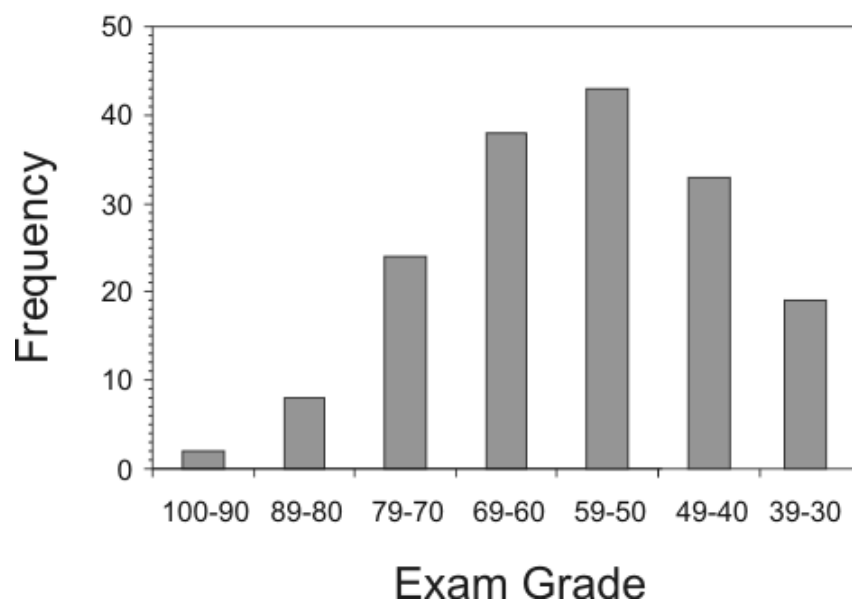
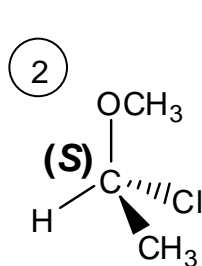


**Exam 2  
Answer Key**

Exam 2 Mean: 58  
Exam 2 Median: 56  
Exam 2 St. Dev.: 14



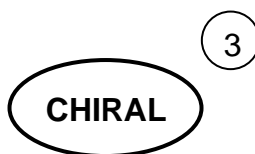
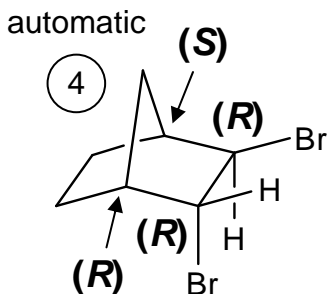
1. (19 pts) On the structures below, **label each chiral center** with its appropriate Cahn-Ingold-Prelog designation [(*R*) or (*S*)]. Then, for each structure, **circle** whether you think the molecule is chiral or achiral.



or

ACHIRAL ?

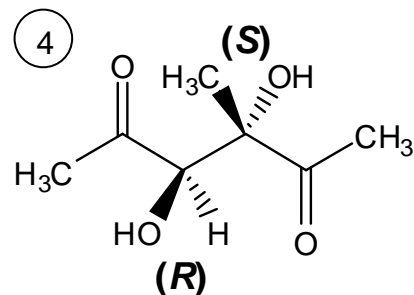
You could look at the mirror image and try to superimpose it, but there's an easier way—this molecule has one chiral center, so it must be chiral.



or

ACHIRAL ?

As with the molecule to the left, this one was probably easier to answer without trying to superimpose mirror images. The molecule is (*R,R*), and so its mirror image would be (*S,S*)—by definition, a different molecule. So, because the molecule is not the same as its mirror image, it's chiral.



or

ACHIRAL ?

This molecule is (*R,S*), so it could be chiral, but it could also be *meso*. It would be *meso* only if the (*R*) and (*S*) centers had the same groups attached, but they don't—one has an H, the other has a CH<sub>3</sub>. So the molecule is chiral.

**Rubric:**

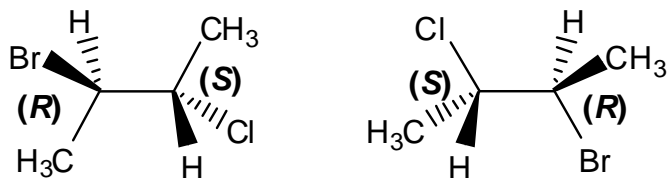
2 points for each stereocenter labeled in molecules 1 and 3.

-2 points for each achiral center labeled as chiral.

Molecule 2 was a lot trickier than I designed it to be—when I wrote the exam, I initially thought it had only two stereocenters. So we just gave everyone an automatic 4 points for this molecule.

3 points for each circle.

2. (12 pts) How would you describe the relationship between each of the pairs of structures below? Are they enantiomers or diastereomers, or are they just two ways of illustrating the same molecule? **Circle one answer** for each pair.



ENANTIOMERS

or

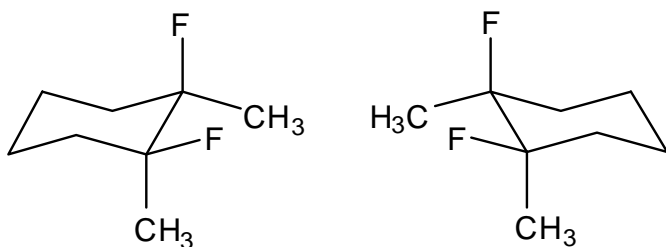
DIASTEREOMERS

or

**SAME MOLECULE**

4

One way to answer this question was to rotate the left molecule to see if it looked like the right molecule. But I think an easier approach was to assign (*R*) and (*S*) labels to the centers, and see that the (*R*) centers for the two molecules are the same and the (*S*) centers are the same. So, these must be the same molecule.



ENANTIOMERS

or

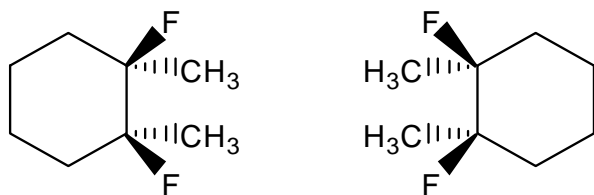
DIASTEREOMERS

or

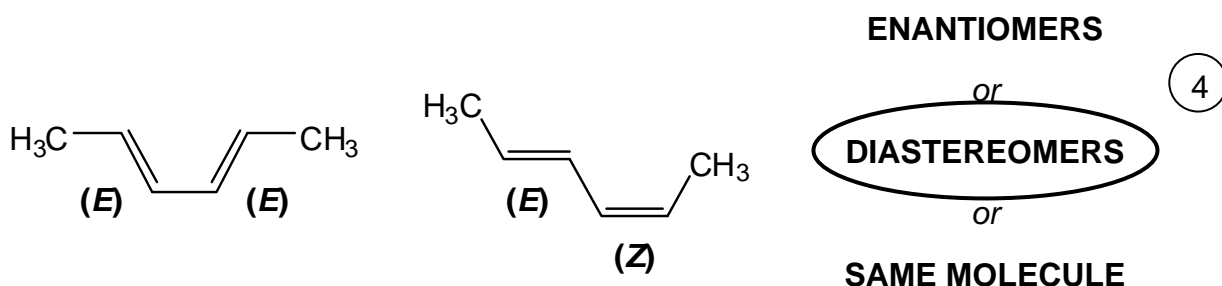
**SAME MOLECULE**

4

If we re-draw these molecules so that they are flat,



they are the same molecule (and achiral). The two drawings represent the two chair conformations of this one molecule.

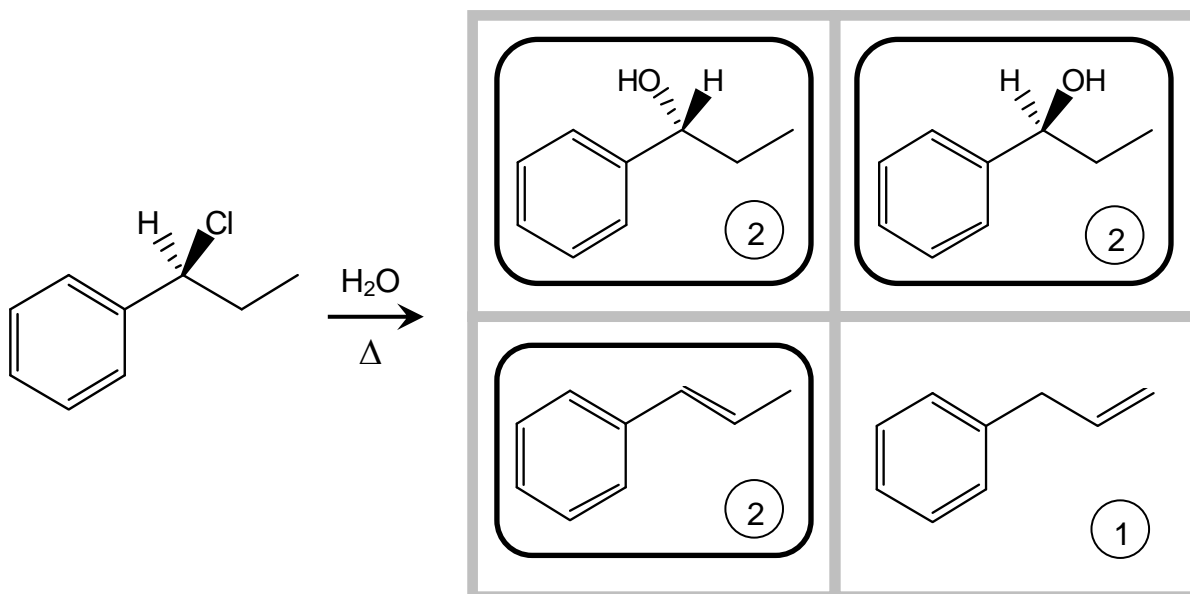


The alkenes on the right-hand side of each molecule have the same groups attached, but different spatial arrangements of those groups, so the two molecules are stereoisomers. The molecules are achiral (because they are flat), so they cannot be or have enantiomers. Two molecules that are stereoisomers, but not enantiomers, are by definition diastereomers.

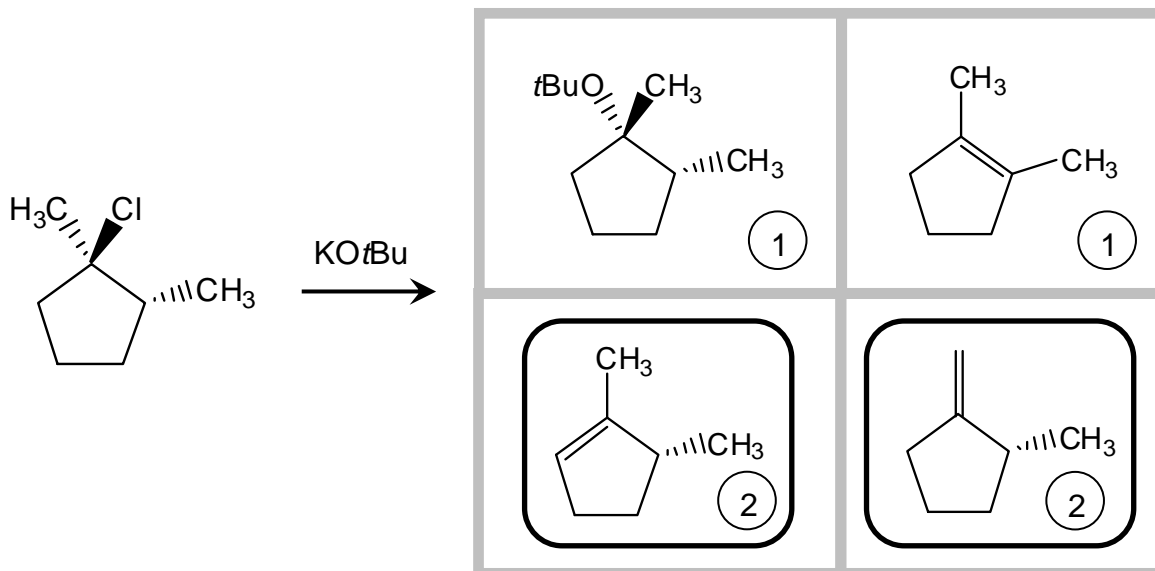
Rubric: 4 points each.

3. (16 pts) For each reaction shown below, **circle all potential products**.

Rubric: 2 points for each box with a correctly circled product.  
1 point for each box with an incorrect product *not* circled.

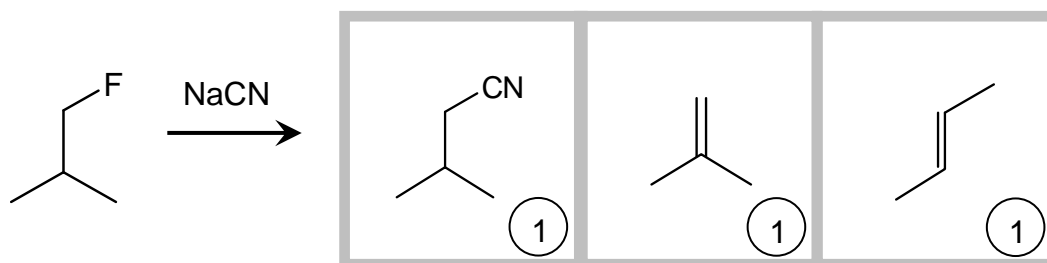
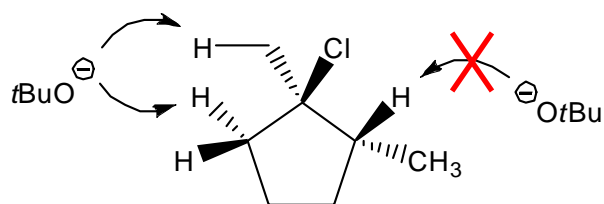


This starting material would react by  $S_N1$  (to produce both substitution enantiomers) and  $E1$  (to make the alkene). The second alkene would not be a product by any mechanism—the alkene is on the wrong carbons.



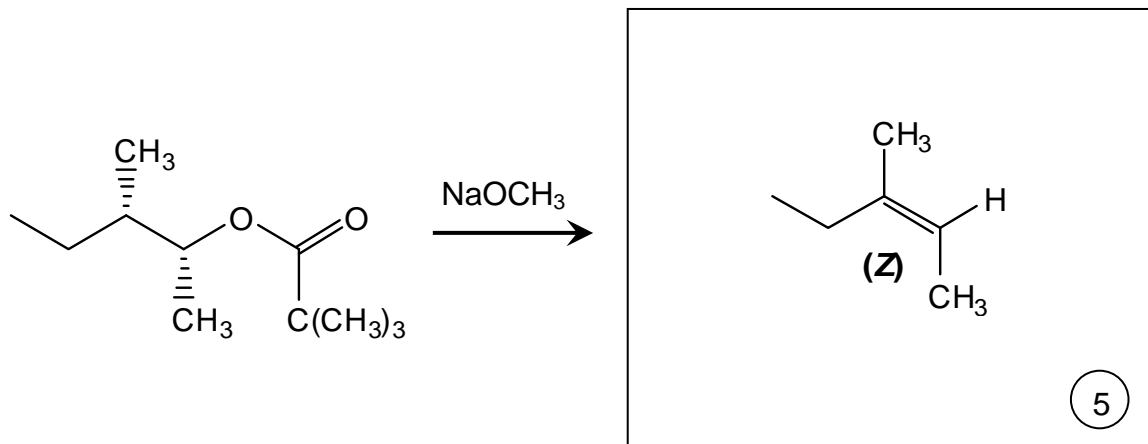
Potassium *t*-butoxide is a very strong base, and is sterically hindered, such that it reacts almost exclusively as a base in E2 reactions. So the first S<sub>N</sub>2 substitution product would not be formed. (Also, the substitution site is tertiary, which would bias the reaction against S<sub>N</sub>2 even further.)

The other three molecules would be the elimination products that would be formed by deprotonation at the three different protons α to the leaving group. Of these three deprotonations (shown at right with curved arrows), the deprotonation on the right side wouldn't occur, because there's no way to orient the H and the Cl leaving group so that they are anti-coplanar. So, the tetrasubstituted alkene would *not* be formed.

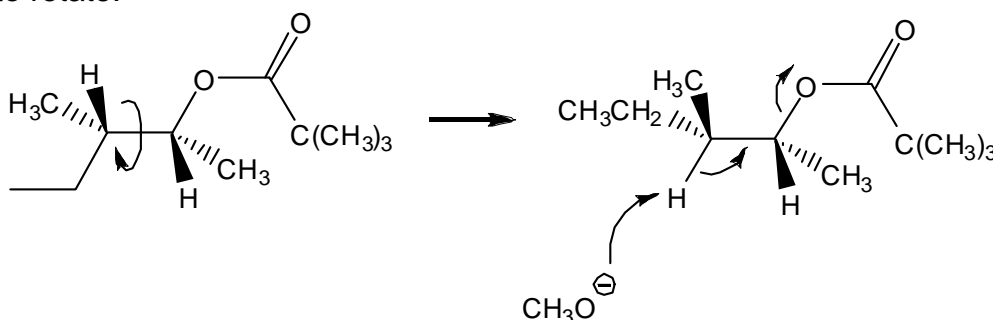


Fluoride is a horrible leaving group—it doesn't react by substitution or elimination. (This is the reason why 3M's perfluorinated chemicals, like PFOS, are so persistent in the environment. They do not degrade by the mechanisms that clear other functionalized molecules from wastewater.) None of the products would be formed.

4. (15 pts) Draw the missing reactant or product in the empty boxes. For products, give the predominant, most favored product. Illustrate stereochemistry in your answer where appropriate. For reactions that yield multiple enantiomers, draw only one enantiomer in the box, and include the note “+ enantiomer”.



$\text{CH}_3\text{O}^-$  is a better base than it is a nucleophile, so it will do E2. It is also small, so it will produce the most stable (Zaitsev) alkene product by taking a proton from the alkyl chain (and not from the methyl group). In order to do this, the H being taken and the leaving group have to be anti-coplanar. To get there, the central C-C bond has to rotate:



The only alkene product that could form from this starting material, as a result, is the (Z)-isomer.

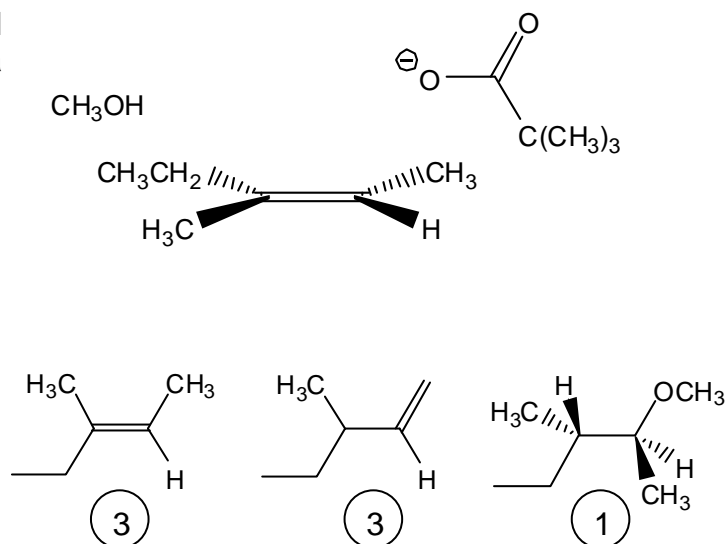
Rubric:

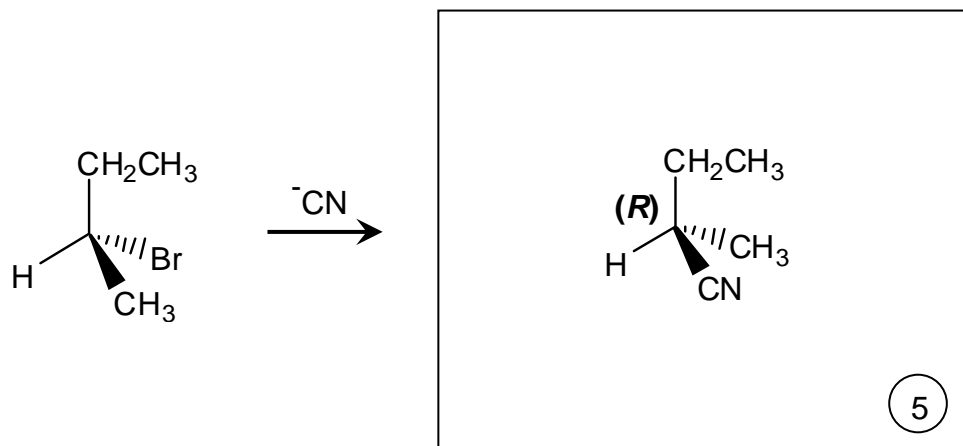
5 points for correct structure.

3 points partial for alkene with wrong stereochemistry or wrong regiochemistry.

1 point partial for substitution product.

-2 points for each clearly trivial structure mistake.





$\text{CN}^-$  is a better nucleophile than base, so this reaction will go  $\text{S}_{\text{N}}2$ . (Secondary halides are OK for  $\text{S}_{\text{N}}2$  as long as they don't have anything else wrong with them.) Inversion of stereochemistry gives the (*R*) product selectively.

Rubric:

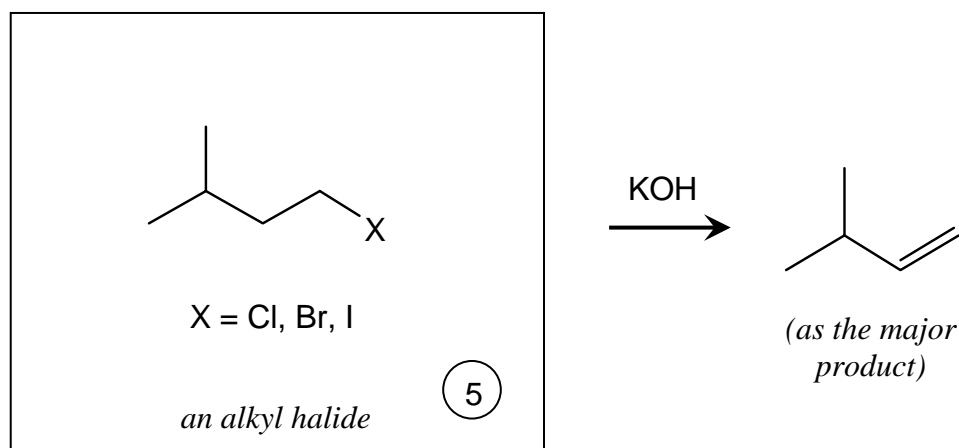
5 points for correct structure.

4 points partial for "+ enantiomer" or drawing both (as if reaction was  $\text{S}_{\text{N}}1$ )

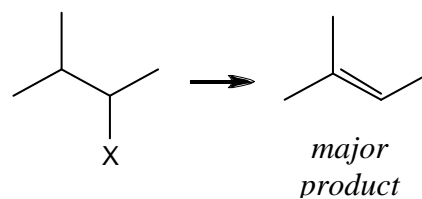
3 points partial for (*S*) stereoisomer only

1 point partial for any butene (elimination product).

-2 points for each clearly trivial structure mistake.



Only the primary halide will give this alkene as the major product. A secondary halide would give it as a minor product, and would yield the more substituted alkene as the major product.



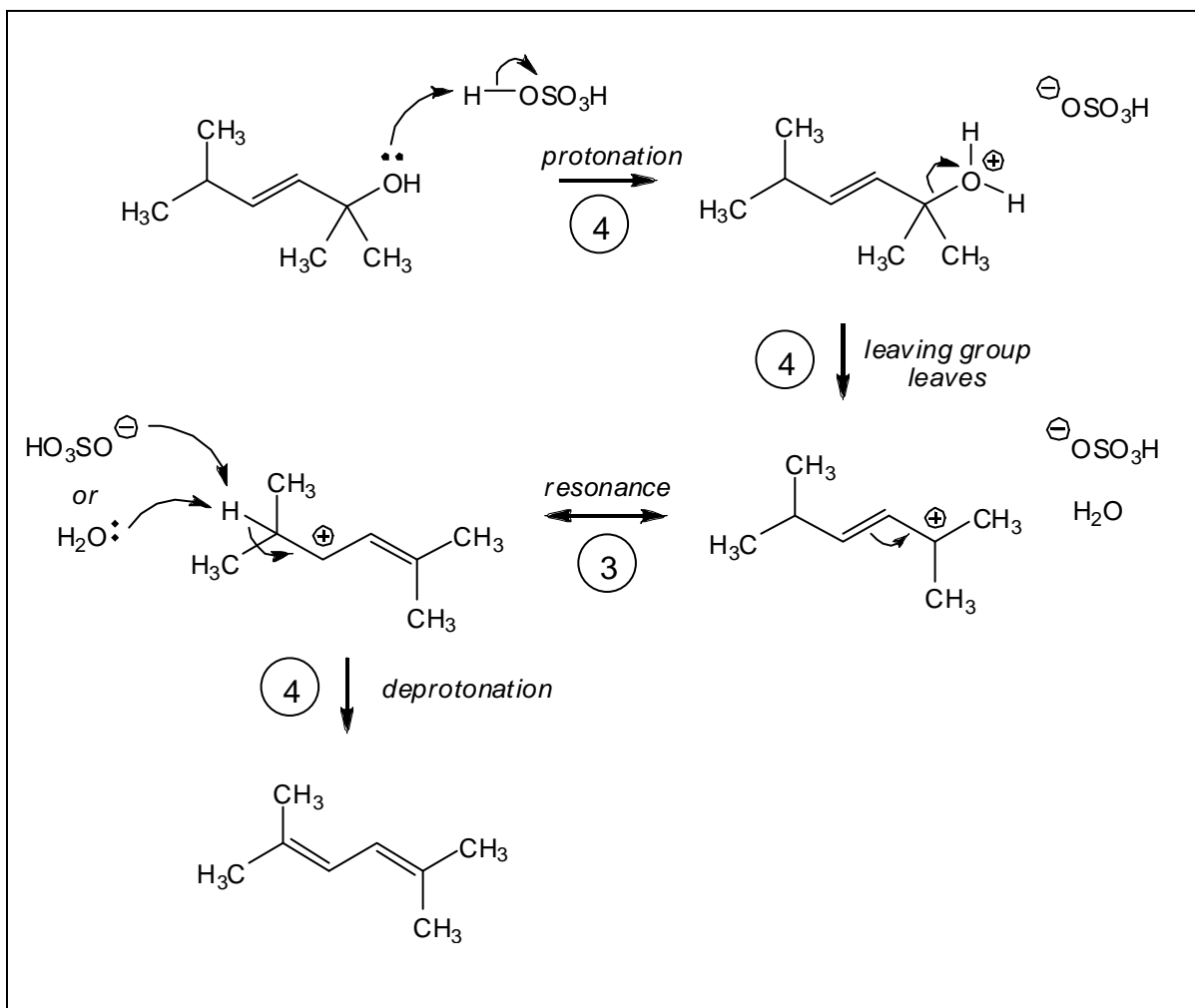
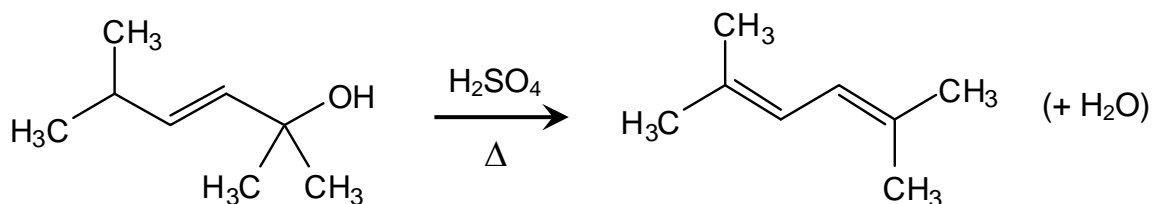
Rubric:

5 points for correct structure.

3 points partial for secondary halide.

-2 points for each clearly trivial structure mistake.

5. (15 pts) For the reaction shown below, draw a mechanism that explains how the product is generated from the starting material. In your answer, make sure that you:
- Draw each step of the mechanism separately;
  - Use “electron pushing” to show where the electrons in each step go;
  - Use only the molecules that you are given; do not invoke reactants or solvents that aren't in the problem.



Important to keep in mind:  $\text{OH}^-$  is a terrible leaving group. But sulfuric acid can make it a better leaving group by protonating it first, so that it leaves as  $\text{H}_2\text{O}$ . We gave only partial credit for answers that invoked  $\text{OH}^-$  as a leaving group.

Rubric:

Overall notes:

*Things that have left (e.g.,  $\text{H}_2\text{O}$ ) and spectators may be omitted.*

*-2 points, for each arrow in each step, for errors in drawing arrows. Arrow must start at an electron pair, and end at nucleus where electrons will newly interact. Can only lose points if you get them.*

*-2 points for each minor error in charge, valency, structure, base, etc.; if error propagates, points are taken off only for initial error.*

*-2 points for each step combined with another (except resonance, see below).*

4 points for protonation by  $\text{H}_2\text{SO}_4$ .

*If you had  $\text{OH}^-$  leave, you do not get these points.*

*2 points partial for proton donated from somewhere else.*

4 points for leaving group leaving to form carbocation.

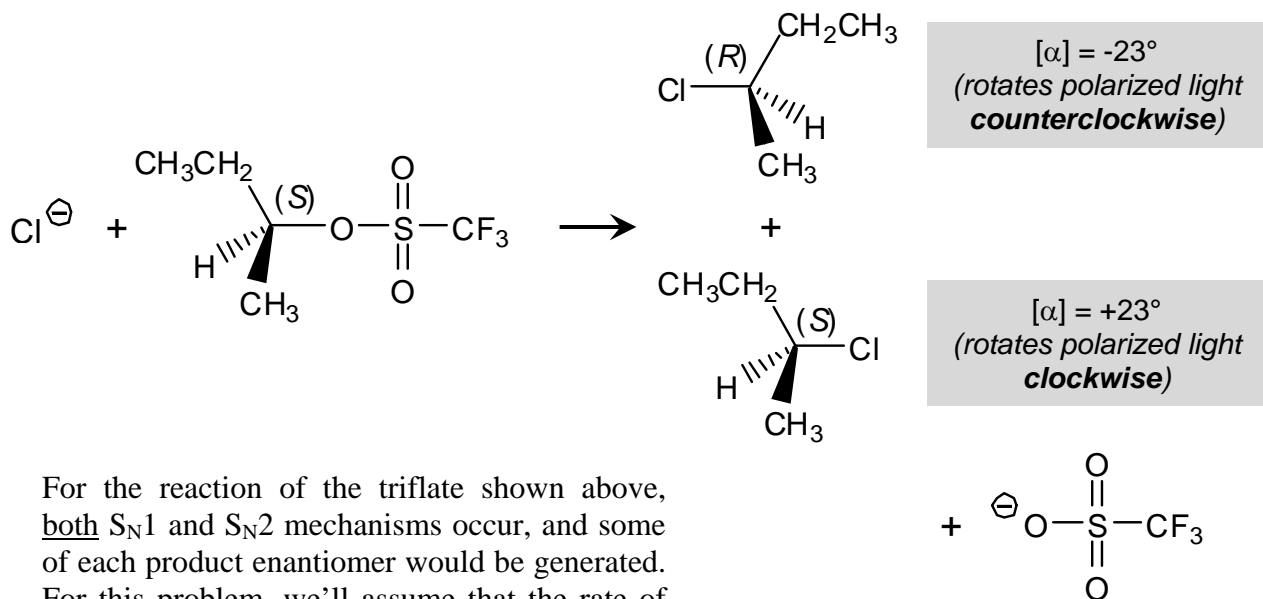
3 points for resonance that moves double bond over to position in product.

*This step may be combined with previous (leaving group) or next (deprotonation) step.*

4 points for deprotonation at correct carbon.

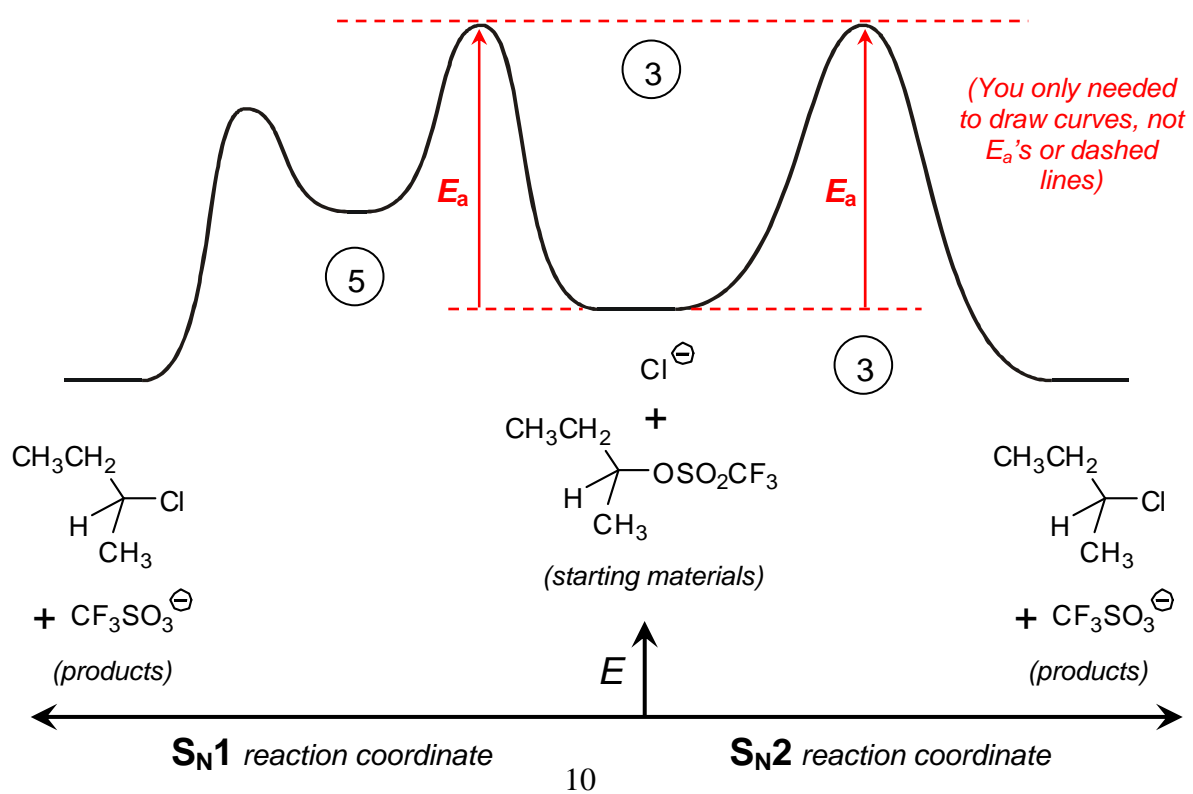
*Base can be just about anything— $\text{HSO}_4^-$ ,  $\text{H}_2\text{O}$ , even starting material alcohol.*

6. (23 pts) The triflate group ( $\text{CF}_3\text{SO}_3^-$ ) is such a good leaving group that alkyl triflates will even undergo nucleophilic substitution reactions with poor nucleophiles, such as chloride ions.



For the reaction of the triflate shown above, both  $\text{S}_{\text{N}}1$  and  $\text{S}_{\text{N}}2$  mechanisms occur, and some of each product enantiomer would be generated. For this problem, we'll assume that the rate of  $\text{S}_{\text{N}}1$  and  $\text{S}_{\text{N}}2$  reactions are exactly equal.

- (a) On the diagram below, draw potential energy curves for these two mechanisms. (I have already drawn the energies of starting materials and products; you need to connect them with curves. You do *not* need to draw transition-state structures.) Make sure your curves illustrate the relative energies of the rate-determining transition states for the two mechanisms.



If the rates of the  $S_N1$  and  $S_N2$  reactions are the same, then the activation barrier for the two reactions (i.e., the height of the tallest hill, the rate-determining step) must also be the same.

Rubric for (a): (11 points total for this part.)

5 points for drawing  $S_N1$  curve.

2 points for drawing as two steps.

2 point for drawing second transition state lower than first.

1 point for drawing intermediate higher in energy than starting material.

3 points for drawing  $S_N2$  curve as one step.

3 points for making rate-determining transition states of the two reactions the same height.

(b) Once the reaction is complete, and all the starting material has been converted to products, would the product mixture rotate plane-polarized light? If so, in which direction? (Circle one answer.)

The product mixture  
rotates polarized light  
**CLOCKWISE**

3

The product mixture  
rotates polarized light  
**COUNTERCLOCKWISE**

The product mixture  
**DOES NOT ROTATE**  
polarized light

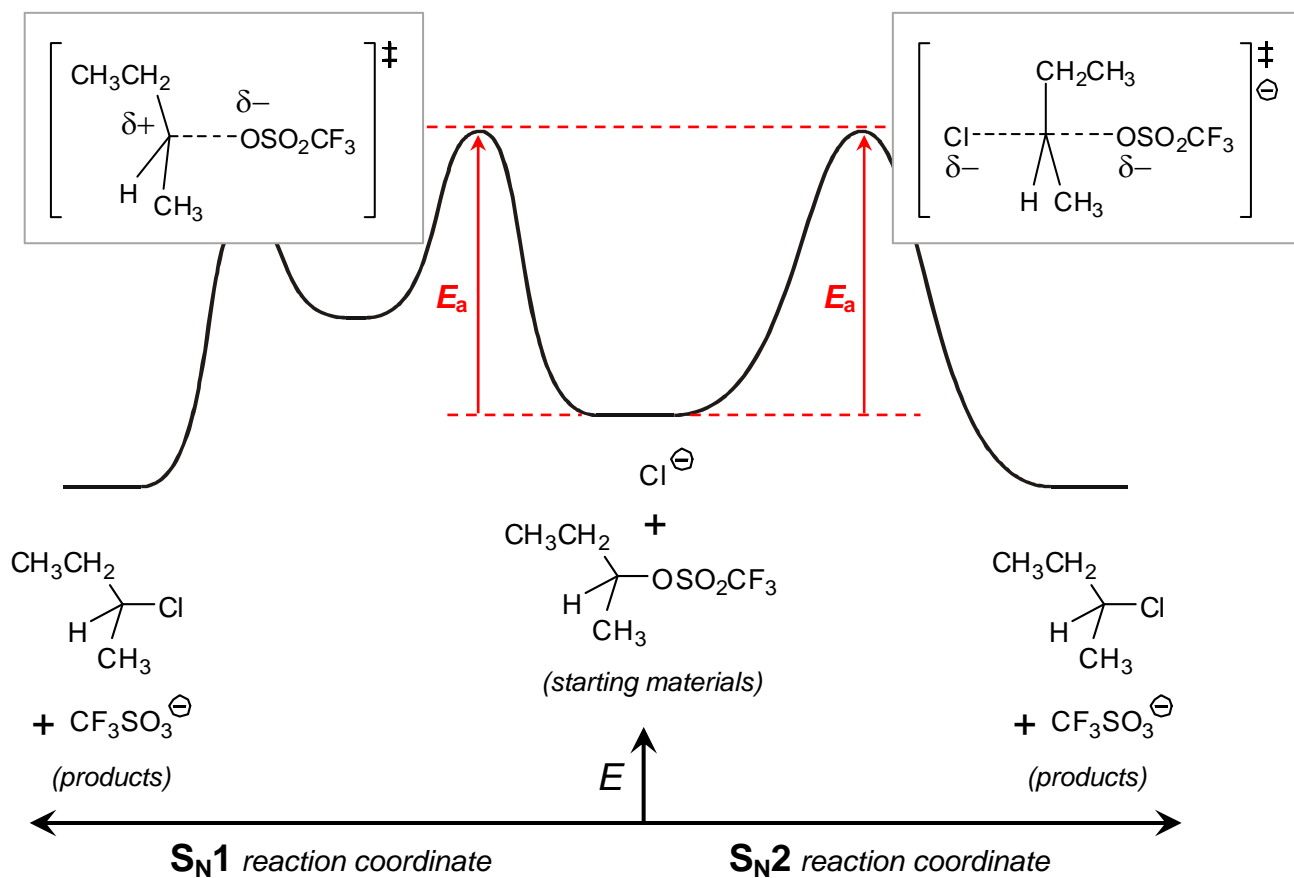
The  $S_N1$  mechanism will produce equal amounts of the (*R*) and (*S*) stereoisomers, but the  $S_N2$  mechanism will produce only the (*R*) stereoisomer (with inversion of the original *S* stereochemistry). If their rates are equal, in fact, the combination of these two mechanisms will produce 75% (*R*), 25% (*S*). Because that mixture will rotate plane-polarized light more counterclockwise (from the *R* fraction) than clockwise (from the *S* fraction), overall the product mixture will rotate light counterclockwise.

Rubric for (b-d): 3 points each circle (12 points total on page 8).

- (c) What would happen if iodide ( $I^-$ ) were used as the nucleophile instead of chloride? How would the activation energies ( $E_a$ ) for the  $S_N1$  and  $S_N2$  mechanisms be affected? (Circle one answer in each column.)

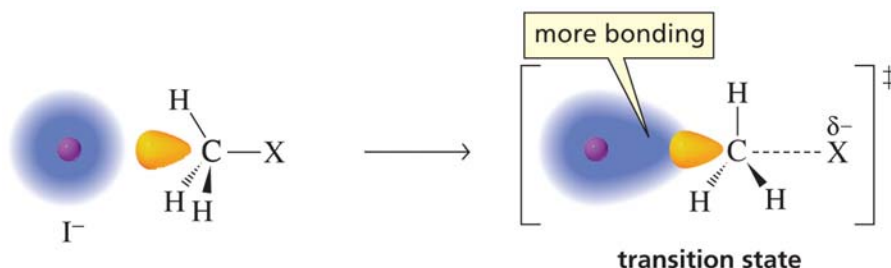
<p>The activation energy (<math>E_a</math>) for the <b><math>S_N1</math></b> mechanism would be</p> <p><b>LARGER</b></p> <p>or</p> <p><b>SMALLER</b></p> <p>or</p> <p><b>THE SAME</b></p> <p>if <math>I^-</math> were used instead of <math>Cl^-</math></p>	<p>The activation energy (<math>E_a</math>) for the <b><math>S_N2</math></b> mechanism would be</p> <p><b>LARGER</b></p> <p>or</p> <p><b>SMALLER</b></p> <p>or</p> <p><b>THE SAME</b></p> <p>if <math>I^-</math> were used instead of <math>Cl^-</math></p>
<p>(3)</p>	<p>(3)</p>

To answer this, we've got to go back to the potential energy diagram and think about the rate-determining transition states.



The  $S_N1$  transition state doesn't even involve  $Cl^-$ , so replacing  $Cl^-$  with  $I^-$  would have no effect on the energy of the transition state or on the overall activation energy for the  $S_N1$  reaction.  $E_a(S_N1)$  would be the same.

The  $S_N2$  transition state does involve  $Cl^-$ . We said in class that  $I^-$  was the best nucleophile of the halides, because the polarizability of the electron cloud made it easier for the electrons to "reach" the electrophile center in the transition state.



This effect selectively stabilizes the  $S_N2$  transition state, and makes the activation energy for this reaction smaller.

- (d) So, would the stereoselectivity of the total reaction—that is, the preference for one product enantiomer over the other—increase, decrease, or stay the same if iodide were used as the nucleophile instead of chloride? (Circle one answer.)

Using  $I^-$  as the nucleophile  
would make the substitution

3

**MORE  
STEREOSELECTIVE**

**LESS  
STEREOSELECTIVE**

**EQUALLY  
STEREOSELECTIVE**

relative to using  $Cl^-$  as the  
nucleophile

Of the two mechanisms,  $S_N2$  is stereospecific and  $S_N1$  is not. The faster the  $S_N2$  reaction goes (due to  $I^-$ ), the greater a fraction of (*R*)  $S_N2$  product there will be, and the more stereoselective the reaction will be.