

Stereochemistry

A brief history...

Christian Huygens discovered plane-polarized light in the late 17th century.

In 1815, Jean Baptiste Biot found that certain natural organic compounds, both liquids and solutions, rotate plane-polarized light.

Carl Wilhelm Scheele made an important contribution to stereochemistry when studying the barrels and corks during grape juice fermentation. He discovered racemic acid in 1819 which had the identical structure (same chemical formula) of tartaric acid.

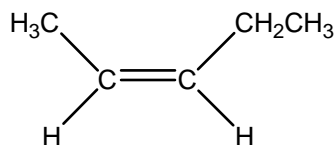
Joesph Achille LeBel and Joobus Henricus van't Hoff, in 1874, proposed carbon is tetrahedral and that a molecule possessing a tetrahedral carbon can exist as a pair of isomers.

(source: Thinkbook 14-C; Hardinger; pgs 11-14)

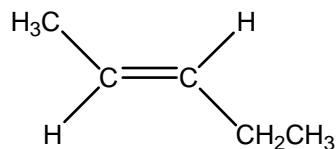
Cis-Trans Isomers (Bruice 4th edition, 5.1)

- A.K.A. geometric isomers
 - Cis isomer: hydrogens lie on same side of the double bond
 - Trans isomer: hydrogens lie on opposite sides of the double bond
- Are a result of restriction rotation cause by a double bond or ring structure

Non-Cyclic Example (Bruice ath edition, pg.183)

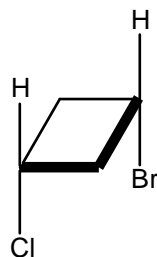


cis-2-pentene

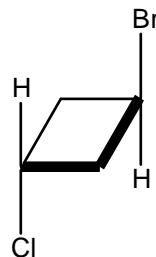


trans-2-pentene

Cyclic Example (Bruice 4th edition, pg. 183)



cis-1-bromo-3-chlorocyclobutane



trans-1-bromo-3-chlorocyclobutane

Chirality (Bruice 4th edition, 5.2)

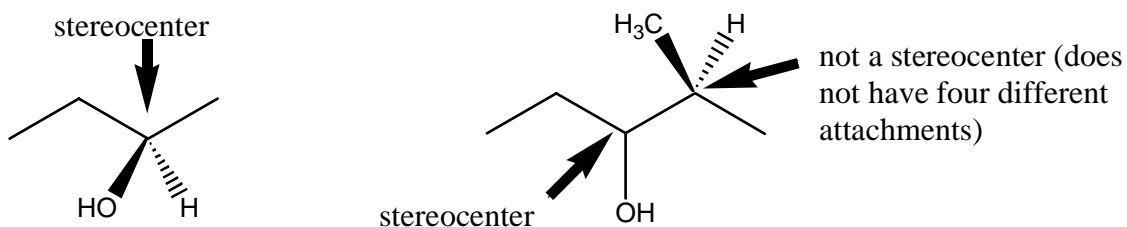
- Chiral: object with a nonsuperimposable mirror image
 - Ex: hands, left hand looks like right hand in mirror; molecule with one asymmetric carbon
- Achiral: object that has a superimposable image
 - any object that isn't chiral

- Ex: a spoon

Asymmetric Carbons, Chirality Centers, and Stereocenters (Bruice 4th edition, 5.3, 5.17, Hardinger Thinkbook 14C, pg.13)

- Asymmetric carbon: a carbon with 4 different substituents
 - A.K.A Chirality Center (there are other types of chirality centers, see below)
 - the most usual cause of chirality in compounds
 - only sp³ hybridized carbons can be asymmetric carbons since sp and sp² hybridized carbons can't have four substituents
- Chirality Centers
 - A type of stereocenter
 - An asymmetric carbon, nitrogen, or phosphorus can be a chirality center
 - Need 4 different substituents and tetrahedral geometry
 - Compounds with a chirality center can exist as enantiomers and be separated (except if a substituent attached to a nitrogen is a lone pair because of amine inversion)
- Stereocenter: atom at which the interchange of two groups produce a stereoisomer
 - Ex. Atom with 4 different attachments; asymmetric carbon
 - make sure to draw in all hydrogen atoms because it will help find stereocenters (look at example below)
- Stereoisomer: isomers that differ only in the position of the atoms in space, and that cannot be interconverted by rotation around a single bond
 - Can't be separated since all physical properties of enantiomers are identical (except direction of polarized light)

Examples: (Hardinger online tutorial; Stereochemistry- Identifying Stereocenter)



*Remember that a stereocenter needs to have 4 **different** attachments*

Isomers with One Asymmetric Carbon (Bruice 4th edition, 5.4)

- Compounds with one asymmetric carbon can exist as two different stereoisomers; both which are nonsuperimposable mirror images (chiral images but more specifically... enantiomers)
- Enantiomers: nonsuperimposable mirror-image molecules
 - molecules that do have superimposable mirror images are referred to as achiral, just like objects
 - have identical physical properties

Notice the difference between “chiral” and “enantiomers”... “chiral” refers to any object and “enantiomers” strictly refers to molecules

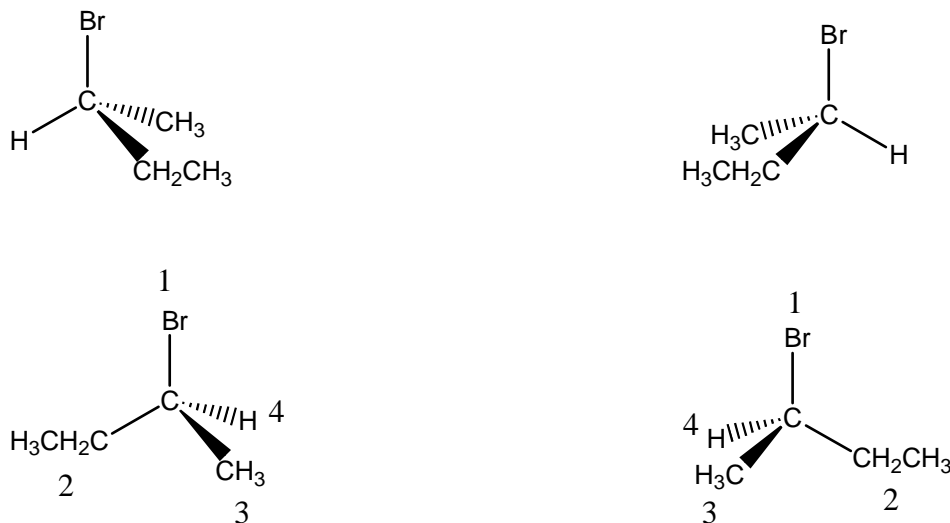
Example of Enantiomers: 2-bromobutane (Bruice, pg. 187)

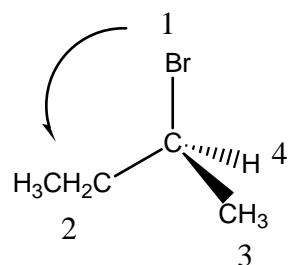


Naming Enantiomers: R,S System of Nomenclature (Bruice 4th edition, 5.6; Hardinger online tutorial on Stereochemistry)

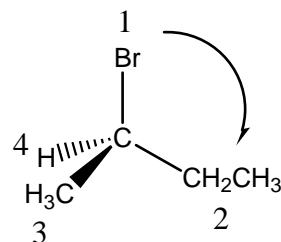
- this system helps indicate the arrangement of atoms (or groups) around the asymmetric carbon
- To determine the configuration of a asymmetric carbon:
 1. Rank the substituents in order of priority (remember that the highest priority is given to atoms with higher atomic numbers... if two atoms have the same atomic number then look at the next atom attached to that atom and so forth). (1) being the highest priority and (4) being the lowest
 2. Rotate the molecule so that the group with the lowest priority (4) is directed away from you. Draw an arrow from the group with highest priority (1) to the group with the next highest priority (2). If the arrow points:
 - clockwise- the asymmetric carbon has the R configuration
 - counterclockwise- the asymmetric carbon has the S configuration

Example: Naming the two enantiomers of 2-bromobutane (Bruice 4th edition, pg. 189)





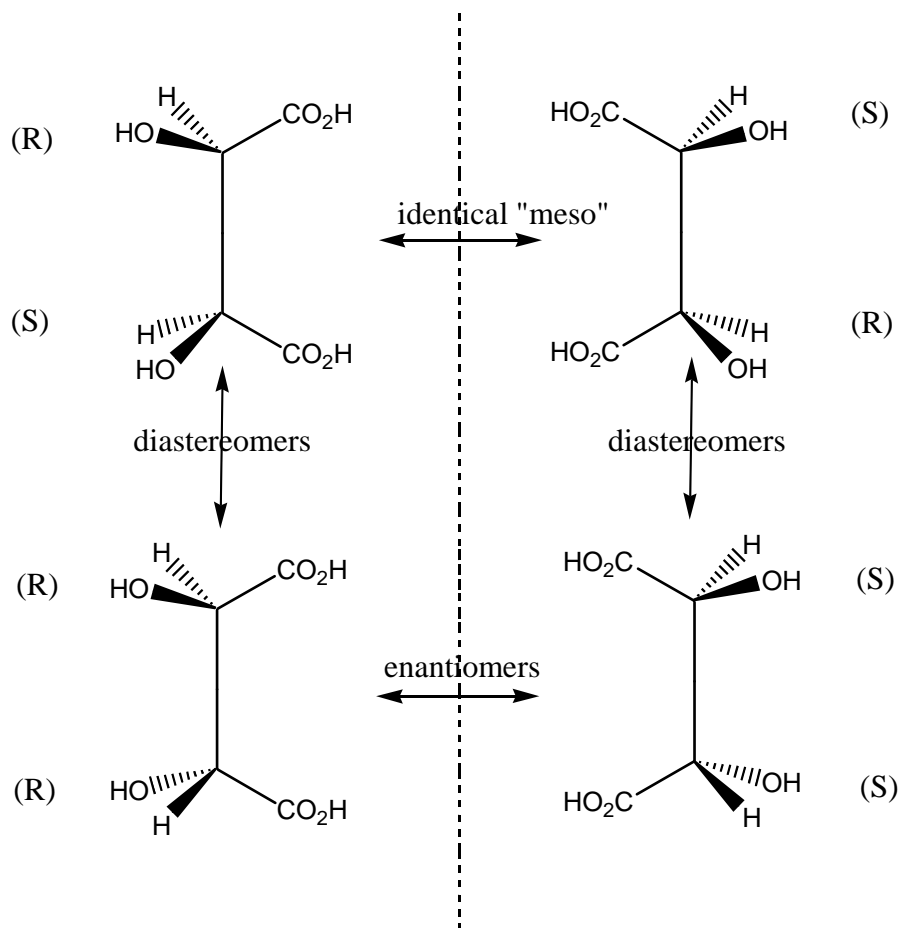
(S)-2-bromobutane



(R)-2-bromobutane

Isomers with More than One Asymmetric Carbon (Bruice 4th edition, 5.9)

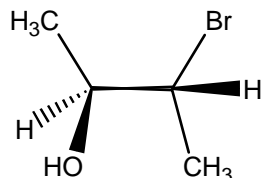
- Meso compound: achiral compounds with more than one stereocenter
- more asymmetric carbons= more possible stereoisomers
 - Max number of stereoisomers: 2^n (where n is the number of asymmetric carbons)
- Diastereomers: stereoisomers that are not enantiomers



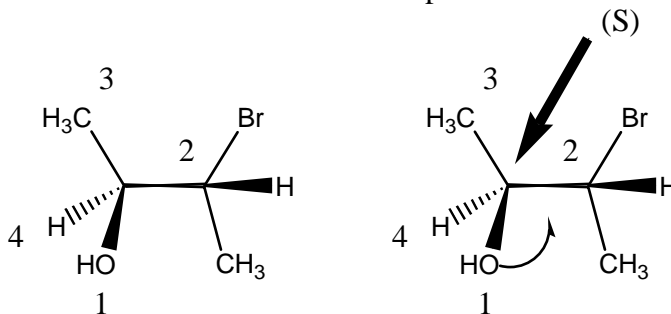
The R, S System of Nomenclature for Isomers with More than One Asymmetric Carbon (Bruice 4th edition, 5.11)

- R or S configuration needs to be determined for each asymmetric carbon

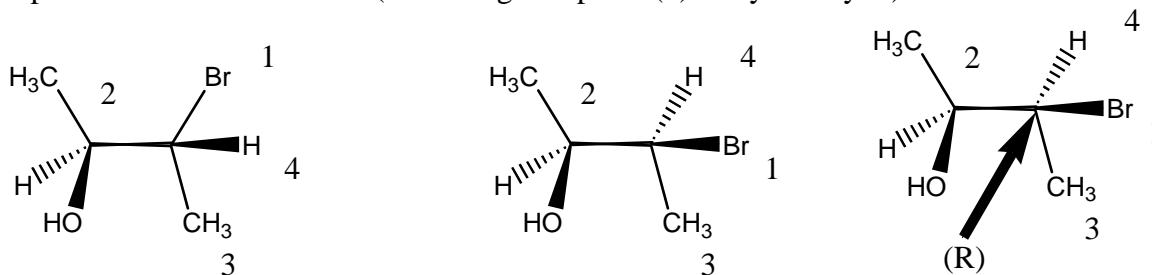
Example: 3-bromo-2-butanol (Bruice 4th edition, pg. 204)
stereoisomer



then label priorities



repeat for other stereocenter (don't forget to place (4) away from you)



So the isomer name is **(2S, 3R)-3-bromo-2-butanol**

Optical Activity (Bruice Bruice 4th edition, 5.7; Hardinger 14C Thinkbook pgs. 11-14)

- Normal light vs. Plane Polarized light (polarized light)
 - normal light- electromagnetic waves that oscillate in all directions
 - plane-polarized light- light that has been filtered so that electromagnetic components lie in a single plane
- Achiral compounds do not rotate polarized light therefore they are:
 - optically inactive: compound that does not rotate polarized light
- Chiral compounds rotate polarized light therefore they are:
 - optically active: compound that has the ability to rotate polarized light
- Rotation of polarized light:
 - Dextrorotatory: optically active compound that rotates plane-polarized light in a clockwise direction (+)
 - Levorotatory: optically active compound that rotates plane-polarized light in a counterclockwise direction (-)

- when you are dealing with a pair of enantiomers, one will be dextrorotatory and the other will be levorotatory

Do not confuse R and S with (+) and (-). R and S refer to arrangement of the substituents about an asymmetric carbon and (+) and (-) refer to the direction in which and optically active compound rotates polarized light.

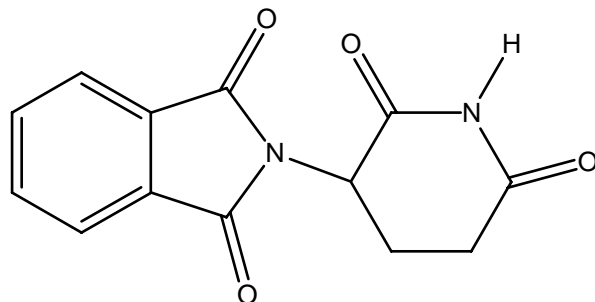
Synthesis and Resolution (Thinkbook 14C, pg. 14)

- Racemic mixture: equimolar mixture of enantiomers
- Resolution: separation into enantiomers
 - convert enantiomers to diastereomers (since they have different physical properties) by adding one stereocenter (minimum)
 - separate diastereomers
 - recover enantiomers from separated diastereomers
- enantiomers have identical physical properties (with the exception of the direction that they rotate polarized light) so you can't separate without using resolution

Biological Significance (Lecture Supplement by Dr. Hardinger given on 1-23-06; Thinkbook pg. 14; Bruice 4th edition, pg. 215)

- Importance of using proper enantiomer

Example: Thalidomide



Thalidomide stops tumor from asking for blood (needed for growth)

- (R) stereoisomer- sedative, now used to treat leprosy and melanomas; dextrorotatory (+)
- (S) stereoisomer- teratogen: caused fetal abnormalities; levorotatory (-)