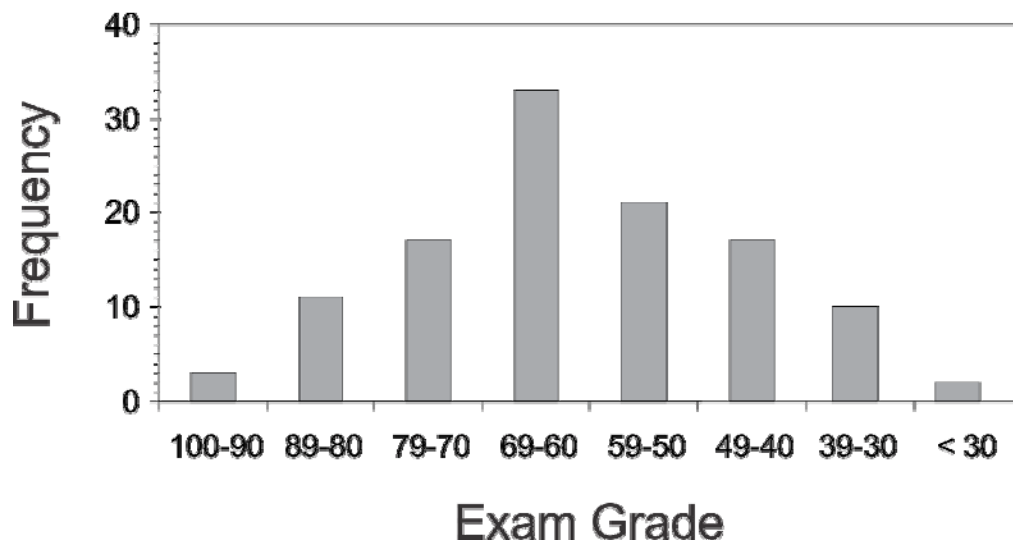
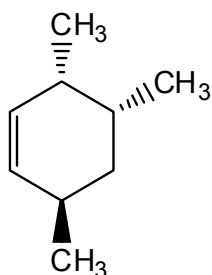
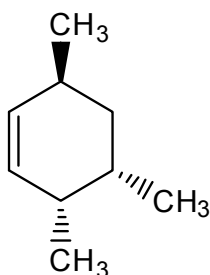


**Exam 2
Answer Key**

Exam 2 Mean: 61
Exam 2 Median: 61
Exam 2 St. Dev.: 15



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 (4)

or

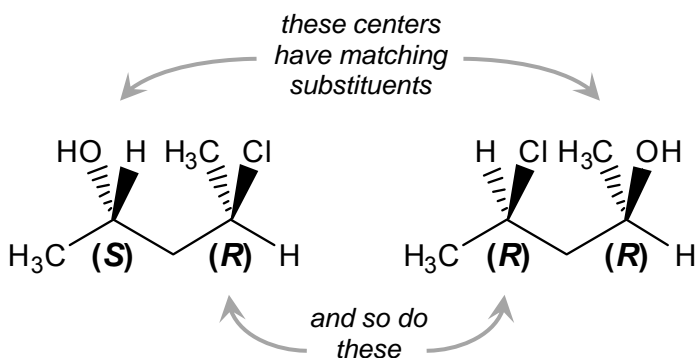
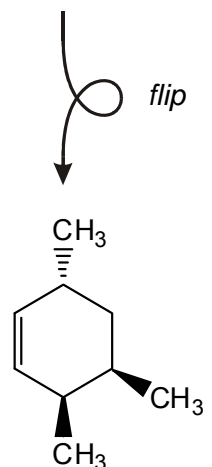
DIASTEREOMERS

or

SAME MOLECULE

I think the easiest way to answer this question was to flip the second molecule to see if you could make it the mirror image of the first.

The flipped molecule has opposite stereochemistry at all three stereocenters, so it is the enantiomer of the first molecule.



ENANTIOMERS

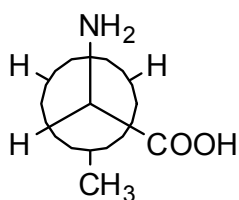
or

DIASTEREOMERS (4)

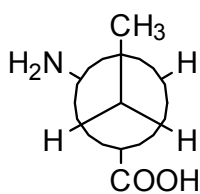
or

SAME MOLECULE

Not opposites, and not the same—these stereoisomers must be diastereomers.



is



is

ENANTIOMERS

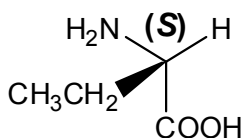
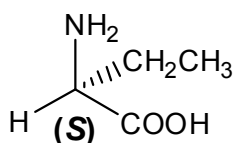
or

DIASTEREOMERS

or

SAME MOLECULE

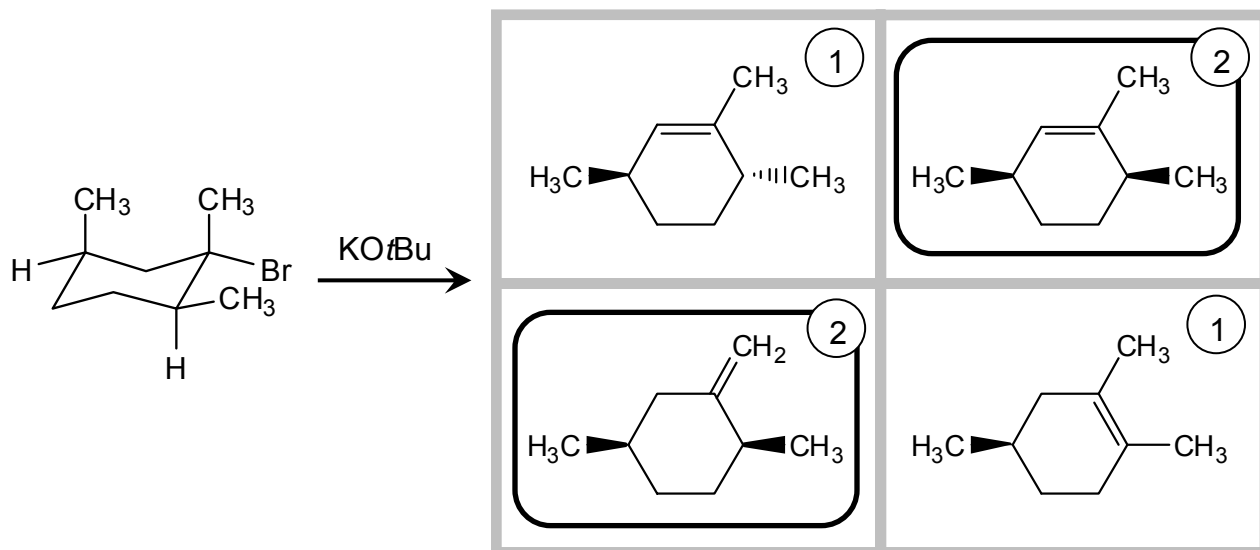
4



Rubric: 4 points each circle.

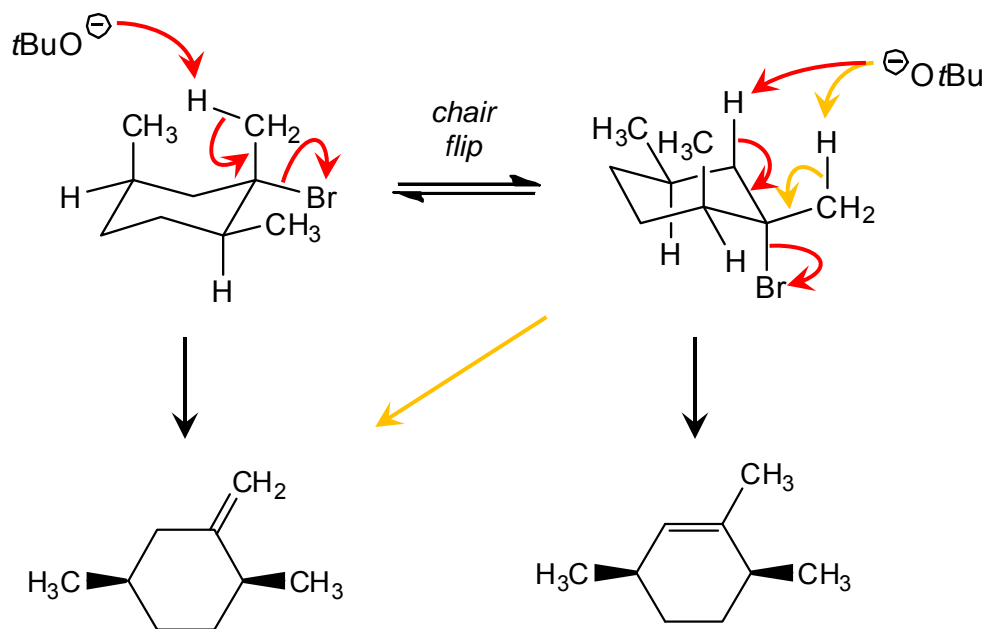
2. (16 pts) For each reaction shown below, **circle all potential products**. Keep in mind that, for each case, you might circle one, multiple, or no molecules.

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

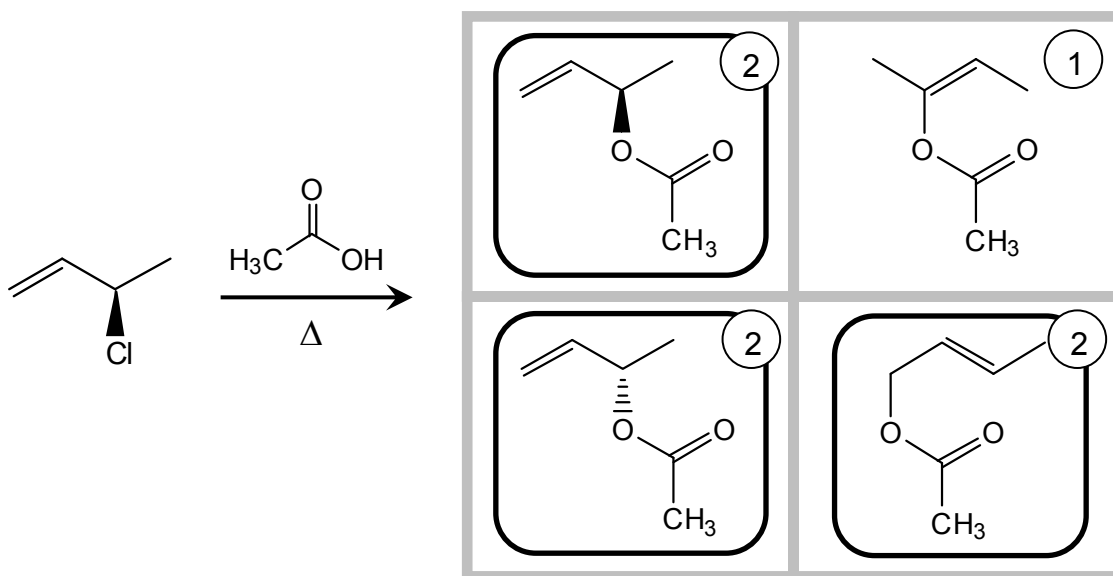


KOtBu is a strong base and a hindered nucleophile, and so it will react via E2 wherever it can. E2 requires an anti-coplanar (“zig-zag”) arrangement of a hydrogen and the leaving group. In the chair drawn above, the only H that is anti-coplanar to

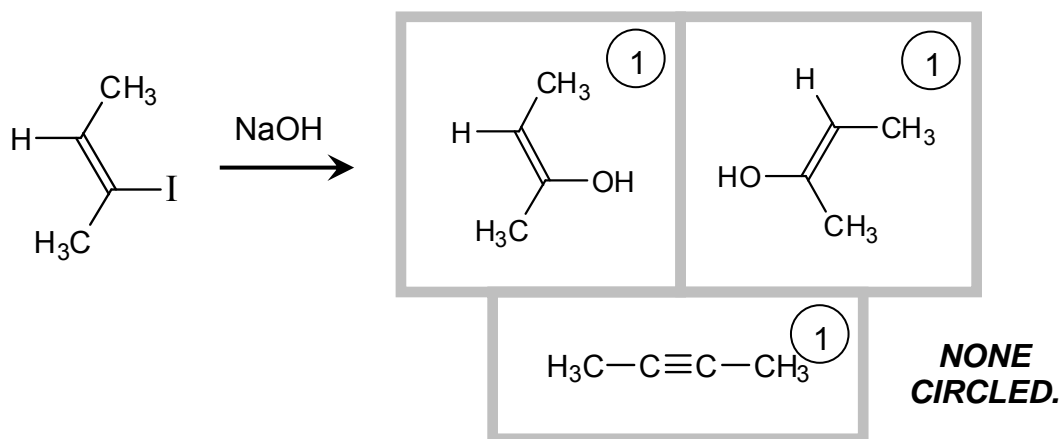
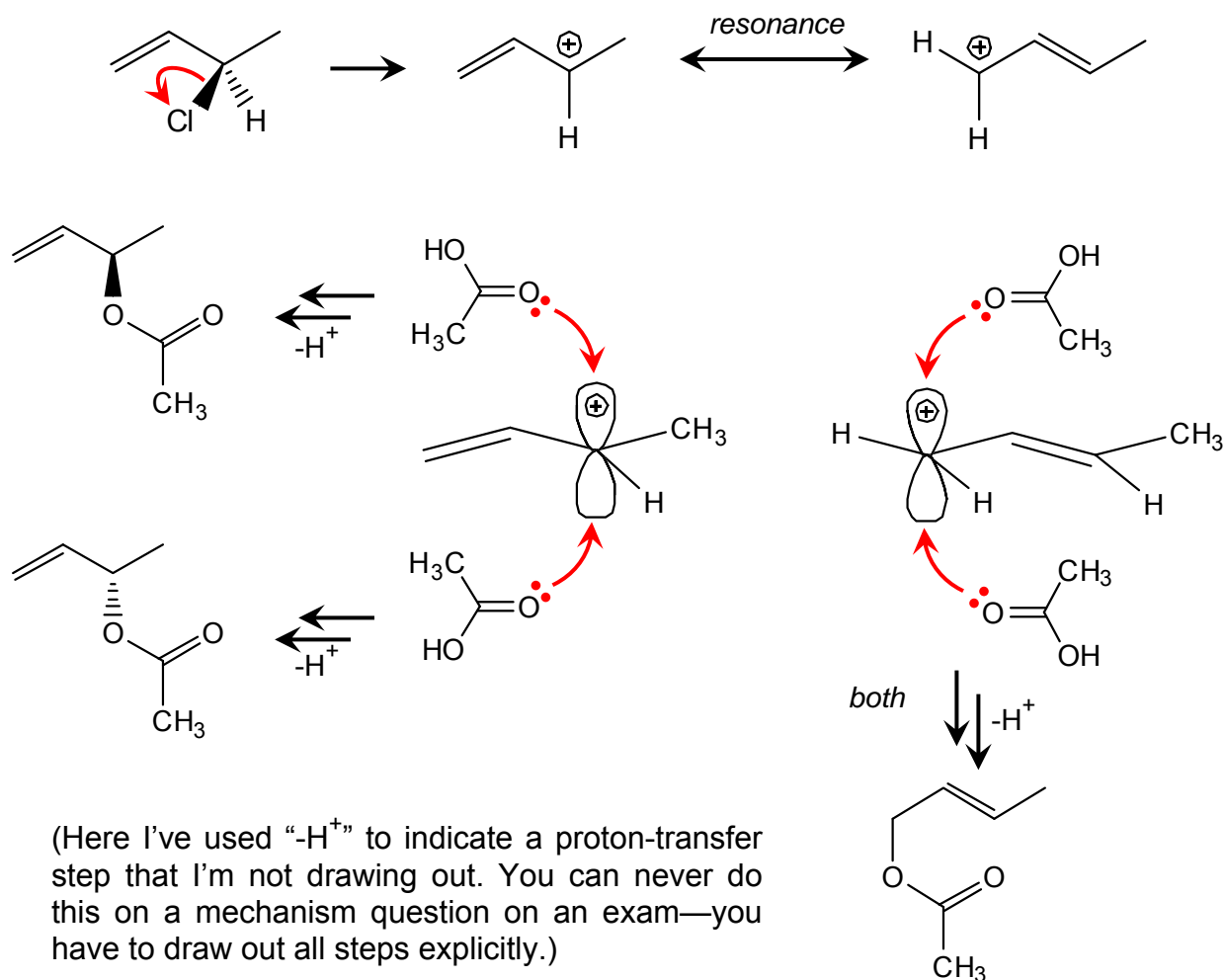
the Br is one on the adjacent methyl group. However, the Br atom can also be anti-coplanar to an H in the chair body if the chair flips (which happens spontaneously, all the time):



And those are the only two possible anti-coplanar arrangements possible for this bromine leaving group.

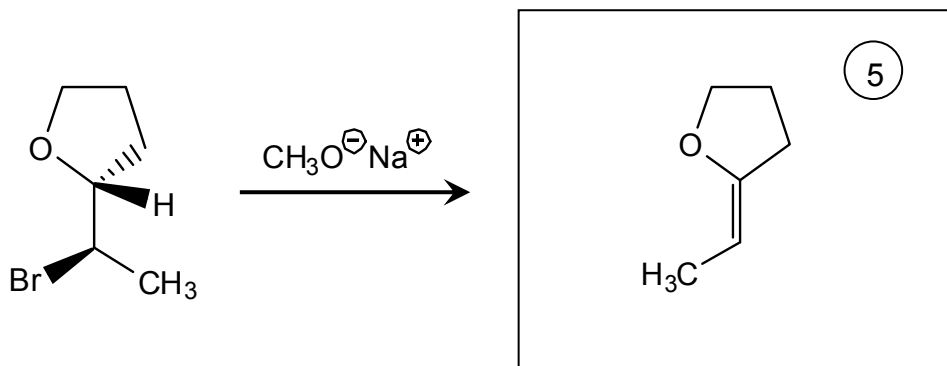


This reaction will proceed via S_N1 because of the stability of the resonance-stabilized cation, and because the acetic acid is a poor nucleophile.



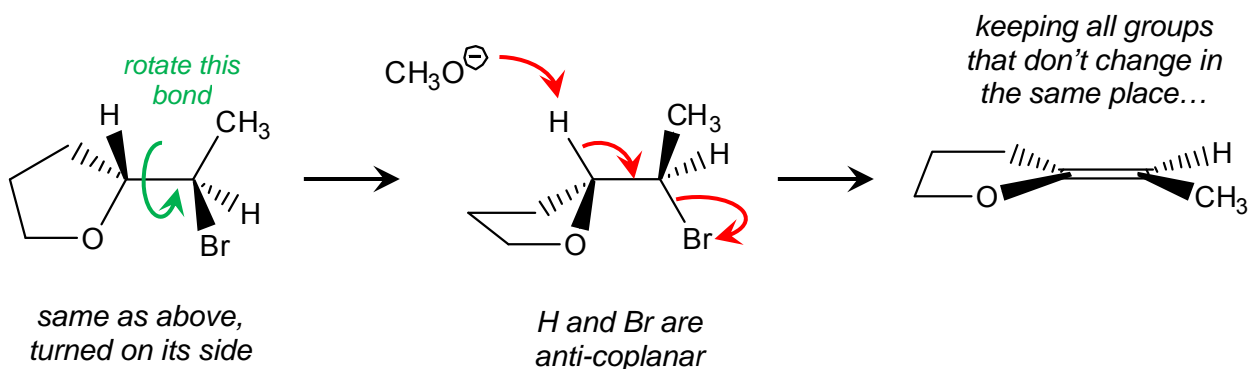
S_N2 , S_N1 , E2 and E1 reactions don't take place at sp^2 -hybridized carbons; they only work when everything is sp^3 . (In lecture I mentioned a single, somewhat obscure exception to this. This reaction is not that exception.) Because the iodide leaving group is bound to an sp^2 -hybridized carbon, none of these products will be formed.

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".



In general, sodium methoxide is a strong base, and a better base than it is a nucleophile, so it will react with this halide via E2 if it can. There are two H's on carbons adjacent to (α to) the leaving group—the methyl group, and the wedge H on the ring. The ring H would give the more substituted alkene product, so we'll focus on it.

E2 requires anti-coplanar arrangement of the H being taken and the leaving group. The way the molecule is drawn, the H and Br are not on opposite sides of the C-C bond that connects them, so that bond will need to rotate to put them in position:



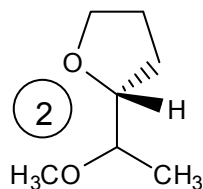
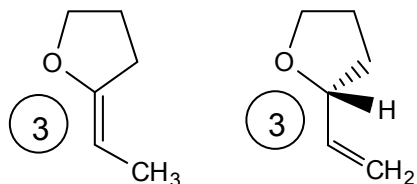
Rubric for this part:

5 points for correct structure.

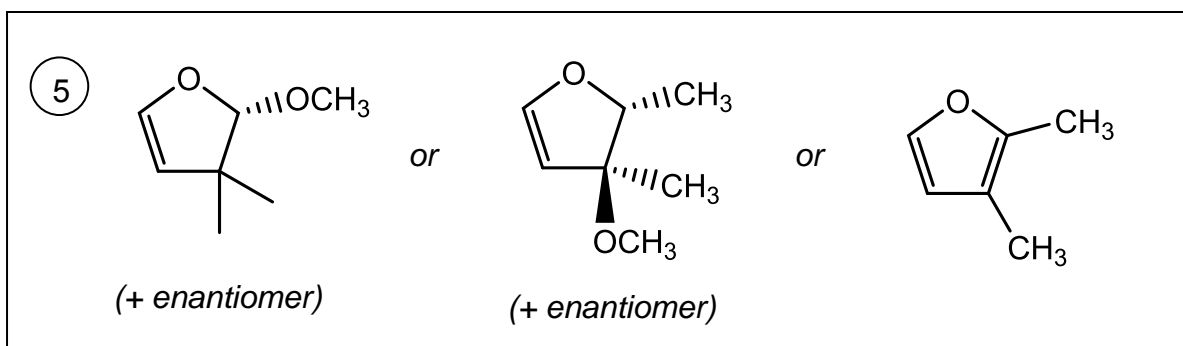
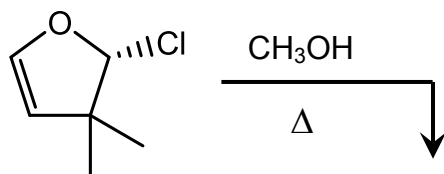
3 points partial for bromine elimination product with wrong or unclear stereochemistry or wrong regiochemistry.

2 points partial for any bromine substitution product.

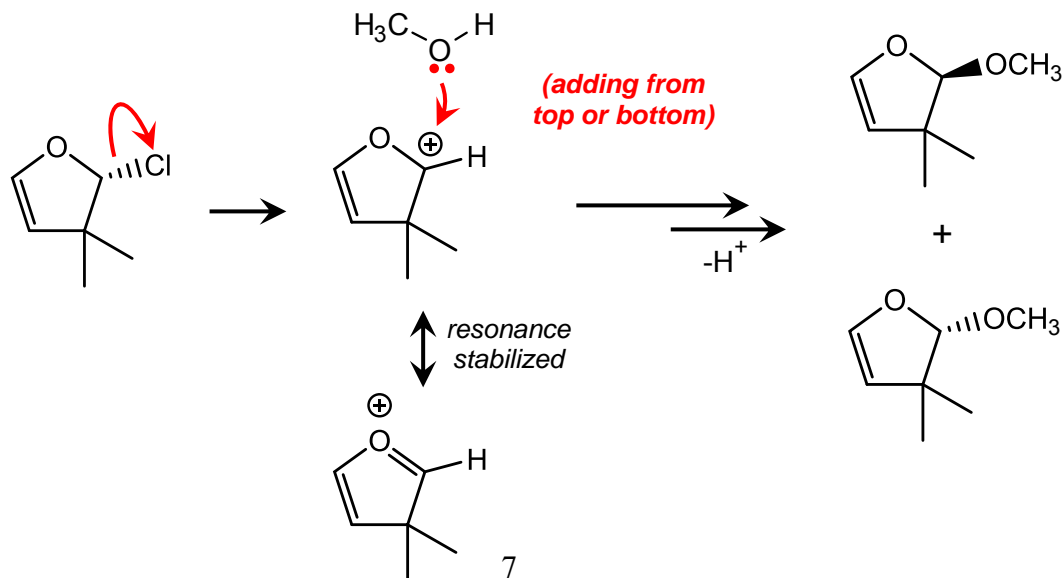
-2 points for each clearly trivial structure mistake. The answer that you intend needs to be clear for you to get these points.



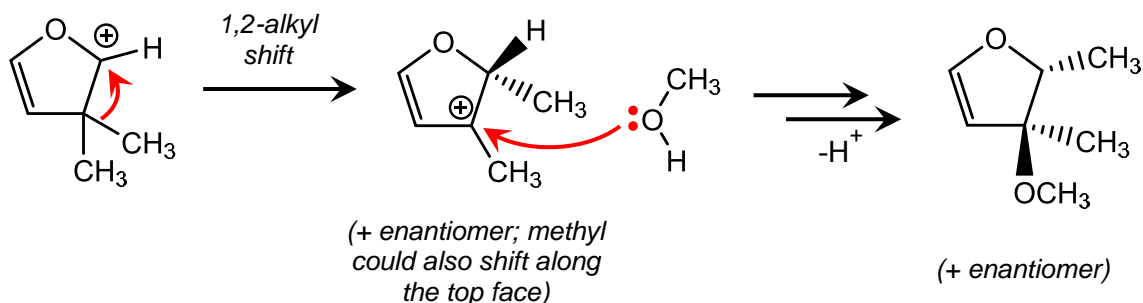
(with any stereochemistry at -OCH₃)



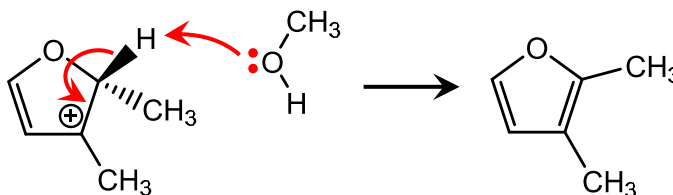
The conditions listed—poor nucleophile, resonance-stabilized cation intermediate—would promote reaction by S_N1 or E1. When I constructed this problem, I imagined that the molecule couldn't react via E1, because there is no proton that can be taken one carbon away from the leaving group. So I imagined this had to be an S_N1 reaction.



However, a couple of test-takers pointed out that the secondary, resonance-stabilized carbocation could become a tertiary resonance-stabilized carbocation by 1,2-alkyl shift. 1,2-alkyl shifts are uncommon, and require heat to overcome a significant kinetic barrier, but they can happen when they lead to further stabilization of an intermediate carbocation. Though I didn't see it when I wrote this problem, that could happen here:



Here, I have methanol adding as an S_N1 nucleophile to the opposite face of the carbocation from the adjacent, sterically hindering $-CH_3$ group. Alternately, the reaction could go $E1$:



Not many of you proposed answers with 1,2-alkyl shifts (which is good, because they are very unusual), but for those of you that did, we accepted these two alternative answers.

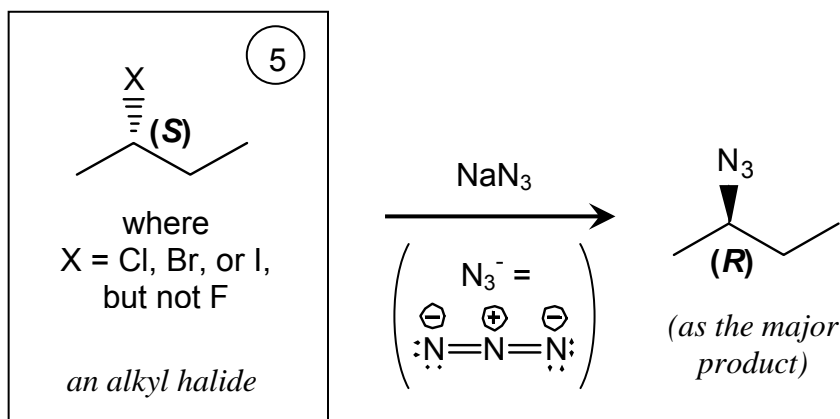
Rubric for this part:

5 points for correct structure and for including "+ enantiomer" in the box.

4 points partial for omitting "+ enantiomer" from an answer that required it.

3 points partial for inversion of stereochemistry only (as if reaction were S_N2), or for not illustrating stereochemistry in your answer.

-2 points for each clearly trivial structure mistake.



Azide (N_3^-) is a good nucleophile, so this can be introduced via $\text{S}_{\text{N}}2$ substitution. $\text{S}_{\text{N}}2$ involves inversion of configuration (stereochemistry), so our starting material will have the leaving group with the opposite stereochemistry relative to the product azide.

Rubric for this part:

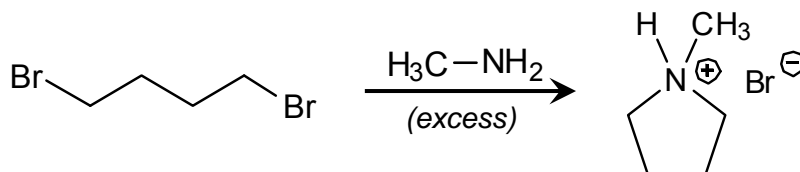
5 points for correct structure, with correct stereochemistry. It doesn't matter how you oriented/drew your answer, as long as it was (S).

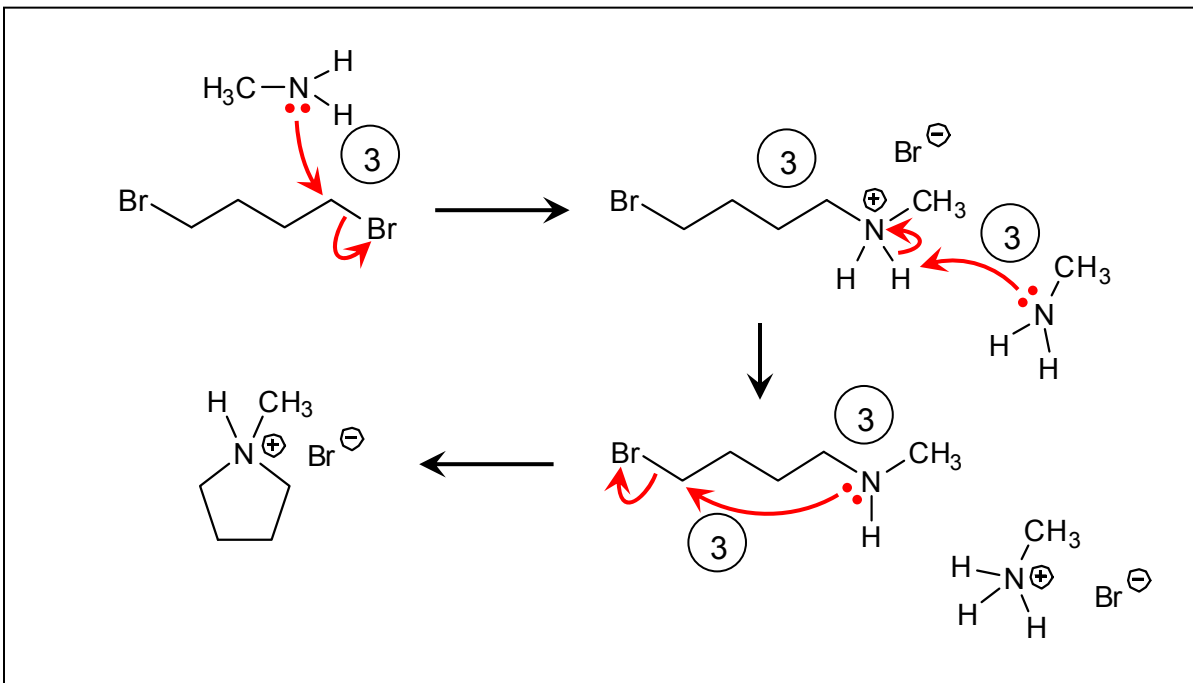
3 points partial for retention of stereochemistry (R), for not illustrating stereochemistry, or for writing "+ enantiomer".

-2 points for each clearly trivial structure mistake.

4. (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.





Rubric:

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 for good (e.g., Br^- , CH_3NH_3^+) and spectators may be omitted.

-2 points for each step combined with another. (Say, an $\text{S}_{\text{N}}2$ step and an acid-base step.)

-2 points for each use of a generic or incorrect acid/base. For example, the amine is your only base; you can't use OH^- or any other base you may have used in other problems.

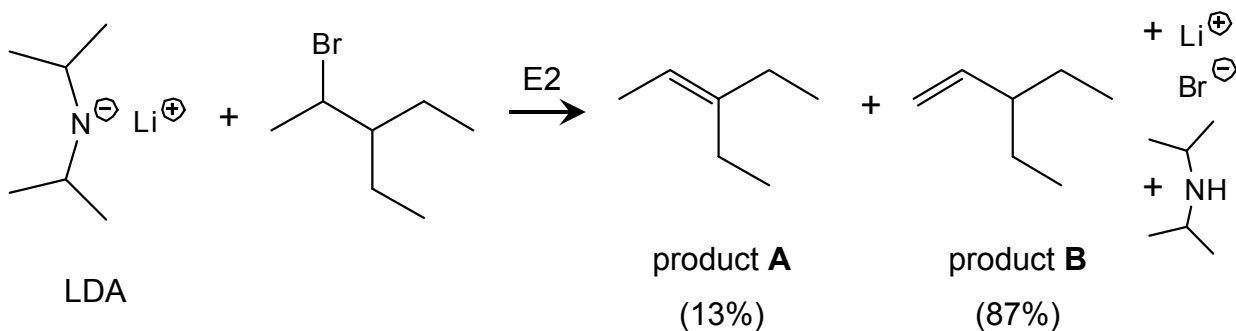
3 points for each set of electron-pushing arrows.

-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.

3 points for each intermediate.

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

5. (23 pts) Lithium diisopropylamide (LDA) is a strong, sterically hindered base that reacts with alkyl halides preferentially via E2 elimination. For example, LDA reacts with 2-bromo-3-ethyl-pentane to yield two alkenes:

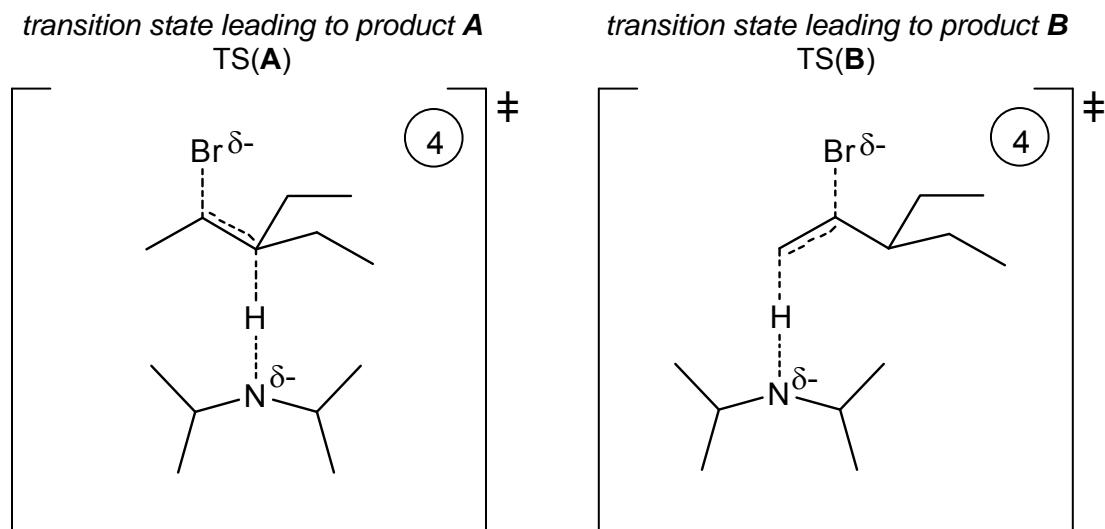


- (a) Which of the two alkenes is more substituted, **A** or **B**? (Circle one.)
- (b) Which of the two products is more stable, **A** or **B**? (Circle one.)

Product **A** is a trisubstituted alkene, and product **B** is a monosubstituted alkene. So **A** is more substituted. More substituted alkenes are more stable alkenes, so **A** is also more stable.

The unusual aspect of this reaction is that the less stable alkene—product **B**—is the predominant product. Hammond's Postulate says that this isn't usually the way things happen; the more stable product is usually associated with the more stable transition state, which controls product selectivity. Here, something must be making the more stable product have the less stable transition state.

- (c) In the brackets below, draw the structure of the transition state encountered on the path to each product.



Rubric for part (c):

4 points for each TS structure (8 points total for part c).

2 points partial for base nitrogen (1 point) attached to correct proton (1 point).

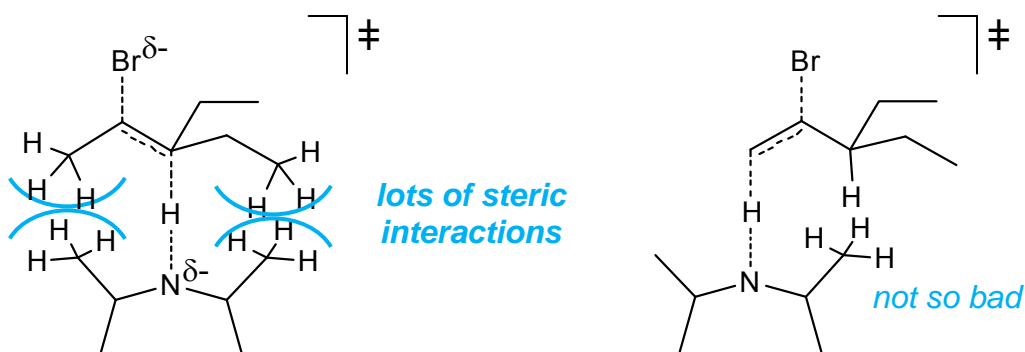
1 point partial for all bond orders (including partial, dashed bonds) correct.

1 point partial for both partial charges correct (and no extra ones).

(d) Which transition state is more stable, **TS(A)** or **TS(B)**? (Circle one.)

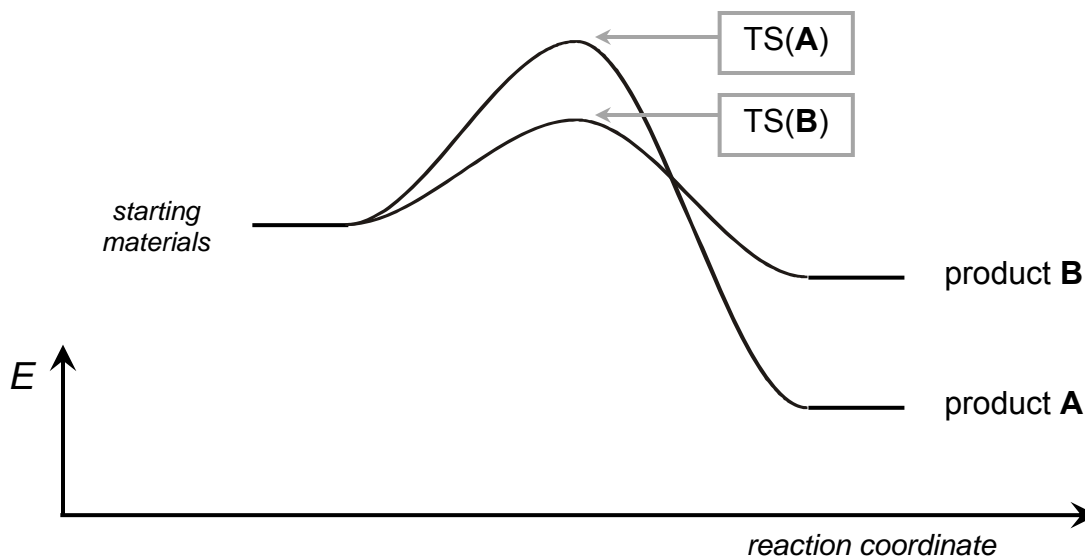
2

The transition state on the way to product **A** is much more sterically hindered than the transition state to product **B**:



This means **TS(B)** is more stable than **TS(A)**. This explains the product distribution at the beginning of the problem; product **B** is favored (87%).

(e) Draw a potential energy diagram that describes the generation of both products **A** and **B** from starting materials. Your diagram should have one curve leading to each product. Label transition-state ["**TS(A)**" and "**TS(B)**"] and product ("**A**" and "**B**") energy levels on your drawing. Your answer should also clearly illustrate the relative energies of transition states and products. I have already drawn the starting material energy for you.



Rubric for part (e):

9 points total for potential energy diagram.

2 points partial for drawing two curves with one step each.

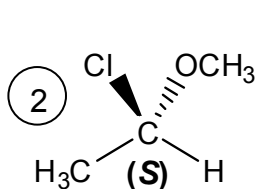
2 points for drawing product energy levels consistent with answer to (b). It doesn't matter whether they are correct or incorrect, only that they are consistent with (b).

2 points for drawing transition state energy levels consistent with answer to (d). Again, only criterion for points is consistency with (d), not correctness.

1 point for making both reactions exothermic.

2 points for drawing the correct answer. You can get these points even if you don't get previous ones.

6. (19 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.

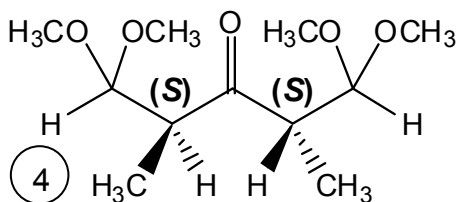


CHIRAL

or

ACHIRAL ?

This molecule has one chiral center, so it must be chiral.

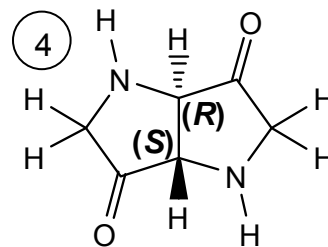


CHIRAL

or

ACHIRAL ?

This molecule is (*S,S*), and so its mirror image would be (*R,R*)—a different molecule. So, because the molecule is not the same as its mirror image, it's chiral.



CHIRAL

or

ACHIRAL ?

A molecule is *meso* if the (*R*) and (*S*) centers have the same groups attached. That is the case here, so the molecule is achiral.

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.

3 points for each circle.