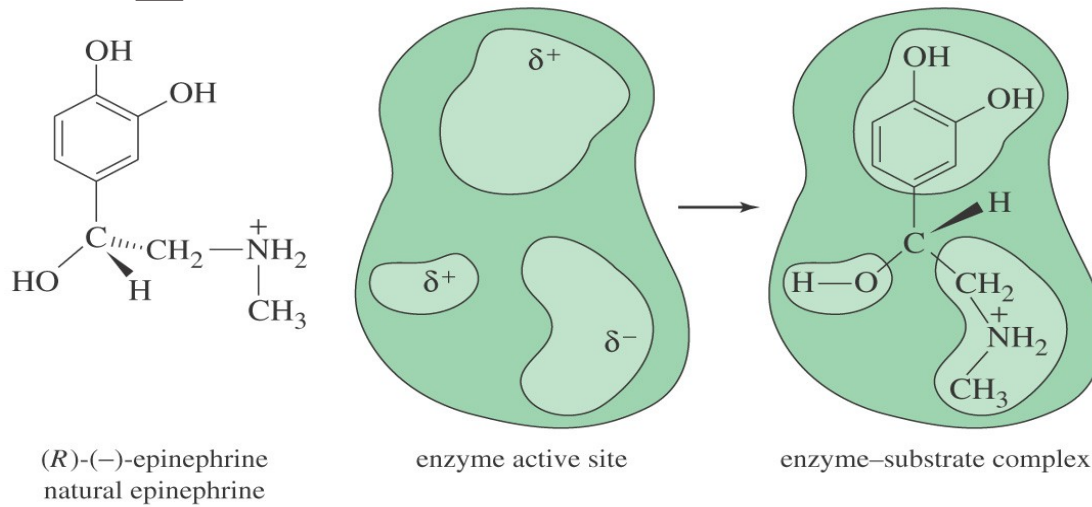


Polarimetry

- 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

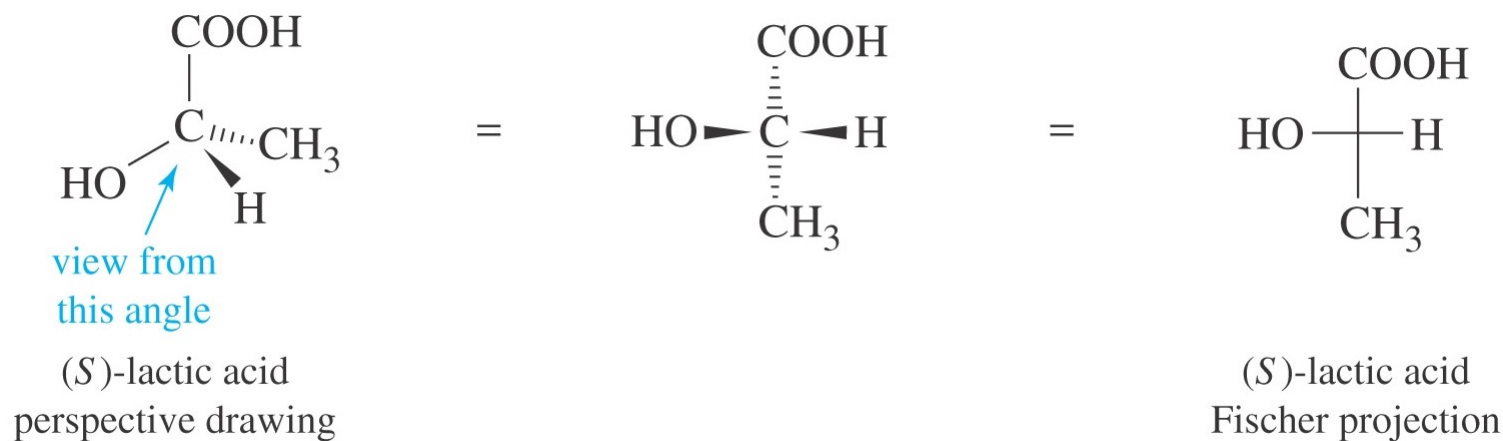


Racemic Mixtures

- Equal quantities of *d*- and *l*- enantiomers a 50/50 mixture.
- Notation: (*d,l*) or (\pm)
- 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.

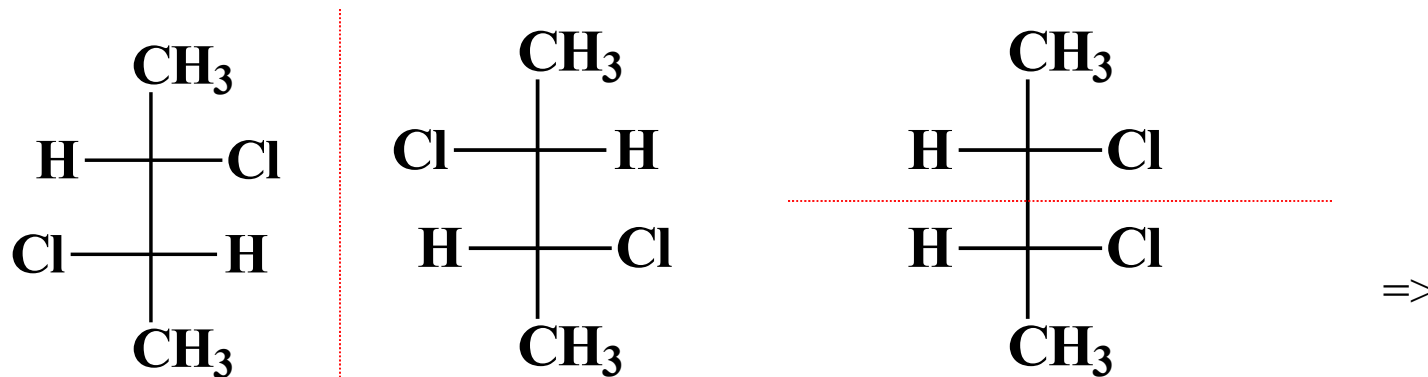


Fischer Rules

- 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

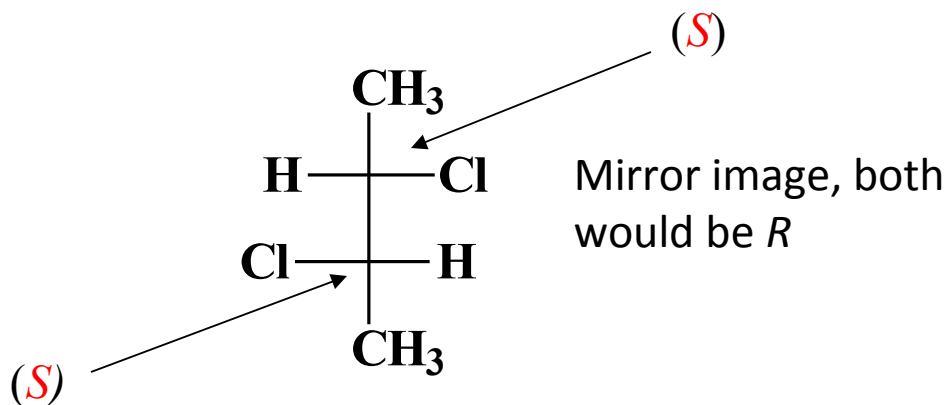
- Easy to draw, easy to find enantiomers, easy to find internal mirror planes.
- Examples:



A meso compound

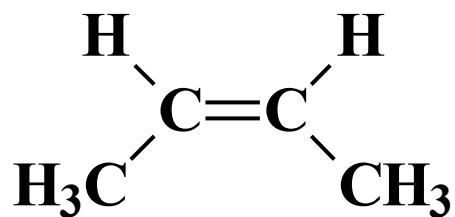
Fischer (R) and (S)

- 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:

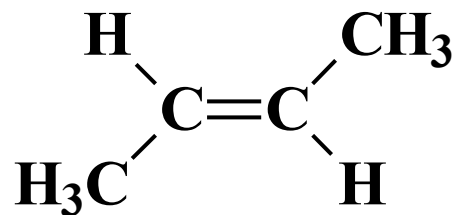


Diastereomers

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



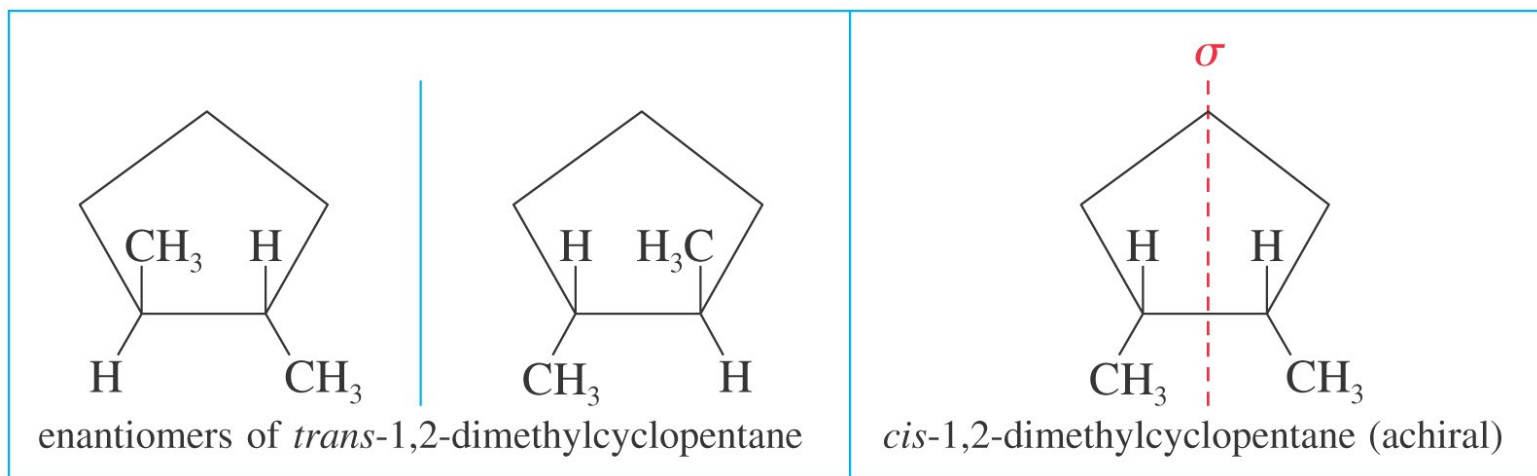
cis-2-butene



trans-2-butene

Ring Compounds

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



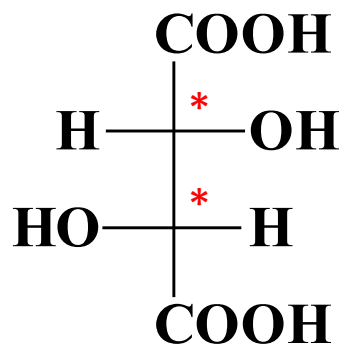
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diastereomers

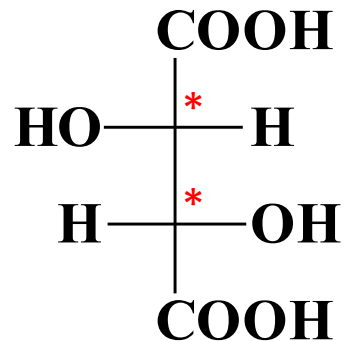
Two or More Chiral Carbons

- 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

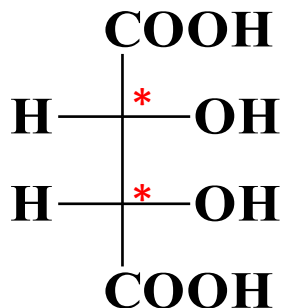


(2*R*,3*R*)-tartaric acid



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

enantiomers



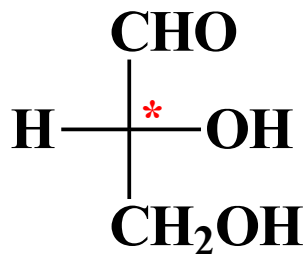
(2*R*,3*S*)-tartaric acid

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

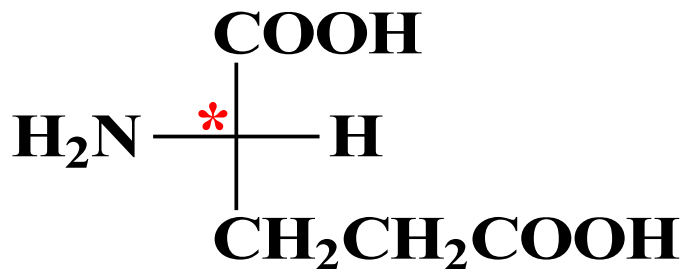
Fischer-Rosanoff Convention

- 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

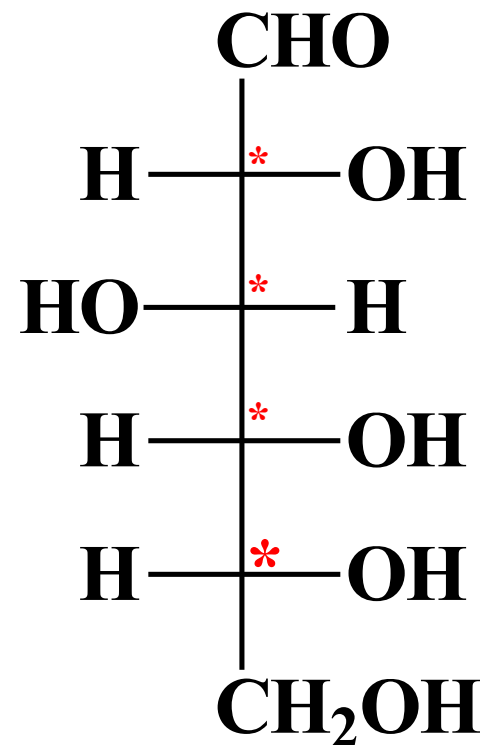


D-(+)-glyceraldehyde



L-(+)-glutamic acid

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.



D-(+)-glucose

Properties of Diastereomers

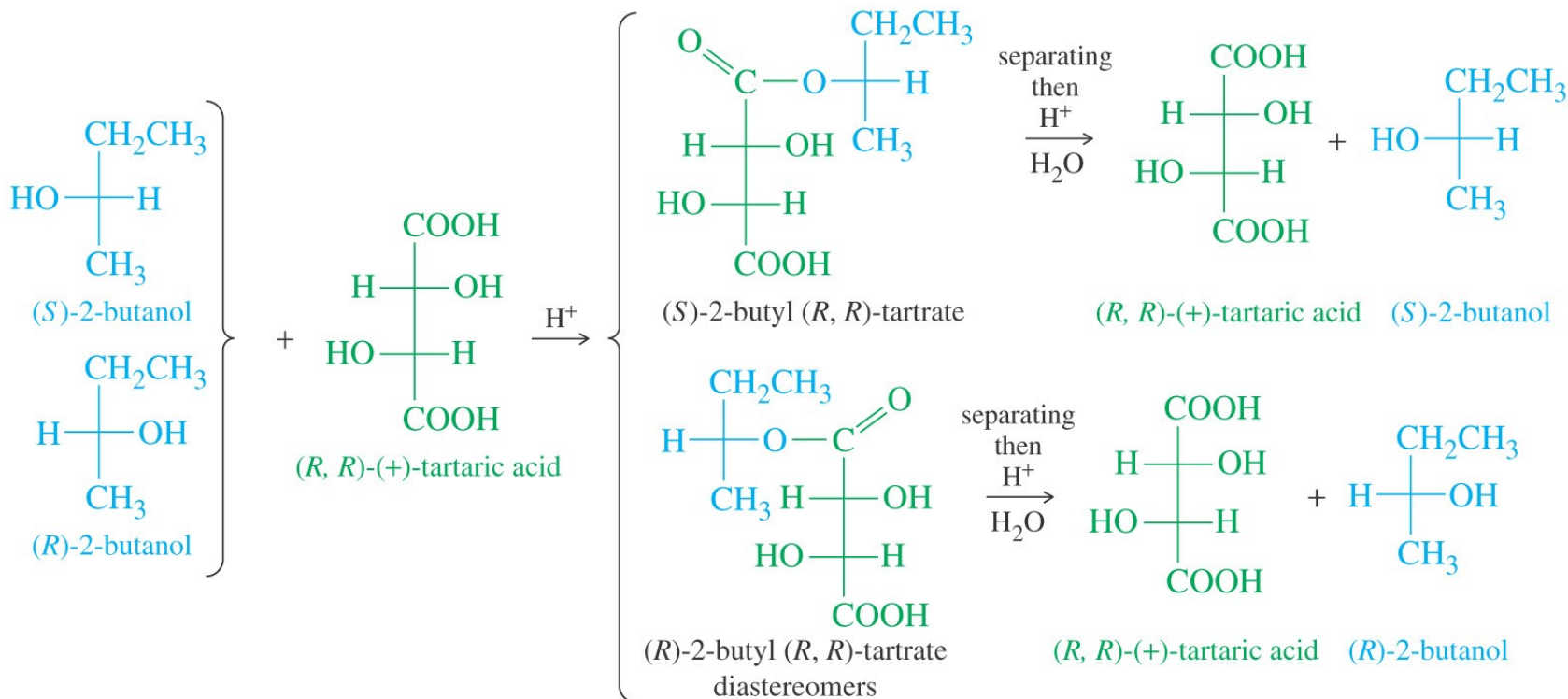
- Diastereomers have different physical properties: m.p., b.p.
- They can be separated easily.
- Enantiomers differ only in reaction with other chiral molecules and the direction in which polarized light is rotated.
- Enantiomers are difficult to separate

Resolution of Enantiomers

- Pasteur was the first to resolve an enantiomeric mixture, using a magnifying glass and tweezers.
- Animals can consume a racemate and metabolize one of the two 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



References

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Michael B. Smith

Jerry March

(SIXTH EDITION)



Advanced Organic Chemistry

FRANCIS A. CAREY

RICHARD J. SUNDBERG

(FIFTH EDITION)

-Thank you