

1. (14 pts) For each of the pairs of acids (or bases) below,
- Draw the conjugate base (or acid).
 - Circle whether you think the first acid (or base) is more or less acidic (or basic) than the second.

Acid	Conjugate Base	Base	Conjugate Acid
$\text{H}_3\text{C}-\text{C}(=\text{O})-\text{OH}$	<div style="border: 1px solid black; padding: 10px; display: inline-block;"> $\text{H}_3\text{C}-\text{C}(=\text{O})-\text{O}^-$ </div> <div style="text-align: right; margin-top: -10px;">(2)</div>	$\text{H}-\text{C}(=\text{O})-\text{H}$	<div style="border: 1px solid black; padding: 10px; display: inline-block;"> $\text{H}-\text{C}(=\text{O})-\text{H}^+$ </div> <div style="text-align: right; margin-top: -10px;">(2)</div>
is		is	
MORE ACIDIC	<div style="border: 2px solid black; border-radius: 15px; padding: 5px; display: inline-block;"> LESS ACIDIC </div>	MORE BASIC	<div style="border: 2px solid black; border-radius: 15px; padding: 5px; display: inline-block;"> LESS BASIC </div>
than	(3)	than	(3)
$\text{F}_3\text{C}-\text{C}(=\text{O})-\text{OH}$	<div style="border: 1px solid black; padding: 10px; display: inline-block;"> $\text{F}_3\text{C}-\text{C}(=\text{O})-\text{O}^-$ </div> <div style="text-align: right; margin-top: -10px;">(2)</div>	$\text{H}-\text{N}(\text{H})-\text{H}$	<div style="border: 1px solid black; padding: 10px; display: inline-block;"> $\text{H}-\text{N}(\text{H})-\text{H}^+$ </div> <div style="text-align: right; margin-top: -10px;">(2)</div>

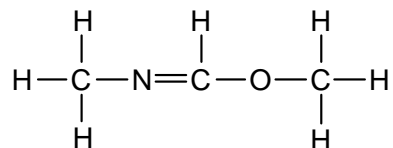
The electronegative fluorine atoms on the bottom trifluoroacetate anion stabilize the negative charge, via inductive effects, better than the $-\text{CH}_3$ group on the acetate anion. Because the bottom conjugate base is more stable, the bottom acid is more acidic.

Both of the cation conjugate acids have the same number of resonance structures. But the nitrogen is less electronegative than the oxygen, and accommodates the positive charge better. Because the bottom cation is more stable, the corresponding bottom base is more basic.

Rubric:

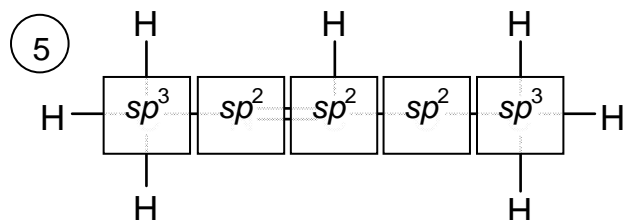
- 2 points per conjugate acid/base structure. No partial credit.
- 3 points per circled more/less acidic/basic.

2. (14 pts) For the molecule drawn at right, in the boxes provided:

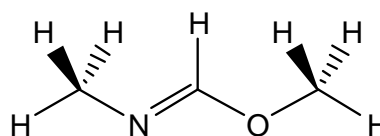


- Draw all significant resonance structures. In each structure, draw all atoms, bonds, lone pairs of electrons, and formal charges.
- Draw a Lewis wedge/dashed-bond structure that illustrates the most stable three-dimensional conformation of the molecule. Draw all atoms, bonds, and charges, but omit lone pairs.
- In the boxes provided, write the hybridization state on any atom heavier than hydrogen.

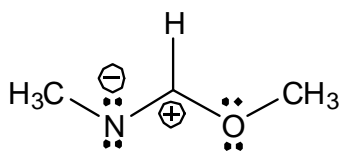
atom hybridizations:



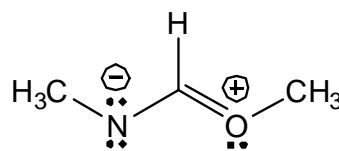
3-dimensional representation



resonance structure



resonance structure



Rubric:

-1 point for mistakes in structure (left out an H, etc.)

Hybridizations: 1 point each. (5 points this part.)

3-D drawing: 3 points total.

1 point for flat, *anti* (180°) H-C-X-C.

1 point for flat, *anti* (180°) C-X-C-X.

1 point for correct wedges and dashes (same side) on -CH₃ groups.

Resonance structures: 3 points each.

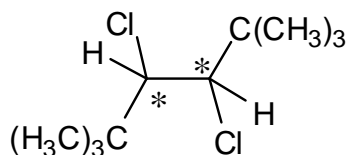
1 point for formal charges (both charges must be correct).

1 point for lone pairs (all must be correct).

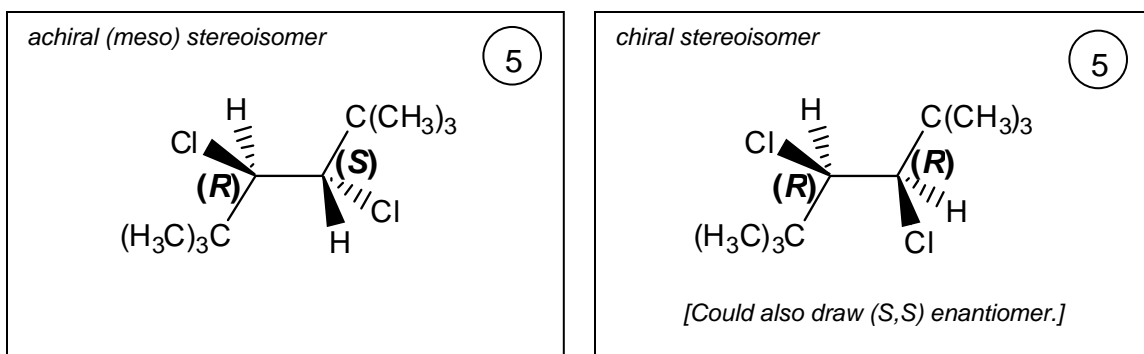
1 point for bonds (all must be correct).

Resonance structures need not be in 3-D, or have correct bond angles.

3. (39 pts) The molecule below has two chiral centers (marked with asterisks) and three stereoisomers; one stereoisomer is achiral (*meso*), and two are chiral. Each stereoisomer reacts with NaOCH₃ via E2 elimination to yield, selectively, a single alkene product.



- (a) I have drawn the molecule above entirely in the plane of the page, without any stereochemical information. **Using wedge and dashed-bond lines**, draw the achiral stereoisomer and one of the two chiral stereoisomers as three-dimensional structures. Then, **label each stereocenter** in your structures “(R)” or “(S)”.



Rubric (part a):

3 points for each correct wedge-dash structure. *No partial credit.*

1 point for each Cahn-Ingold-Prelog assignment. (2 total each structure.)

Full credit for assigning correct letters to incorrect structure.

- (b) What is the stereochemical relationship between the two molecules you drew above? Are they

enantiomers

or

diastereomers

or

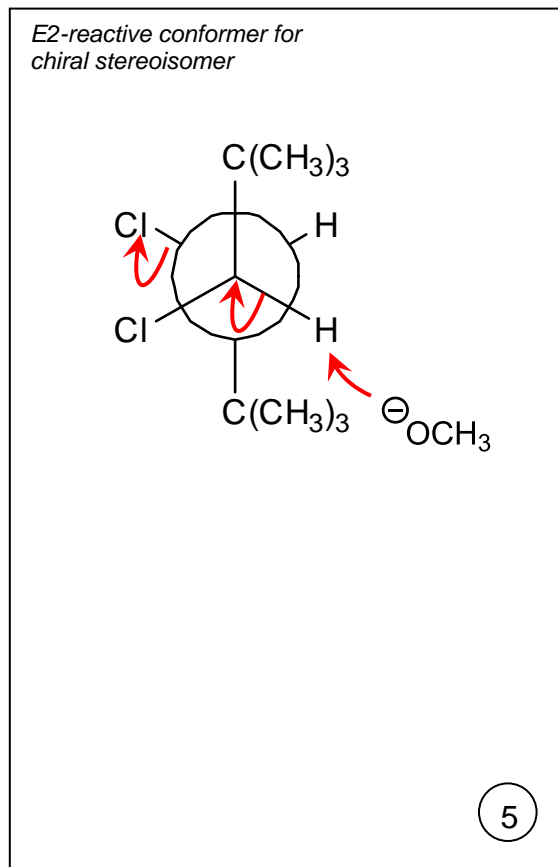
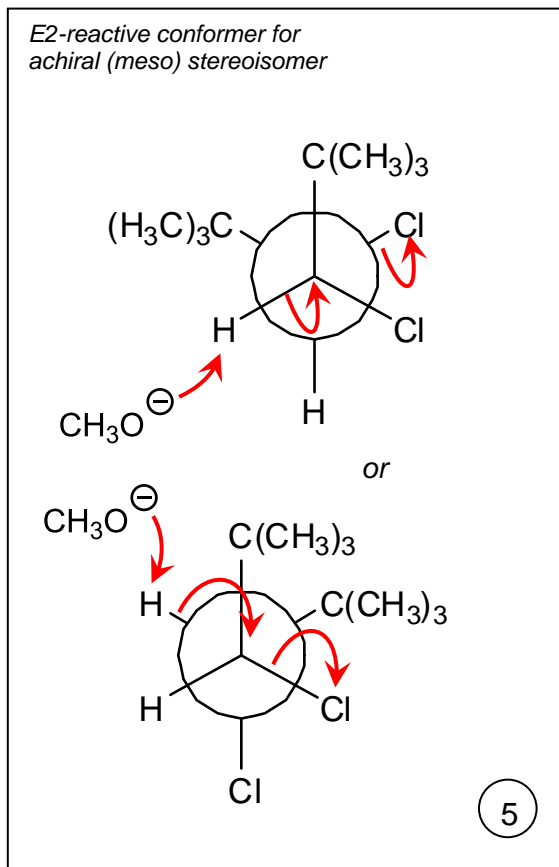
neither

?

3

Rubric (part b): Full credit for any answer that is consistent with part (a).

- (c) E2 elimination requires a very specific geometric relationship between the leaving group and the proton being taken by the incoming base. In the boxes below, draw a Newman projection for each of the stereoisomers you drew above that puts the proton and leaving group in the right orientation to undergo E2. Then, “push arrows” on each diagram to illustrate the mechanism of the E2 elimination.



Rubric (part c):

3 points for each Newman projection.

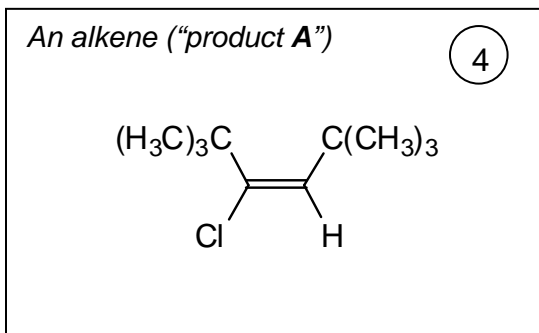
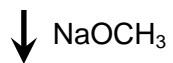
Answers that are consistent with (a) receive full credit, even if (a) is incorrect.

-1 point for each trivial structural mistake.

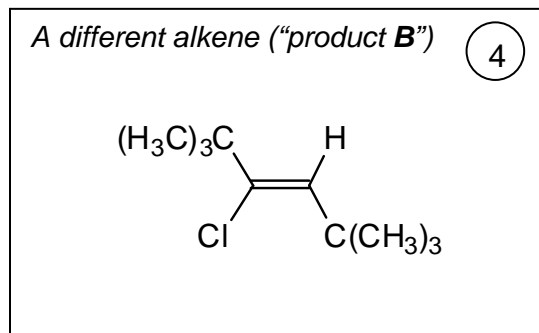
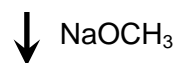
2 points for correct arrow pushing.

(d) Which alkene product will be generated via E2 from each of the two stereoisomers you drew?

achiral (meso) stereoisomer



chiral stereoisomer



Rubric (part d):

4 points for each alkene. (8 total.)

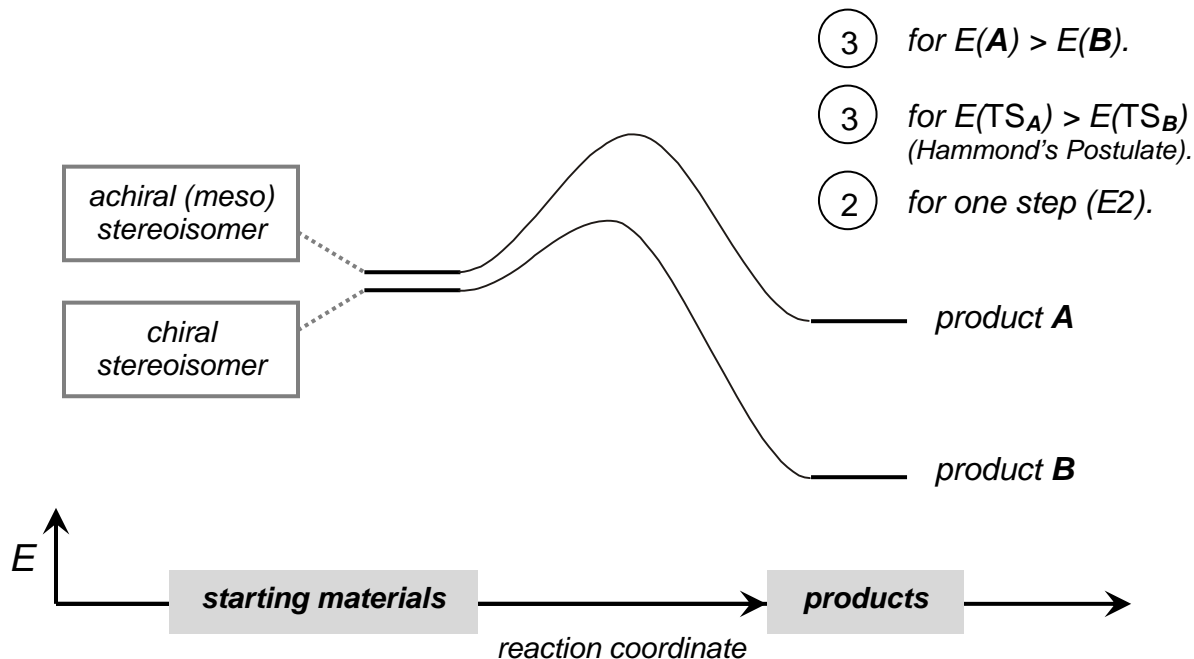
Full credit for stereochemistry that is consistent with (c). So if answers to (d) are switched because answers to (c) are switched, full credit is possible.

2 points partial for incorrect alkene stereochemistry.

If same answer drawn twice, credit only given for one of two answers. This is true even if answers to (c) are drawn twice/the same.

(e) On the potential energy diagram below, draw curves that represent the E2 elimination of each starting material to products **A** and **B**. The starting material energies have already been drawn for you (we will assume they are equal in energy)—you need to connect these starting points to transition state and product energies. Your curves should answer the following questions:

- Is product **B** higher, lower, or equal in energy relative to product **A**? Label your diagram so that it is clear which product energy level corresponds to which product.
- How many steps, and how many transition states, does each E2 pathway have?
- Is the overall activation energy for making product **B** larger, smaller, or equal to the activation energy for making product **A**?



In product **A**, the two bulkiest groups—the *tert*-butyl groups—are *cis*- to one another, whereas those same groups are *trans*- in product **B**. So, steric interactions will make product **A** less stable than product **B**. The E2 mechanism involves just one concerted step, with one transition state. Hammond's Postulate says that the relative transition-state energies for the two pathways should reflect that difference in product energies, meaning that the barrier to product **A** should be higher.

Rubric (part e):

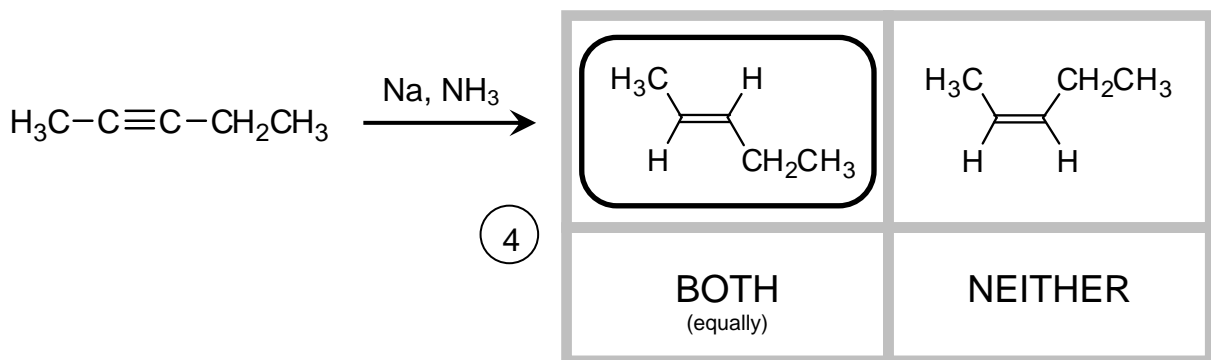
Scoring depends entirely on answers to part (d). If answer to (d) is incorrect, but the relative energy of the two products in (d) is accurately depicted in the potential energy diagram, you can get full credit.

3 points for ordering product energies correctly [here, $E(\mathbf{A}) > E(\mathbf{B})$].

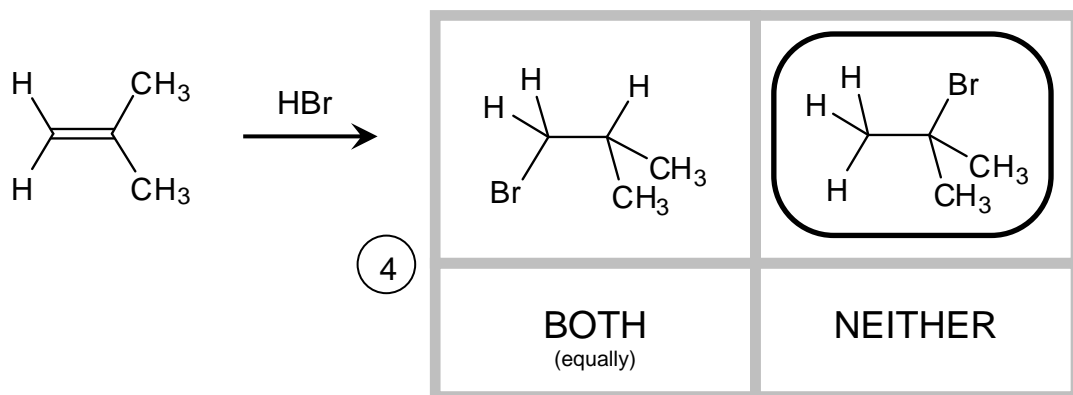
3 points for ordering transition-state energies the same [$E(\text{TS}_A) > E(\text{TS}_B)$], with a larger gap than starting materials.

2 points for both curves having just one hump.

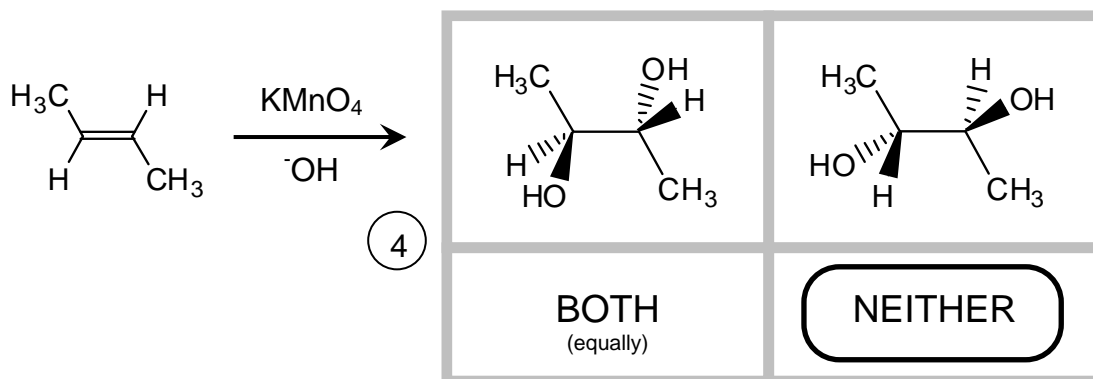
4. (20 pts) Each of the reactions below is drawn with two possible products. If one of the two products predominates, circle that preferred product. If the two products are produced equally, circle "BOTH". If neither product would result from the reaction, circle "NEITHER". **Circle one answer only.**



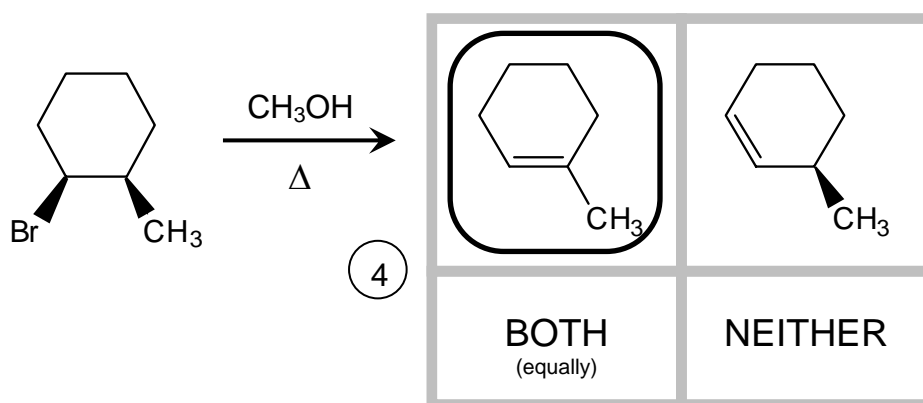
This protocol gives *trans*-alkenes. (As opposed to hydrogenation on "poisoned" Pd/BaSO₄, which gives *cis*-alkenes.)



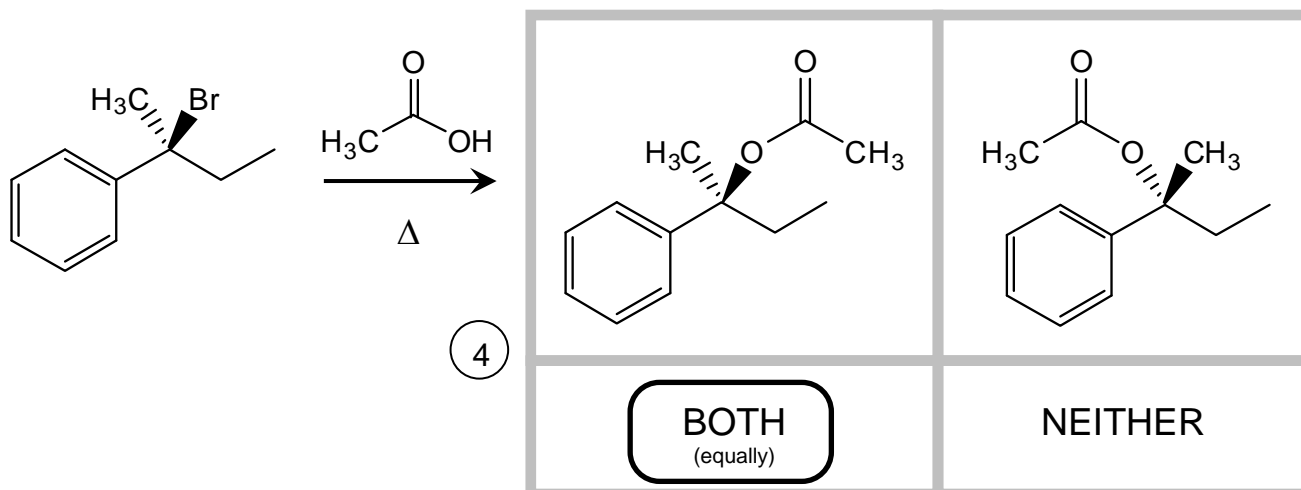
HBr adds to the double bond with Markovnikov regioselectivity (with X = Br attached to the more substituted carbon).



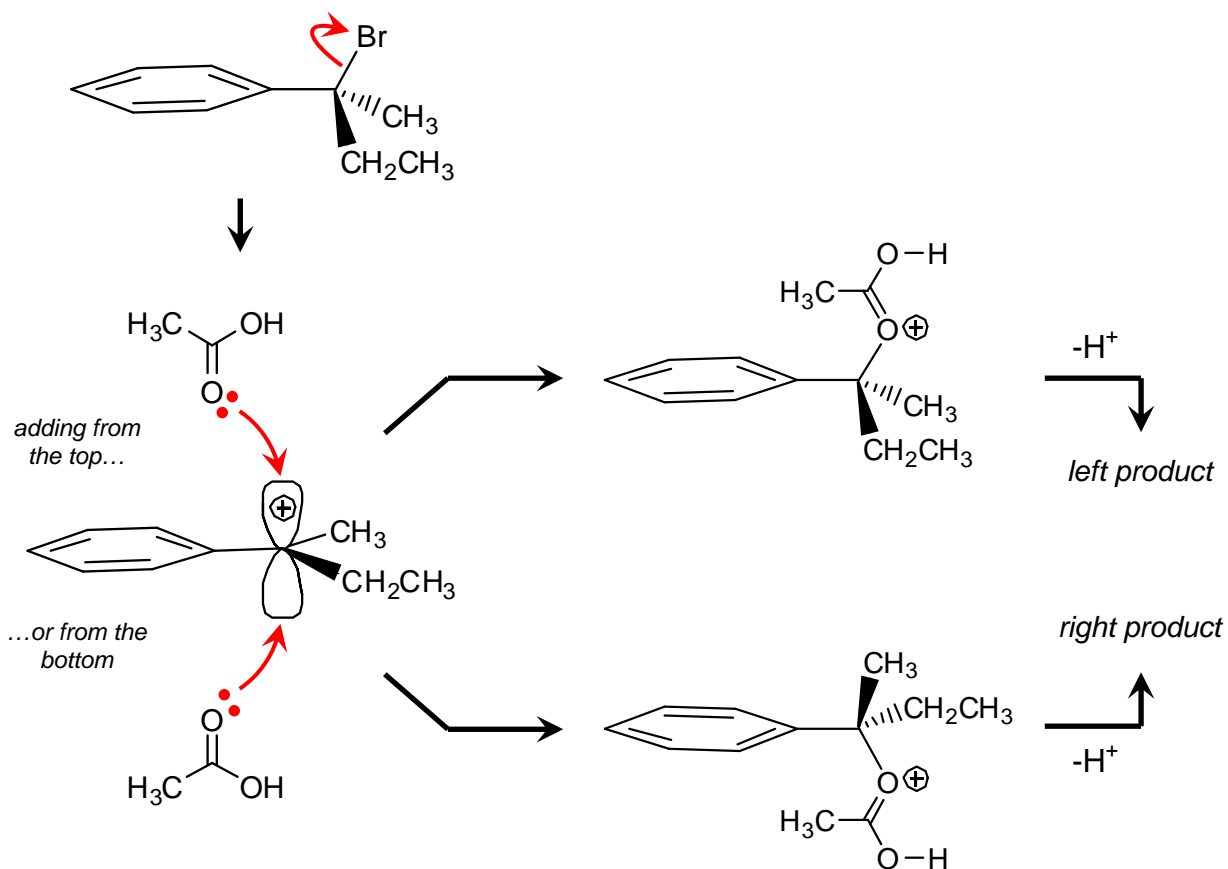
KMnO_4 performs *syn*-dihydroxylation on alkenes. Both of these products represent anti addition of two $-\text{OH}$ groups—that is, addition of the two groups to opposite faces of the original alkene. (In fact, I accidentally engineered this problem such that the two products are the same molecule.)



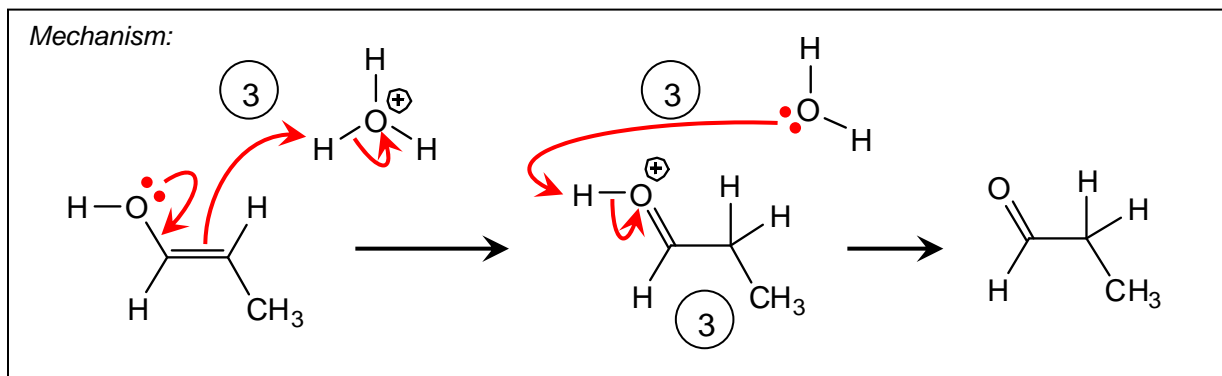
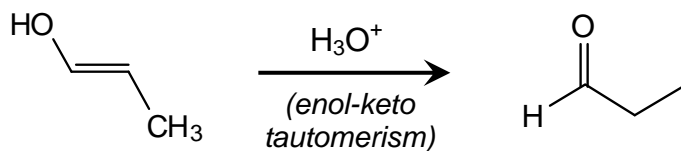
This is an $\text{S}_{\text{N}}1$ reaction, which will preferentially generate the most substituted (and thus most stable, or the “Zaitsev”) alkene.



This is an S_N1 reaction which passes through an intermediate carbocation. The flat carbocation can combine with acetic acid on either its top or bottom faces:



5. (9 pts) Draw a mechanism (using “electron pushing”) for each of the reactions shown below. Draw each mechanistic step explicitly; don’t cheat by combining multiple processes in a single step. Use only the molecules shown in the problem; don’t invoke generic species. (E.g., don’t use “H-A” as a generic acid.)



Rubric: (9 points total)

Overall notes:

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

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

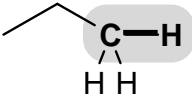
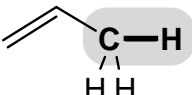
-4 points—two taken from each step—for putting steps in the opposite order. In acid (H_3O^+), there would be no base strong enough to deprotonate the alcohol and generate an anion first.

-6 points (out of 9 total) for drawing this as a one-step process (for combining the two steps).

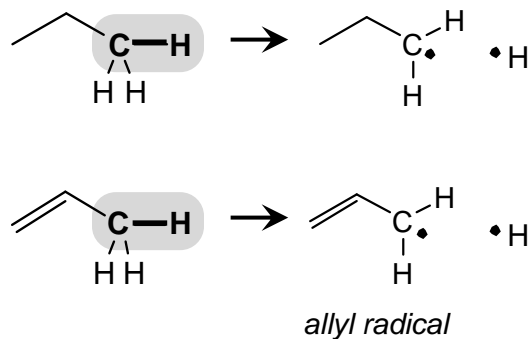
3 points for each arrow-pushing step;

3 points for intermediate.

6. (9 pts) Of the C-H bonds highlighted below, which:

(check one box in each column)	has a larger bond dissociation energy?	is broken to form a more stable radical?	would be converted more rapidly to a C-Br bond by Br_2 and light?
	<input checked="" type="checkbox"/> (3)	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input checked="" type="checkbox"/> (3)	<input checked="" type="checkbox"/> (3)
NEITHER (they are the same)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

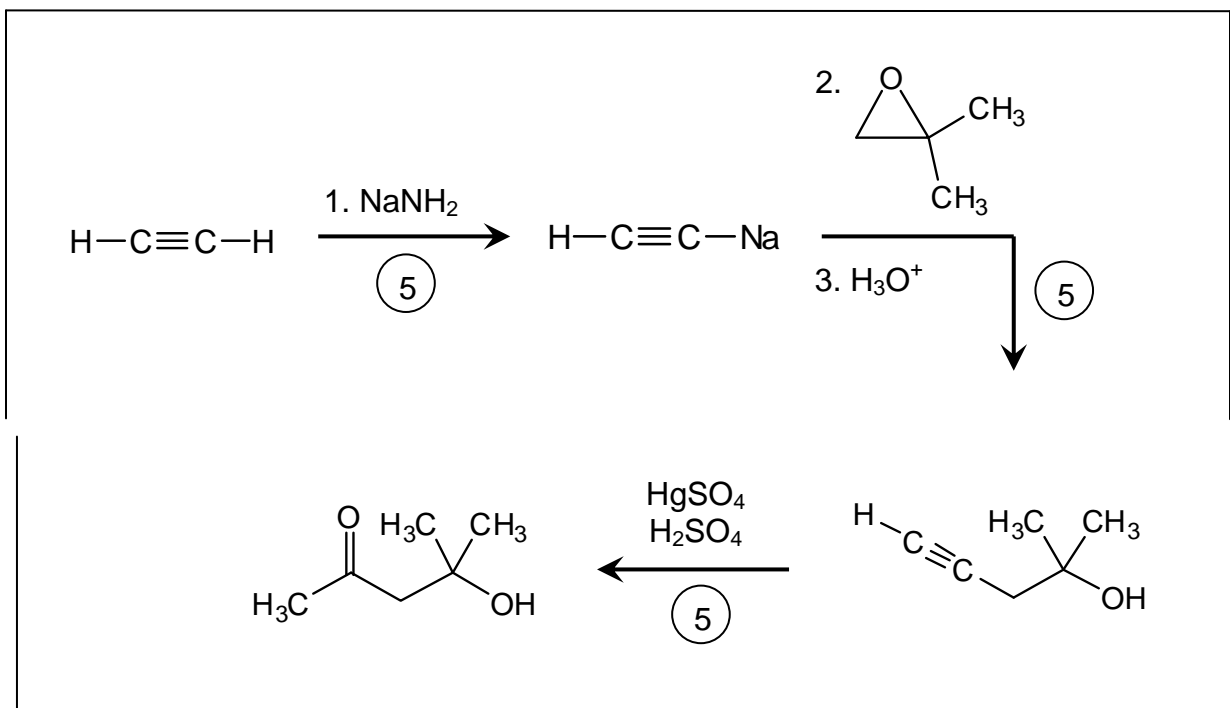
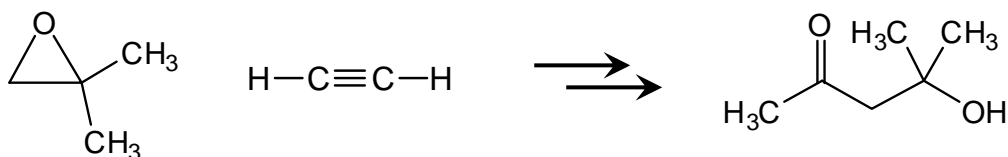
In a way, these three questions are actually all the same question. "Bond dissociation energy" (BDE) is the amount of energy it costs to break a bond into component radicals. The more stable the product radicals are, the less energy it takes to make them. These two C-H bonds would both generate primary radicals, but the second starting material would generate a resonance-stabilized allylic radical:



The allyl radical is more stable than the plain primary radical, and so the cost of making the allylic radical is lower and the BDE of the allylic C-H bond is smaller. That smaller BDE translates to a lower activation energy for generating that radical in the rate-determining step of halogenation, such that bromination at an allylic site is much more rapid than bromination at any ordinary alkyl site (no matter what the substitution pattern).

Rubric: 3 points each column.

7. (15 pts) For the starting materials and products shown below, **propose a multistep synthesis**. In addition to the molecules shown, you can use any reagents and reactions we've learned about in class. You might discover multiple answers to this problem; draw only your best (one) synthetic route. Feel free to draw an incomplete route—we will give you partial credit where we can.



Rubric:

General notes:

-1 point for each minor error in structures or reagents; if error propagates, points are taken off only for initial error.

-2 points if step reagents are incorrect, but reaction could otherwise be accomplished with correct reagents.

-2 points if reagents are correct, but product is wrong. If this happened, and you were led down an incorrect synthetic path by your mistake, you can also lose later points.

5 points for deprotonating alkyne with NaNH_2 .

There is no need to show alkynyl anion/alkynylsodium itself; just “ NaNH_2 ” is enough.

5 points for combining alkynylide with epoxide.

Can omit workup step.

Can combine this step with previous step on the same synthetic arrow.

5 points for converting alkyne to internal ketone (via Markovnikov addition of H-OH, followed by enol-keto tautomerism).

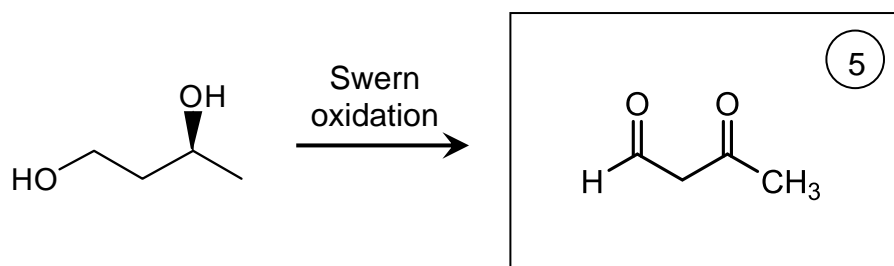
3 points partial for any multi-step approach to this last part. For example:

Lindlar or Na, NH_3 hydrogenation of alkyne to alkene, Markovnikov hydration, then oxidation to ketone;

Cleavage of alkyne with O_3 or KMnO_4 to give carboxylic acid, followed by addition of methyl lithium to give ketone;

...plenty of other options.

8. (18 pts) For each of the reactions on the following pages, fill in the empty box corresponding to the major product. Wherever appropriate, illustrate stereochemistry in your drawings (using wedge and dashed bonds). If multiple enantiomers or diastereomers are produced, indicate this in the answer box (e.g., by writing “+ enantiomer”, etc.)



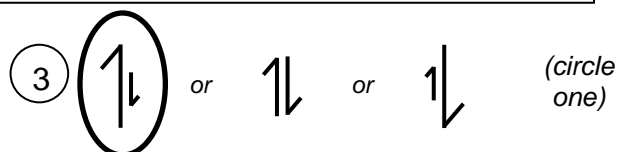
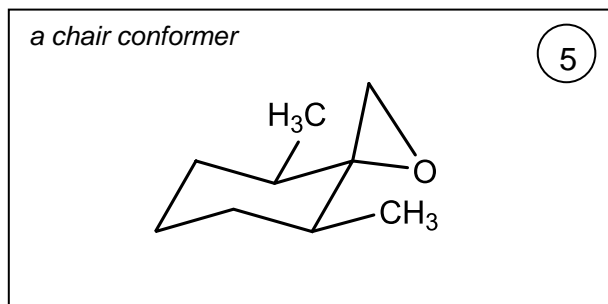
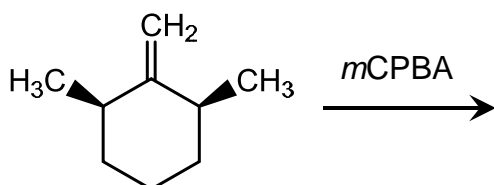
Swern oxidation is a mild oxidizing method, and will oxidize alcohols to aldehydes and ketones only. For the primary alcohol, that's an aldehyde; for the secondary alcohol, it's a ketone.

Rubric:

5 points for correct structure.

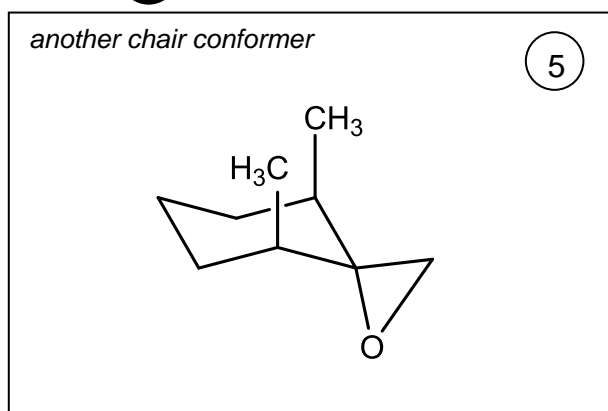
3 points partial for any other oxidized product, for either alcohol.

-2 points for each trivial structural mistake (omitting a carbon, etc.)



Special instructions for this part:

- Draw the preferred product as two equilibrating chair conformers (one per box). Feel free to omit H atoms from your structure.
- Indicate that one conformer is more stable than the other, or that they are equally stable, by circling the appropriate equilibrium arrow.



In principle, mCPBA could add to the alkene on the top face or the bottom face. I think there will be some preference for addition on the opposite face from the two methyl groups, with the oxygen atom added to the underside, but I think it could also go either way.

Rubric:

5 points each correct chair structure.

3 points partial (each chair) for diol. mCPBA doesn't have water present, so it would form an epoxide, not a diol.

-1 point for each (non-hydrogen) substituent drawn incorrectly. Equatorial substituents must be parallel to a ring C-C bond. Axial substituents must go up or down in same direction as attached carbon does.

It is not sufficient to just write labels "axial" and "equatorial" on your substituents; they need to be drawn correctly in 3-D.

3 points for correct equilibrium arrow.

To get these points, your chairs must interconvert. However, chairs do not need to be correct.