Learning Guide for Chapter 6 - Stereochemistry

I. Stereoisomers containing C=C p 1
II. Introduction to chirality - compounds with one stereoisomer - p 5 Chirality Recognizing chiral compounds Labeling stereocenters as R or S
III. Compounds with two or more stereoisomers - p 9 Diastereomers and meso compounds Fischer projections
IV. Physical properties of chiral compounds - p 14 Melting point, boiling point, etc Biological environments Optical activity Separation of enantiomers Determination of stereochemical correlation

I. Stereoisomers containing C=C

What do two compounds which are constitutional isomers have in common? How are they different?

same molecular formula

different bonding sequence

Give the molecular formula and one constitutional isomer for each of the following compounds.



Are these compounds constitutional isomers of each other? no - different formula

What do two compounds which are stereoisomers have in common? How are the different?

same molecular formula

same bonding sequence stereoisomers can only occur under certain conditions different shape

Draw line structures for two different molecules with the condensed structure shown.

CH₃CH=CHCH₃ make models!

What keeps these two compounds from being the same?



draw a picture of sigma and pi bonds

they can't rotate around the C=C

Why aren't these two structures the same as the ones above? What relationship do they have?



two conformations of the same compound

can rotate around C-C bond

Draw a constitutional isomer, a stereoisomer, and a conformation of the following compound.

$\frown \frown$	constitutional isomer	stereoisomer	conformation
	$\sim \sim$		
same formula?	yes	yes	yes
same bonding sequence?	no	yes	yes
same shape?	no	no	no
same compound	? no	no	yes

How many stereoisomers are possible for a compound containing a C=C? two max Do all compounds containing a C=C have stereoisomers? no

How many stereoisomers does the following compound have? Why?



How can you tell if a compound with a C=C will have a stereoisomer?

look at both sides of the C=C; both groups must be different from each other

Determine whether or not the compounds below will have a stereoisomer, and for those that will, draw it.



What is a stereocenter?

carbon - switch two substituents, get a new compound



Can a compound containing a C=C have only one stereocenter?

no - it must either have 2, or none

When can we use <u>cis</u> and <u>trans</u> to label the two stereoisomers?

when there is only one substituent on each side of the C=C

Which of these is <u>cis</u>, and which is <u>trans</u>?



Why can't cis and trans be used on the following compound?



more than one group on each side - can't tell what to compare

In the following examples, the #1 substituent has priority over the #2 substituent. Which is \underline{E} and which is \underline{Z} ?



Label the following as \underline{E} or \underline{Z} and explain why. If they were the same all the way out, then what? no stereochemistry



II. Introduction to Chirality

What does it mean to say that an object is chiral? What about achiral?

chiral - its mirror image is different from the original object achiral - its mirror image is the same as the original object

Many everyday objects are chiral. Consider the following. Are they chiral or achiral? Is the mirror image of the object the same, or different?

hand chiral	scissors chiral
spoon achiral	gloves chiral
fork achiral	nail achiral
knife achiral (unless is has an edge)	screw chiral
socks achiral	DNA helix chiral
shoes chiral	folding student desk chiral
Tetris shapes	
achiral chiral	achiral chiral
striped quilt triangles	
chiral o	chiral achiral

How can a molecule be chiral?

most common way - asymmetric carbon: 4 different groups

Using models, make the compound below. Then construct its mirror image



What is the relationship between these two compounds?

Br OH H Br OH same molecular formula same bonding sequence different shape non-superimposable mirror images enantiomers (type of stereoisomer) Are the central carbon atoms stereocenters?

yes - switching any two substituents gives the other enantiomer

Construct the compound below, and its mirror image.



Are these compounds superimposable? yes Is the original compound chiral? no Does the original compound have an enantiomer? no

How can you determine if a molecule is chiral?

1) Is the mirror image superimposable? yes - achiral only completely reliable test

:OH

: OH ŧ

OH

enantiomers

chiral

:OH

:OH

same compound

achiral

2) Is there a plane of symmetry in the molecule?



There are other, rarer kinds of symmetry that can also make the molecule achiral.



3) How many asymmetric carbons are in the molecule?

None - molecule is probably not chiral. One - molecule is chiral. Two or more - molecule is chiral unless there is a plane of symmetry.



more about molecules with more than one stereocenter shortly

2 asymmetric C's no plane of symmetry chiral

2 asymmetric C's plane of symmetry achiral

Which of the following molecules are chiral? Which have planes of symmetry? Where are the asymmetric carbons? Where are the stereocenters?



LG Ch 6 p 8

How are enantiomers labeled?

- 1) Prioritize the groups
- 2) Rotate so that the last priority group is pointed away.
- 3) Look at the 1-2-3 direction.

clockwise - R counterclockwise - S

<u>S</u> <u>і</u> w

when last group is already back, you're set



use overhead of clock!

when last group is forward, you're looking at it from behind go 1-2-3, then reverse





when last group is in the plane of the page, use models! at 1st glance it looks R

Practice:









How is this label included in the name?

(S)-3-methylhexane



 $(1\underline{S},2\underline{R})$ -1-ethyl-2-methyl-cyclopentane



(<u>cis</u>)-1,4-dimethylcyclohexane



(or a mixture of both!)

III. Compounds with two or more stereocenters

Consider the following compound. How many stereocenters does it have? How many stereoisomers could it have?



one stereocenter is the same, the other opposite	RR-RS
	RR-SR
	SS-SR
	SS-RS

Next, consider the following compound. How many stereocenters does it have? How many stereoisomers does it have?



LG Ch 6 p 10

What is the difference between the following compounds?



Consider the following compound. How many stereocenters does it have? How many stereoisomers does it have?



All of the isomers we have seen so far can be related as follows:



Fischer Projections

When are Fischer projections useful?

showing multiple stereocenters biological molecules like sugars

Draw a Fischer projection of the following molecule: 1) main C chain up and down

most oxidized C at the top



Convert the following Fischer projection to a line structure.



Why are the OH's all on the right in the Fischer projection, but some up and some down on the line structure?

line structure - staggered Fischer projection - eclipsed

have to rotate to change between them

Which shows the relationship between the stereocenters better? Fischer projection

Which is the more stable conformation? line structure

What is the relationship between the following molecules?





Label each stereocenter as R or S:



Label each of the following molecules as D or L:



What is the relationship between the first two molecules? What about the second two? What about the middle two?

Since D and L only give the stereochemistry of one stereocenter, how can you tell what the rest are?

each set of enantiomers has a different name

D, L just tells you which of the pair it is

IV. Physical Properties of Chiral Compounds

Regular physical properties

What are some of the physical properties that we regularly talk about with organic compounds?

melting point, boiling point, solubility, density, color, etc

How are the properties of enantiomers related? they are the same

How are these properties of diastereomers related? they are different

What is the relationship of the pairs of compounds below? What would you predict about their physical properties?



Why is the odor of a compound an exception to this?

receptors in your nose are chiral - can detect different enantiomers



What areas of chemistry are strongly influenced by stereochemistry? Why?

biochemistry, pharmaceuticals

biological molecules are often chiral - amino acids, nucleotides, carbohydrates, neurotransmitters, hormones

Optical Activity

How is plane polarized light different from ordinary light?

ordinary light - light waves in all planes

polarized light - light waves in only one plane

How do you obtain plane polarized light?

put ordinary light through a filter

What would happen if you put two polarizing filters together and then turned them at right angles?

no light would get through

Why do polarizing sunglasses work?

reflected light (glare) is polarized - filter blocks it out

What happens when polarized light passes through a solution containing chiral molecules?

it rotates the plane of the light waves show overhead

What is this called? optical rotation - angle that the plane is rotated

How is it measured? using a polarimeter

What factors affect the optical rotation? Which is the most useful? How do we eliminate the effect of other factors?

structure this is what we are interested in

concentration standard concentration - 1 g/ml

distance traveled - path length standard path length - 1 dm (10 cm)

temperature always measure at 25°C

wavelength of light always use the same wavelength (D line of sodium)

The optical rotation of a compound measured under these conditions is called:

specific rotation - $[\alpha]$ there are tables where you can look these up



We can use a different concentration or path length and correct for them using what equation? Why does this work?

 $\alpha = [\alpha] x c x 1$ optical rotation is directly proportional to c and 1

The specific rotation of (\underline{S})-2-butanol is -13.5°. If a sample is made by dissolving 6 g of the compound in 40 ml of solvent, and a 2 cm cell was used to measure the optical activity, what angle of rotation will be observed?

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[\alpha] = -13.5^{\circ}
c = 6 g / 40 ml \alpha = (-13.5^{\circ})(6/40)(0.2) = -0.405^{\circ}
l = 0.2 dm
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If given an observed rotation, how could you figure out the specific rotation?

 $[\alpha] = \alpha / cl$

What is the relationship between the following molecules? How would their melting points and specific rotations be related?



What can you tell about R and S vs. + and - rotations? What can't you tell?

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can tell: if R is + S is -; if R is -, S is + why?
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can't tell: if R will be + or -

What does it mean to say a solution is optically active?

it rotates the plane of polarized light - has an α

Would a solution of the following compound(s) be optically active?



Why are racemic mixtures common?

both compounds have the same energy, formed in the same amounts.

If a solution has 40% optical purity, what does this mean?

the optical rotation has been reduced by 40% by having some of the other enantiomer

If a pure enantiomer has an optical rotation of 20°, what rotation will a solution have which has a 40% optical purity?

80

What equation describes this? %o.p. = rotation of solution rotation of pure enantiomer What proportion of enantiomers will give you a 40% optical purity?

% o.p. = % e.e. = % R - % S 70% - 30% = 40%)

Take 3 mol of R, 7 mol of S



If the specific rotation of (<u>S</u>)-2-butanol is 13.75° , and a mixture of (<u>R</u>)- and (<u>S</u>)-2-butanol has a rotation of -6.75, what is the optical purity of the solution? What is the % e.e.? What percentage of the two isomers is present?

 $\frac{-6.75^{\circ}}{13.5^{\circ}} = .5$ % o.p. = 50% % e.e. = 50% 75% - 25% = 50% since S is + and mixture is -, must be 75% R, 25% S



Separation of Enantiomers

Where do enantiomerically pure compounds come from?

1. many found in nature

→ 2. separation of enantiomers (resolution)

3. stereoselective reactions (Ch 7)

Why can't enantiomers be separated by operations like chromatography, distillation, etc?

same physical properties

What must be done to separate them?

turn them into diastereomers - now they will have different properties

Consider the following example:



Determining the stereochemical correlation

What does it mean to determine the stereochemical correlation for a pair of enantiomers?

match up R and S structures with + and - rotations

Why is this difficult?

you can't tell by looking at the structure whether it is + or -



What method has been developed?

- 1 get a pure sample
- 2 measure its rotation
- 3 evaporate to get a crystal
- 4 do x-ray crystallography to get 3D structure
- 5 see if structure is R or S

Once the stereochemical correlation of one compound has been discovered, how can it be used to determine another without x-ray crystallography?

change molecule in a predictable way (structure still known), measure rotation

