Stereochemistry

*Students can bring models to class!

A. Introduction

What is this thing called stereochemistry?

-recall constitutional isomers have _____

Example, C_4H_{10}: Butane and 2-methylpropane

There is another important kind of isomer….

STEREOISOMER! (a.k.a. _____isomers) = same molecular formula, same bonding order, _____

B. Cis/trans isomers

Klein 5.1

-a.k.a. _____ isomers

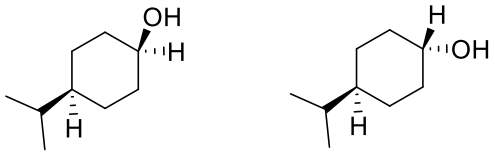
-a type of "_____"

(= _____)

**occurs in _____ and _____

1. _____ and cis/trans isomers

a) Example:



-cis= groups on _____ side of ring

-trans=groups on _____ side of ring

b) Notes:

*neither of these can be interconverted, because they are _____. Bonds would have to be _____ for the cis isomer to become the trans isomer.

-If >2 groups, then you just _____.

2. _____ and cis/trans isomers
Klein 5.1 and 5.11

-two methods of naming:

a) cis/trans stereoisomers (old fashioned terminology)

-follow _____

-if C chain is on the same side of alkene, then _____; if on the opposite, then _____

b) _____ nomenclature system (more modern/Cahn-Ingold-Prelog system)—Klein 5.11

method:
(1) identify _____ priority group on ***each*** C of alkene

**Priority based on atomic number of atom

(2) if highest priority groups are on _____ side of alkene, then Z (zusammen=

_____); if highest priority groups are on _____ sides, then E

(entgegen=_____).

c) examples

(1) 2-hexene: draw the cis, trans, E and Z versions of 2-hexene → $CH_3CH_2CH_2CH=CHCH_3$

trans and E name: trans-2-hexene or (E)-2-hexene	cis and Z

(2) 2-bromo-2-hexene → $CH_3CH_2CH_2CH=C(Br)CH_3$

trans, but … name: (Z)-2-bromo-2-hexene	cis, but…. name: (E)-2-bromo-2-hexene

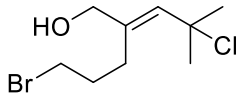
d) Notes:
*Alkene carbon groups must be _____!!

-pi bonds _____the C chain into a configuration.

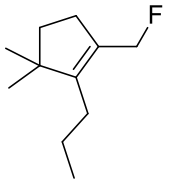
-alkenes with different substituents can therefore have two configurations
_____
!
-C's of alkene are considered _____ → _____ 2 groups on C

produces a different stereoisomer

2nd example:



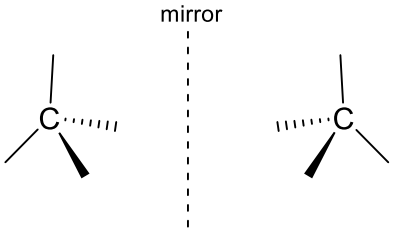
3rd example:



*REMEMBER THESE PRIORITY RULES! THEY APPLY IN THE NEXT SECTION.

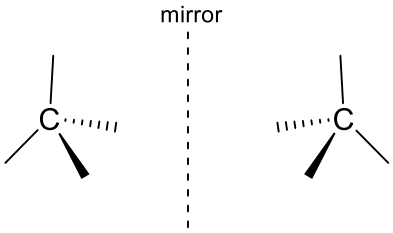
C. Stereoisomers with Asymmetric Centers

1. Draw a tetrahedral structure for the C-1 carbon of ethanol, CH_3CH_2OH



-note:

2.Contrast with lactic acid:$CH_3CH(OH)CO_2H$



<u>Key difference:</u>

-These are _____ mirror images!

-the central carbon is a _____!

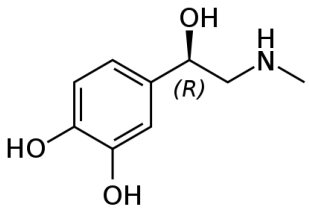
-we call these two compounds "_____"

The two different forms of lactic acid are called _____!

3. Biological relevance= many biomolecules are _____ and only one

_____ is found or only one has the _____.

-example: epinephrine (adrenaline)...R is _____ and S is _____



4. Chiral objects=_____

-there are lots of everyday objects that are chiral!

-*achiral*= _____ chiral

5. Important terms

a) <u>chiral or asymmetric center</u> =

-must be C's_____

b) stereocenter= _____;

includes _____ and_____.

**Therefore it is a _____ category.

c) enantiomers= _____

D. Stereochemistry Nomenclature

1. Cahn-Ingold-Prelog (CIP) system

a) Find asymmetric center--> look for _____

b) _____ on chiral center

-highest atomic no. = _____

-1st atom same rank, then….

-double and triple bonds = _____ bonds to same atom respectively

c) Orient molecule with _____ in back.

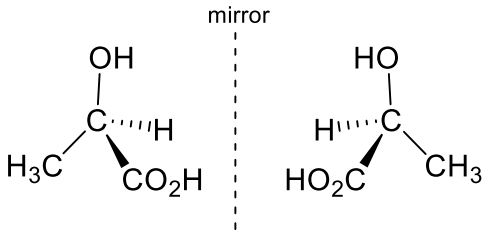
d) Determine direction of _____

-CAUTION: third priority group must NOT be between highest and second in orientation determination!

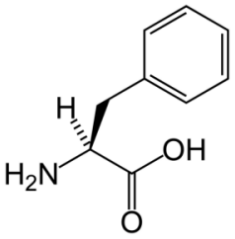
Clockwise= _____

-Counterclockwise= _____

Example:

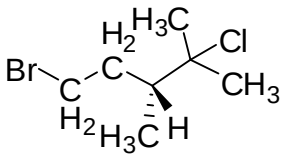


2nd example…



phenylalanine

3rd example…



E. Fun stereochemistry activities:

1. Finding stereocenters and asymmetric centers

a) stereocenters of cis/trans isomers

-find alkene with _____

-find a cycloalkane with _____

b) asymmetric (chiral) centers

-must have _____ on a tetrahedral C (or N, P or S) for asymmetric center

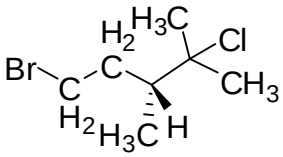
2. Determining R or S with a trick

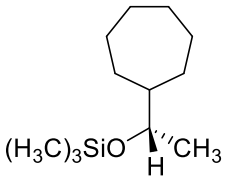
-you can follow standard description above, but...IF you have difficulty rotating molecules in space, then...

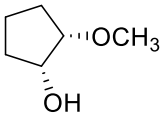
a) *Lowest priority group in front* (wedge)…

TRICK 1: determine R or S orientation with groups as drawn, then _____

-examples:







Caution: lowest group with _____is the trickiest situation!

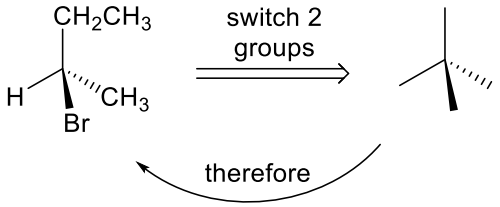
b) *Lowest priority group to side* (flat line)….

TRICK 2: switch two groups to put _____

-determine priority orientation of _____

-due to original switch,……

-example with H in front:



3. Drawing a particular stereoisomer.

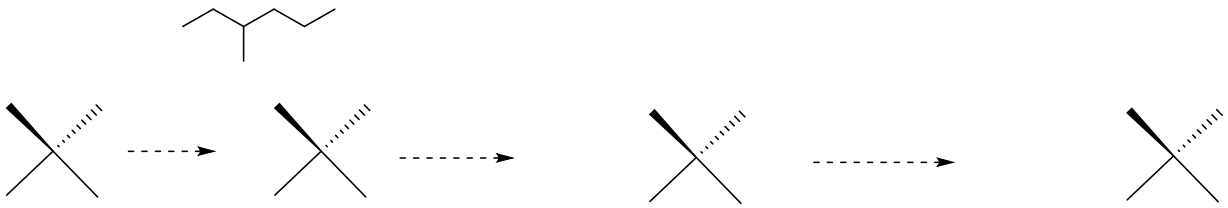
-draw a tetrahedral C

-put _____ on dash bond (going back)

-put _____ on line bond

-put next highest priority group either _____.

Example:
(S)-3-methylhexane

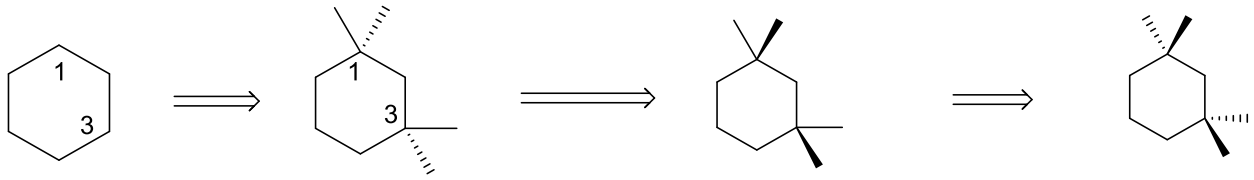


A cyclic example where the procedure above needs to be modified…

2nd example: (1S, 3R)-1-ethyl-3-methylcyclohexane
(1) draw _____

(2) put _____ with wedge at chiral centers
(3) analyze
(4) switch if necessary

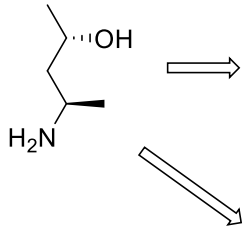
*Note: rings can't rotate chiral centers _____, so you don't necessarily need both _____!



4. Drawing an enantiomer of a chiral molecule

-if given one stereoisomer, just _____.

-example:

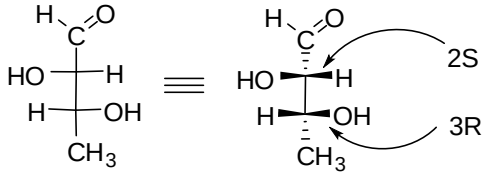


5. Fischer projections

a) Fischer projections vs. typical chemistry structural depictions

-e.g. D-(+)-glyceraldehydes

2nd example:



F. Multiple asymmetric centers

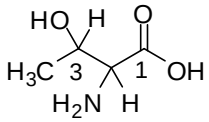
1. Introduction

-more _____ centers = more _____

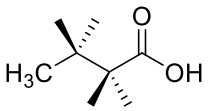
-n= no. of _____ centers, then 2^n = no. of _____

2. Molecules with _____ chiral centers

a) e.g. threonine



four stereoisomers:

 2S, 3R-threonine	2S, 3S-threonine
2R, 3R-threonine	2R, 3S-threonine

*Note:
-2S, 3R and 2R, 3S are _____ or an _____

-2R, 3R and 2S, 3S are _____

-2S, 3R and 2S, 3S are _____

-2R, 3R and 2R, 3S are _____

b) Summary: two chiral centers affords _____.

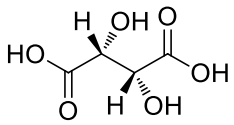
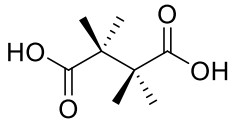
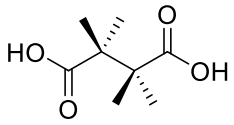
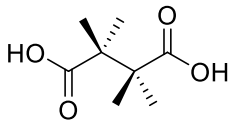
These _____ of the other enantiomers.

-enantiomers=_____

-diastereomers=_____

3. Special topic: <u>Meso compounds</u>= _____

a) example: tartaric acid (hugely historic compound; found in wine)

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

b) Highlights:

(i) *Note: the 2R,3S stereoisomer = the _____ stereoisomer!This is a _____ compound. It is NOT chiral (=achiral)!
-you can expect that a meso compound will _____.

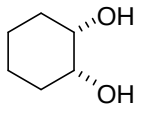
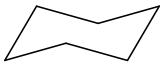
(ii) *Note: the conformations on the right are _____ based on our earlier discussions, but they best show the symmetrical nature of the molecule.

(iii) **Therefore, tartaric acid has _____ stereoisomers:
_____

c) Identifying a meso compound/cyclic examples

-look for _____ in structure.

(i)example: cyclohexane structure:

*therefore the cis-1,2-cyclohexanediol is _____.

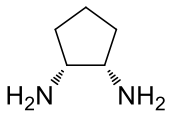
-trans-1,2-cyclohexanediol would _____.

-1,4-disubstituted cyclohexanes are _____.

-cis-1,3-disubstituted cyclohexanes are _____.

Note: the two chair conformations of cis-1,2-cyclohexanediol are _____!

(ii) Another example with a cyclopentane structure



Conclusion of meso discussion:
Dr. Mal Maxim: IF A MOLECULE CAN ADOPT A _____ THAT YIELDS A

_____ STRUCTURE, THEN THE MOLECULE IS _____.

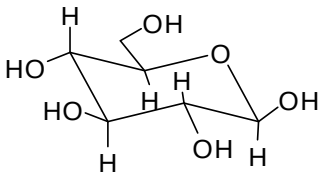
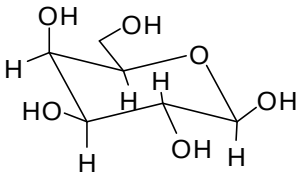
4. Molecules with 3 or more chiral/asymmetric centers

-enantiomer pairs _____; so will _____ relationships

-since there will be _____

-epimers= multi-stereocenter molecules with _____ different; they are a specific type of diastereomer

Examples:

D-glucose:	D-galactose:
	

G. Summary of Isomers

H. Physical properties of stereoisomers

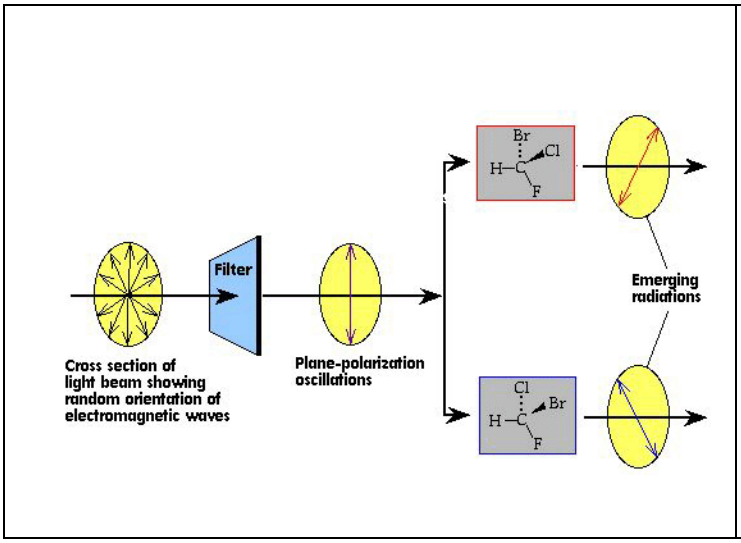
1. Enantiomers

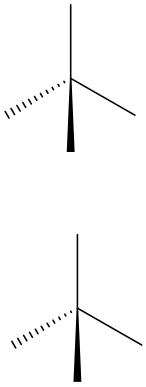
-all properties of enantiomers are the _____

EXCEPT….._____!!

a) Plane-polarized light

(plane-polarized light is explained in Klein sect. 5.4)





-optical rotation=_____

b) Two important terms:

(i) *dextrorotatory=_____→ + rotation

(ii) *levorotatory=_____→ - rotation

This will be represented as follows:

(R)-(+)-glyceraldehyde has an optical rotation of +13.5°

-R tells you the arrangement of the groups around the tetrahedral C

-(+)- has _____ with atom arrangements!!

Some _____ enantiomers are also (+) and vice versa.

e.g. lactic acid:

CAUTION: D and L designations are relative to _____and have no relation to

_____ configuration assignments!

Relationship of D and L to dextrorotatory or levorotatory??

c) Racemic mixture= _____ mixture of enantiomers will have an optical rotation of _____.

*__Racemization__ = ….

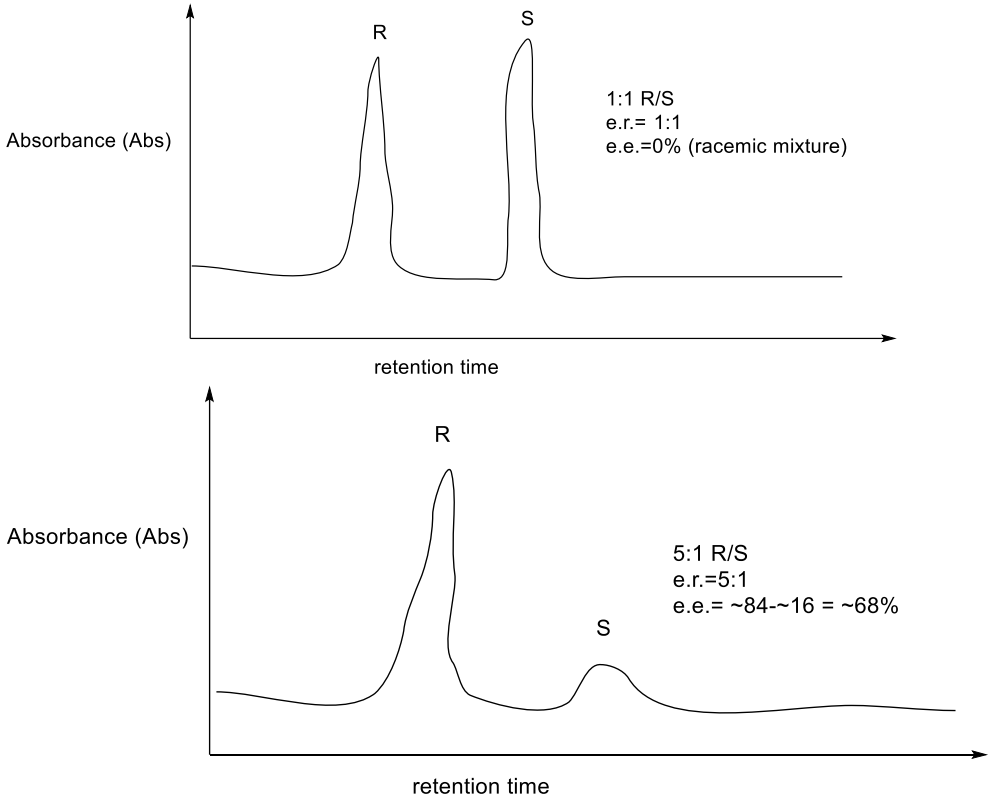
d) Modern approaches to enantiomer analysis

-liquid chromatography (LC) with a chiral stationary phase (often _____)

-You can think of this as creating a_____!

-when done, you get two separate peaks in the chromatogram and their areas correspond to the relative amount of each present

Illustrated:



2. Diastereomers

-_____! Different m.p., b.p., NMR, chromatography, etc.

Therefore they can be much more easily analyzed!

I. Special topics

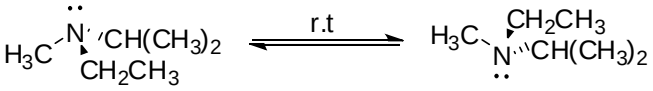
1. Amine and Phosphorus stereochemistry

a) Most amines are _____

-amines rapidly _____;

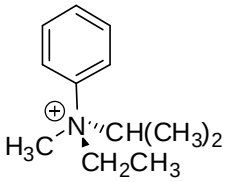
phosphines do not and are _____

Amine inversion leading to racemization:



~25 kJ/mol E required for amine inversion (recall ~80 kJ/mol of E available at r.t.)

b) Quaternary ammonium salts are _____



Stereochemistry?