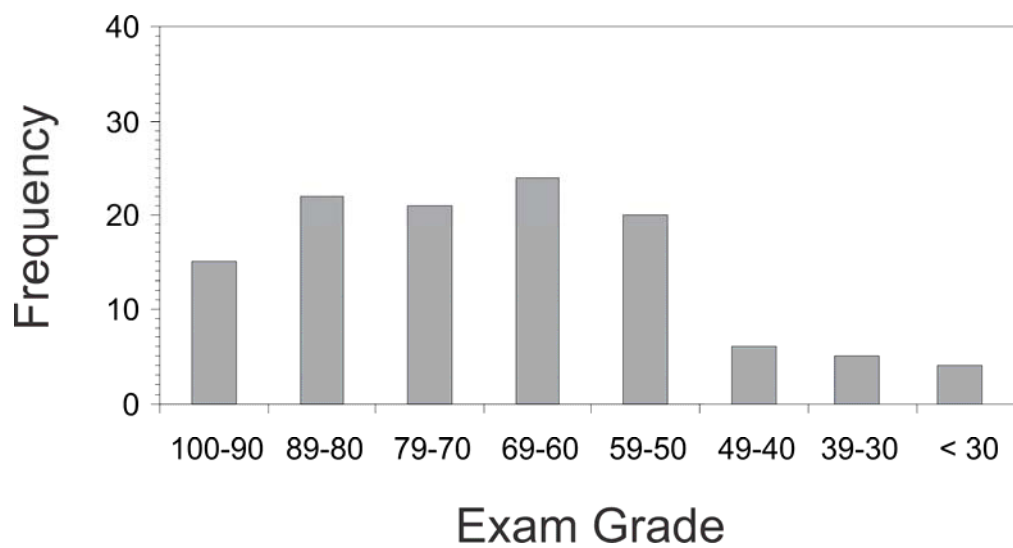
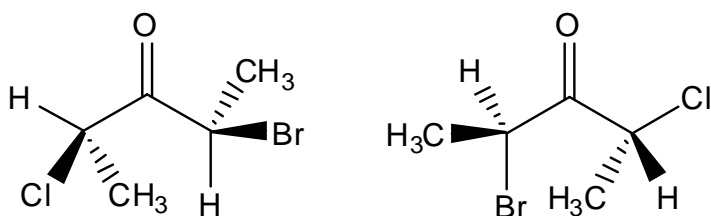


**Exam 2
Answer Key**

Exam 2 Mean: 68
Exam 2 Median: 68
Exam 2 St. Dev.: 18



1. (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

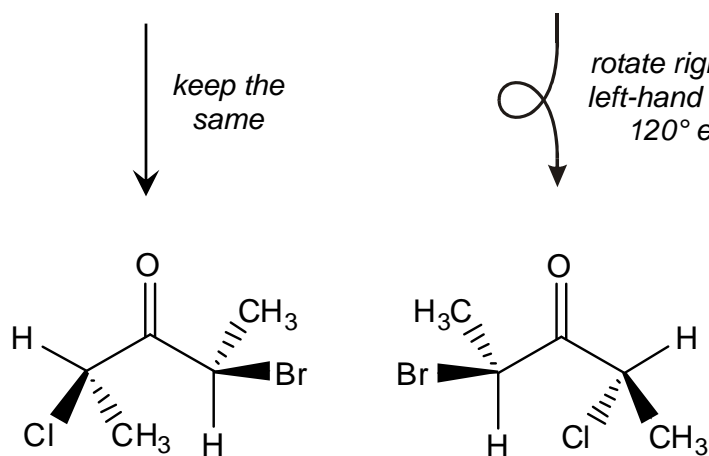
DIASTEREOMERS

or

SAME MOLECULE

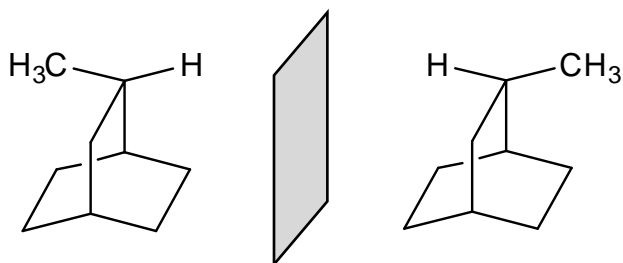
4

One way to answer this question was to rotate the central bonds of the molecule to see if you could make mirror images:



These are not mirror images, so they cannot be enantiomers or the same molecule. They must be diastereomers.

But I think an easier approach was to assign (*R*) and (*S*) labels to the centers, and see that the left-hand molecule is (*R,R*) and the right-hand molecule is (*S,R*). Again, the molecules must be diastereomers.



ENANTIOMERS

or

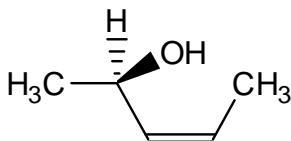
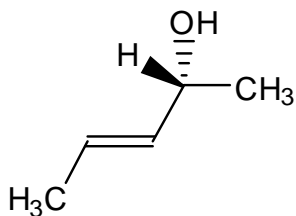
DIASTEREOMERS

or

SAME MOLECULE

4

These two molecules are clearly mirror images of one another, meaning they are enantiomers (if they are chiral) or the same molecule (if they are achiral). They can't be superimposed, so they are chiral.



ENANTIOMERS

or

4

DIASTEREOMERS

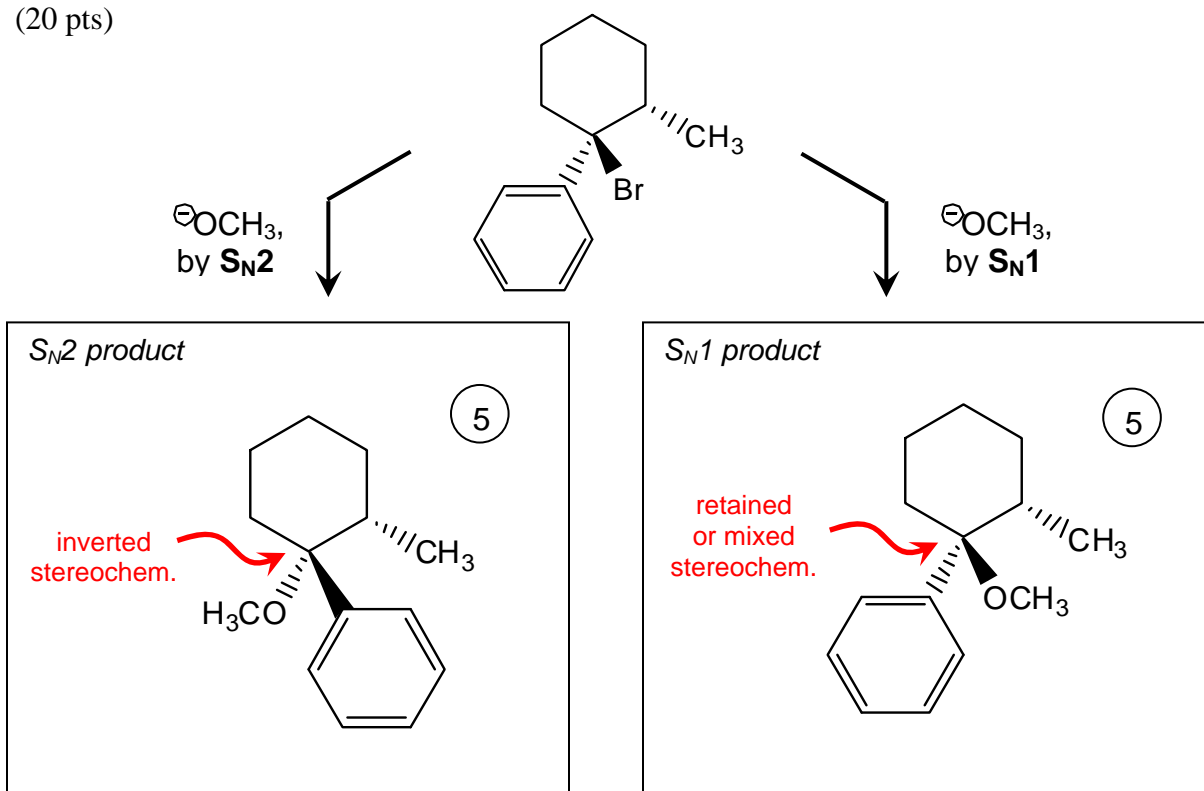
or

SAME MOLECULE

These molecules are stereochemically related—they have all of the same atoms attached to all of the same other atoms, just in a different arrangement—but the difference between the *trans*- double bond on the left and the *cis*- double bond on the right clearly makes these molecules different (not the same molecule). The molecules are also clearly not mirror images of one another, so they can't be enantiomers. We said in class that stereoisomers that are not enantiomers are, by default, diastereomers. So that's what these are.

Rubric: 4 points each circle.

2. (20 pts)



S_N2 reactions proceed with inversion of stereochemistry. So, when the CH₃O⁻ displaces the Br⁻, it will come from behind the molecule and end up on the underside.

Rubric for this part:

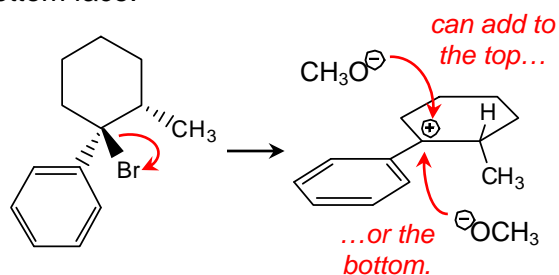
5 points for correct structure.

4 points partial for "+ enantiomer" or drawing both (as if reaction was S_N1).

3 points partial for retention of configuration only

-2 points for each clearly trivial structure mistake.

S_N1 reactions proceed through an intermediate cation. In principle, CH₃O⁻ could add to this flat cation on the top or bottom face.



I think the -CH₃ group will sterically block the bottom face a little, and favor addition to the top. But it's hard to say, so we also accepted mixed stereochemistry in your answer.

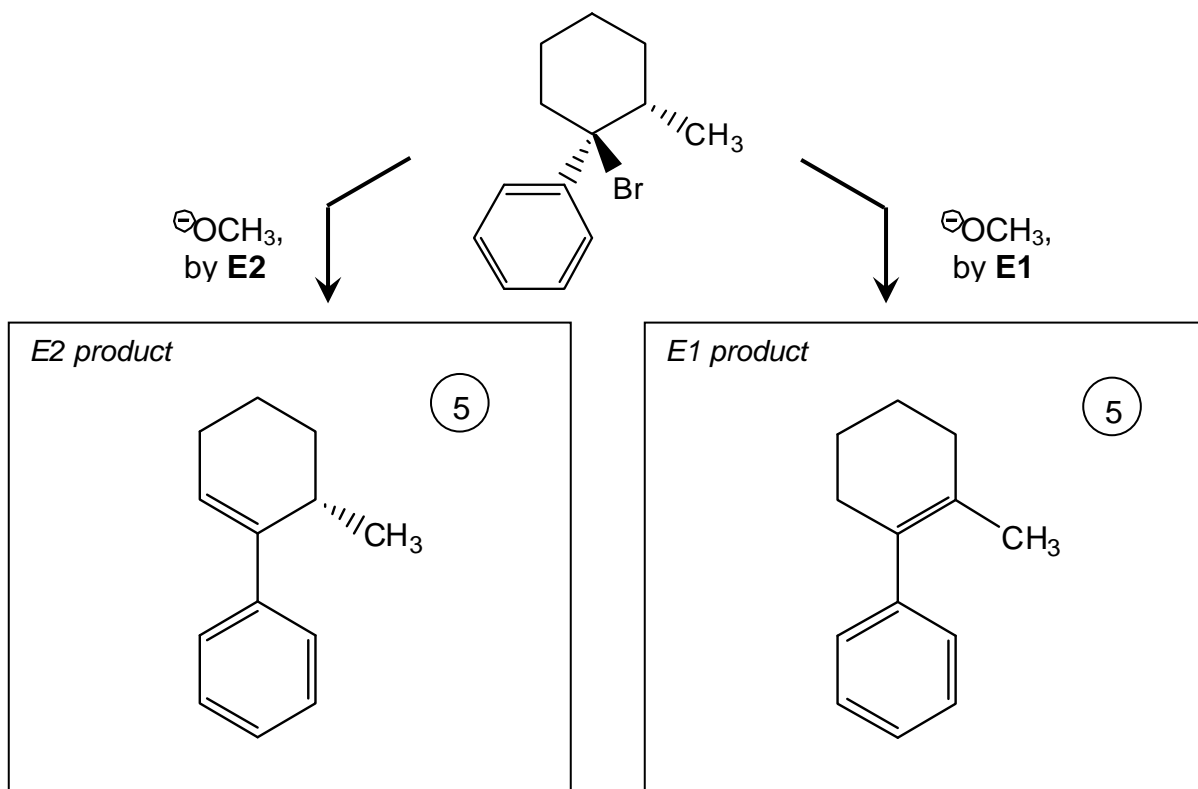
Rubric for this part:

5 points for correct structure.

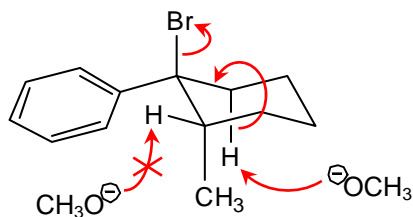
Full credit for "+ enantiomer" (which is technically incorrect here), "+ diastereomer" (which is actually correct), or for not illustrating stereochemistry in your answer.

4 points partial for inversion of configuration only.

-2 points for each clearly trivial structure mistake.

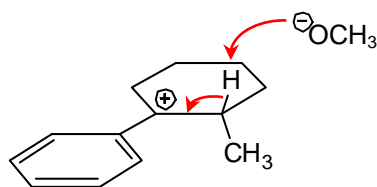


E2 reactions involve a base taking a proton and a leaving group departing at the same time. The E2 mechanism requires that the proton and the leaving group be oriented anti-coplanar (across from one another). In the starting material, there is no way to orient the H at the methyl carbon opposite the leaving group. So CH_3O^- could only react via E2 on the left-hand side of the ring:



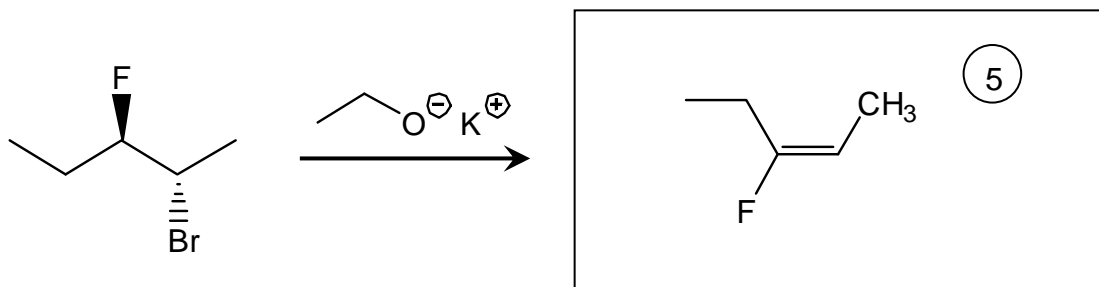
Rubric for this part:
 5 points for correct structure (less substituted alkene).
 3 points partial for more substituted alkene.
 2 points partial for any alkene.
 -2 points for each clearly trivial structure mistake.

E1 reactions proceed through the same intermediate cation as $\text{S}_{\text{N}}1$ reactions. As a result of this, E1 reactions don't have the same anti-coplanar constraint that E2 reactions have, and the most substituted proton can be removed to generate the most stable product:

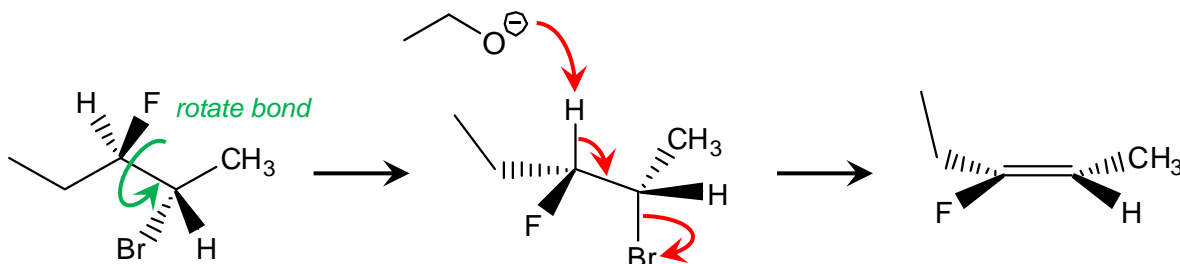


Rubric for this part:
 5 points for correct structure.
 3 points partial for less substituted alkene.
 2 points partial for any alkene.
 -2 points for each clearly trivial structure mistake.
 -1 for not illustrating alkene as flat.

3. (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".

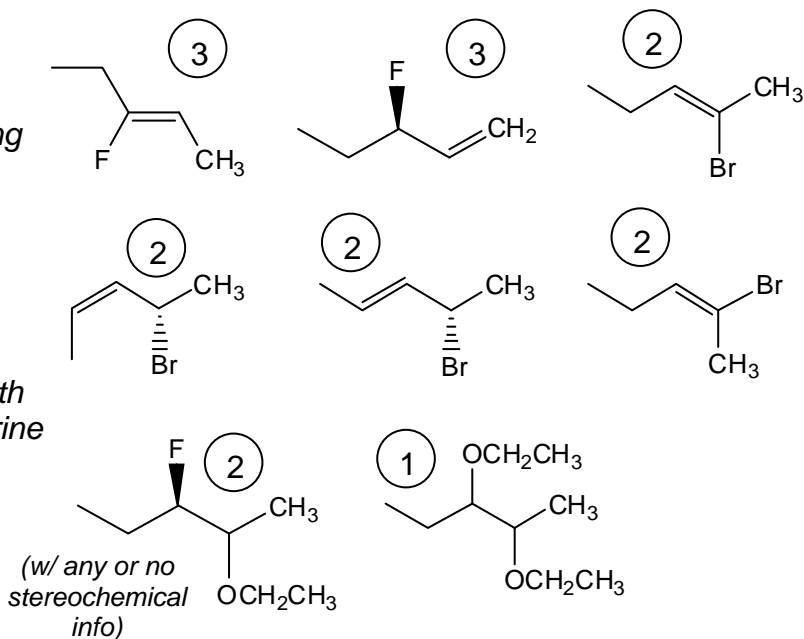


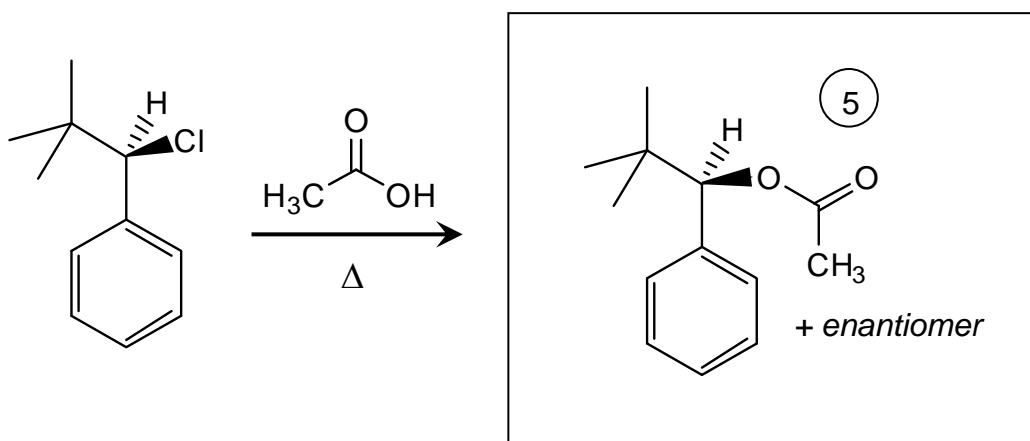
EtO^- is a better base than it is a nucleophile, so it will do E2. It is also small, so it will produce the most stable (Zaitsev) alkene product by taking a proton from the alkyl chain (and not from the methyl group). In order to do this, the H being taken and the leaving group have to be anti-coplanar.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



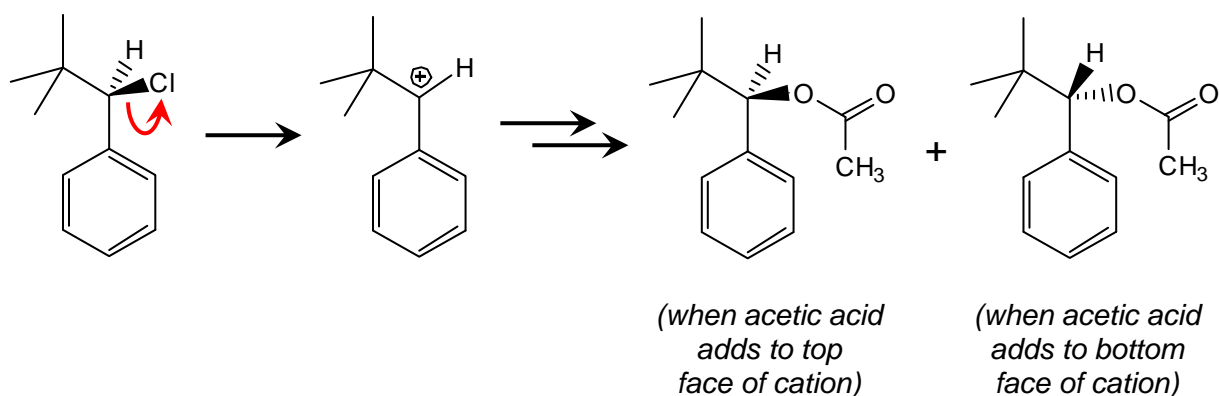
Rubric for this part:

- 5 points for correct structure.
- 3 points partial for bromine elimination product with wrong stereochemistry or wrong regiochemistry.
- 2 points partial for eliminating fluorine instead of bromine.
- 2 points partial for any bromine substitution product.
- 1 point partial for substituting both bromine and fluorine, or fluorine only.
- 2 points for each clearly trivial structure mistake.

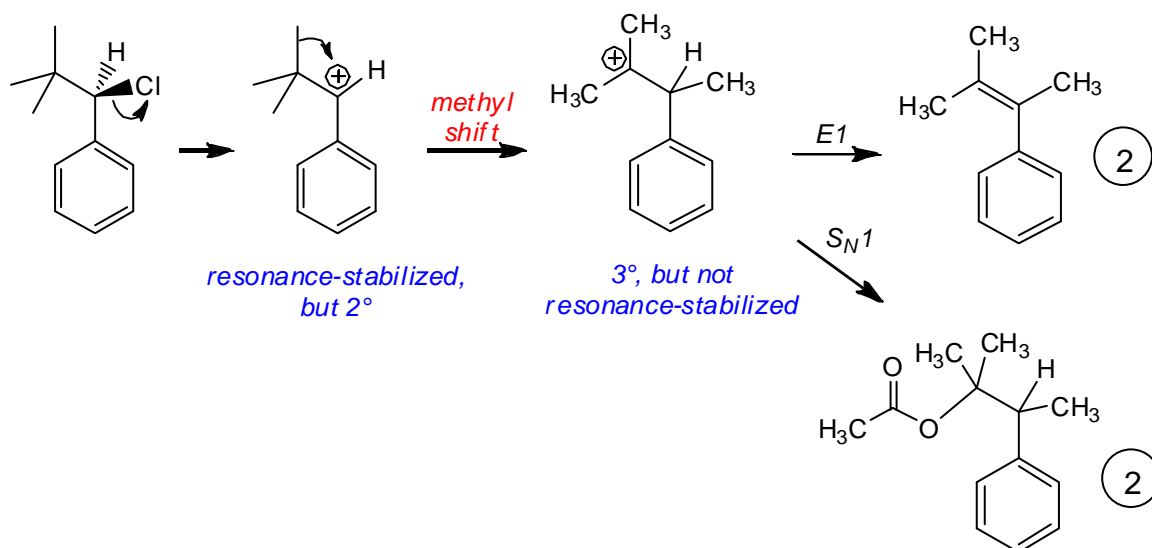




Acetic acid is a poor nucleophile, and the added heat tips us off that this should be an S_N1 or $E1$ reaction. There are no protons α to the Cl leaving group, so it cannot be $E1$; this must be S_N1 . S_N1 passes through an achiral carbocation intermediate, which reacts to generate a racemic mixture of products:



Less likely answers involved a methyl shift of the intermediate cation:



In class, we said that even though 1,2-hydride and 1,2-alkyl shifts were uncommon, they can occur when the rearranged cation is more stable than the original cation. A tertiary cation is normally more stable than a secondary cation, *all other things being equal*. But here the tertiary cation has lost its resonance stabilization, and resonance is almost always more important than substitution in determining ion stabilization. So, the shift shown above would never happen. We gave these answers partial credit.

Rubric for this part:

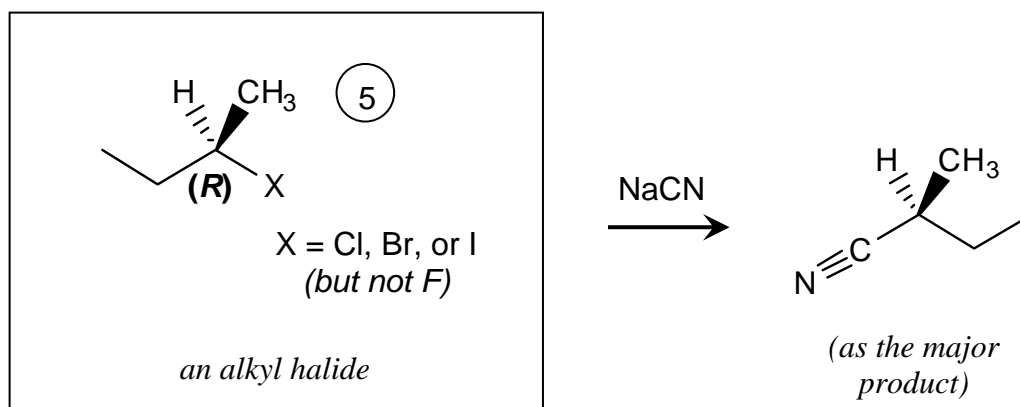
5 points for correct structure and either (a) including "+ enantiomer" or (b) not illustrating stereochemistry (which infers racemate).

4 points partial for omitting "+ enantiomer".

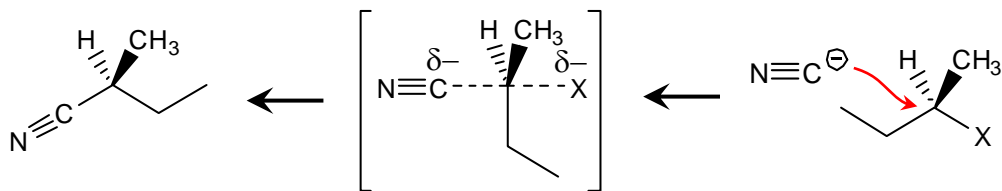
3 points partial for inversion of stereochemistry only (as if reaction were S_N2).

2 points partial for methyl migration products.

-2 points for each clearly trivial structure mistake.



Cyanide (CN^-) is a great nucleophile, so this can be easily configured as an S_N2 substitution. S_N2 involves inversion of configuration (stereochemistry), so our starting material will have the leaving group on the opposite side of where the CN^- group ends up:



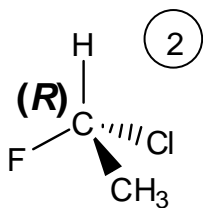
Rubric for this part:

5 points for correct structure, with correct stereochemistry. It doesn't matter how you oriented your answer, as long as it was (*R*).

3 points partial for retention of stereochemistry (*S*), for not illustrating stereochemistry, or for writing "+ enantiomer".

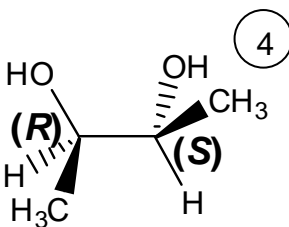
-2 points for each clearly trivial structure mistake.

4. (22 pts) On the structures below, **label each chiral center** with its appropriate Cahn-Ingold-Prelog designation [(*R*) or (*S*)]. Make it clear which atom in the drawing you are labeling. Then, for each structure, **circle** whether you think the molecule is chiral or achiral.



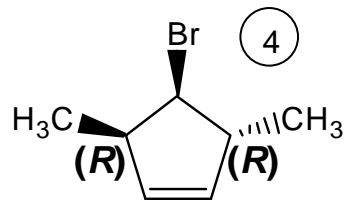
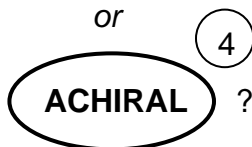
or

ACHIRAL ?



CHIRAL

or



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.

This molecule is (*R,S*), so it could be chiral, but it could also be *meso*. A molecule is *meso* only if the (*R*) and (*S*) centers have the same groups attached. That is the case here, so the molecule is achiral.

This 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.

Rubric:

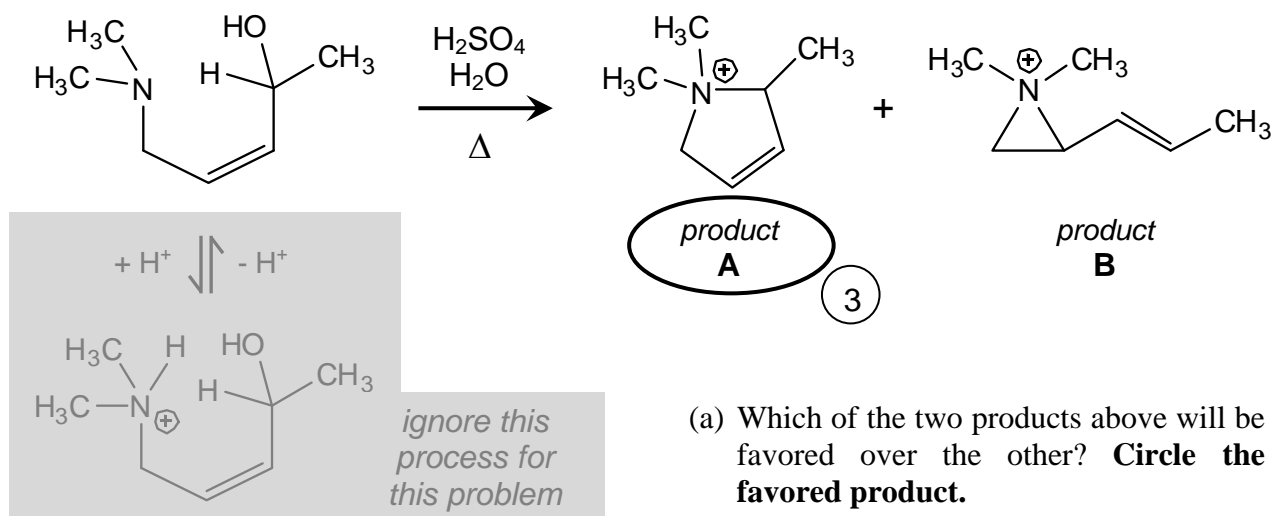
2 points for each labeled stereocenter.

No partial credit for labeling correct center with incorrect letter.

-2 points for each achiral center labeled as chiral.

4 points for each circle.

5. (31 pts) The starting material shown below can interact with an acid (like H_2SO_4) in two ways: (i) it can be reversibly protonated at nitrogen, which we will ignore in this problem; or (ii) it can react to form products **A** and **B**.



- (a) Which of the two products above will be favored over the other? **Circle the favored product.**

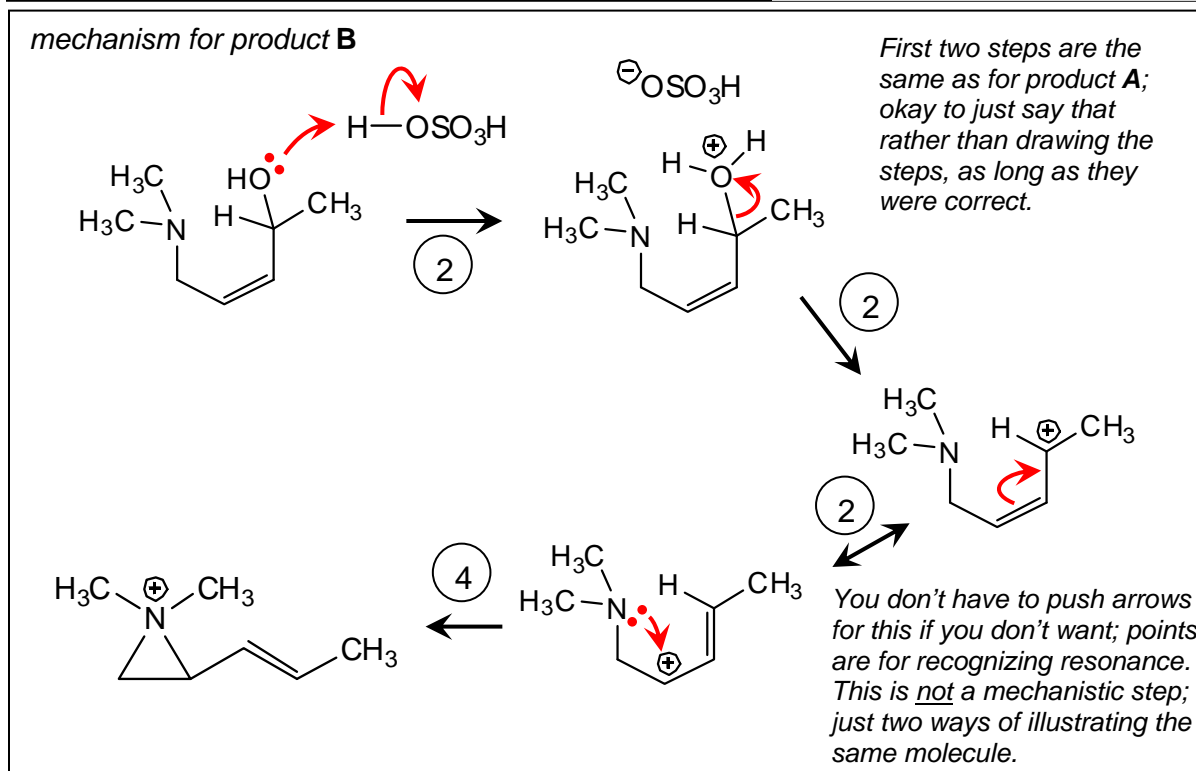
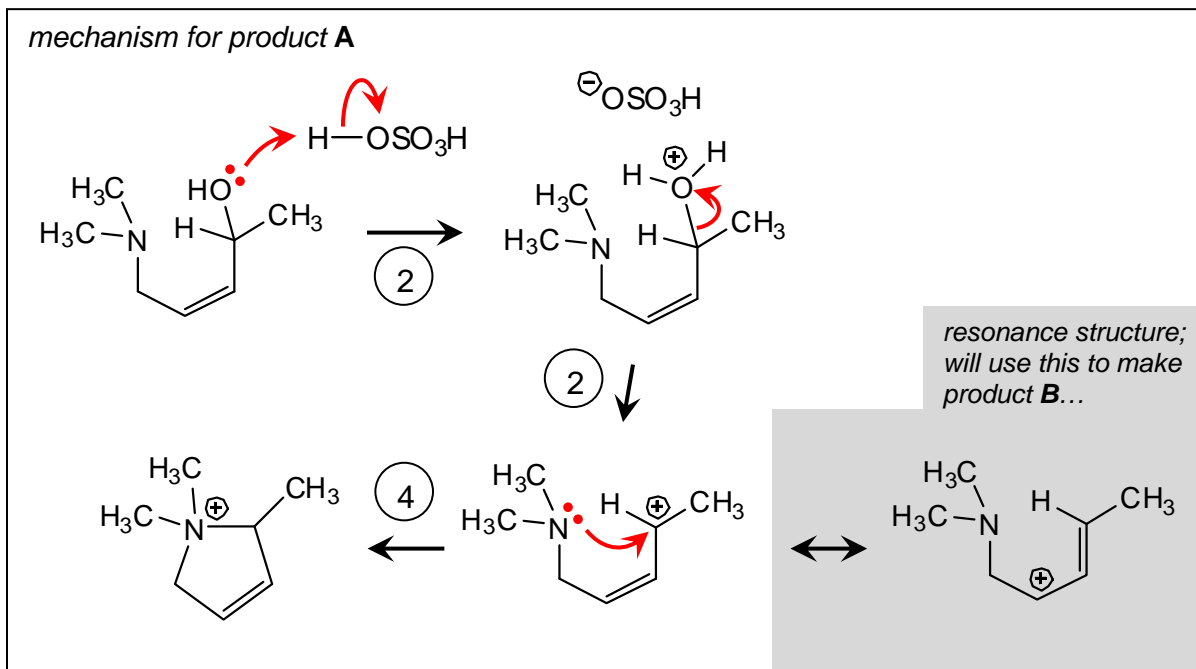
We can assume, at first glance, that the product distribution will be determined by the relative stability of the two products. In class we talked about how *trans*-disubstituted alkenes are generally more stable than *cis*-disubstituted alkenes, and you might conclude that product **B** was favored on that basis. But the energy difference between a *cis*- and *trans*-alkene is not that big (only about 1 kcal/mol), and drives product distribution if all else is equal. By contrast, the energy difference between a 5-membered ring and a 3-membered ring is large (~21 kcal/mol). So the impact of ring strain here should be larger, and would drive the reaction to prefer product **A**.

Rubric for part (a): 3 points.

If you got this incorrect, you can still get full credit for the rest of the problem; we based grading on the other parts on your answer (even if incorrect) to this part.

(b) Draw mechanisms that explain how products **A** and **B** are formed from starting material. **Each mechanism should be three steps long.** In each 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.



Rubric for part (b):

Overall notes:

Overall, the minimum score for each step is zero; errors in a step cannot earn you negative points that count against another, correct step.

Things that have left (e.g., $\text{^-OSO}_3\text{H}$ from HOSO_3H) and spectators may be omitted.

No partial credit for any step containing an error, including omission, in drawing arrows. (This is because most steps involve just one arrow.) Arrow must start at an electron pair (either a bond or a lone pair), and end at nucleus where electrons will newly interact.

-1 point for each error in charge, valency, structure, base, etc.; if error propagates, points are taken off only for initial error.

-2 points for combining first step (protonation) with another. (So, you would lose all points for protonation step, but not for the subsequent step.) You can, however, combine resonance with another step, or combine H_2O leaving with nitrogen attack (as if last step were $\text{S}_{\text{N}}2$, though I think it would be $\text{S}_{\text{N}}1$).

-2 points for each use of a generic or incorrect acid/base. H_2SO_4 and H_3O^+ can be used interchangeably as acids, and $\text{^-OSO}_3\text{H}$ and H_2O can be used as bases, but that's it. You also lose these same two points for creating any negatively charged intermediate (other than $\text{^-OSO}_3\text{H}$), though I can't imagine how you would do that here.

(c) On the diagram below, **draw potential energy curves for each of your two mechanisms**. For each curve:

- Draw energy levels for all transition states and intermediates, and connect them with curves. You do not need to draw any chemical structures, just energies.
- Energy levels for the starting material and the two products are given. Choose which product energy corresponds to which product, by circling one letter (**A** or **B**) for each.
- Because each mechanism is three steps long, you will need to draw two intermediates and three transition states on each curve.
- If your two mechanisms share any common intermediates or transition states, you only need to draw their (common) energy levels once.

Three features were important here:

- Each pathway was three steps long—meaning you needed to draw two intermediates (valleys) and three transition states (hills) between the starting material and product for each pathway.
- The first two steps of the two mechanisms are the same. That means that the two reactions follow the same path over the first two hills, and then they diverge.
- Product **B** is higher in energy (less stable) than product **A**, because its 3-membered ring has a lot more ring strain than the 5-membered ring of product **A**. Hammond's Postulate says that this difference should also be reflected in the transition state energies of the third step, so that the barrier to product **A** is lower than the barrier to product **B**.

