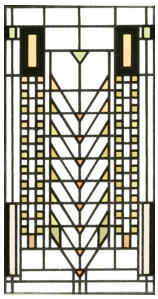
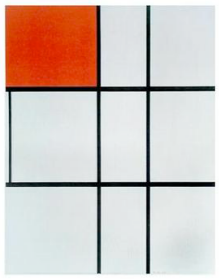
Symmetry

Monarch butterfly:
bilateral symmetry=
mirror symmetry





Whenever winds blow
butterflies find a new place
on the willow tree
-Basho (~1644 - 1694)

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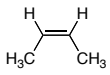
Chapter 7: Stereochemistry - three-dimensional arrangement of atoms (groups) in space

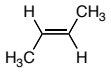
Stereoisomers: molecules with the same connectivity but different arrangement of atoms (groups) in space

cis-1,2-dimethylcyclopropane

trans-1,2-dimethylcyclopropane



cis-2-butene



trans-2-butene

geometric isomers (diastereomers)

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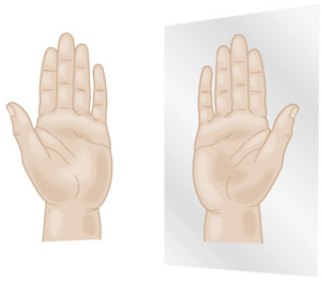
7.1: Molecular Chirality: Enantiomers
Enantiomers: non-superimposable mirror image isomers.

Enantiomers are related to each other much like a right hand is related to a left hand

Enantiomers have identical physical properties, i.e., bp, mp, etc.

Chirality (from the Greek word for hand). Enantiomers are said to be *chiral*.



Left hand Right hand

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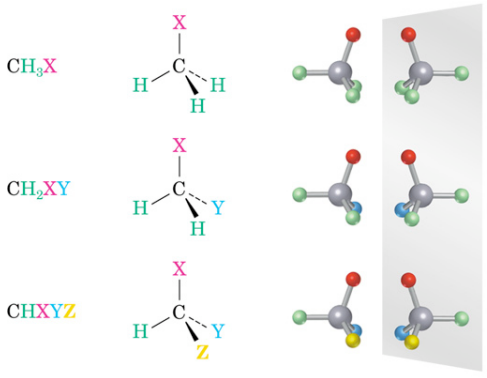
Molecules are <u>not</u> chiral if they contain a plane of symmetry: a plane that cuts a molecule in half so that one half is the mirror image of the other half. Molecules (or objects) that possess a mirror plane of symmetry <u>are</u> superimposable on their mirror image and are termed *achiral*.

7.2: The Chirality Center - A molecule containing a carbon with four different groups results in a chiral molecule, and the carbon is referred to as a *chiral,* or *asymmetric,* or *stereogenic* center.



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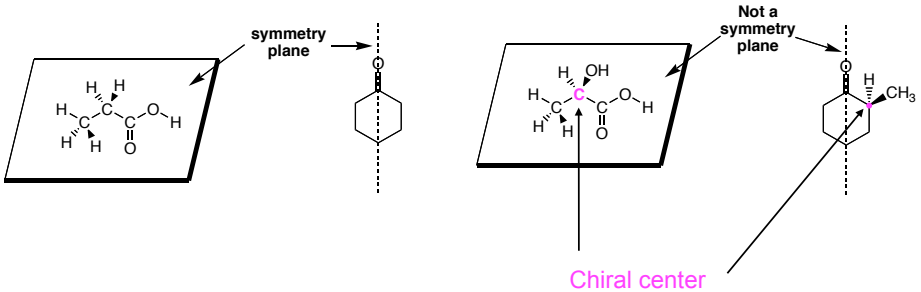
Enantiomers: non-superimposable mirror image isomers

7.3: Symmetry in Achiral Structures - Any molecule with a plane of symmetry or a center of symmetry must be achiral.

achiral

chiral



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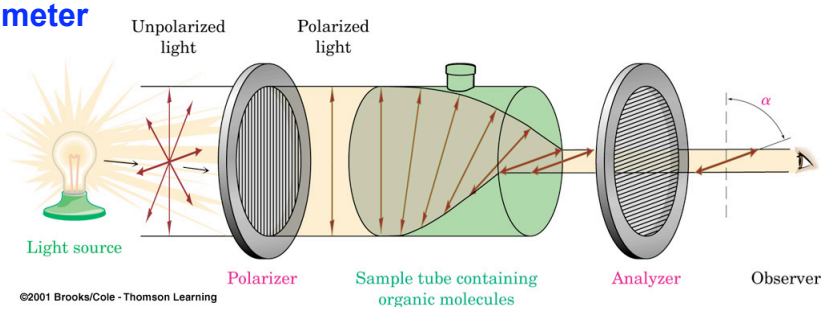
7.4: Optical Activity - molecules enriched in an enantiomer will rotate plane polarized light are said to be *optically active*. The optical rotation is dependent upon the substance, the concentration, the path length through the sample, and the wavelength of light.

Polarimeter

589 nm - D-line of a sodium lamp



Plane polarized light: light that oscillates in only one plane

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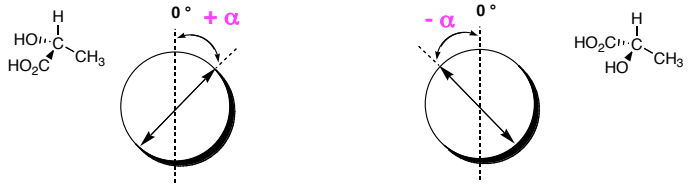

dextrorotatory (*d*): rotates light to the right (clockwise)

levorotatory (*l*): rotates light to the left (counterclockwise)

α: angle (# of degrees) plane polarized light is rotated by an optically active sample. Expressed in degrees.

Enantiomers will rotate plane polarized light the same magnitude (α) but in opposite directions (+ or -)

90% (+) + 10% (-) will rotate light 80% of pure (+)
75% (+) + 25% (-) will rotate light 50% of pure (+)
50% (+) + 50% (-) will be optically inactive

50:50 mixture of enantiomers (+/-): racemate or racemic mixture

Each individual molecule is chiral, however the bulk property of the substance is achiral, if it is in an achiral environment.

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Specific Rotation $[\alpha]_D$: a standardized value for the optical rotation

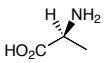
$$[\alpha]_\lambda^T = \frac{100\ \alpha}{l \bullet c}$$

α = optical rotation in degrees
l = path length in dm
c = concentration of sample in g/100 mL
T = temperature in °C
λ = wavelength of light, usually D for the D-line of a sodium lamp (589 nm)

The specific rotation is a physical constant of a chiral molecule

The $[\alpha]_D$ may also depend upon solvent, therefore the solvent is usually specified.

for alanine:



$[\alpha]_D^{20}$ = +14.5° (*c* 10, 6N HCl)

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An optically pure substance consists exclusively of a single enantiomer.

Optical purity of a optically active substance is expressed as the *enantiomeric excess* = % one enantiomer – % other enantiomer

7.5: Absolute and Relative Configuration

Absolute configuration is the precise three-dimensional arrangement of atoms in space

Relative configuration compares the three-dimensional arrangement of atoms in space of one compound with those of another compound.

$[\alpha]_D$= +33.0 $[\alpha]_D$= -7.0

There is NO correlation between the sign of the optical rotation and the three-dimensional arrangement of atoms

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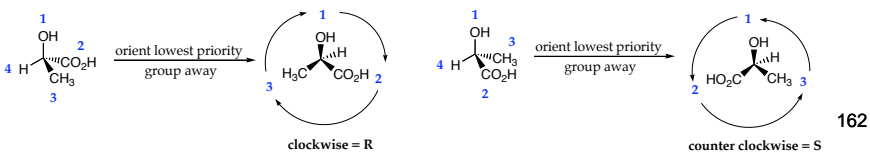
7.6: The Cahn-Ingold-Prelog *R-S* Notational System

Assigning the Absolute Configuration

1. Use the Cahn-Ingold-Prelog priority rules (Chapter 5) to assign priority (one through four) to the four groups on the "chiral" atom.

3. Orient the molecule so that the lowest priority atom is in the back (away from you). Look at the remaining three groups of priority 1-3. If the remaining three groups are arranged so that the priorities 1→2→3 are in a *clockwise* fashion, then assign the chiral center as **R** ("rectus" or right). If the remaining three groups are arranged 1→2→3 in a *counterclockwise* manner, then assign the chiral center as **S** ("sinister" or left)



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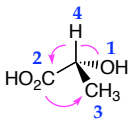
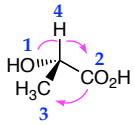
3. Or use the "Hand Rule." Orient the lowest priority group up. Point your thumb in the direction of the lowest priority group. If you need to use your *right hand* so that your fingers point in the direction of the group priorities in the order 1→2→3, then the stereogenic center is assigned **R** ("rectus" or *right*). If your *left hand* is required so that your fingers point in the direction of the group priorities 1→2→3, the the stereogenic center is assigned **S** ("sinister" or *left*).



(R)-(-)-Lactic acid
(Right Hand)

(S)-(+)-Lactic acid
(Left Hand)



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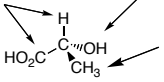
You must be able to draw tetrahedral carbons properly!!

In the plane of the paper and in the same plane as the tetrahedral carbon (adjacent position off the tetrahedral carbon)

Dash: projecting behind the plane of the paper away from you

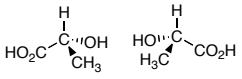
Dash and Wedge are on adjacent position off the tetrahedral carbon

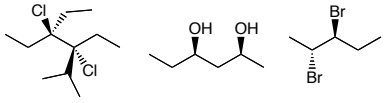


Wedge: projecting out of the plane of the paper toward you

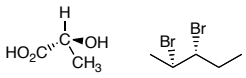
LINEAR ALKANES: You should draw the carbon backbone in the plane of the paper, and draw substituents either coming towards you (with wedges) or going away from you (with dashes). Note that each carbon should look like a tetrahedron.

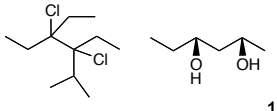
Correct ☺





Incorrect ☹





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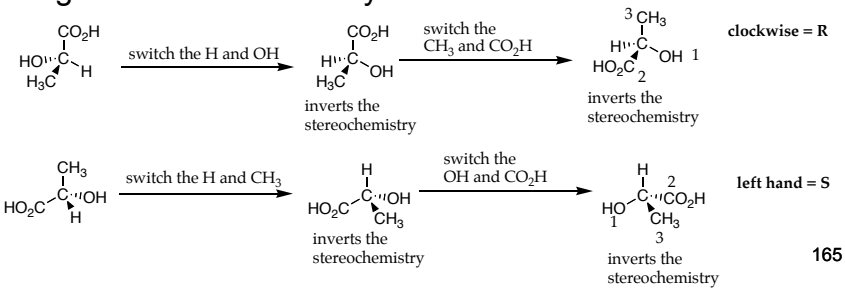
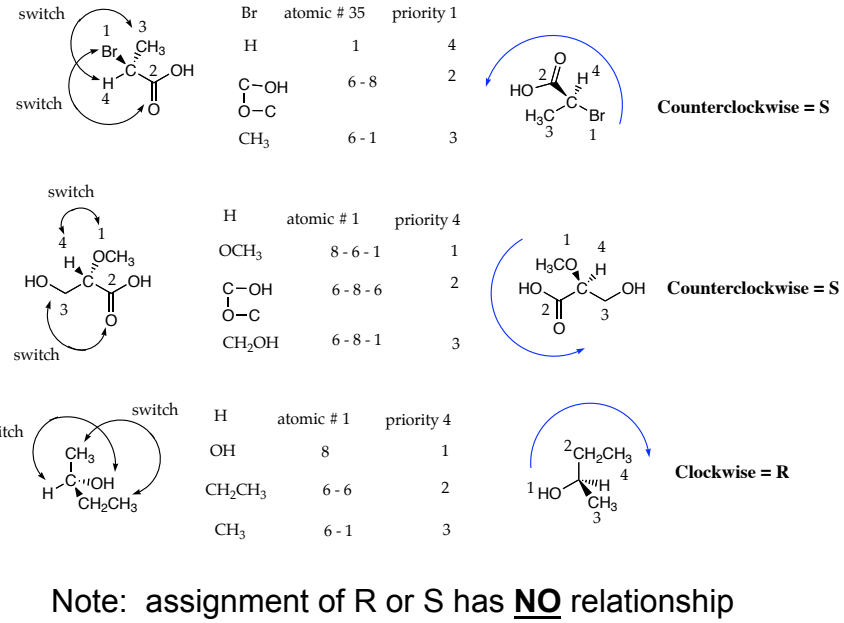
Do the Double-Switch Dance!!

In order to assign the stereochemistry you must be able to manipulate the structure on paper so that the lowest priority group is in the proper orientation (back for the steering wheel rule or up for the hand rule)

Interchanging any two groups inverts the stereochemistry. So switch the lowest priority group to the desired position. Then switch the other two groups. The "double-switch" does not change the stereochemistry.



165



Note: assignment of R or S has **NO** relationship with the optical rotation (+) or (-).

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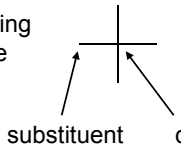
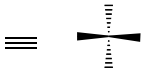
7.7: Fischer Projections - representation of a three-dimensional molecule as a flat structure. A tetrahedral carbon is represented by two crossed lines:

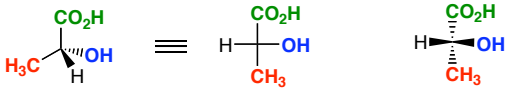
horizontal line is coming out of the plane of the page (toward you)



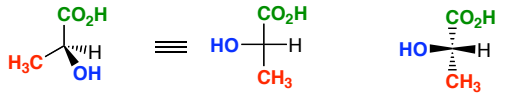
vertical line is going back behind the plane of the paper (away from you)



(*R*)-lactic acid



(*S*)-lactic acid



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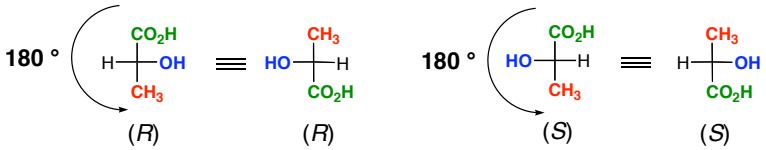
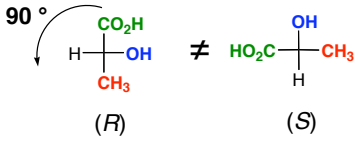
Manipulation of Fischer Projections

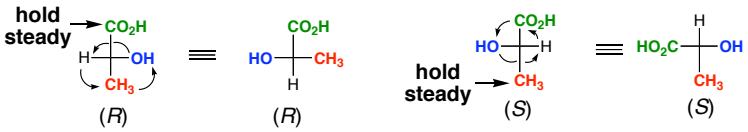
1. Fischer projections can be rotated by 180° only!



a 90° rotation inverts the stereochemistry and is illegal!



2. If one group of a Fischer projection is held steady, the other three groups can be rotated clockwise or counterclockwise.



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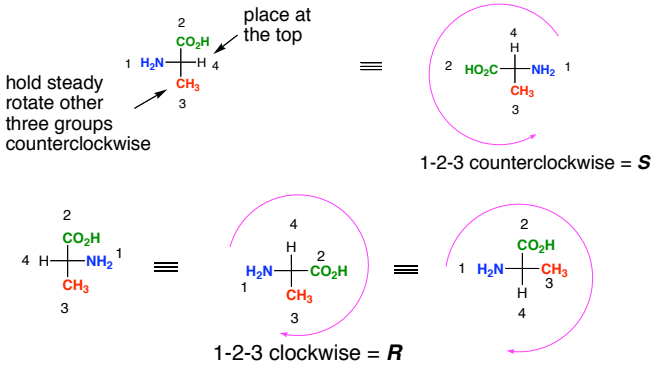
Assigning R and S Configuration to Fischer Projections

1. Assign priorities to the four substitutents according to the Cahn-Ingold-Prelog rules
2. Perform the two allowed manipulations of the Fischer projection to place the lowest priority group at the top (or bottom).
3. If the priority of the groups 1→2→3 are clockwise then assign the center as *R*, if 1→2→3 are counterclockwise then assign the center as *S*.



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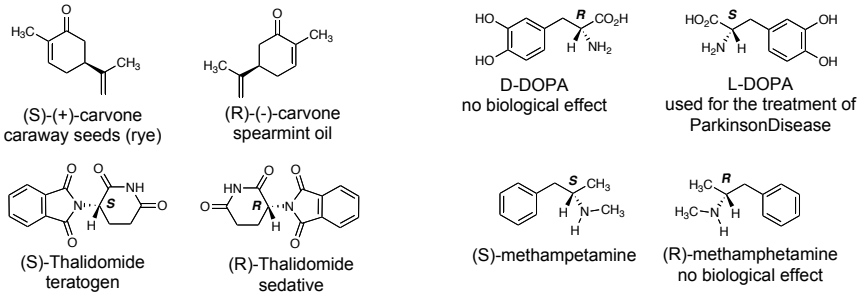
7.8: Properties of Enantiomers

In general, enantiomers have the same physical properties (bp, mp, density, etc). Enantiomers will rotate plane polarized light the same magnitude (α) but in opposite directions (+ or -).



Enantiomers can have significantly different biological properties

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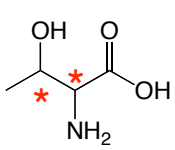
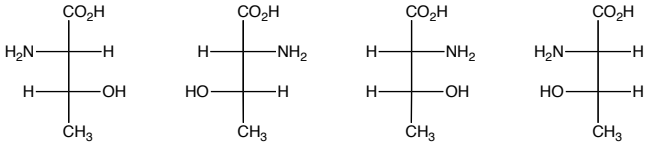
7.10: Chiral Molecules with Two Chirality Centers



Threonine



(2*S*, 3*R*) (2*R*, 3*S*) (2*R*, 3*R*) (2*S*, 3*S*)

mirror images (enantiomers) **mirror images (enantiomers)**

Natural threonine possesses the 2S, 3R stereochemistry

non-mirror image (diastereomers)

What is the relationship between these stereoisomers?

(2*R*,3*R)* and (2*S*,3*S*) are enantiomers

(2*R*,3*S*) and (2*S*,3*R*) are enantiomers

Diastereomers: non-mirror image stereoisomers. Occurs when more than one chiral centers are present in a molecule.

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Enantiomers must have the opposite configuration at **all** chiral centers.

In general, enantiomers have identical physical properties except optical rotation (which is equal in magnitude but opposite in sign). Diastereomers may have completely different physical properties.

For a molecule with n chiral centers, there are 2^n number of stereoisomers possible, not including geometric stereoisomers of double bonds.

Erythro: substituents on same side of a Fischer projection
i.e., (2*R*, 3*R*)- and (2*S*, 3*S*)-threonine

Threo: substituents on opposite sides of a Fischer projection
i.e., (2*S*, 3*R*)- and (2*R*, 3*S*)-threonine

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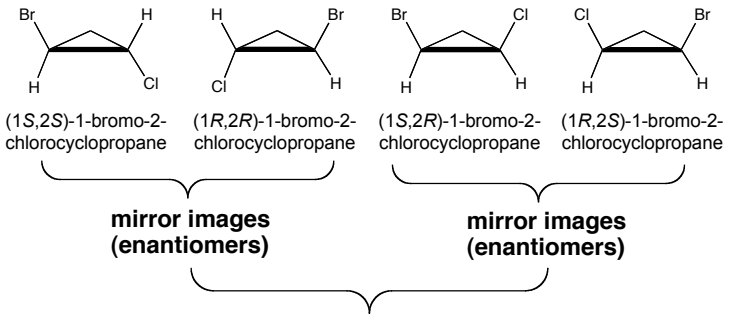

7.11: Achiral Molecules with Two Chirality Centers

meso (achiral) chiral

Meso: molecules that contain chiral atoms but are achiral because they also possess a plane of symmetry.

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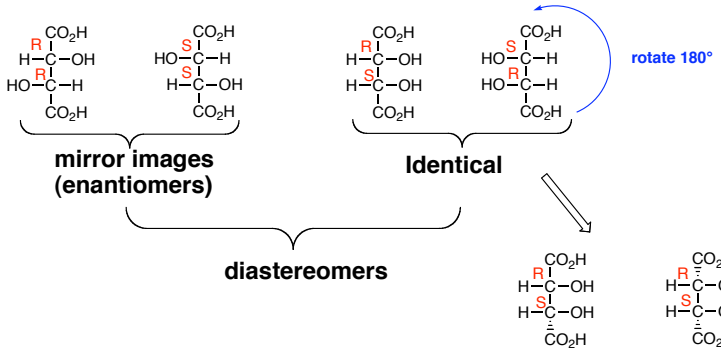

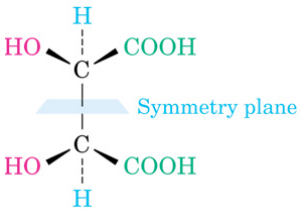

meso tartaric acid: The groups on the top carbon reflect (through the symmetry plane) onto the groups on the bottom carbon

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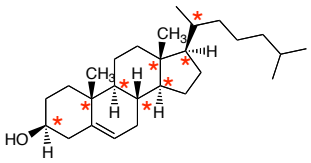
7.12: Molecules with Multiple Chirality Centers

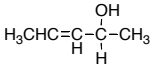
Maximum number of stereoisomers = 2^n.

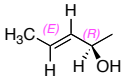
where *n* = number of structural units capable of stereochemical variation.

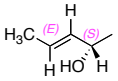
Structural units include chiral centers and cis (E) and/or trans (Z) double bonds.

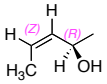


Cholesterol: eight chiral centers
2^8 = 256 possible stereoisomers
(only one of which is naturally occurring)









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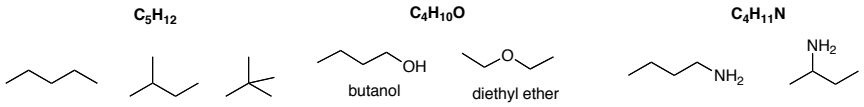
A Brief Review of Isomerism

Isomers: compounds with the same chemical formula, but different arrangement of atoms

Constitutional isomer: have different connectivities (not limited to alkanes)



different carbon skeleton | different functional group | different position of FG

Stereoisomers: Atoms connected in the same way, but different three-dimensional arrangement of atoms or groups (topology)

enantiomers: non-superimposable mirror image isomers
diastereomers: non-superimposable, non-mirror image isomer (more than one chiral center.
geometric isomers (diastereomers): E / Z alkene isomers

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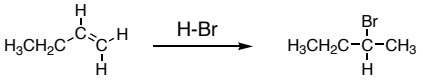
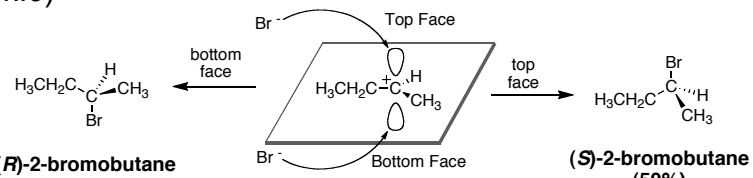
7.9: Reactions That Create a Chirality Center - reactions of achiral reactants may generate product with chiral centers



1-butene (achiral) **2-bromobutane (chiral)**

However, the products of such reactions with be optically inactive (*racemic*)



(*R*)-2-bromobutane (50%) **(*S*)-2-bromobutane (50%)**

There is an equal chance for Br^- to add from the top face or the bottom face resulting in a 50:50 mixture. The two products are enantiomers. The two transitions states are enantiomeric and have identical activation energies

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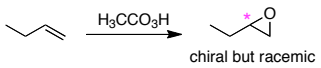
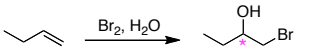
Optically inactive starting materials cannot give optically active products



chiral but racemic



chiral but racemic

racemic chiral but racemic

chiral but racemic

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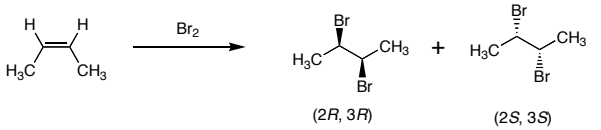
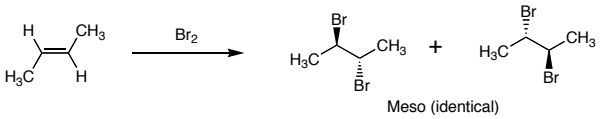
7.13: Reactions That Produce Diastereomers

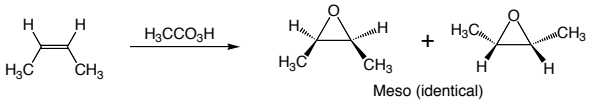
The stereochemical outcome of a reaction is dependent on the reaction mechanism

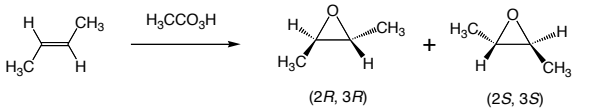
Addition of Br_2 to 2-butene (*anti*-addition)





Epoxidation to 2-butene (s*yn*-addition)





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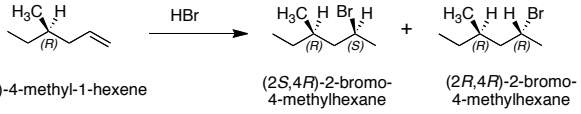
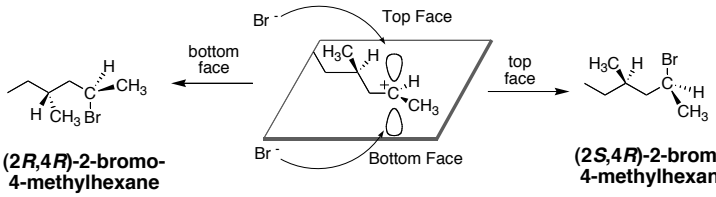
A reaction of a chiral reactant with an achiral reagent may give diastereomeric products, which may or may not be formed in equal amounts.





7.14: Resolution of Enantiomers (please read) - a process of separating a racemate into pure enantiomers. The enantiomers of the racemate must be temporarily converted into diastereomers.

50:50 mixture of enantiomers is a racemic mixture or racemate, denoted by (±) or (*d,l*)

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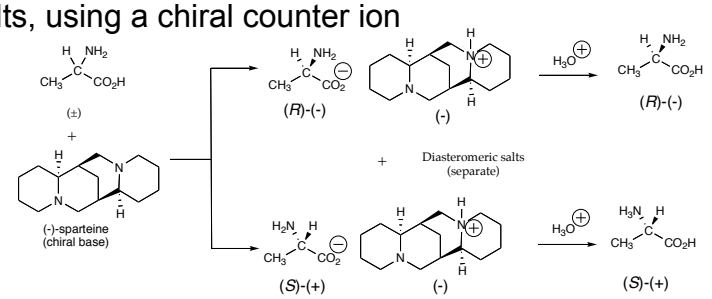
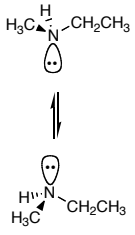
Resolution of a racemic amino acids by crystallization of their salts, using a chiral counter ion



7.15: Stereoregular Polymers (please read)

7.16: Chirality Centers Other Than Carbon (please read)

Stereochemistry at atoms other than carbon: N, Si, P, S, and other atoms have the potential to be chiral (assymmetric, stereogenic) centers



Barrier to inversion is very low

Inversion is a racemization process

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