Lecture 16

Organic Chemistry 1

Professor Duncan Wardrop

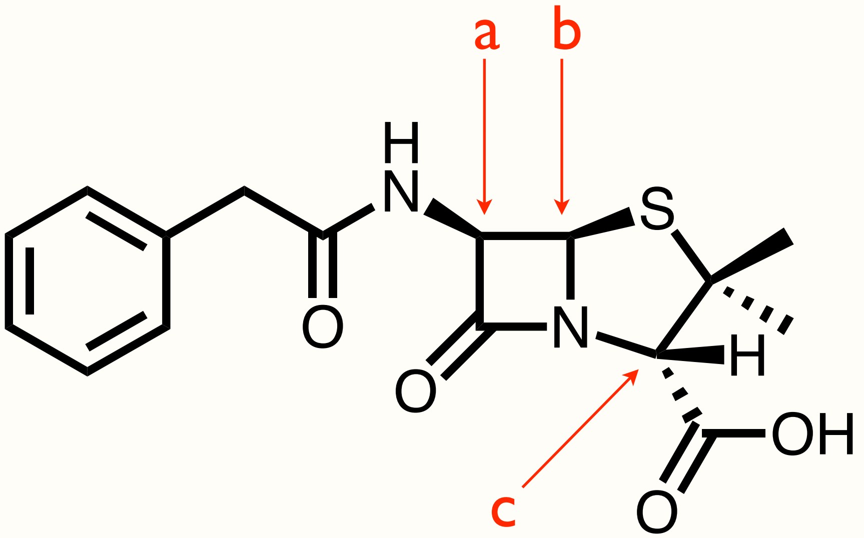
March 4, 2010

Stereochemistry

Section 7.9 - 7.13

Self Test Question

The three asymmetric carbon atoms in penicillin G are labeled a-c. List the *R/S* configuration of each in order of a,b,c.



A. *R,R,S*

B. *S,S,R*

C. *R,S,R*

D. *S,R,S*

E. *S,R,R*

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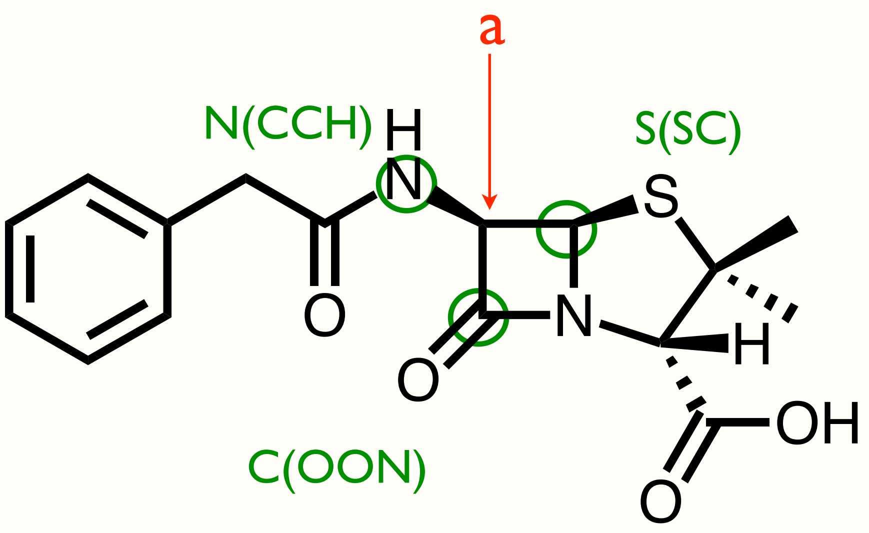

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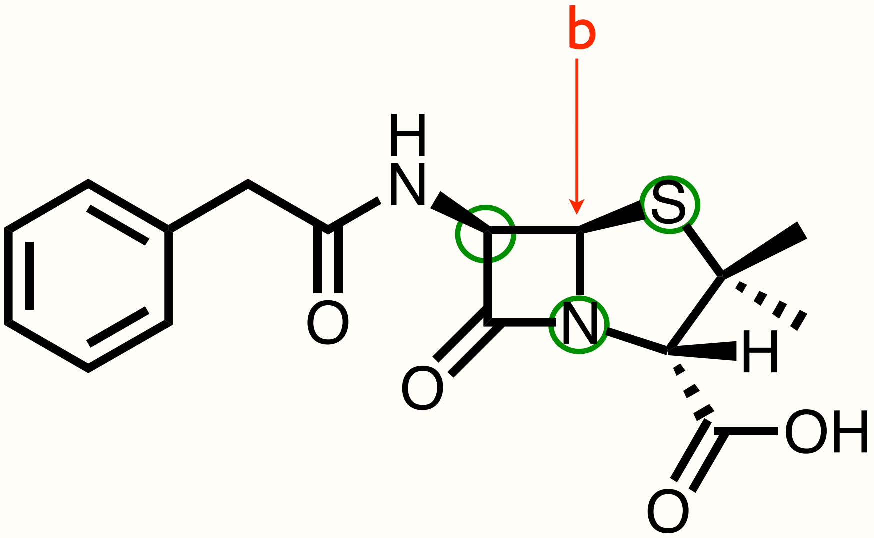

A. *R,R,S*

B. *S,S,R*

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E. *S,R,R*

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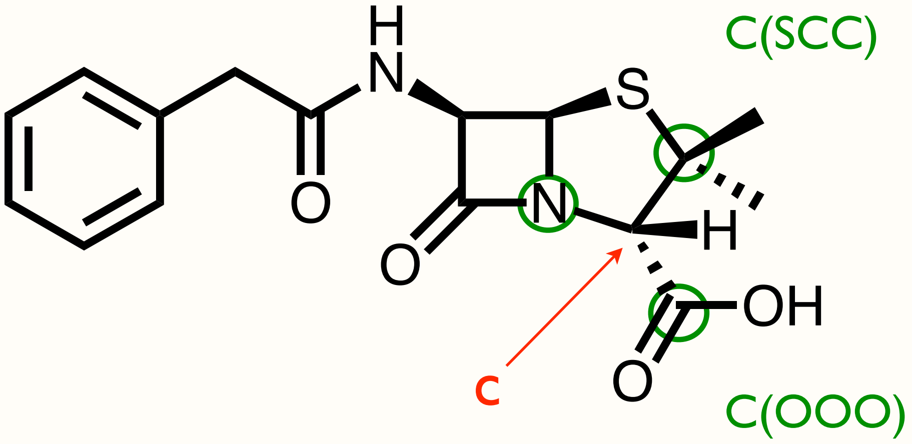

A. *R,R,S*

B. *S,S,R*

C. *R,S,R*

D. *S,R,S*

E. *S,R,R*

Self Test Question

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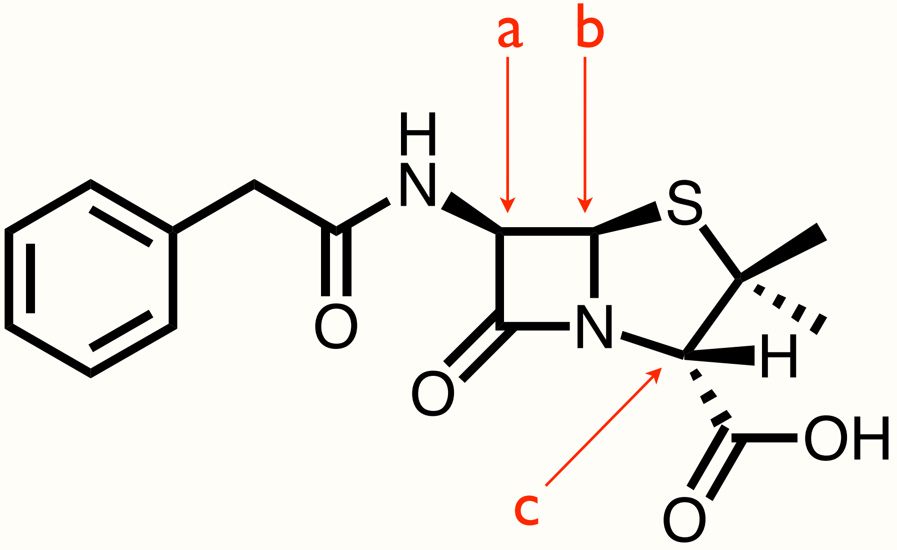


[✓ A.] *R*,*R*,*S*

B. *S*,*S*,*R*

C. *R*,*S*,*R*

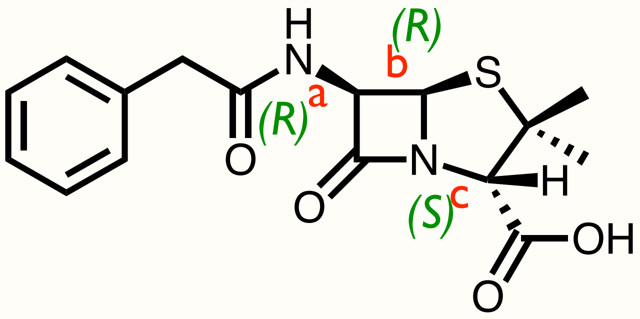
D. *S*,*R*,*S*

E. *S*,*R*,*R*

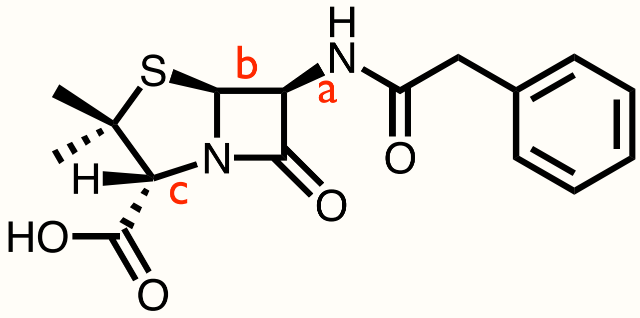
Self Test Question

List the R/S configuration of each asymmetric carbon in the enantiomer of penicillin G in the order a,b,c.

Remember: enantiomers have opposite configurations at every chirality center.



penicillin G



enantiomer of
penicillin G

A. R,R,S

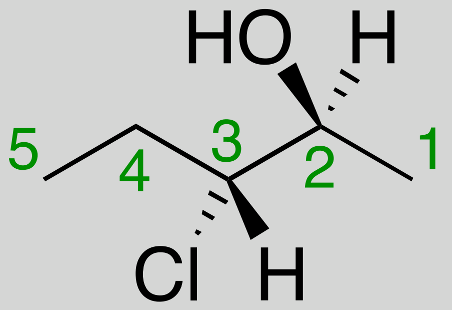
[✓ B.] S,S,R

C. R,S,R

D. S,R,S

E. S,R,R

Stereoisomers with >1 Chirality Center



(2*S*,3*R*)-3-chloro-2-hexanol or (2*S*,3*R*)-3-chlorohexan-2-ol

Steps:

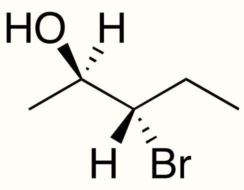
1. Number longest chain so that highest priority group has lowest locant.
2. List locants of asymmetric carbons in increasing order within parentheses at the beginning of name.
3. List stereodescriptor (R/S) after each asymmetric locant.

Conventions/Rules:

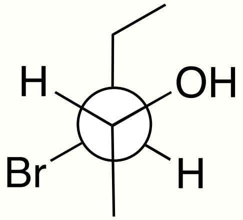
- *R* & *S* are italicized when typed
- a comma separates each steredescriptor (no spaces)
- stereodescriptors are not considered when alphabetizing subgroups
- asymmetric locants are not written if their exclusion is unambiguous

(	**chiral locant**	**R/S**	,	**chiral locant**	**R/S**	)-	**parent**	**class suffix**

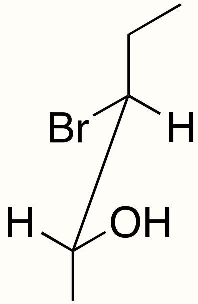
Drawing Fisher Projections



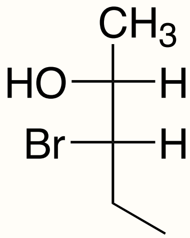
bond-line



Newman Projection

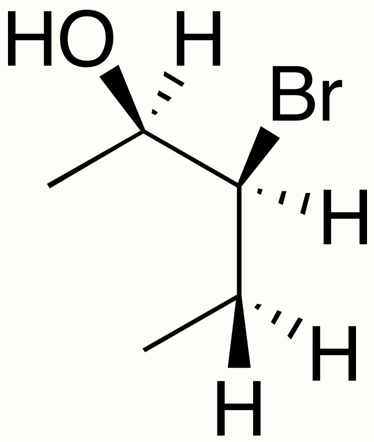


Sawhorse Projection

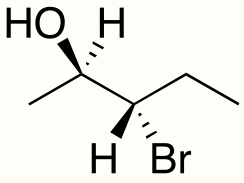


Fisher Projection

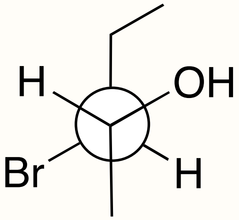
Step One: Draw (imagine) totally eclipsed conformation



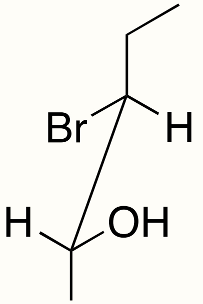
Drawing Fisher Projections



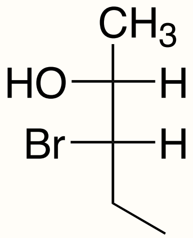
bond-line



Newman Projection

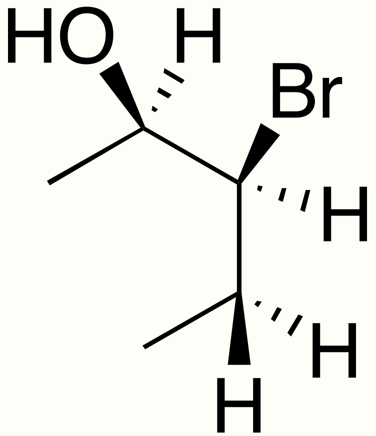


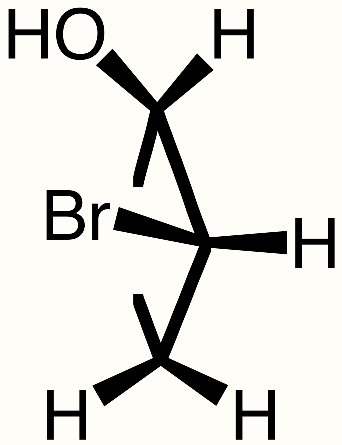
Sawhorse Projection



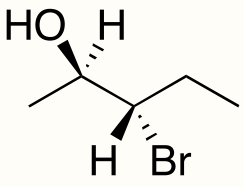
Fisher Projection

Step Two: Imagine that the carbon skeleton atoms form a "C" and you are looking at the back of the C.

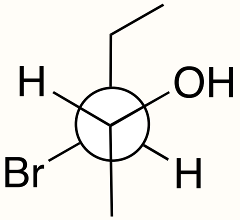




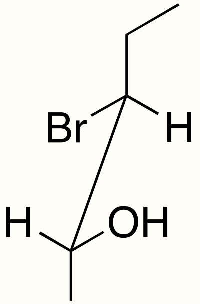
Drawing Fisher Projections



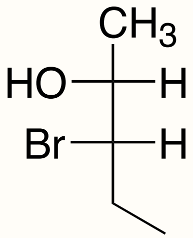
bond-line



Newman Projection

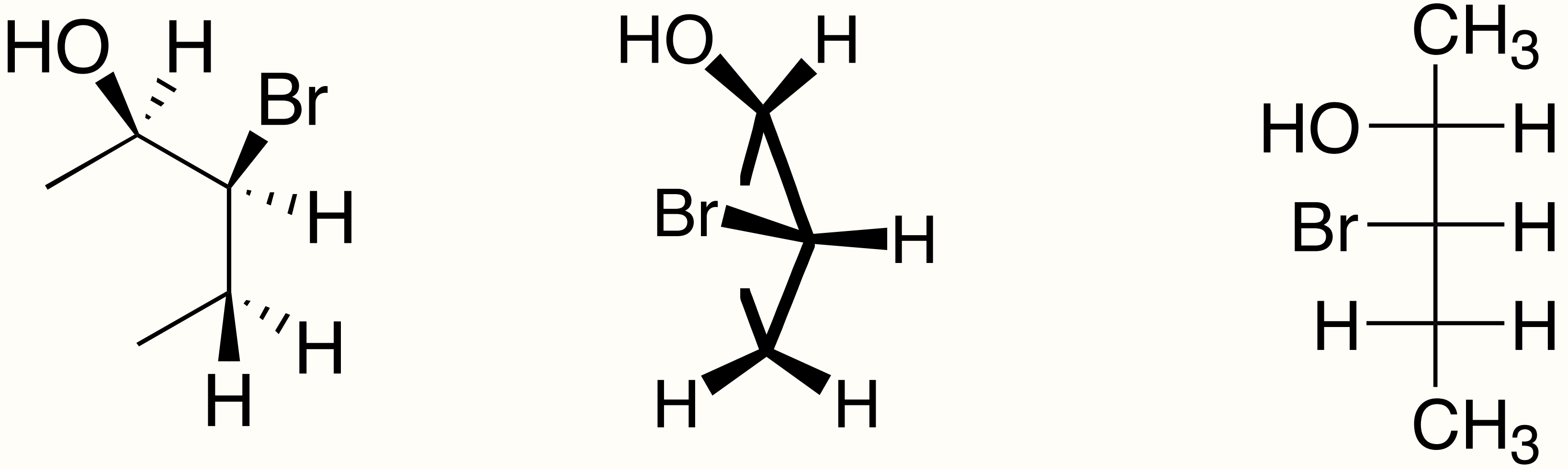


Sawhorse Projection



Fisher Projection

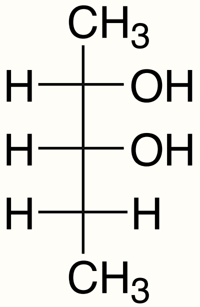
Step Three: Flatten out the "C" so vertical bonds point away from you and horizontal toward you.



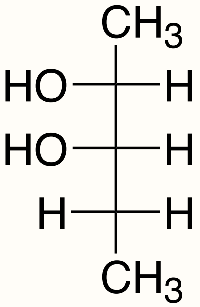
Self Test Question

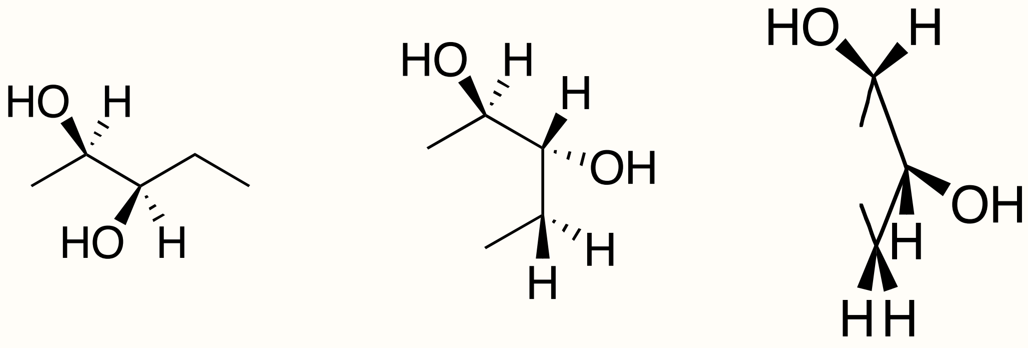
Which Fisher project is (2R,3R)-2,3-pentandiol?

A

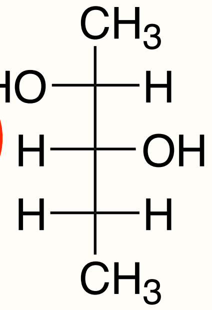


C

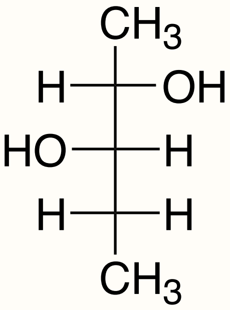




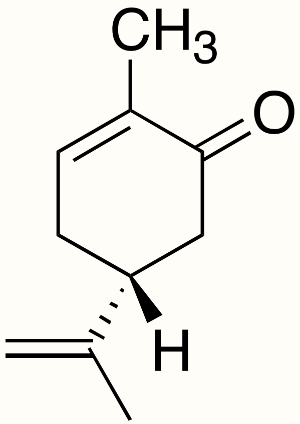
B



D

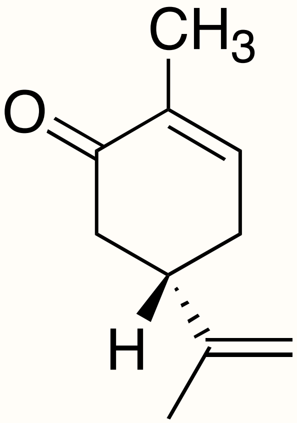


Properties of Enantiomers



(*R*)-(-)-carvone

boiling point = 231 °C
density = 0.96
^{1}H-NMR δs = same as (*S*)
^{13}C-NMR δs = same as (*S*)
IR spectrum $\bar{\nu}$s = same as (*S*)
optical rotation = –61°
smell = earthy



(*S*)-(+)-carvone

boiling point = 231 °C
density = 0.96
^{1}H-NMR δs = same as (*R*)
^{13}C-NMR δs = same as (*R*)
IR spectrum $\bar{\nu}$s = same as (*R*)
optical rotation = +61°
smell = spearmint

Properties of Enantiomers

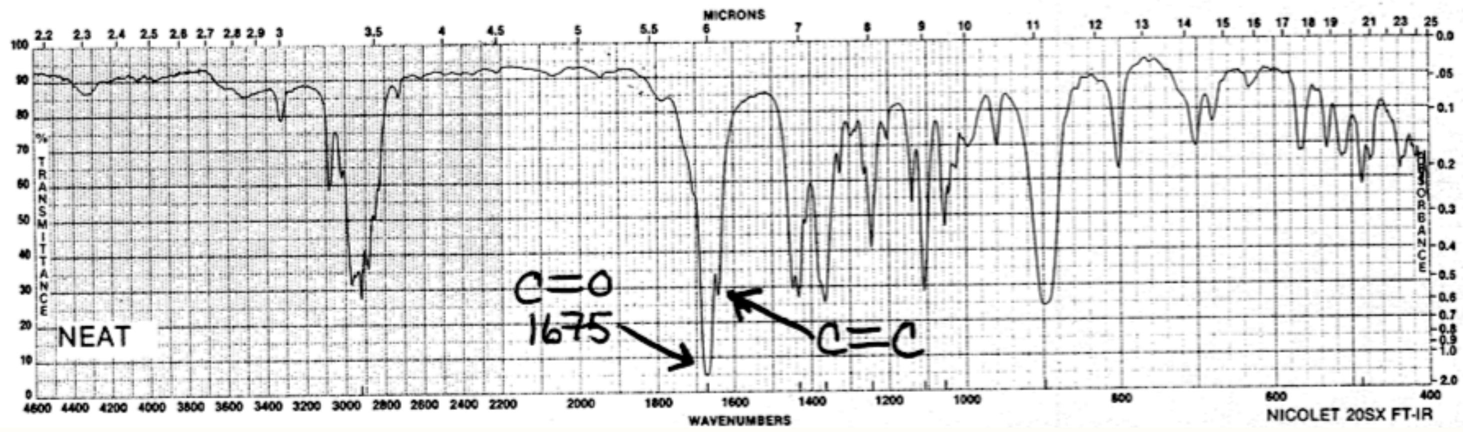
(*S*)-(+)-Carvone

FW 150.22
bp 100°C/10mm
d 0.965

Fp 192°F
n_D^{20} 1.4968

IR III, 265F
NMR II, 1,413C
Merck 10,1856

2923.2	1367.2	1057.9
1675.2	1247.0	894.1
1434.6	1110.8	487.9



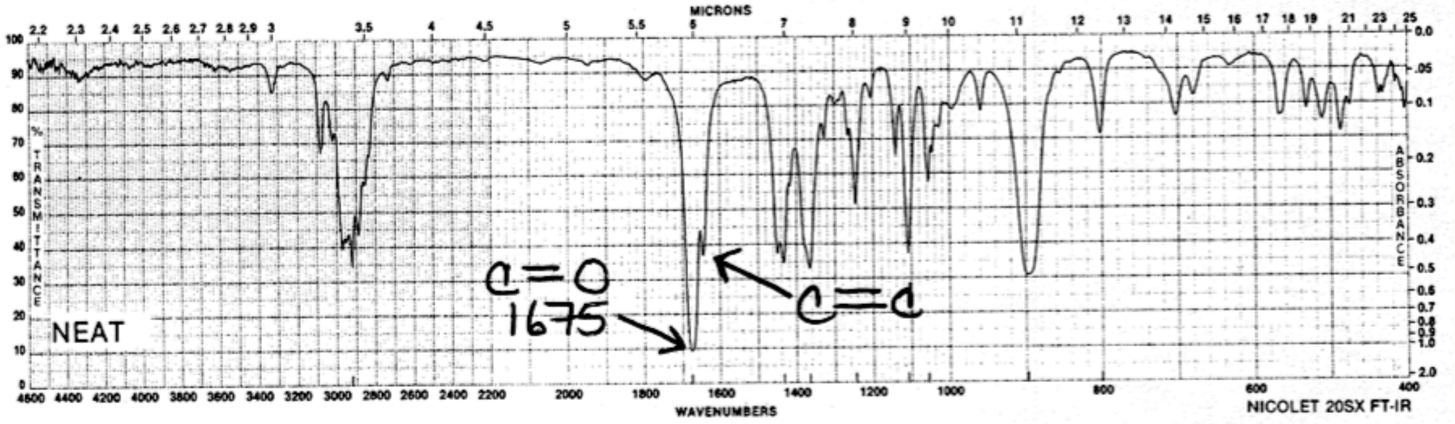
(*R*)-(-)-Carvone

FW 150.22
bp 227-230°C
d 0.959

Fp 192°F
n_D^{20} 1.4985

IR III, 265G
NMR II, 1,413D
Merck 10,1856

2922.7	1367.0	1057.8
1674.9	1246.8	899.0
1434.3	1110.7	802.2



(*S*)-carvone is the enantiomer of (*R*)-carvone

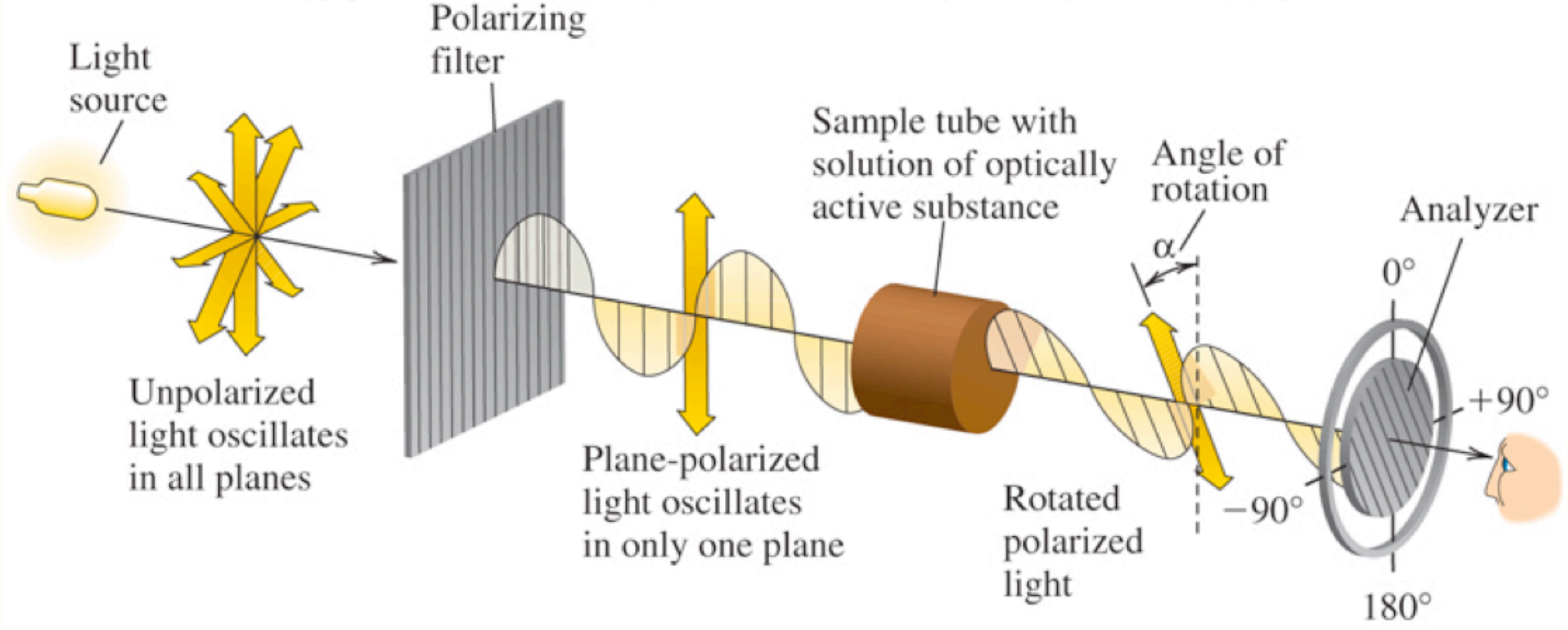
↓

Enantiomers have the *same* physical properities including IR vibrational frequencies, mp, bp, R_f, etc.

↓

IR spectra for both enantiomers of carvone--and for any two enantiomeric compounds--are identical.

Optical Rotation



(–) = counterclockwise = levorotary
(+) = clockwise = dextrorotary

enantiomers rotate plane polarized light an equal magnitude, but in opposite directions

Optical Rotation

- degree of optical rotation depends on concentration of a solution containing the chiral compound
- [α]: specific optical rotation; determined in specified concenetration and path length units for universal comparison

$$[\alpha]_D^{25} = \frac{(100)(\alpha)}{(c)(l)}$$

α = degree of rotation determined by polarimeter
c = concentration (g/dL); 10 dL = 1 L
l = path length (cm)

Optical Rotation

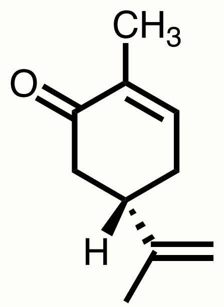
- racemic mixture = contains equal quantities of both enantiomers (1:1, 50/50, etc); $[\alpha] = 0°$
- enantiomeric excess (ee) = |% A enantiomer - % B enantiomer|

% A enantiomer	% B enantiomer	enantiomeric excess (ee)
100	0	100
75	25	50
50	50	0
25	75	50
0	100	100

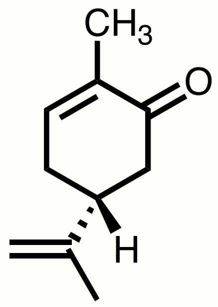
racemic mixture

R/*S* versus (+)/(-)

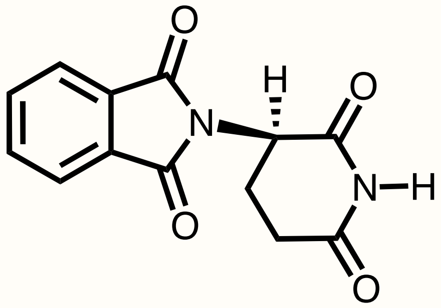
- Enantiomers have equal magnitudes, but opposite signs of specific rotation
- **Caution:** the sign of rotation (+/-) cannot be determined from R/S configuration!



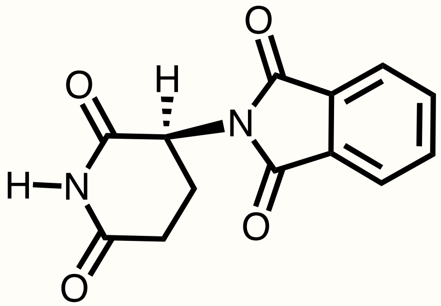
(*S*)-(+)-carvone
[α] = +61°



(*R*)-(–)-carvone
[α] = –61°

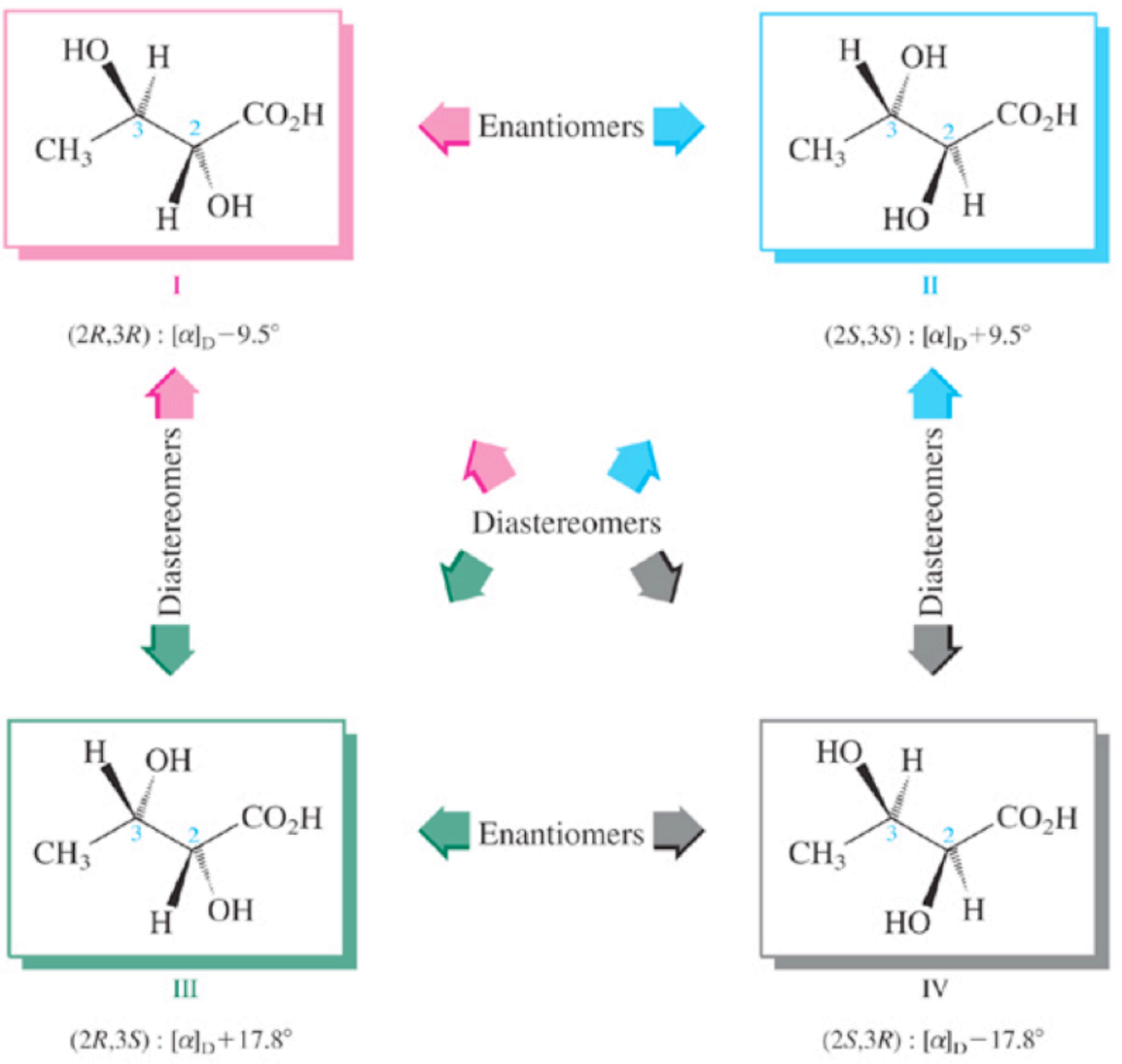


(*S*)-(–)-thalidomide
[α] = –64°



(*R*)-(+)-thalidomide
[α] = +64°

Diastereomers:Chiral Molecules with >1 Chirality Center

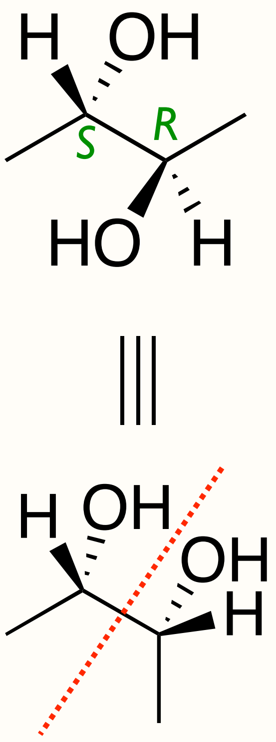


diastereomers:

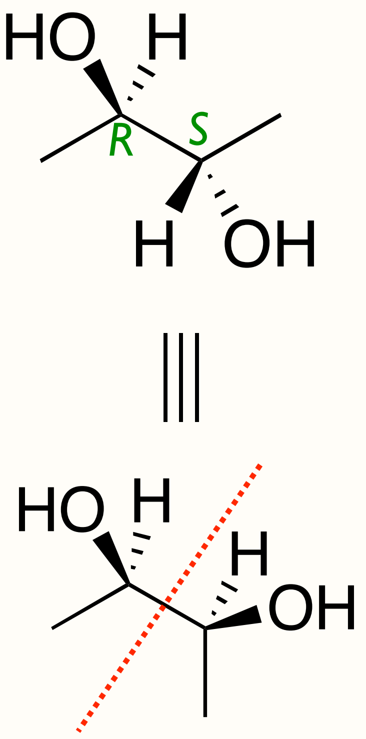
- stereoisomers that are not mirror images
- stereoisomers with ≥ 2 chirality centers that are not all opposite
- diastereomers may have different physical properties!

Meso Forms

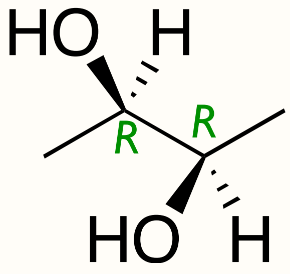
meso forms = achiral molecules with chirality centers
meso forms are optically inactive (0° optical rotation)

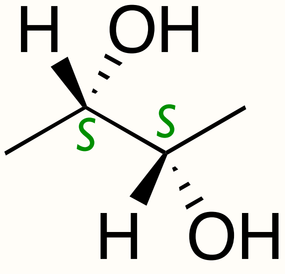


meso



meso



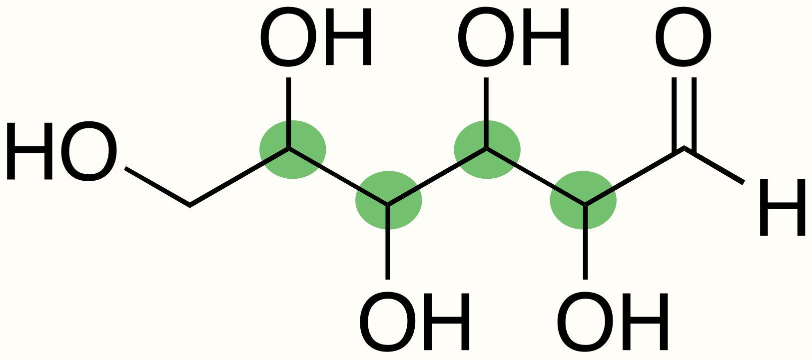


Two tests for *meso*:

1. plane or center of symmetry
2. two chirality centers with same groups, but opposite configurations

Determining the Number of Stereoisomers

2^n = maximum number of stereoisomers
n = chirality centers



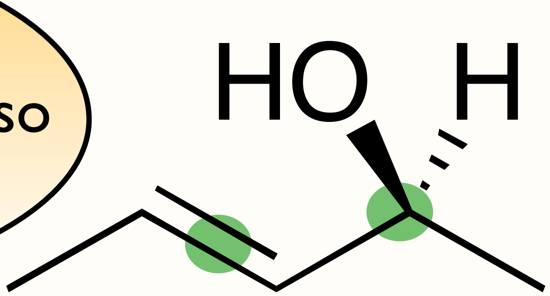
$2^n = 2^4 = 16$ stereoisomers

Determining the Number of Stereoisomers

2^n = maximum number of stereoisomers

n = chirality centers

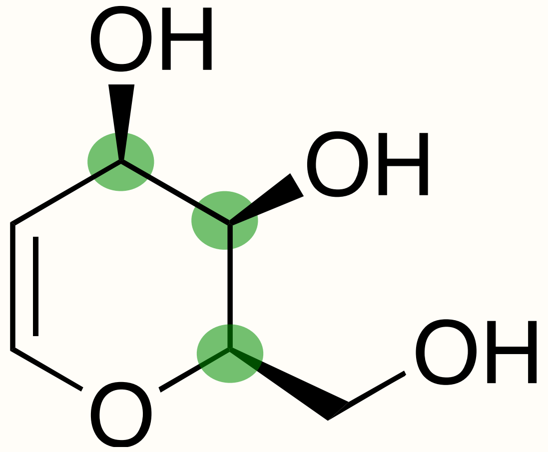
alkenes that have geometrical isomers are also a type of chirality center!



$2^n = 2^2 = 4$ stereoisomers

Determining the Number of Stereoisomers

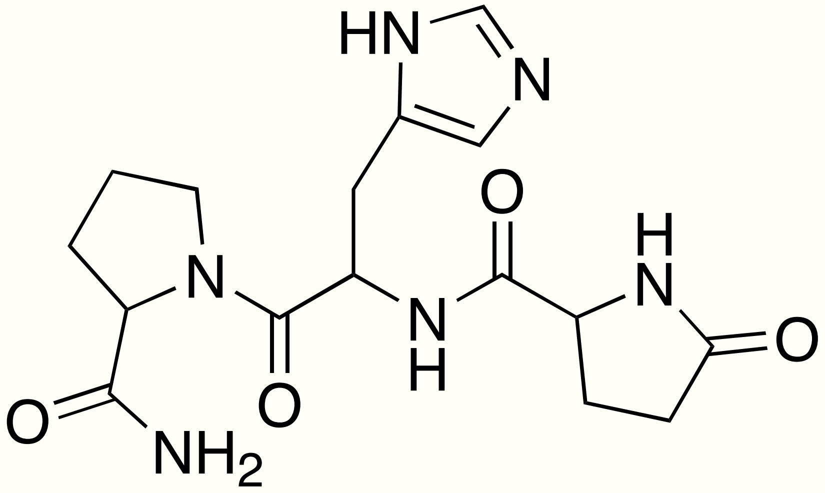
2^n = maximum number of stereoisomers
n = chirality centers



$2^n = 2^3 = 8$ stereoisomers

Self-Test Question

Thyrotropin releasing hormone (TRH) stimulates the anterior pituitary to release thyroid stimulating hormone (TSH); the thyroid gland regulates metabolism. How many stereoisomers are possible in TRH?



TRH

A. 2
B. 4
[✓ C. 8]
D. 16
E. 32

Reactions that Produce Stereoisomers

Sections: 7.9 & 7.13
You are responsible for section 7.16.
We will not cover sections 7.14-7.15.

Reactions That Create a Chirality Center

- Many reactions convert **achiral** reactants to **chiral** products. However, if all starting components are achiral (reactant, catalyst, solvent, etc.), any chiral product will be formed as a racemic mixture.
- Optically inactive starting materials cannot produce optically active products.

$$CH_3CH{=}CHCH_3 + HBr \longrightarrow CH_3\underset{\displaystyle Br}{\underset{|}{C}}HCH_2CH_3$$

cis- or *trans*-2-Butene (achiral)

Hydrogen bromide (achiral)

2-Bromobutane (chiral, but racemic)

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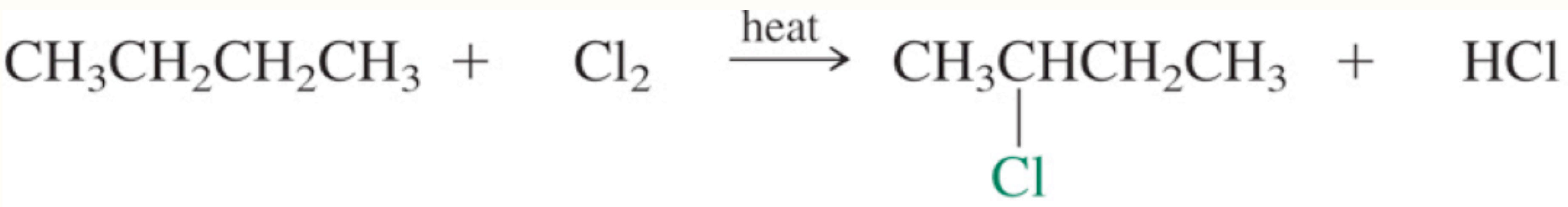

$$CH_3CH_2CH_2CH_3 + Cl_2 \xrightarrow{\text{heat}} CH_3\underset{\displaystyle Cl}{\underset{|}{C}}HCH_2CH_3 + HCl$$

Butane	Chlorine	2-Chlorobutane	Hydrogen chloride
(achiral)	(achiral)	(chiral, but racemic)	

Reactions That Create a Chirality Center

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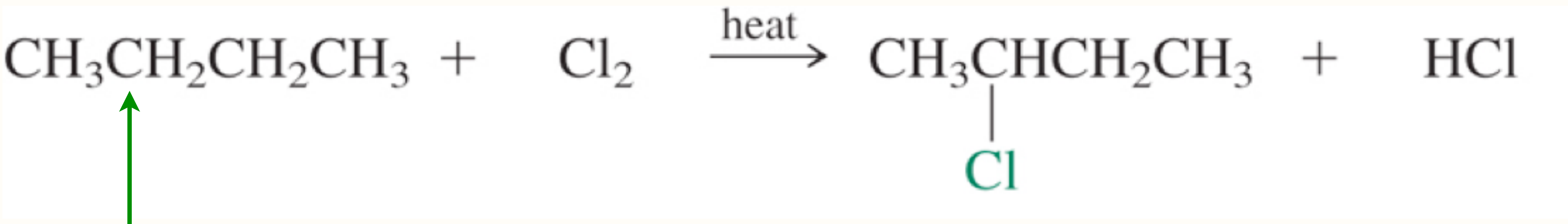
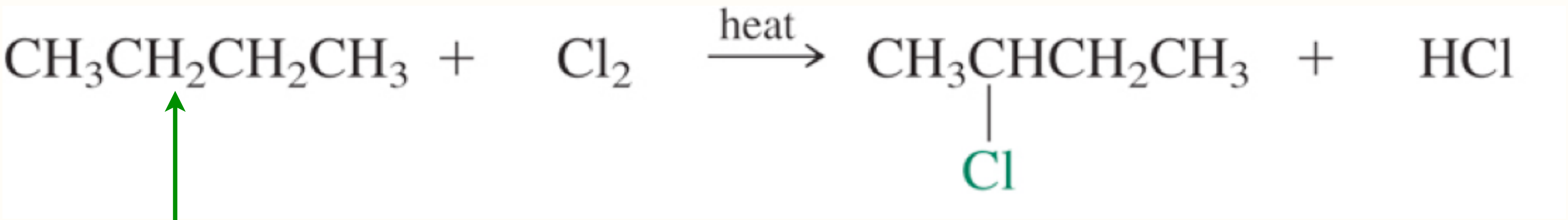


$$\mathrm{CH_3CH_2CH_2CH_3} + \mathrm{Cl_2} \xrightarrow{\text{heat}} \mathrm{CH_3}\underset{\underset{\mathrm{Cl}}{|}}{\mathrm{C}}\mathrm{HCH_2CH_3} + \mathrm{HCl}$$

prochirality center: replacement of one group will produce a chiral product

Reactions That Create a Chirality Center

- Many reactions convert **achiral** reactants to **chiral** products. However, if all starting components are achiral (reactant, catalyst, solvent, etc.), any chiral product will be formed as a racemic mixture.
- Optically inactive starting materials cannot produce optically active products.

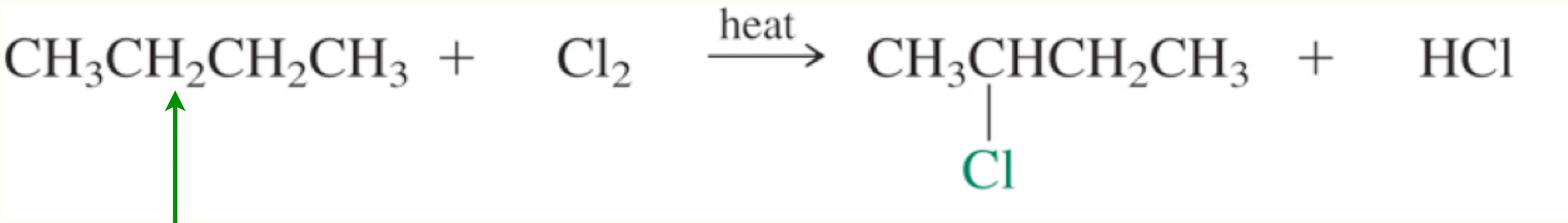


$$CH_3CH_2CH_2CH_3 + Cl_2 \xrightarrow{\text{heat}} CH_3\underset{\underset{\displaystyle Cl}{|}}{C}HCH_2CH_3 + HCl$$

enantiotopic hydrogens: replacement of each hydrogen atom in two different molecules with a test group gives enantiomers

Reactions That Create a Chirality Center

- Many reactions convert **achiral** reactants to **chiral** products. However, if all starting components are achiral (reactant, catalyst, solvent, etc.), any chiral product will be formed as a racemic mixture.
- Optically inactive starting materials cannot produce optically active products.



$$CH_3CH_2CH_2CH_3 + Cl_2 \xrightarrow{heat} CH_3\underset{\displaystyle Cl}{\underset{|}{C}}HCH_2CH_3 + HCl$$

enantiotopic hydrogens are equally reactive toward achiral reagents; both react equally to give optically inactive products

Reactions That Create a Chirality Center

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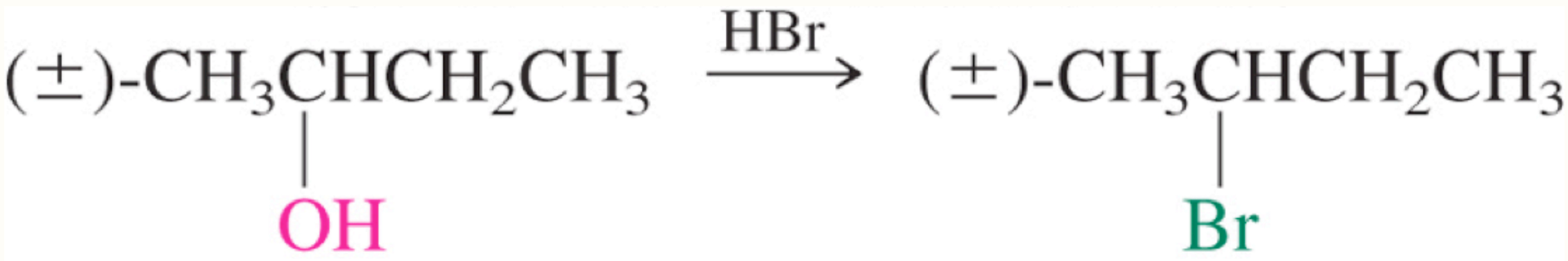


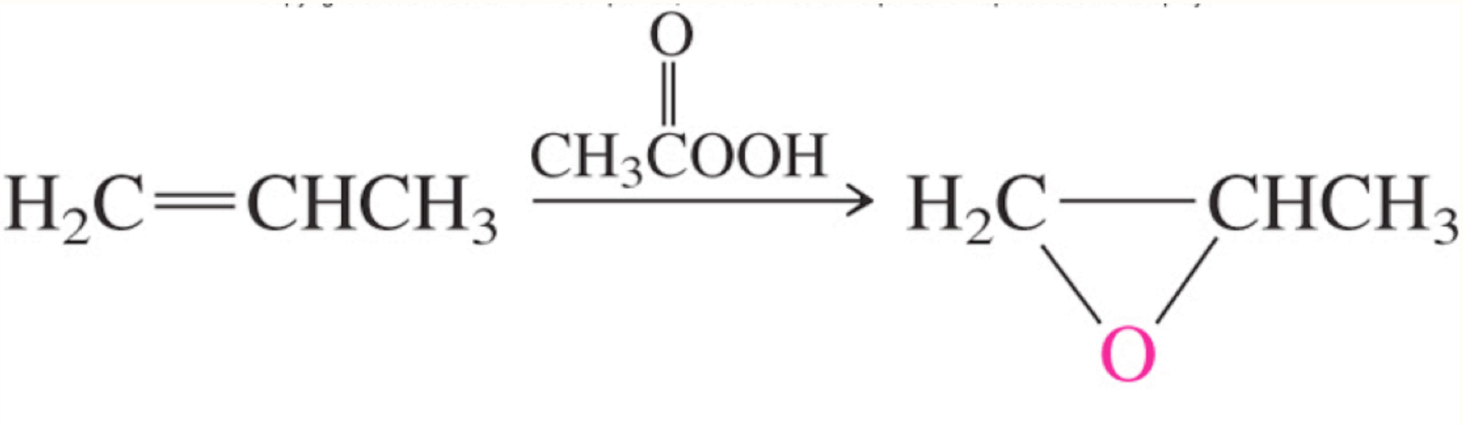
$$(\pm)\text{-}CH_3\underset{\displaystyle OH}{\underset{|}{C}}HCH_2CH_3 \xrightarrow{HBr} (\pm)\text{-}CH_3\underset{\displaystyle Br}{\underset{|}{C}}HCH_2CH_3$$

2-Butanol
(chiral but racemic)

2-Bromobutane
(chiral but racemic)

Reactions That Create a Chirality Center

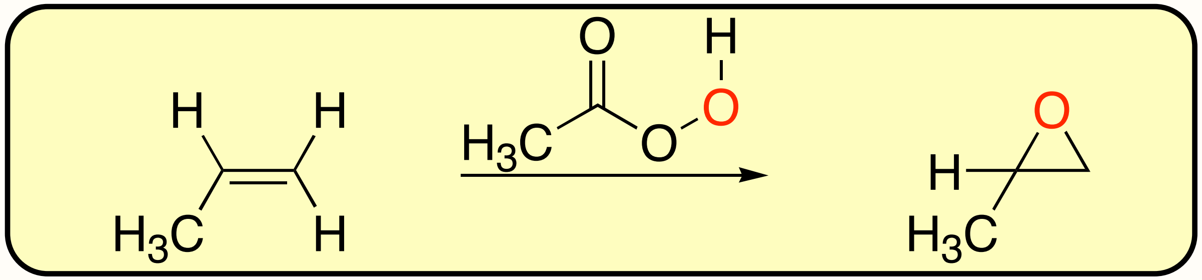
- Many reactions convert **achiral** reactants to **chiral** products. However, if all starting components are achiral (reactant, catalyst, solvent, etc.), any chiral product will be formed as a racemic mixture.
- Optically inactive starting materials cannot produce optically active products.

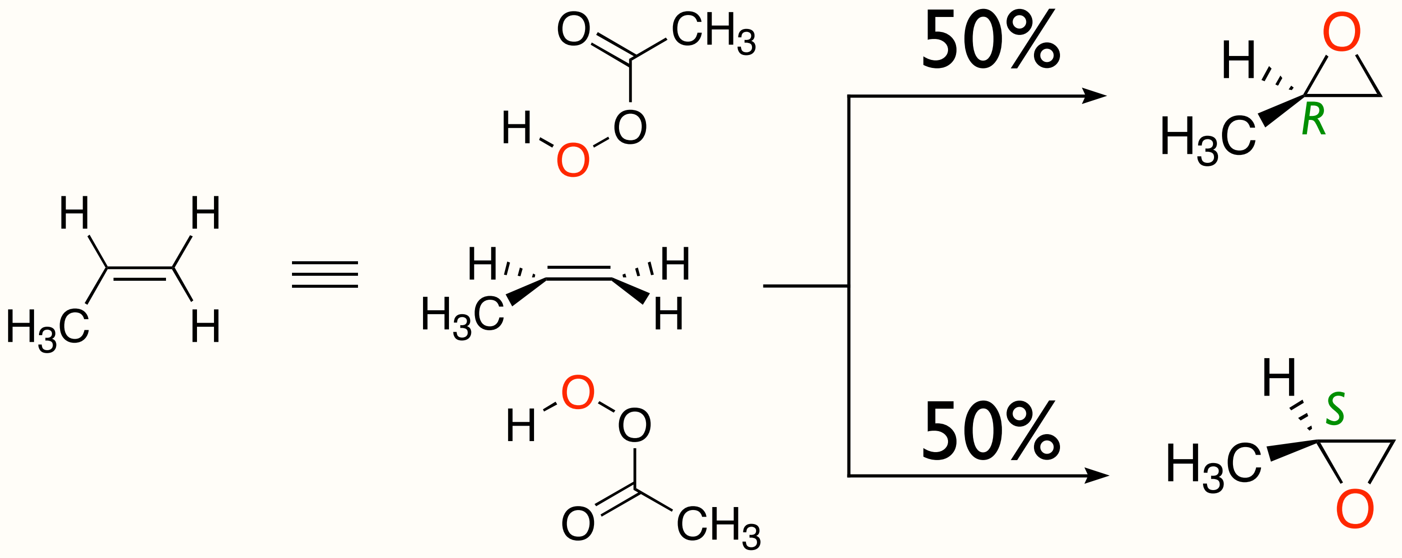


Propene (achiral)

1,2-Epoxypropane (chiral)

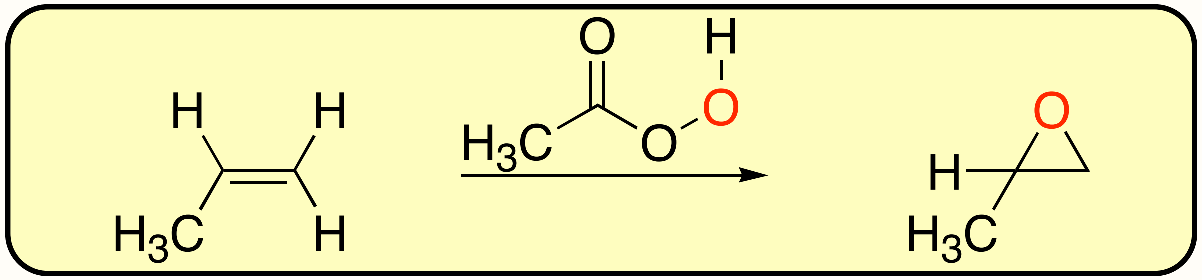
Epoxidation: Prochiral/Enantiotopic Faces

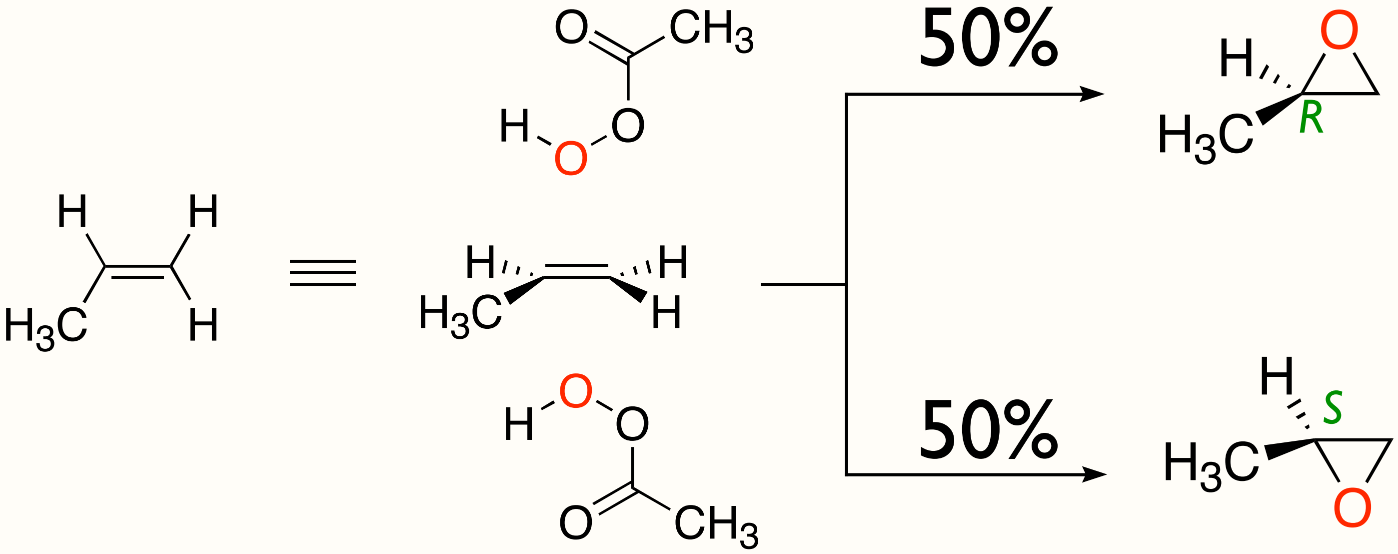




- epoxidation can occur on either face of the alkene
- two stereoisomeric products are formed in equal amounts
- products are enantiomers; mixture is racemic
- racemic = 1:1 mixture of enantiomers

Epoxidation: Prochiral/Enantiotopic Faces

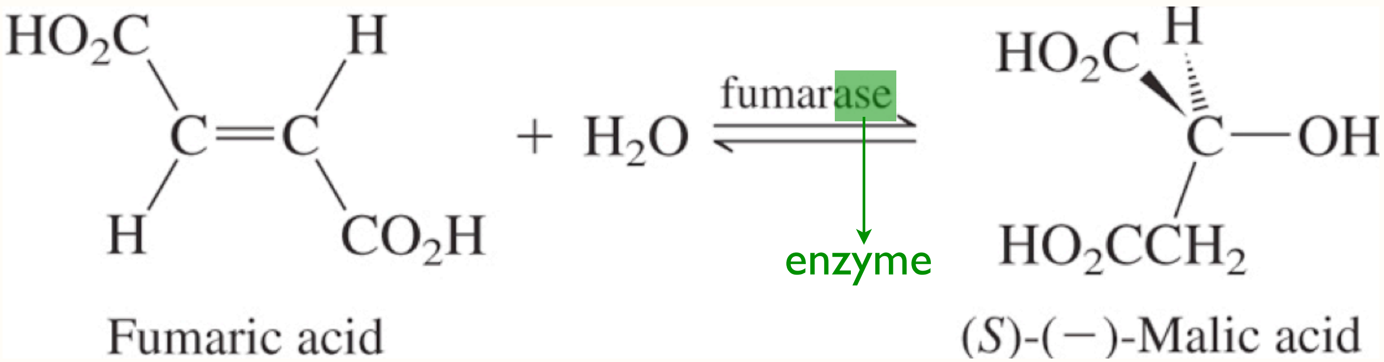




- prochiral face: one side of an sp^2 system where a reaction would produce a chiral product
- enantiotopic faces: reaction at either face of an sp^2 system produces enantiomeric products

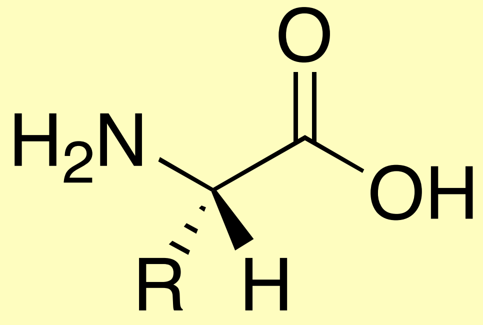
Reactions That Create a Chirality Center

Optically inactive reactants can give optically active products if the reaction utilizes an optically active reagent such as a chiral catalyst.



Fumaric acid

(S)-(−)-Malic acid



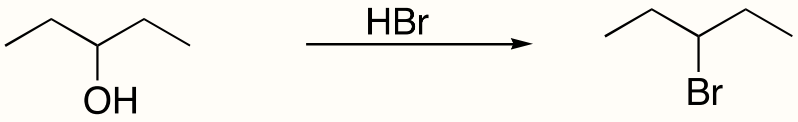
amino acid

- enzymes are proteins catalysts =
- proteins are polymers made of amino acids =
- most amino acids are chiral =
- enzymes are chiral =
- enzymes can form optically active products from optically inactive reactants

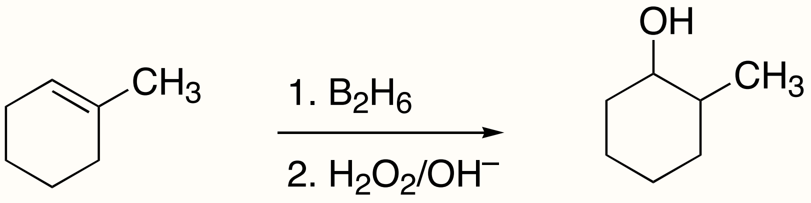
Self Test Question

Which of the following reactions will create a chirality center?

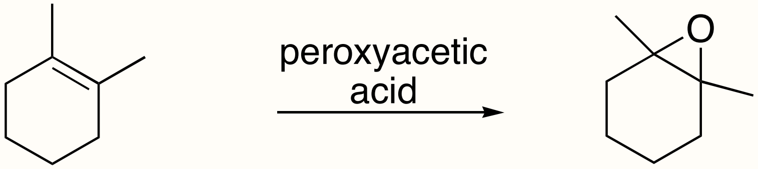
A



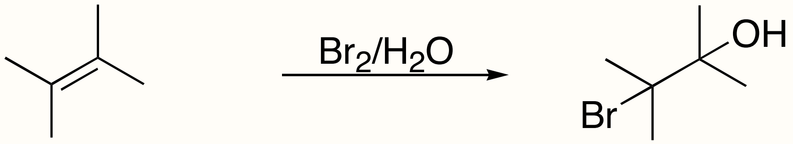
[✓ B]



C

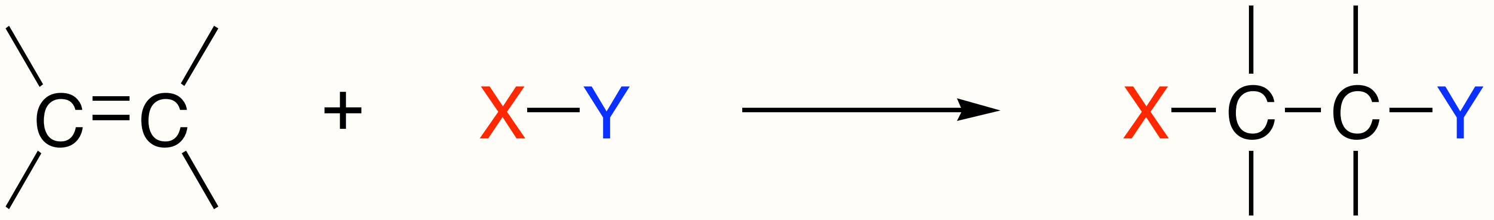


D



Reactions That Produce Diastereomers

Addition across a double bond can produce products that are diastereomers.

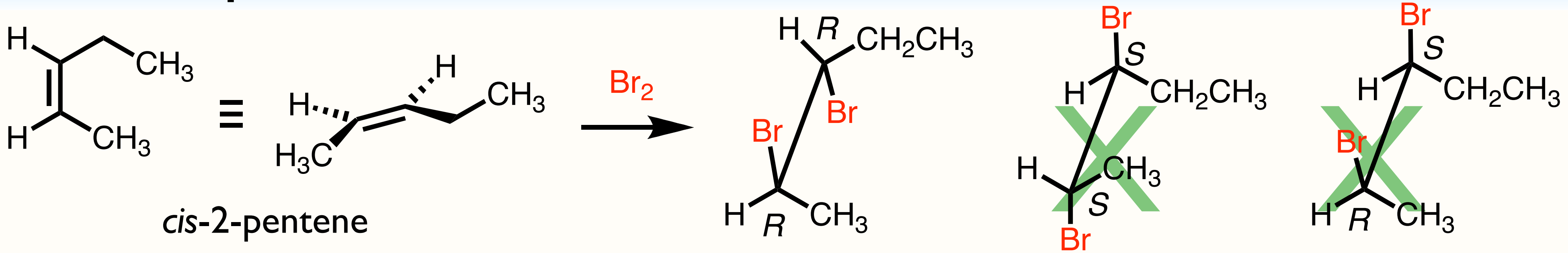


Two factors determine which stereoisomer is formed:

1. Are there geometrical isomers (E/Z) of the alkene?
2. Is the addition across the double bond *anti*, *syn* or neither?

Stereospecific Reaction

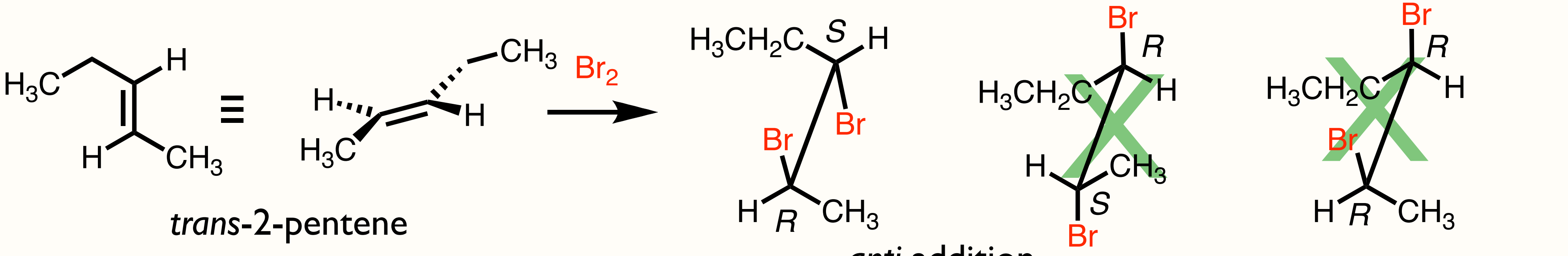
<u>stereospecific:</u> ≥ 2 stereoisomeric reactants <u>could</u> produce products that are stereoisomers of one another



cis-2-pentene

anti addition

syn addition



trans-2-pentene

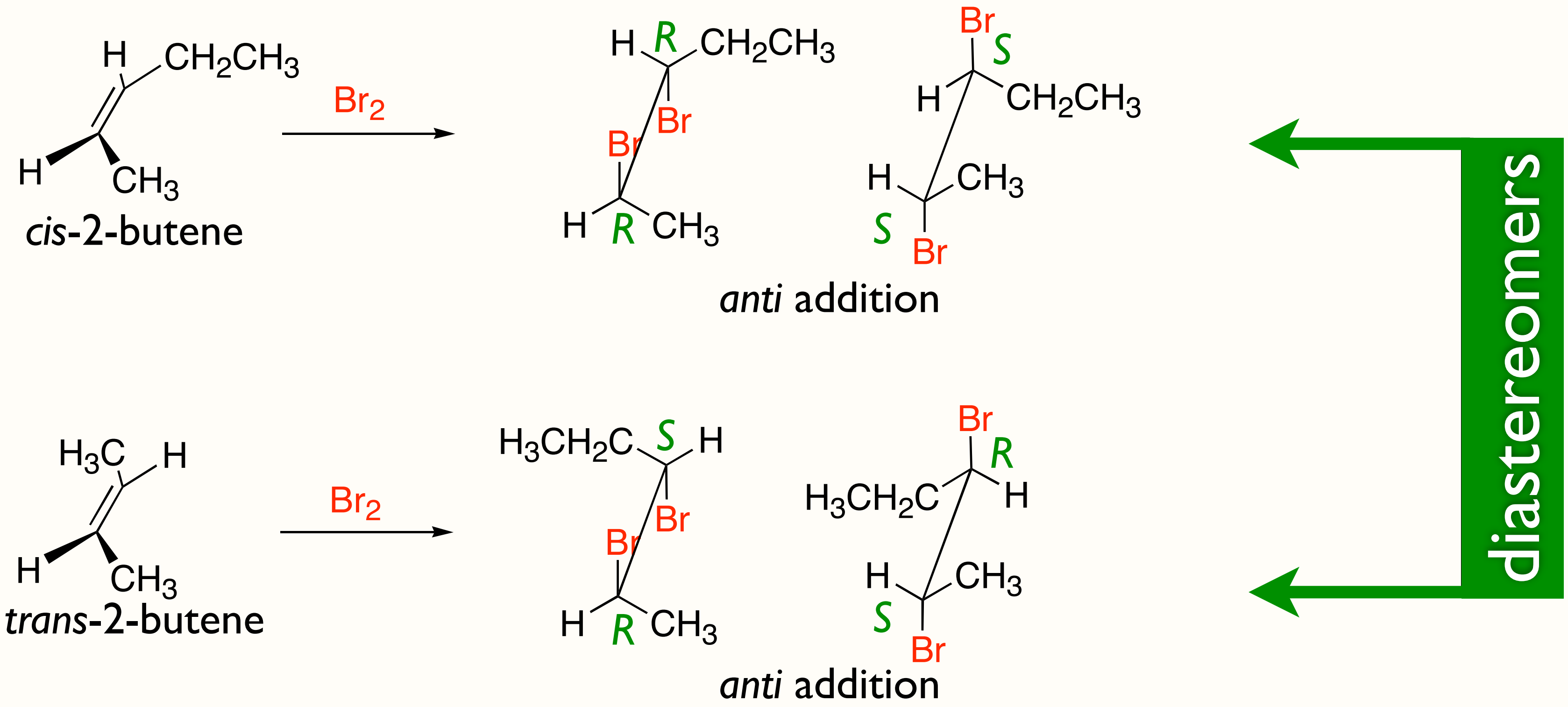
anti addition

syn addition

Since Br atoms are added to opposite <u>faces</u> of the alkene (anti addition) in the mechanism, no *syn* products are observed.

Stereospecific

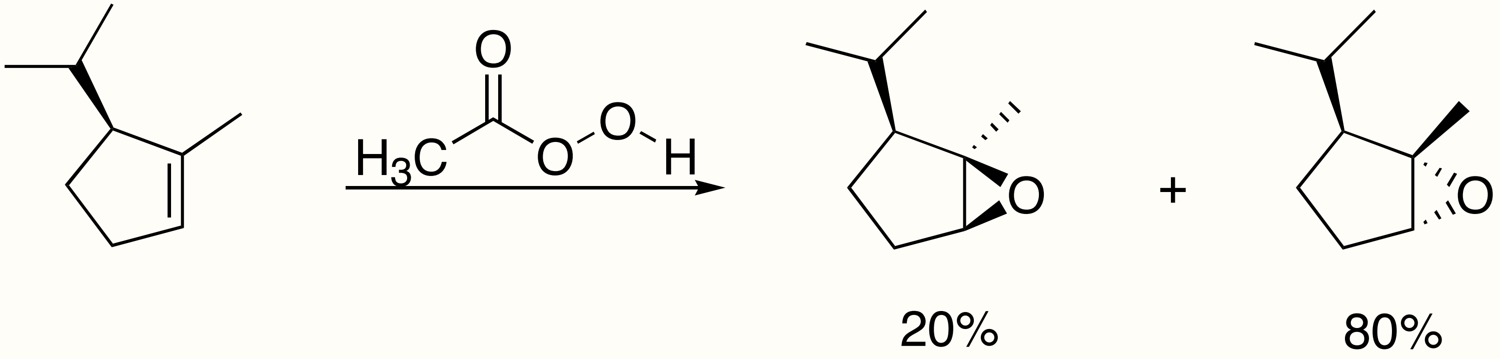
stereospecific: ≥ 2 stereoisomeric reactants could produce products that are stereoisomers of one another



This reaction is also stereoselective since one group of stereoisomers is preferred over another. All stereospecific reactions are also stereoselective, but not all stereoselective reactions are stereospecific.

Stereospecific

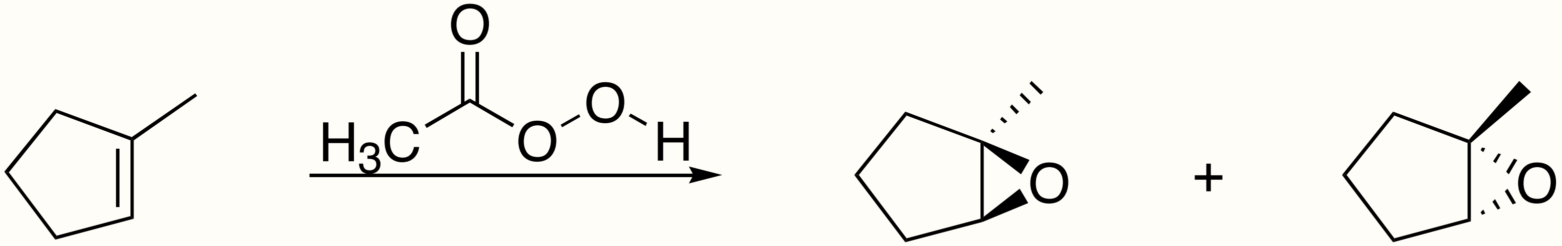
stereospecific: ≥ 2 stereoisomeric reactants could produce products that are stereoisomers of one another



Syn or *anti* addition to small cycloalkenes is also considered stereospecific even though the *trans* geometrical isomer is not possible starting material; it would theoretically give products that are diastereomers to those obtained by addition to *cis*-cycloalkenes.

Stereospecific

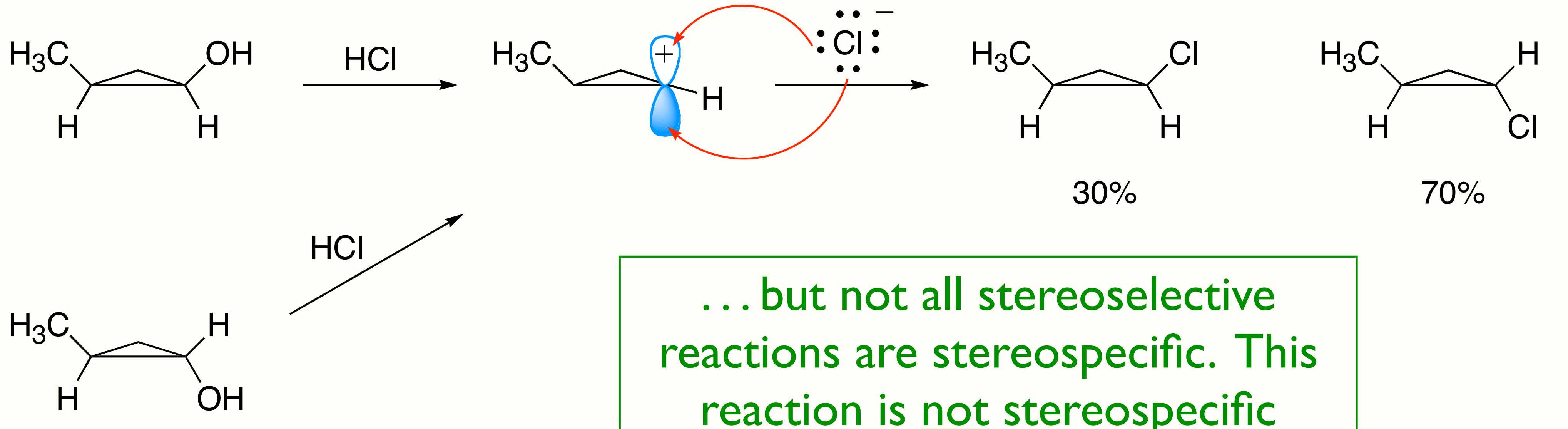
<u>stereospecific:</u> ≥ 2 stereoisomeric reactants <u>could</u> produce products that are stereoisomers of one another



This reaction is also **stereoselective** since only *cis*-addition products are formed. Remember: all stereospecific reactions are stereoselective…

Stereoselective

stereoselective: describes a reaction where a single stereoisomeric reactant produces two or more stereoisomeric products, one of which is favored

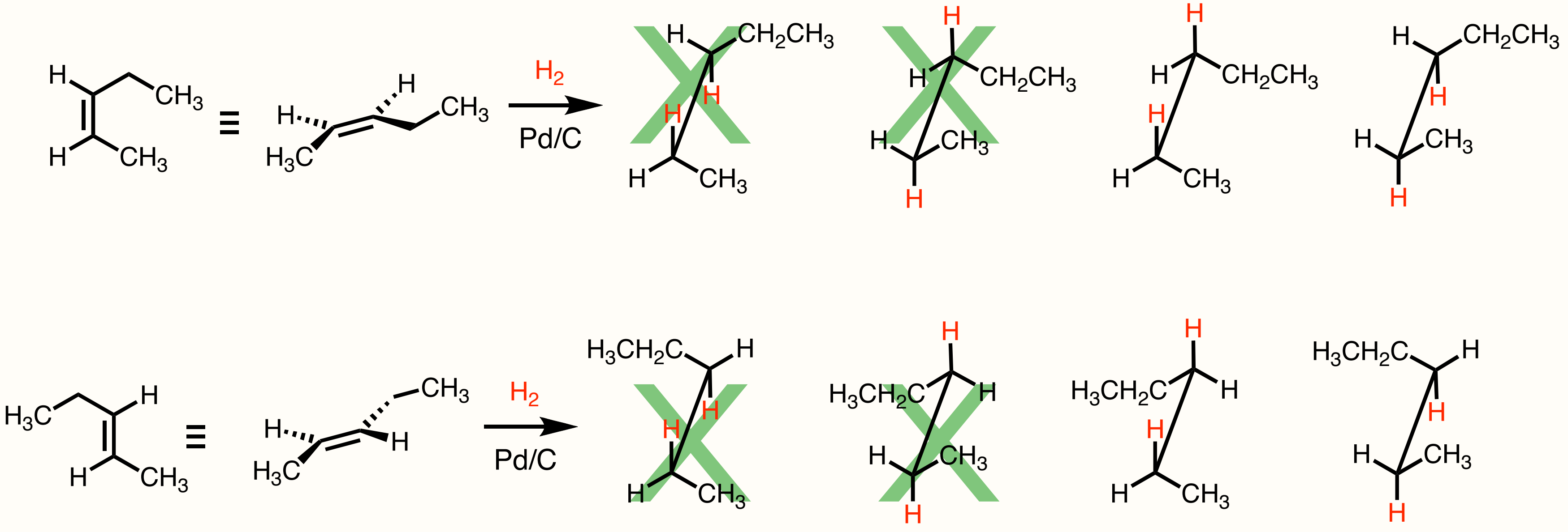


. . . but not all stereoselective reactions are stereospecific. This reaction is not stereospecific because the enantiomeric reactant gives the same set of products.

Self Test Questions

Which best describes the hydrogenation of *cis*-2-pentene and *trans*-2-pentene?

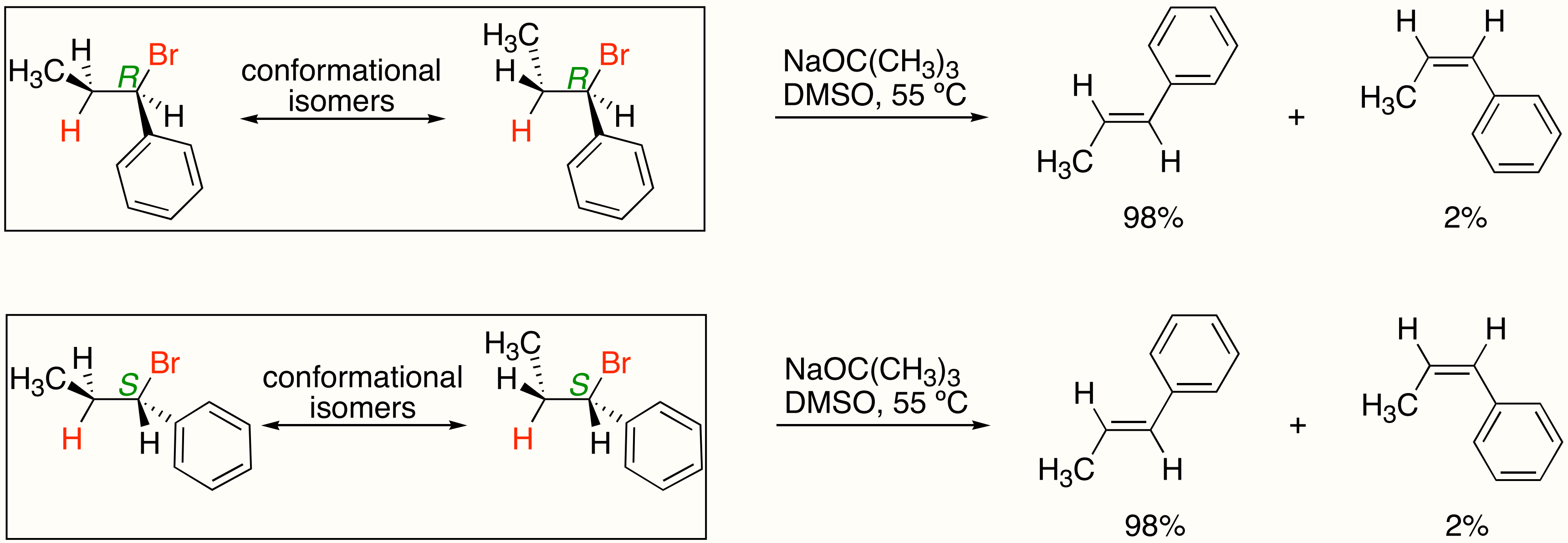
- A. regioselective
- B. stereoselective
- C. stereospecific
- D. B & C
- [✓ E.] none of the above



Self Test Questions

Which best describes the dehydrohalogenation below?

- A. regioselective
- [✓ B.] stereoselective
- C. stereospecific
- D. B & C
- E. none of the above



Next Lecture. . .

Chapter 8: Sections 8.1 - 8.7

Quiz This Week. . .

Chapter 13