Discovering Molecular Models #2:
Stereochemistry: E and Z / R and S

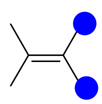
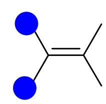
There are no additional tutorial or laboratory notes (you don't need them!). Read and bring your course notes (end of organic unit #2 and all of organic unit #3), as they provide all of the background material necessary to perform these exercises and problems.

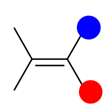
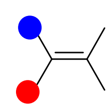
Bring Your Molecular Model Kits!

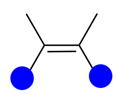
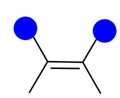
There will be a quiz at the end of this exercise. If you are performing this in the lab, the mark will count towards your lab component of the course. Likewise, if you are performing this in the tutorial room, it will count towards the tutorial component.

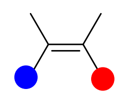
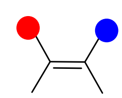
A. Familiarization with Molecular Models

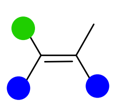
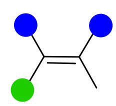
1. Build molecular models of each of the two molecules in each pair illustrated below. For each pair, compare the two models by trying to overlap them. Indicate if they isomers of each other or if they are the same molecule?

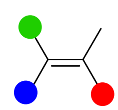
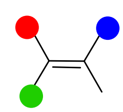
Same  and 

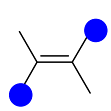
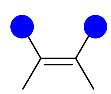
 and  Same

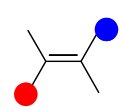
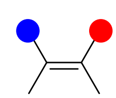
Same  and 

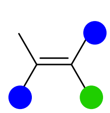
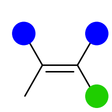
 and  Same

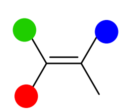
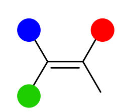
Same  and 

 and  isomers

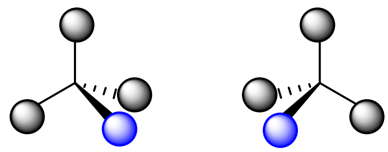
Isomers  and 

 and  isomers

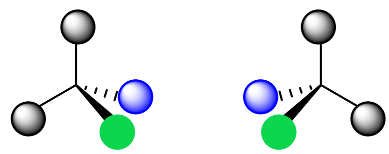
Isomers  and 

 and  isomers

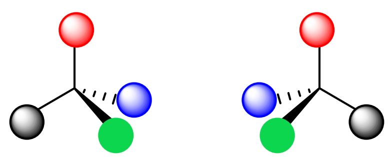
2. Repeat the exercise below, which is from the lecture notes, to be sure you understand the outcome. For each pair of molecules that are mirror images of each other, are they the same or different (can you overlap the two models at every color… yes or no)?



same



same



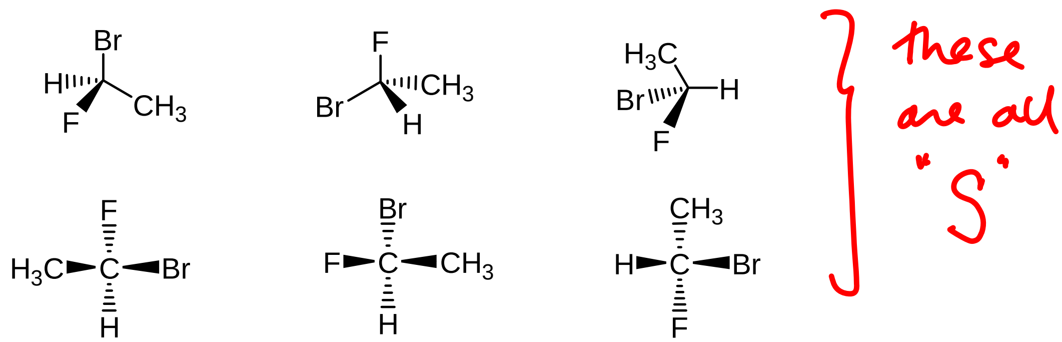
different

these are stereoisomers

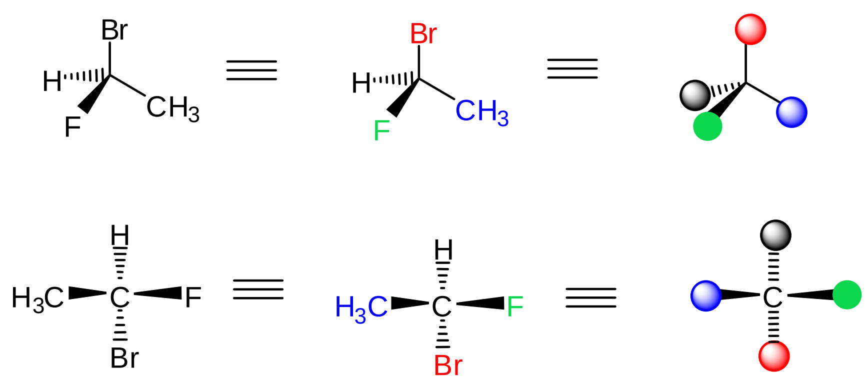
non-superimposable mirror images of each other

They are enantiomers.

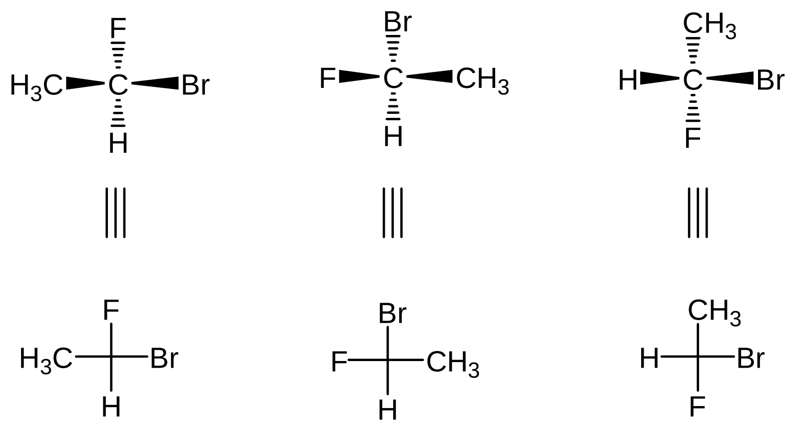
3. Next, we will look at converting different representations of molecules to those on the previous page, so that they can be manipulated to determine the stereochemistry. Convince yourself that all six of the representations below are of the same molecule.



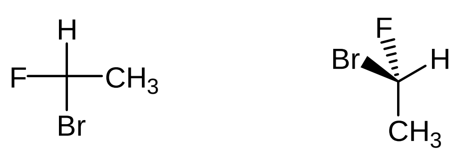
Hint: assign each group on the chiral carbon a different colour and build the corresponding models. For example:



Note: Fisher projections. These molecules could also have been drawn as Fisher Projections, where the molecule is drawn in the form of a cross, with the central carbon atom being the point of intersection. The horizontal lines signify bonds directed out towards you (wedges), while the vertical lines indicate bonds pointing away (dashes).



Exercise: For each of the two molecules below, describe them as being the same as those above, or different. If different, what is the relationship to the others (constitutional isomer or stereoisomer)?

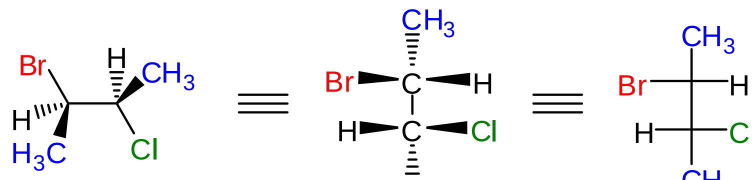


R ∴ enantiomer

S same

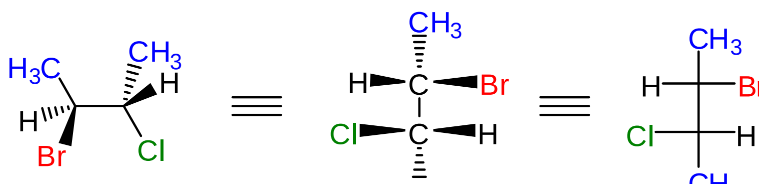
4. Assign each of the stereocentres in the molecules in question 3 as either *R* or *S*. (Assign priorities 1, 2, 3, and 4, and use your models. Recall that you first have to build the model that is an accurate representation of the molecule. Second, assign the group priorities and then label appropriately colored ball. Third, rotate the model such that the lowest priority group is pointing away from you. Fourth, see which way the order of groups 1, 2 and 3 are: counterclockwise = *S*, clockwise = *R*).

5. This is a more complex example, where there are two ~~or more~~ stereoisomers. Build the two models that are representations of molecules **A** and **B** below (shown in three different representations). Are **A** and **B** the same molecule or different? How about **A** and **C**?

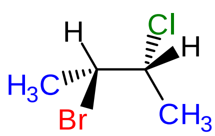


A

A & B are enantiomers



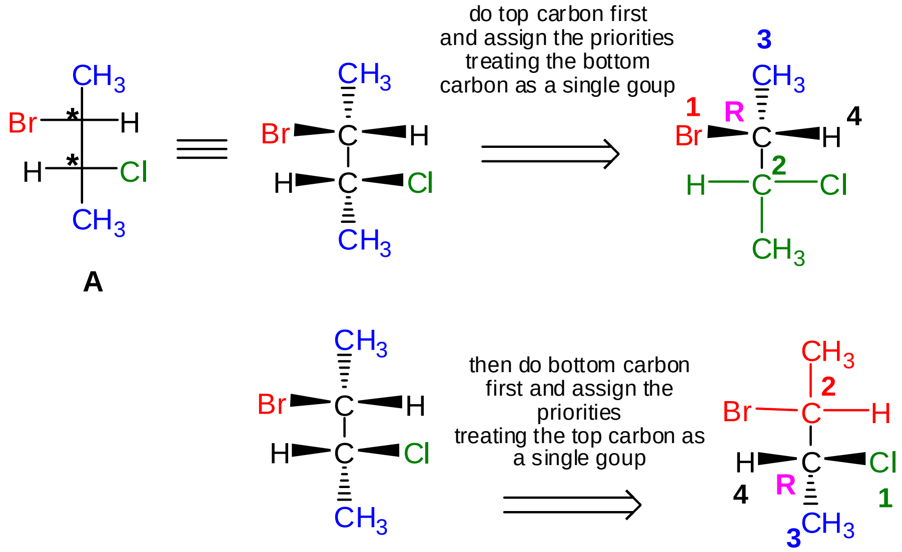
B

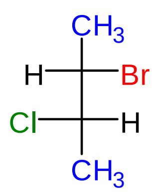


C

A & C are representations of the same molecule.

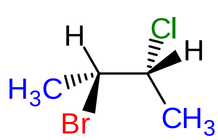
6. The molecules in question 5 each have two stereocentres. Each stereo centre can be either *R* or *S*, so the possible molecules could be *R*, *R*; *S*, *S*; *R*, *S*; or *S*, *R* (four combinations). How does one use models to assign *R* and *S* to larger more complex molecules? Treat each stereo centre separately, and the group containing the other stereo centre is simply regarded as a substituent. Assign *R*/*S* to each chiral carbon in molecules A, B, and C in #5.





B

S
S



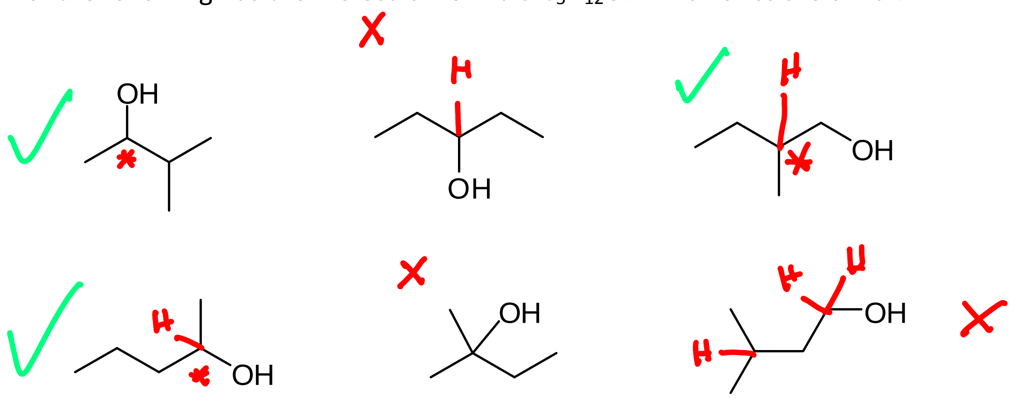
C

R
R

B. Practice Problems. Use your models as necessary!

C with 4 different groups

7. Each of the following has the molecular formula $C_5H_{12}O$. Which ones are chiral?



8. Rank the substituents in each set in order of priority, from highest to lowest.

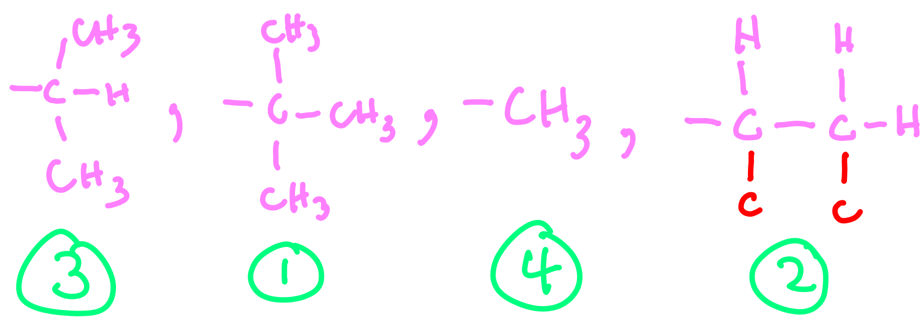
   a. –Cl, –OH, –SH, –H → Cl > SH > OH > H

   b. –H, –OH, –CHO (aldehyde), –CH_3 → OH > CHO > CH_3 > H

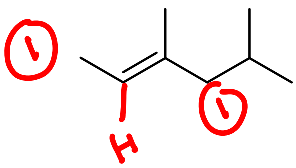
   c. –H, –N$(CH_3)_2$, –OCH_3, –CH_3 → OCH_3 > N$(CH_3)_2$ > CH_3 > H

   d. –CH_3, –CH_2Br, –$CHCl_2$, –-CH_2OH → CH_2Br > $CHCl_2$ > CH_2OH > CH_3

   e. –CH$(CH_3)_2$, –-C$(CH_3)_3$, –CH_3, –CH=CH_2

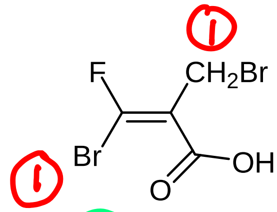


9. Assign the configurations at the double bond of these compounds as *E*, *Z*, or neither.



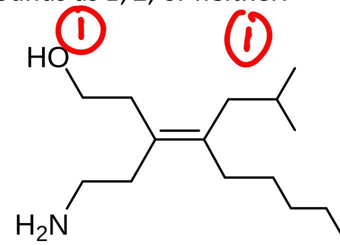
(a)

E



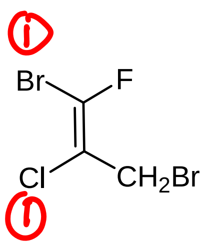
(b)

E



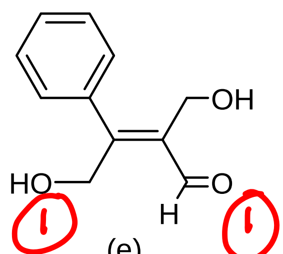
(c)

Z



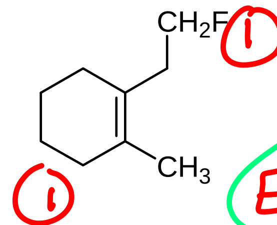
(d)

Z



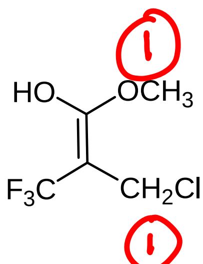
(e)

Z



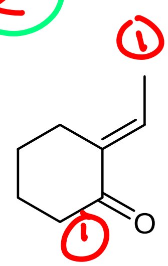
(f)

E



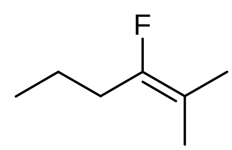
(g)

Z



(h)

E

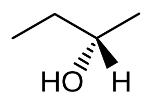


(i)

neither

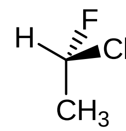
10. Assign *R/S* to each of the stereo centres in the following molecules.

(a)



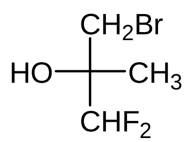
S

(b)



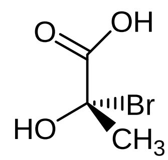
R

(c)



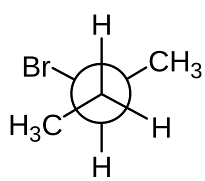
S

(d)



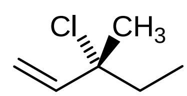
S

(e)



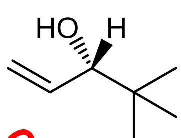
S

(f)



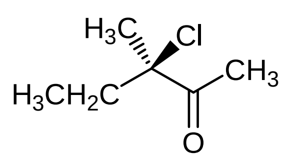
R

(g)



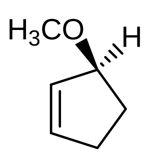
S

(h)



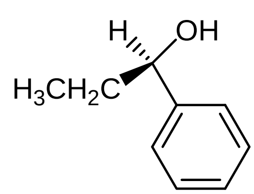
R

(i)



S

(j)

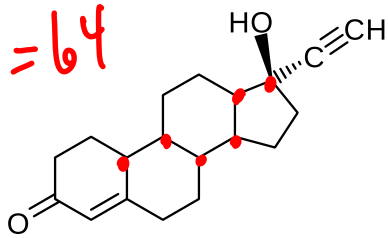


R

stereocenters are indicated • $= 2^n$

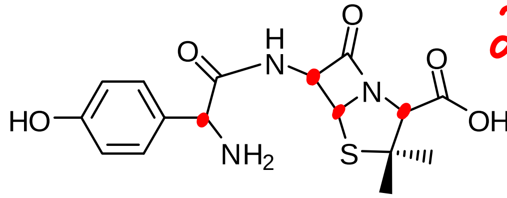
11. Label the stereocentres in each of the following molecules. (Some of these are from your course notes). For each, what is the maximum number of stereoisomers possible?

$2^6 = 64$



norethindrone
(an oral contraceptive)

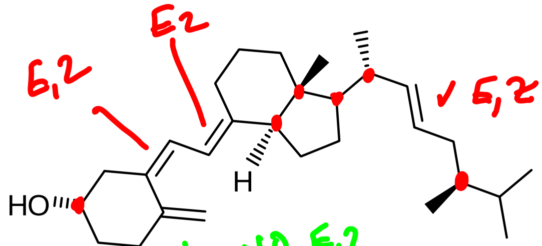
$2^4 = 16$



amoxicillin
(an antibiotic)

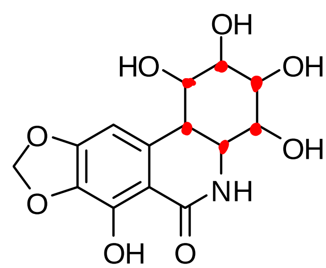
6 chiral centers
3 E/Z

$2^9 = 512$

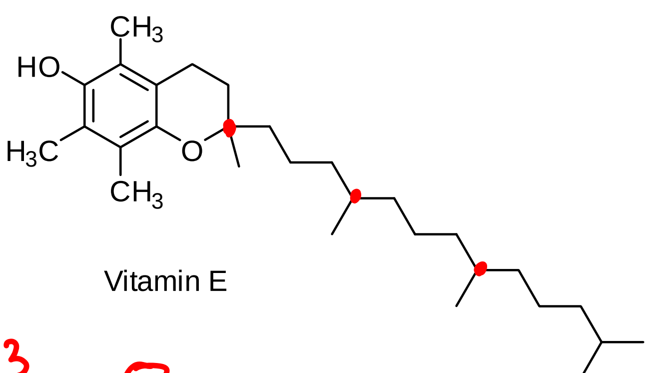


Vitamin D2

$2^6 = 64$

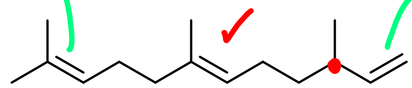


pancratistatin
(an anti-cancer drug)



Vitamin E

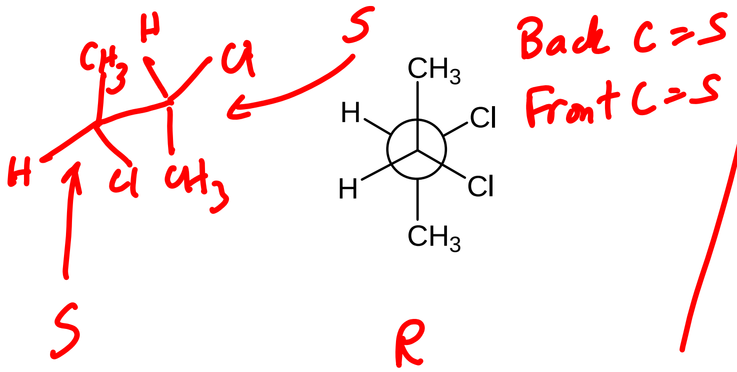
$2^3 = 8$

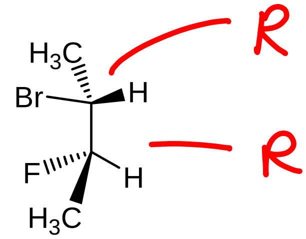


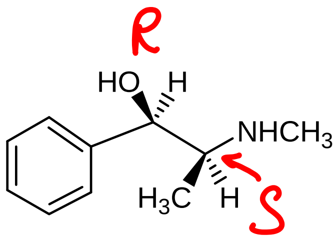
farnesene
(found in the waxing coating of apples)

$2^2 = 4$

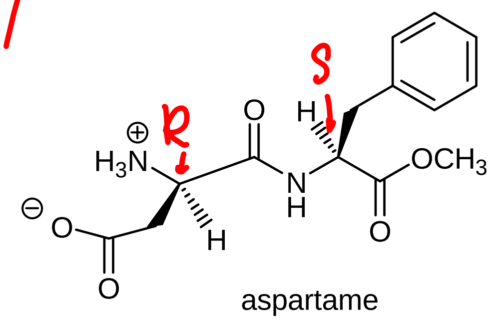
12. Assign *R/S* to each stereocentre in the following molecules.







ephedrine
(brochodilator)



aspartame
(artificial sweetener)

13. How are the compounds in each pair related? Are they identical, enantiomers, constitutional isomers, or not isomers of each other?