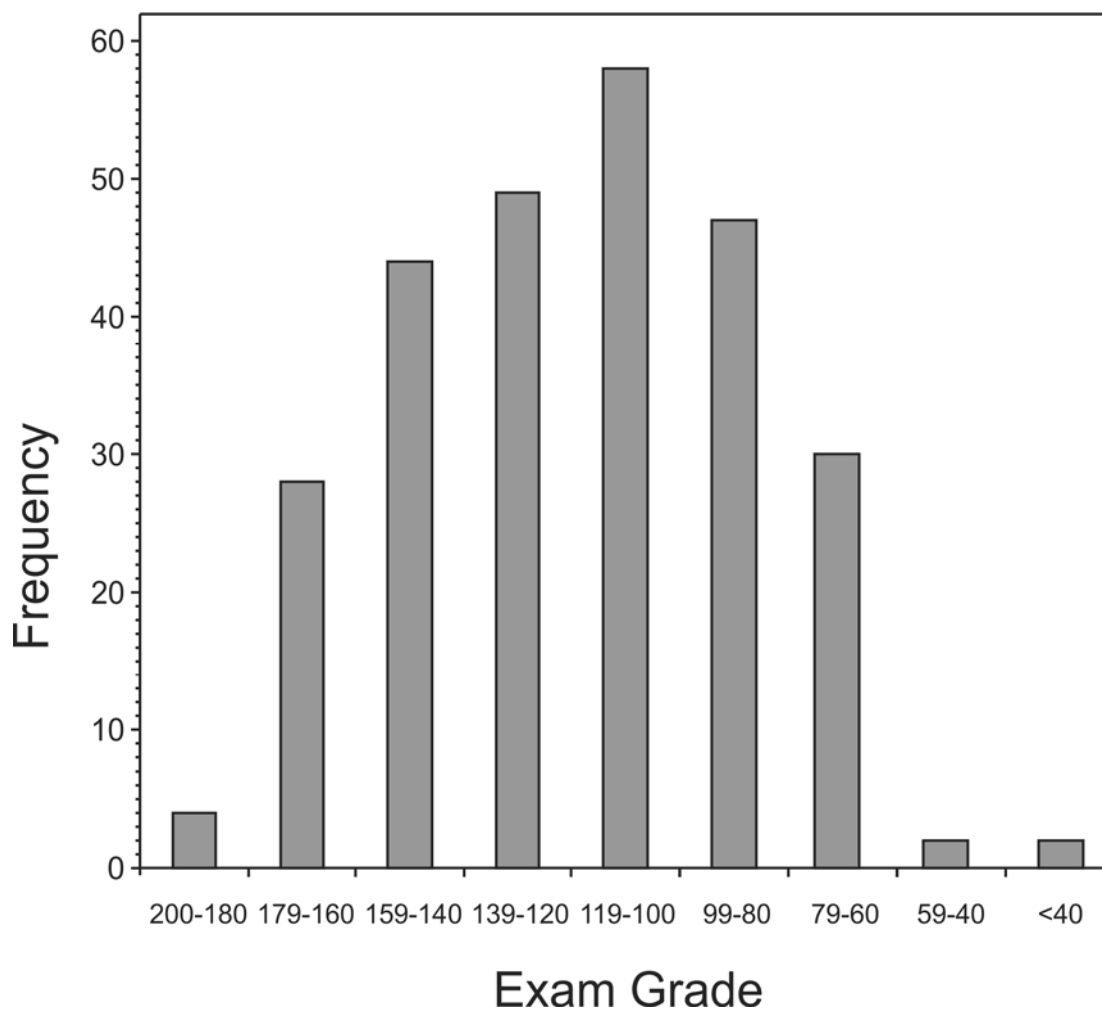


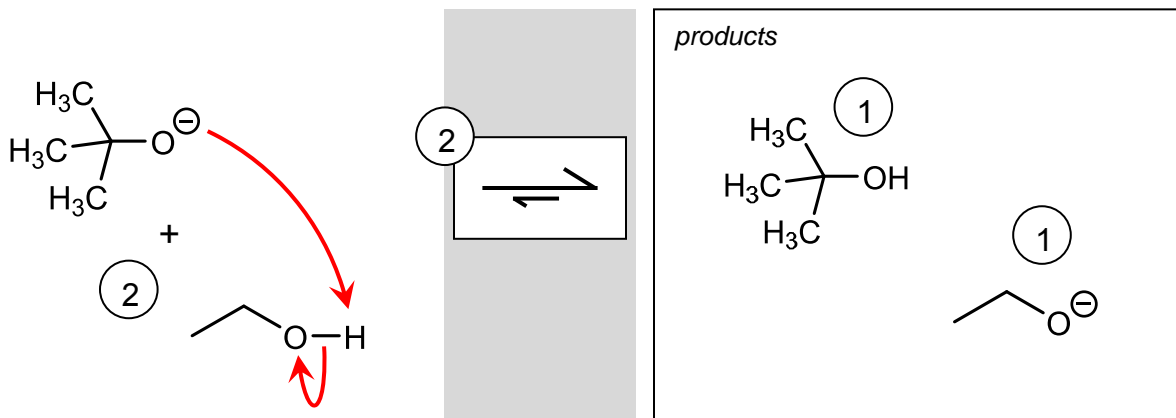
**Final Exam
Answer Key**

Final Exam Mean: 119
Final Exam Median: 117
Final Exam St. Dev.: 32

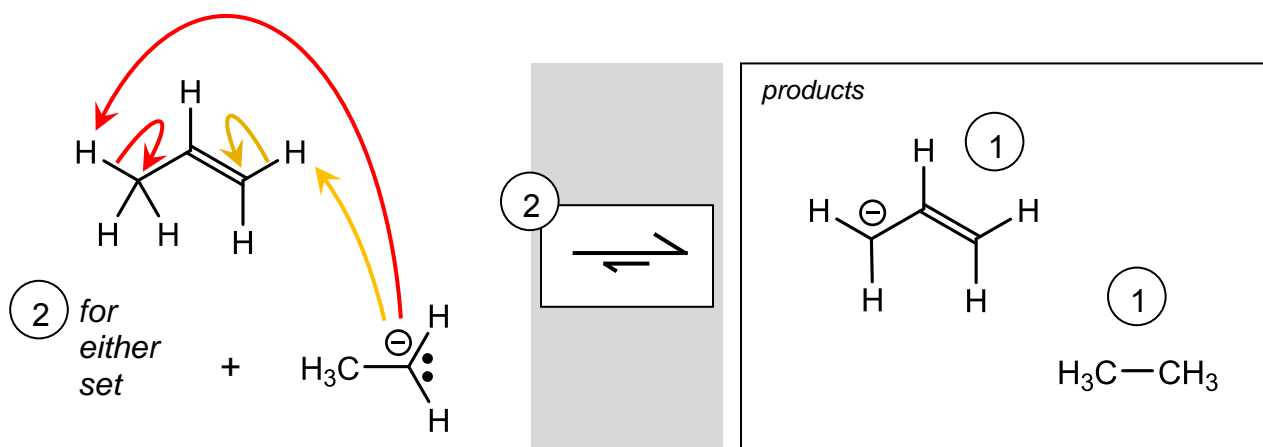


1. (12 pts) For each of the sets of molecules below:

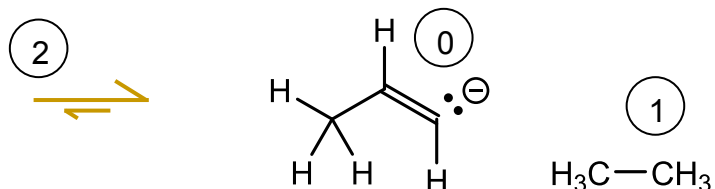
- Using “electron pushing” (with double-barbed arrows), show how the molecules on the left would react in an acid-base reaction to transfer a proton from one to the other.
- In the box on the right, draw the conjugate acid and base products of each reaction.
- In the middle, draw an equilibrium arrow that shows whether you feel the acid-base equilibrium would lie on the left or the right.



Remember that, most often, acidity and basicity are related to the relative stability of charged species on the reactant and product sides of an acid-base reaction. Here, we are comparing the stability of *tert*-butoxide on the left with ethoxide on the right. *tert*-Butoxide is less stable, because its many electropositive methyl groups push electron density towards the negatively charged oxygen. That de-stabilizes the charge, makes *tert*-butoxide less stable, and pushes our equilibrium rightwards.



incorrect answer, but still worth most of credit:



Our sp^3 -hybridized ethyl anion on the left is super unstable; remember that, of all the hybridizations, sp^3 -hybridized atoms act the least electronegative, so we'd expect this carbon to be the least stable with its negative charge. There are actually a couple of different H's that the anion could take: an sp^2 -hybridized C-H bond, which would lead to an anion stabilized more by hybridization, or an H on the other side, which would yield a resonance-stabilized allyl anion. Resonance (when there are multiple major resonance structures) is more important than hybridization, so we would expect the allyl anion to be preferred. (Nevertheless, you only lost one point if you chose the vinyl anion instead.)

Rubric: For each acid-base reaction,

2 points for electron pushing (one point each curved arrow).

You can start arrow from a lone pair or from a negative charge sign (if available).

Products do not have to be correct to receive points for arrow pushing.

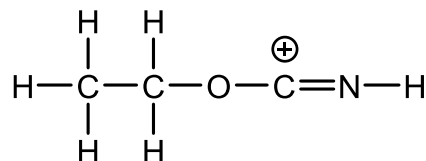
2 points for equilibrium arrow direction.

2 points for each set of products (1 point each).

No partial credit (no point value less than 1).

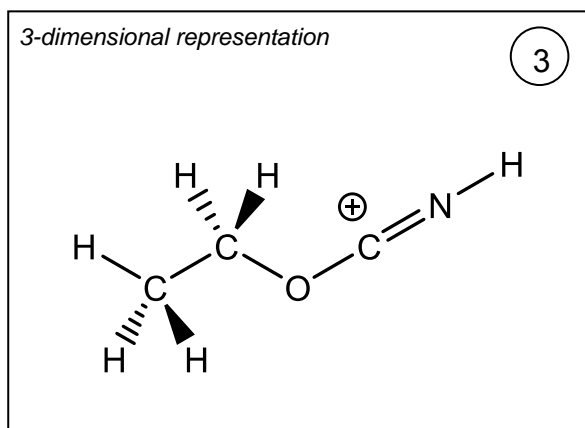
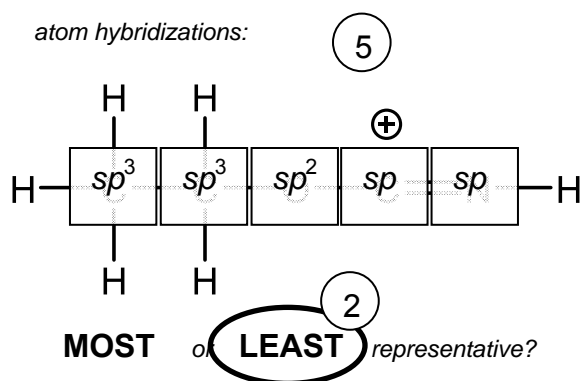
2. (16 pts) For the ion drawn at right, in the boxes provided:

- Draw all significant resonance structures. In each structure, draw all atoms, bonds, lone pairs of electrons, and formal charges. Then, circle which resonance structure you think is the most representative, and which is the least. **Circle only one MOST and one LEAST.**

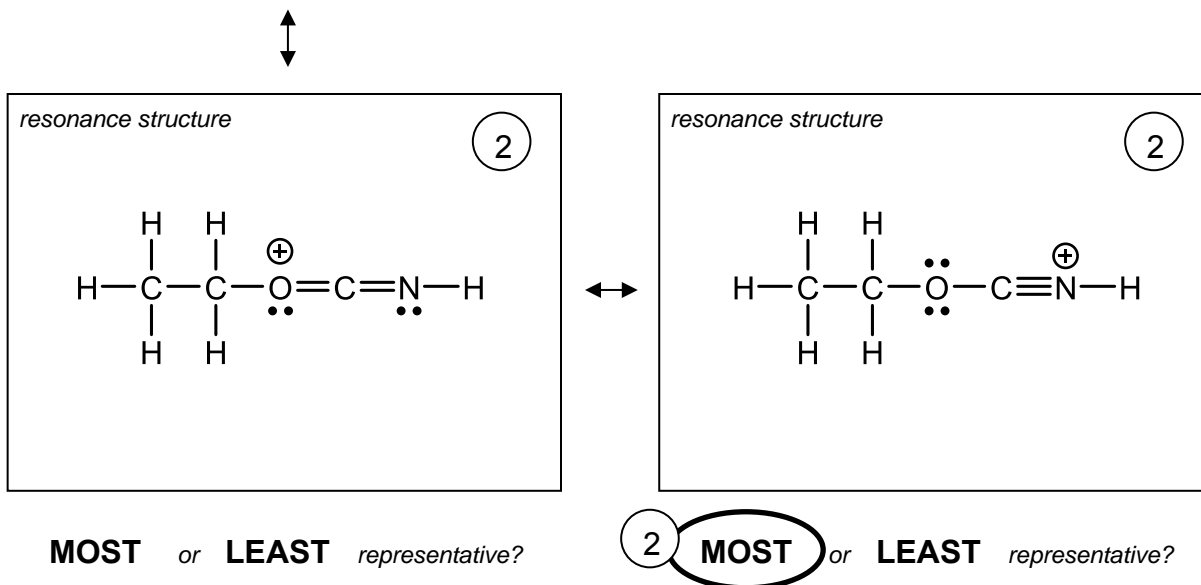


- Draw a Lewis wedge/dashed-bond structure that illustrates the most stable three-dimensional conformation of the molecule. Draw all atoms, bonds, and charges, but omit lone pairs.

- In the boxes provided, write the hybridization state on any atom heavier than hydrogen.



Why is the N *sp*-hybridized? In order to determine hybridization, you have to look at all of the major resonance structures, and pick the lowest hybridization state you see for each atom. This is not a major resonance structure, so you have to look at the major one below.



Rubric:

-1 point for each trivial mistake in structure (left out an H, extra C, etc.)

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

3-D drawing: 3 points total.

1 point for *anti* (180°) dihedral angle at C-C-O-C.

(*Anti conformation puts the largest groups farthest away from each other.*)

1 point for illustrating tetrahedral carbons correctly.

Tetrahedral centers are illustrated as having two bonds in the plane of the page on one side of the center, and two bonds out of the plane (one forward, one back) on the other side. Hydrogens must be staggered.

1 point for 180° centers drawn as linear.

Resonance structures: 2 points each.

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

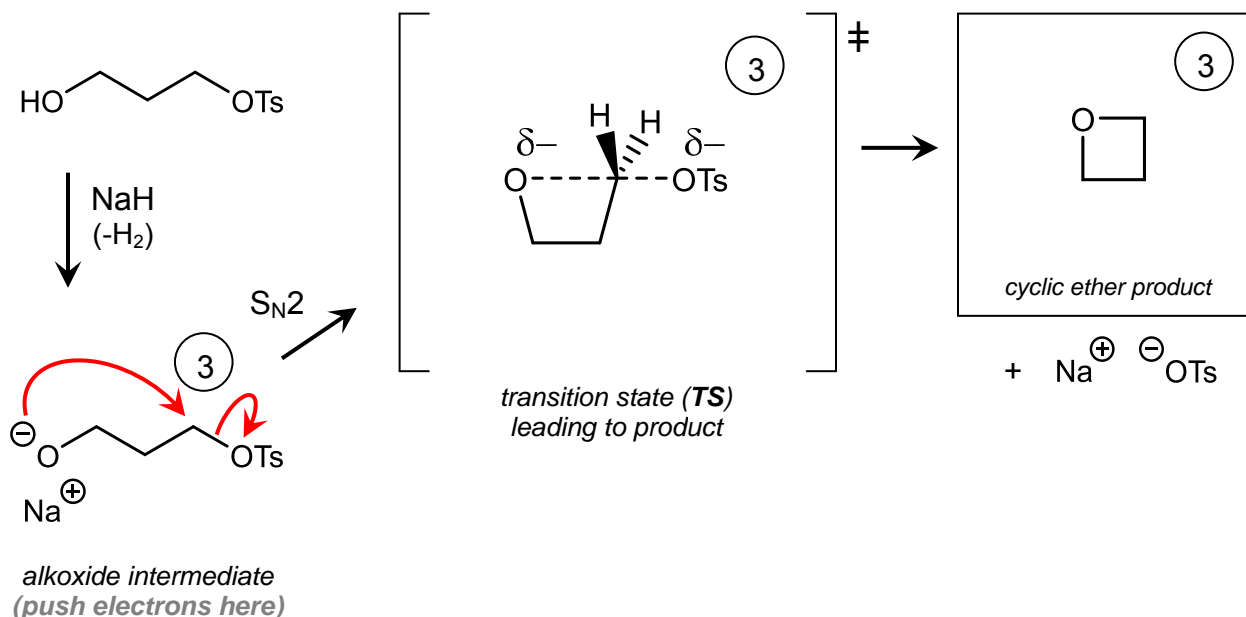
1 point for bonds (all must be correct).

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

Contributions (MOST/LEAST): 2 points each.

No credit for multiple MOSTs or multiple LEASTs.

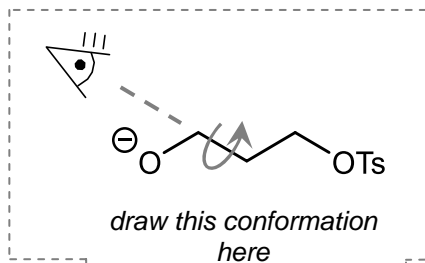
3. (37 pts) Cyclic ethers can often be synthesized by an intramolecular, ring-closing S_N2 reaction. For example, when the alcohol starting material shown on the next page is deprotonated with NaH, the resulting alkoxide reacts with itself to form a cyclic product.
- Draw the product** in the empty box on the right. Then, **draw a transition state structure** that illustrates the conformation of the transition state in the S_N2 reaction.
 - Using “electron pushing”, draw a mechanism that illustrates how the alkoxide intermediate reacts. I’ve drawn the alkoxide for you—**just add curved arrows to my alkoxide intermediate structure**.



Rubric:

- 3 points for electron pushing.
 - 1 point partial if only one arrow is correct.
- 3 points for transition state.
 - 1 point for partial (dashed) bonds.
 - 1 point for partial charges.
 - 1 point for putting nucleophile opposite leaving group. Angle doesn't have to be perfectly 180°, but they do have to be on opposite sides.
- 3 points for correct product.
 - 1 point partial for any cyclic ether.

- c. The alkoxide intermediate can't react in the conformation drawn on the left; the indicated C-C bond has to twist, so that its dihedral angle changes from $\phi = 180^\circ$ to $\phi = 0^\circ$. In the spaces below, **draw Newman projections** for different conformations of the alkoxide that would be encountered by twisting the C-C bond in 60° steps, using the perspective I've provided. Then, indicate whether each Newman projection represents a *gauche*, an *anti*, or an *eclipsed* conformer by circling one answer.



$\phi = 180^\circ$ (3)	$\phi = 120^\circ$ (3)	$\phi = 60^\circ$ (3)	$\phi = 0^\circ$ (3)
<i>gauche</i> or anti (1) or <i>eclipsed</i> ?	<i>gauche</i> or <i>anti</i> or eclipsed (1) ?	gauche (1) or <i>anti</i> or <i>eclipsed</i> ?	<i>gauche</i> or <i>anti</i> or eclipsed (1) ?

Rubric:

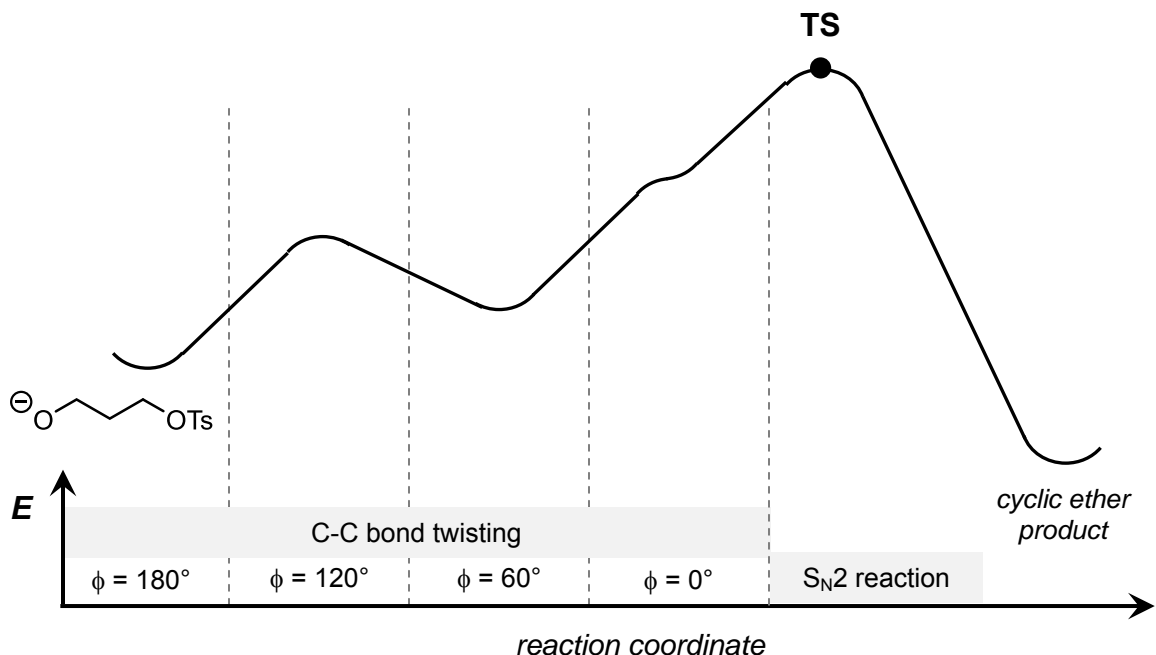
3 points for each Newman projection.

2 points partial for each correct Newman projection at an incorrect angle.

Okay to write "O" group as "OH", and "CH₂OTs" as "OTs".

1 point for each circled identification.

- d. Draw a potential energy diagram that shows everything the alkoxide must do to react—including the C-C bond twisting and the S_N2 reaction. I have already drawn energies for the starting material and product; connect them with one, continuous energy curve. You do not need to draw any molecule structures in this part. Label the S_N2 transition state (“TS”) on your curve.



Rubric: (8 points total for PE curve.)

4 points for C-C bond twist portion.

1 point for drawing 120° as a maximum.

1 point for drawing 60° as a minimum.

1 point for 60° higher in energy than 180° .

1 point for 0° highest energy of all conformations.

(0° region might look like a well, or a hill, or other. No judging shape here.)

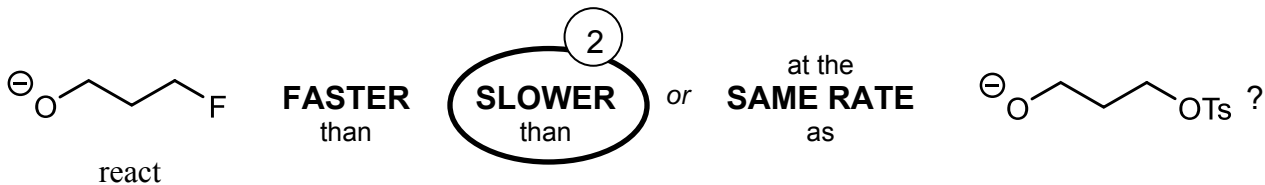
If you drew your Newman projections in a different order than mine, we tried to apply the Rubric to your PE diagram according to your Newman projections.

4 points for S_N2 portion.

2 points for drawing S_N2 hill as highest energy point on landscape.

2 points for labeling **TS**.

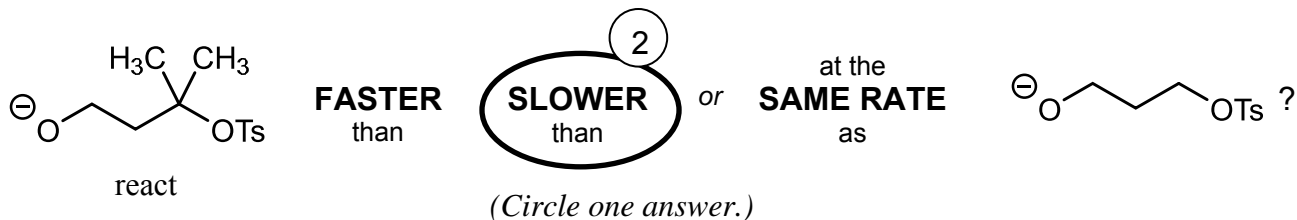
- e. What if the functional group on the right was a fluoride instead of a tosylate? Would



(Circle one answer.)

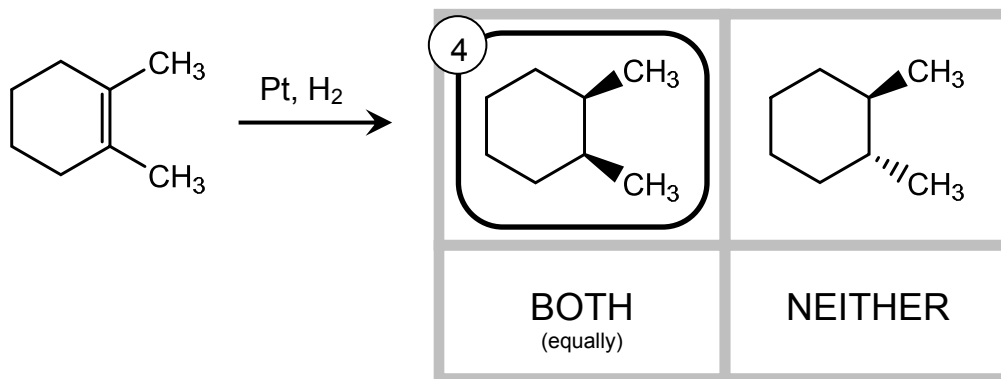
Fluorine is a terrible leaving group--it's not very polarizable, and that makes it difficult to form a partial bond in the S_N2 transition state. (It's also why fluorocarbons are so persistent in our environment--they don't undergo the kinds of substitution reactions that other molecules do.)

f. What if the right-hand carbon also bore two methyl groups? Would

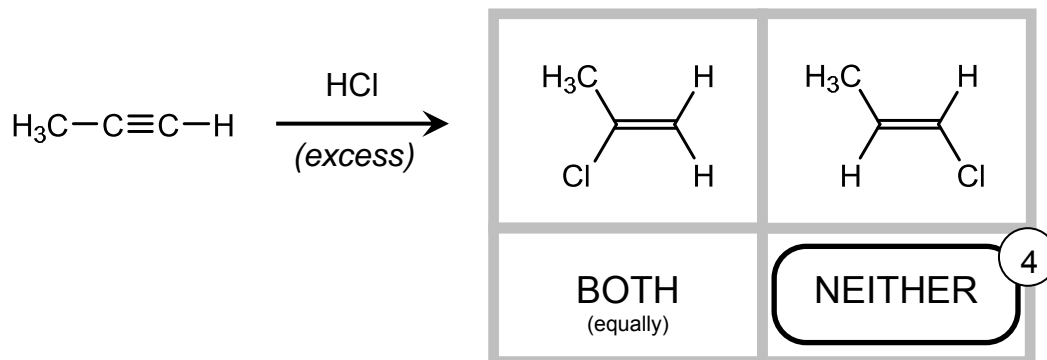
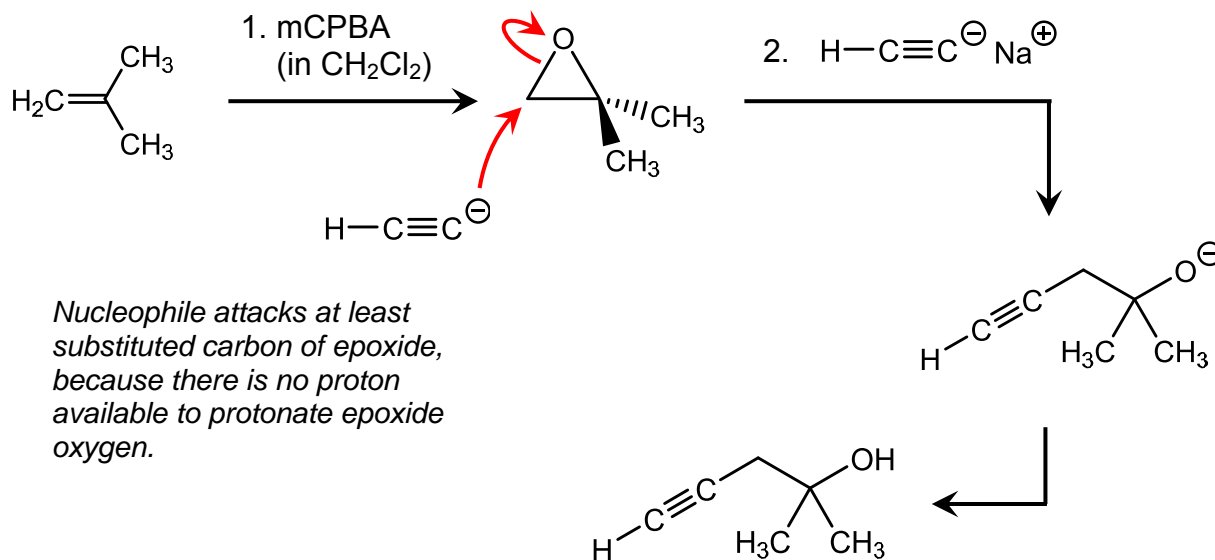
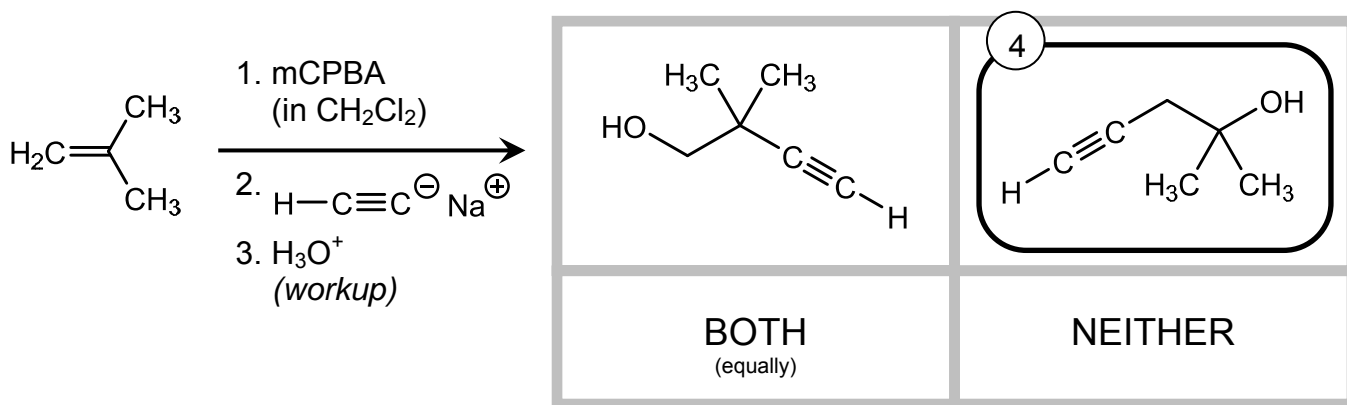


Those methyl groups would sterically hinder the nucleophile's approach, and make the required eclipsed ($\phi = 0^\circ$) conformer a lot less stable.

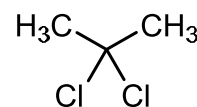
4. (16 pts) Each of the reactions on the next page is drawn with two possible products. If one of the two products predominates, circle that preferred product. If the two products are produced equally, circle "BOTH". If neither product would result from the reaction, circle "NEITHER". **Circle one answer only.**

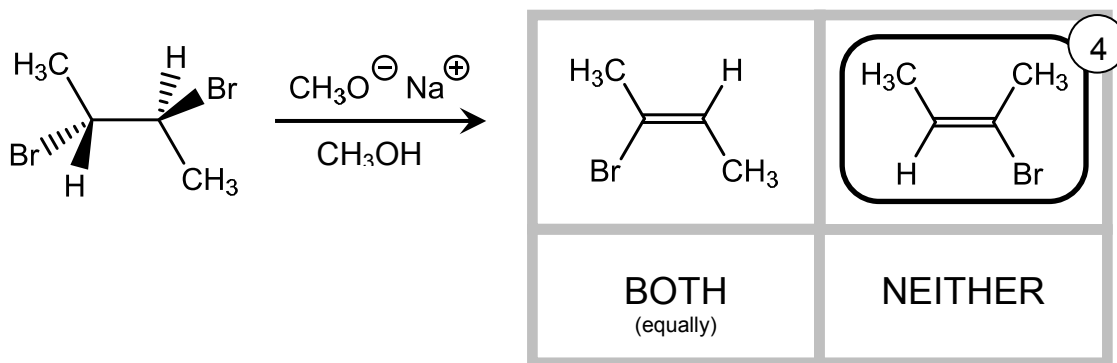


Hydrogenation of alkenes leads to *syn*-addition of two H atoms—addition of the H atoms to the same face of the alkene, to yield the *cis*-dimethyl product.

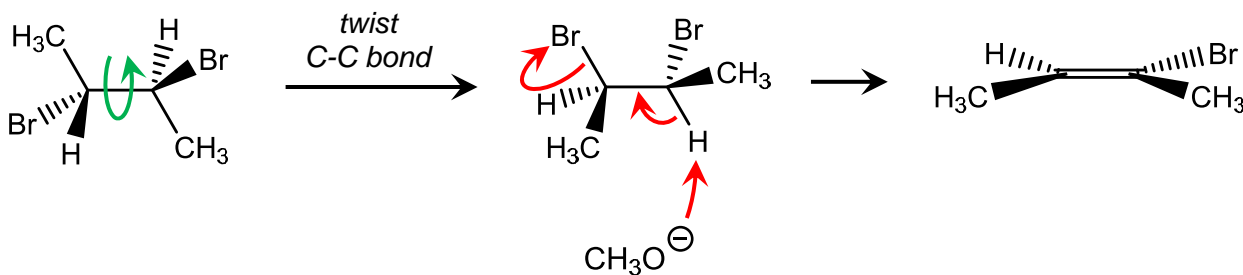


These products show Markovnikov (left) and anti-Markovnikov (right) addition of 1 equivalent of HCl to the triple bond. But in the presence of excess HCl, addition won't stop at one HCl; the Markovnikov product will add another HCl, to make the double-addition product shown at right.

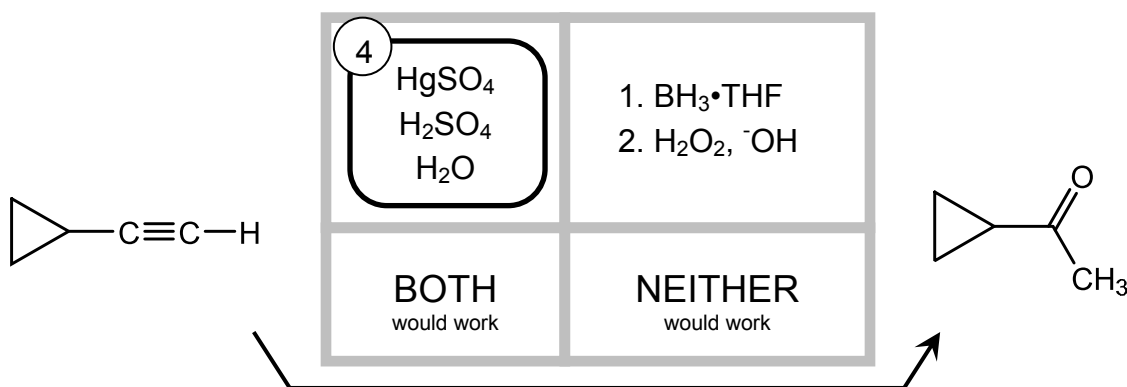




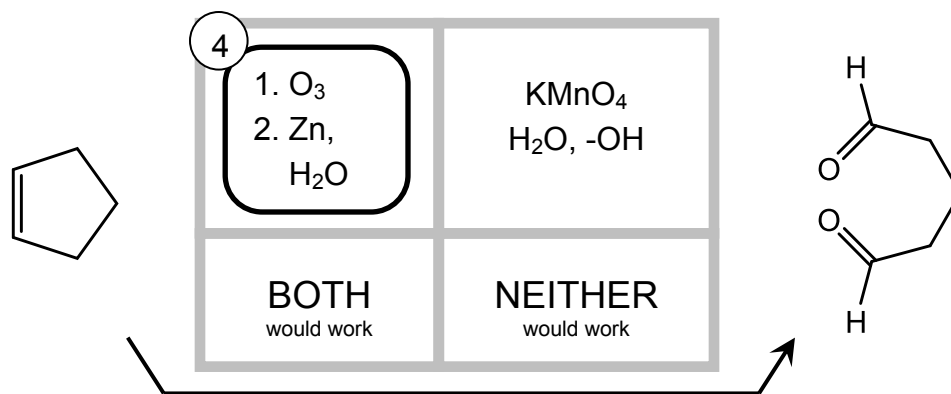
These reaction conditions (strong base) accomplish E2 on the starting material, as long as it can put an -H atom and a leaving group anti-periplanar to each other. Unfortunately, our starting material isn't drawn in a conformation that does that, but we can put it in an E2-reactive conformation by twisting the central C-C bond:



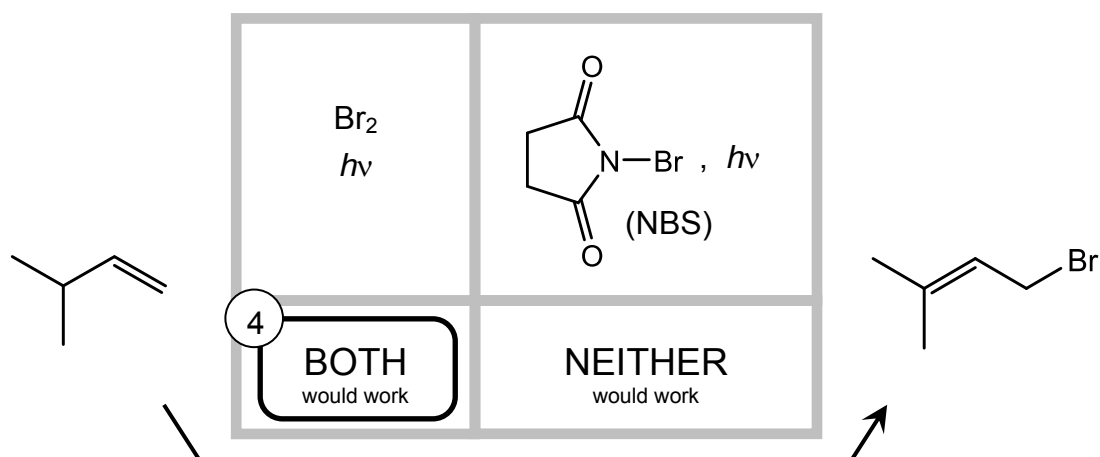
5. (16 pts) Each of the reactions on the next page is drawn with two possible reaction conditions. If only one of the two reaction conditions would generate the given molecule as the major product, circle those conditions. If both sets of conditions would accomplish the reaction, circle "BOTH". If neither set of reaction conditions would succeed, circle "NEITHER". Circle one answer only.



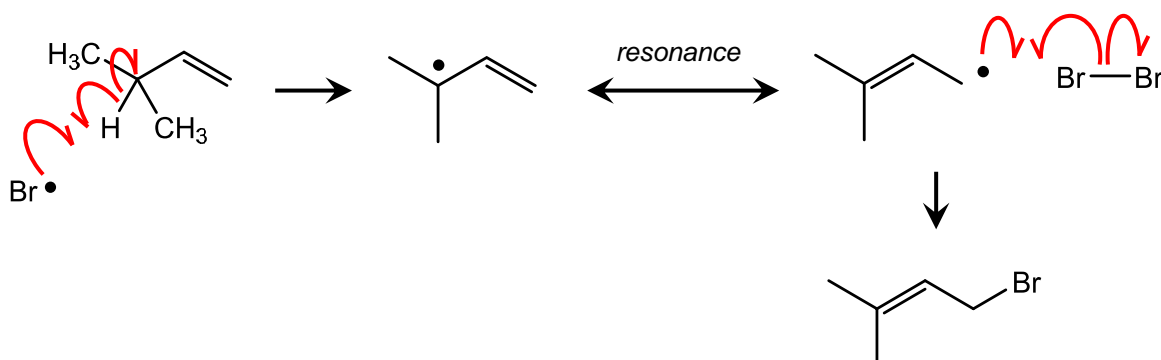
These two reaction conditions represent Markovnikov (left) and anti-Markovnikov (right) addition of H-OH to the alkyne to yield an enol, which then tautomerizes to a ketone (left) or aldehyde (right). Our product is the ketone, with the oxygen at the more substituted carbon of what used to be the alkyne.

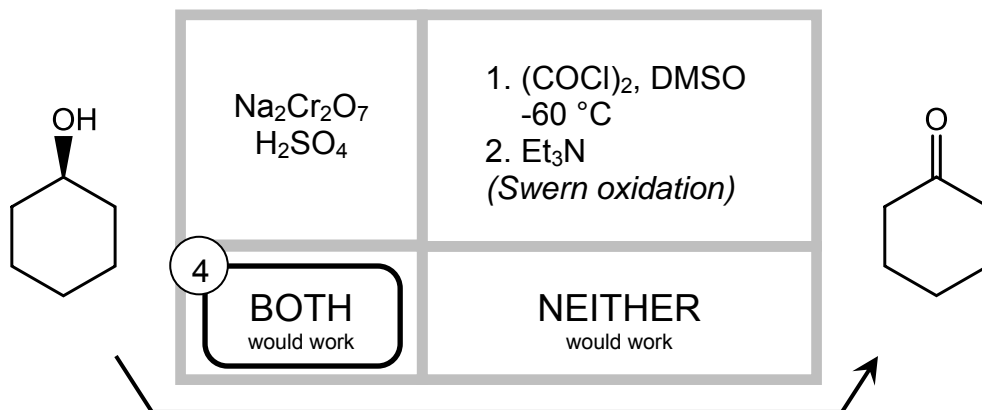


The conditions on the left perform ozonolysis on the alkene, to split it in two. The conditions on the right, on the other hand, will *syn*-dihydroxylate the alkene to yield a *cis*-diol.



Both of these will work, though NBS will work better (because there will be no competing electrophilic addition of Br₂ to the double bond).



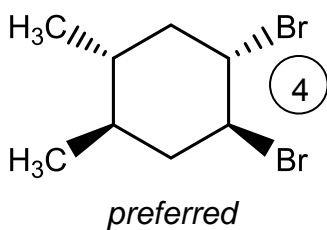
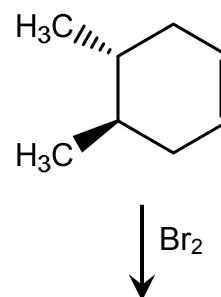


Both of these oxidation methods—strong and mild—will convert an alcohol to a ketone.

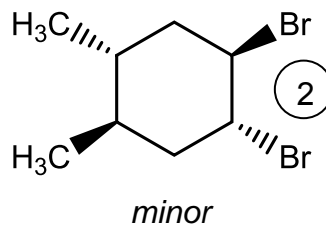
6. (23 pts) The *trans*-dimethylcyclohexene starting material shown at right reacts with Br_2 to yield just one preferred product.

a. **Draw the preferred product** as a pair of equilibrating cyclohexane chair conformers. Draw all non-hydrogen substituents, but feel free to omit H atoms.

b. Which conformer is more stable? Indicate which chair is more stable, or that they are equally stable, by circling one of the three equilibrium arrows between them.



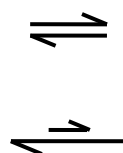
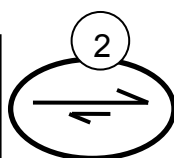
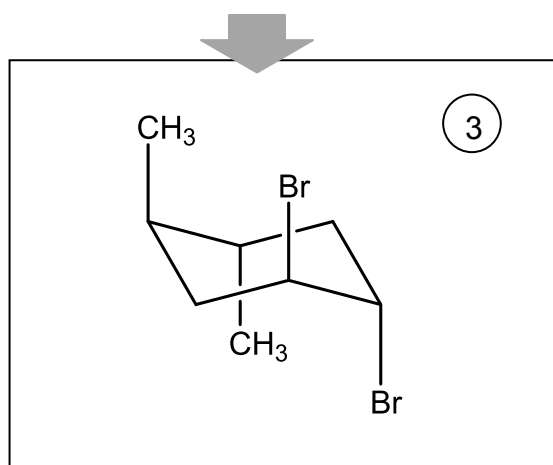
OR



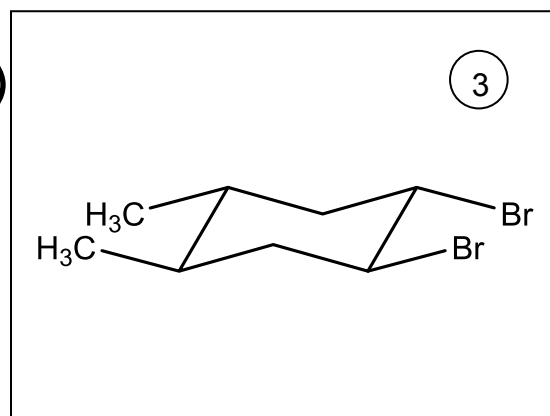
OR

1

any other dibromide, or two dibromide chairs that represent different products



(circle one)



Br₂ adds to the double bond *anti*, to generate a trans-dibromide product. There are two possible *trans*-dibromide products. One, the one shown above, has the most stable, all-equatorial chair, making it the more stable product; the other (labeled minor on the previous page) is less stable, because it doesn't have an all-equatorial chair.

Rubric:

4 points for the most stable dibromide product.

2 points partial for the other, less stable anti-adduct.

1 point partial for any other dibromide (*syn*, or with incorrect positioning of -Br on ring, or for two chairs that represent different dibromides).

.3 points for each chair. (6 points total for two chairs.)

Does not have to be correct dibromide to get all of these points.

1 point for chairs matching.

1 point for drawing a chair. Any chair.

1 point for all substituents in correct position.

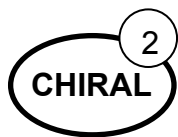
.2 points for equilibrium arrow.

Does not have to be correct dibromide to get all of these points, but chairs do have to match.

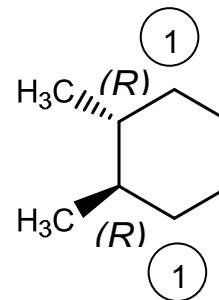
Minor product gets automatic 2 points for any arrow (but loses points for being wrong product, above).

Full credit for an arrow that matches the two chairs drawn.

c. Is the starting material **CHIRAL** or **ACHIRAL** ?
(Circle one.)



d. On the structure on the right, 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.

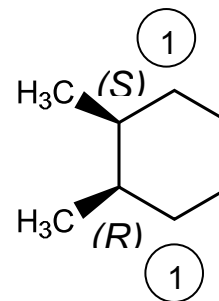


e. What about the *cis*-dimethylcyclohexene at right—is this

CHIRAL or **ACHIRAL** ? (Circle one.)



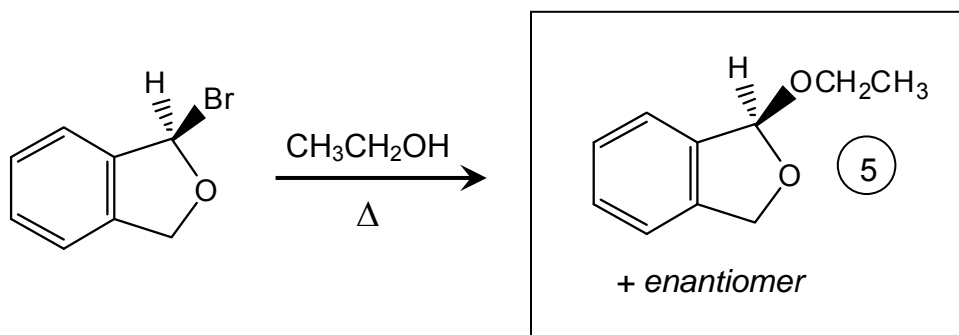
Once again, label each chiral center with its appropriate (*R*) or (*S*) designation.



f. Are the *cis*- and *trans*-dimethylcyclohexenes above

ENANTIOMERS , **DIASTEREOMERS** (3) or **THE SAME MOLECULE** ?

7. (15 pts) For each of the reactions below, **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.)



The conditions in the problem are for E1 and $\text{S}_{\text{N}}1$. In this case, there are no H atoms one carbon away from the Br leaving group, so this starting material can only react via $\text{S}_{\text{N}}1$. $\text{S}_{\text{N}}1$ produces a racemic mixture of products.

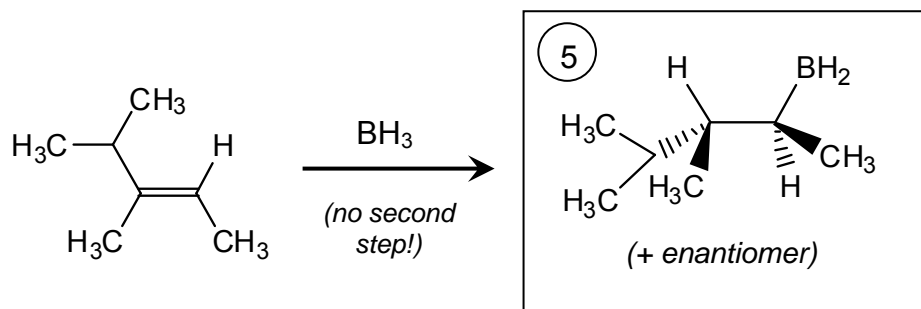
Rubric for this part:

5 points for correct structure and either (a) including “+ enantiomer” or (b) not drawing wedge or dash illustrating stereochemistry (which infers racemate).

4 points partial for omitting “+ enantiomer”.

3 points partial for inversion of stereochemistry only (as if reaction were $\text{S}_{\text{N}}2$).

-2 points for each clearly trivial structure mistake.



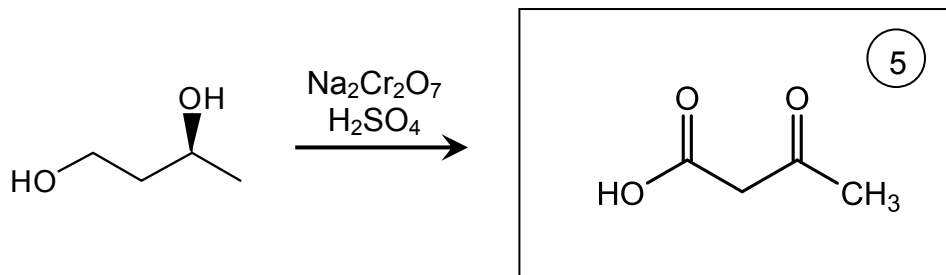
In hydroboration of a double bond, BH_3 adds across the double bond such that an -H is added to the more substituted carbon, and a $-\text{BH}_2$ group is added to the less substituted carbon. Addition is *syn*-, meaning the groups are added to the same face of the alkene. This is typically followed by an oxidation step, in which $\text{H}_2\text{O}_2/\text{OH}^-$ “trades” the $-\text{BH}_2$ for an -OH group; but this step isn’t part of this problem, so the reaction stops at the boration step.

Rubric for this part:

5 points for correct product.

4 points partial for correct answer, but omitting “+ enantiomer”.

3 points partial for incorrect or undetermined stereochemistry.
 3 points partial for correct stereochemistry, but incorrect regiochemistry ($-BH_2$ attached to more substituted carbon).
 2 points partial for anti-Markovnikov alcohol (all else correct).
 -2 points for each trivial structural mistake.



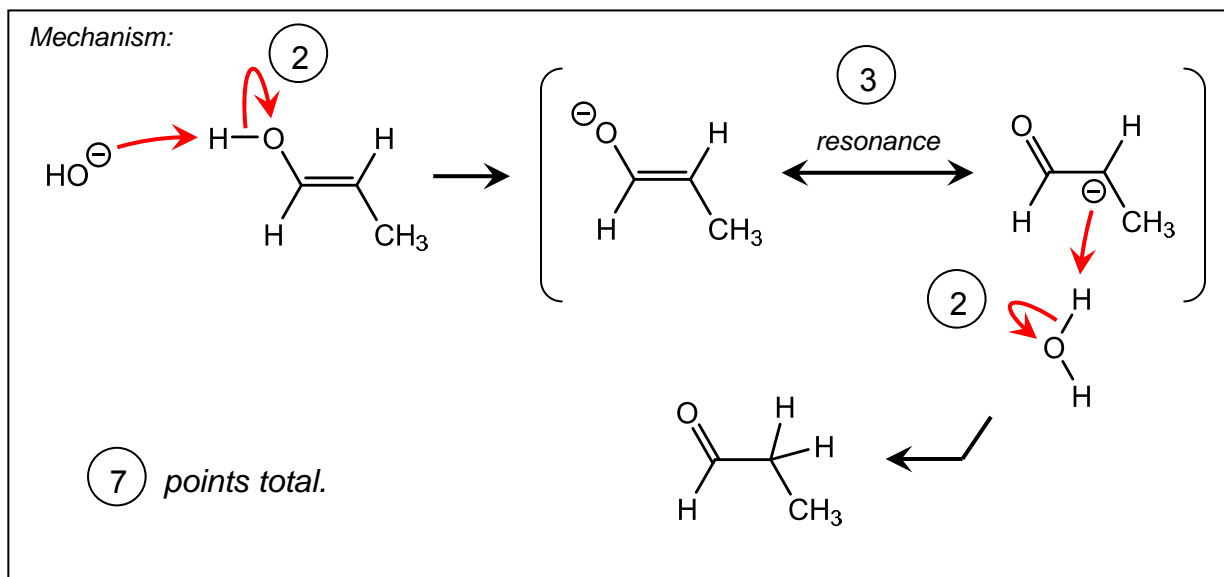
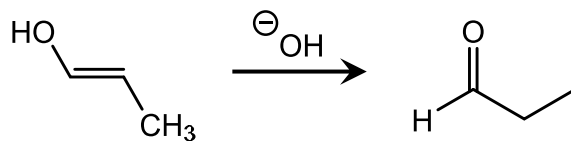
Rubric:

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.)

8. (24 pts) **Draw a mechanism** (using “electron pushing”) for each reaction or series of reactions shown on the next page. 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: (7 points total)

Overall notes:

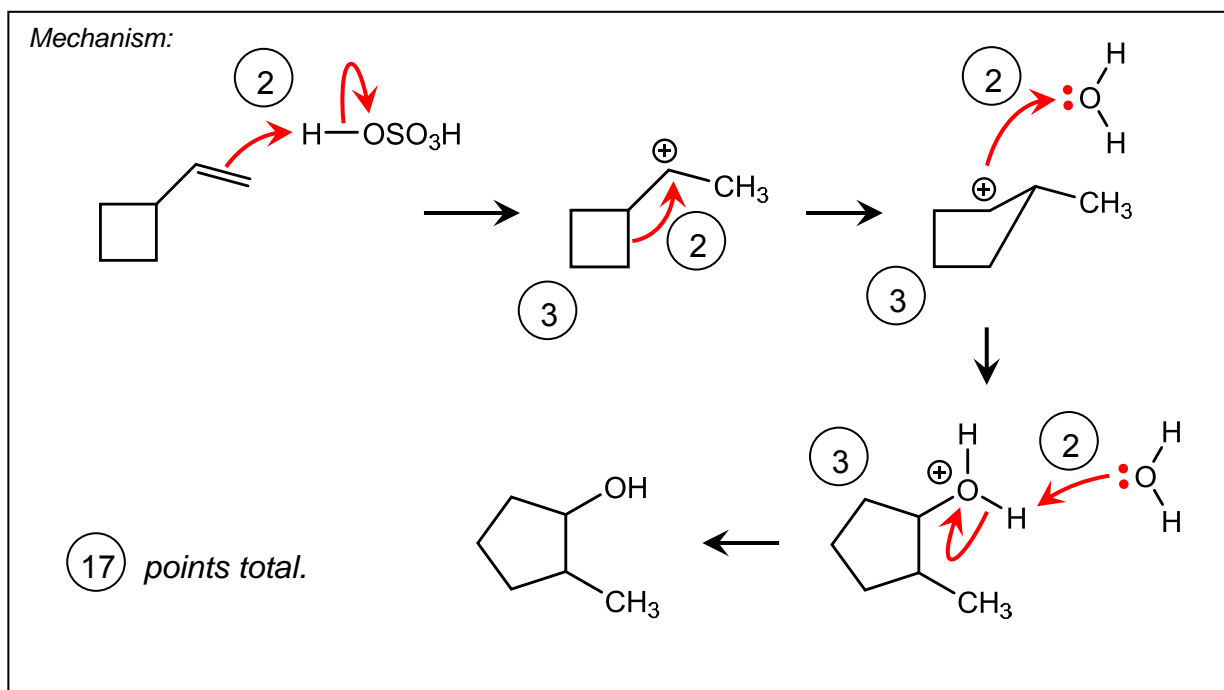
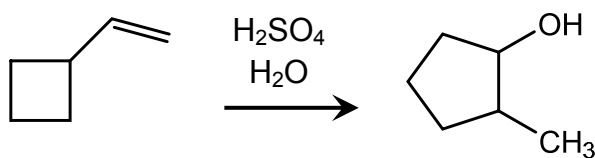
- 1 points, for each arrow in each step, for errors in drawing arrows. Arrow must start at an electron pair, and end at nucleus or bond where electrons will newly interact. Can only lose points if you get them.
- 2 points for each error in charge, valency, structure, base, etc. in intermediate; if error propagates, points are taken off only for initial error.
- 2 points for each step put steps in the wrong order. (So, protonation, then deprotonation). In base (-OH), there would be no acid strong enough to protonate the double bond and generate a cation first.
- 4 points (out of 7 total) for drawing this as a one-step process (for combining the two steps).

We did not judge electron pushing in resonance; resonance is not a mechanistic step, but rather just two ways of illustrating the same molecule. Molecules can be illustrated as any resonance structure, even minor ones. Resonance need not be drawn explicitly; it can be incorporated into an adjoining mechanistic step.

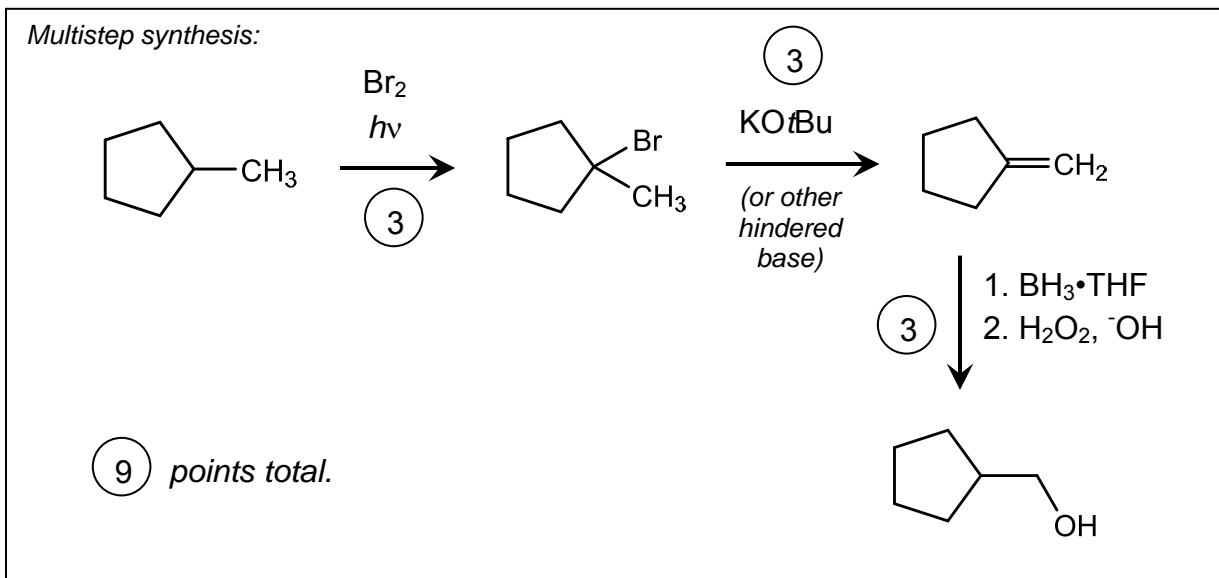
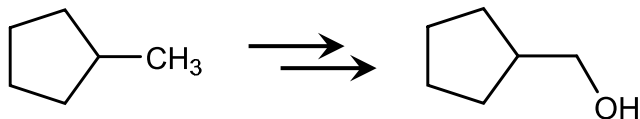
2 points for each arrow-pushing step;

3 points for intermediate.

Intermediate can be shown as either resonance structure.



9. (15 pts) For each set of 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 each 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:

Each task is judged separately, and does not require that the synthesis makes sense, or that other tasks are correct.

-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.

We only gave points for reagents if they connected a starting material and a product in an understandable way. So, for example, making the final -OH from a -Br, by itself, earns no points; sure, it's a reaction that would work, but it doesn't connect the product to the starting material.

3 points for introducing a functional group in starting material.

I can only imagine halogenation ($\text{Br}_2/h\nu$) as the way to do this.

1 point partial for NBS. Wouldn't work as well.

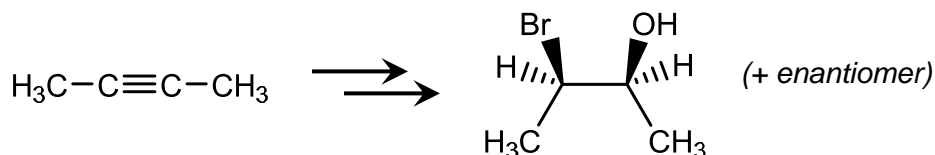
3 points for elimination with sterically hindered base (like KOtBu or LDA).

1 point partial for any other E2 base. This would generate the more substituted alkene within the ring.

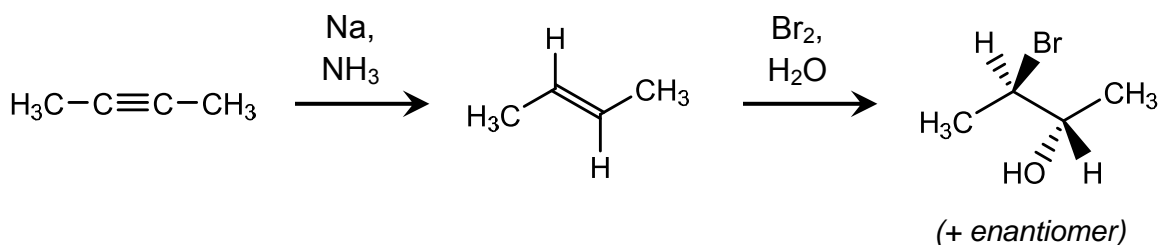
3 points for anti-Markovnikov addition of -OH to alkene (via hydroboration).

2 points partial for combination of anti-Markovnikov addition of HBr (w/ ROOR) followed by SN2 with hydroxide. Would also re-generate alkene via E2.

1 point partial for using H₂SO₄/H₂O as reagent.

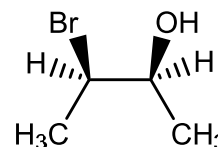


Multistep synthesis:



6 points total.

which is the same molecule as



Rubric:

General notes: Same as above.

3 points for anti-hydrogenation of alkyne.

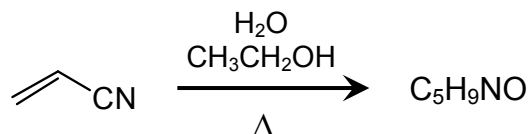
1 point partial for syn-hydrogenation (either listing syn reagents for trans hydrogenation, or doing entire thing syn).

1 point partial for Pt/H₂. This goes all the way to alkane.

3 points for formation of halohydrin.

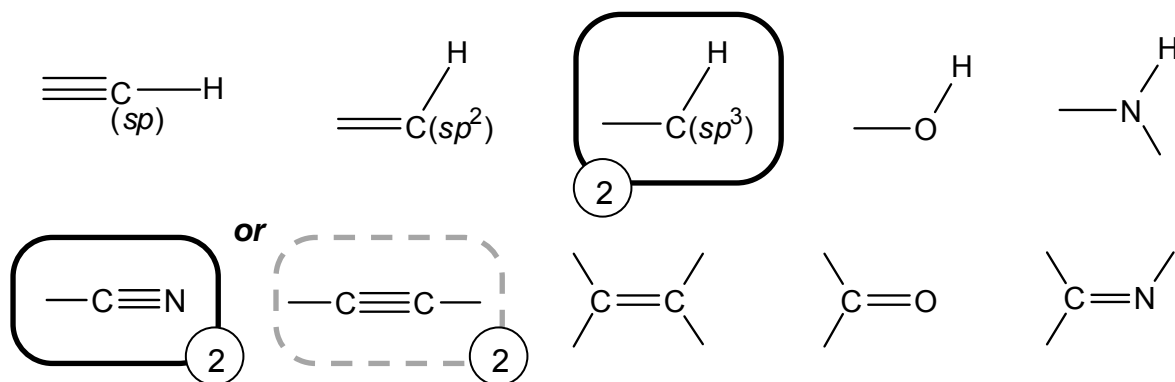
1 point partial for bromination, followed by S_N2 w/ hydroxide. There would be a lot of E2, and tough to control number of SN2 reactions per molecule.

10. (26 pts) Acrylonitrile, the starting material on the right, can be polymerized into polyacrylonitrile (a component of plastic consumer goods) by heating it in solvent, but heating acrylonitrile in a mixture of ethanol and water generates a small molecule product instead. This product was isolated and characterized by NMR and IR spectroscopy and mass spectrometry; the spectra of this product are shown on the next two pages. High-resolution mass spectrometry determined an exact mass of 99.06840 amu for the highest-mass (parent, M^+) peak in the MS spectrum, which corresponds to a molecular formula of C_5H_9NO .



Before we answer any questions about the unknown molecule, this problem already tells us a couple of things. The molecular formula of our molecule changes from C_3H_3N to C_5H_9NO , which means that the molecule picks up two carbons, an oxygen, and some hydrogens, and it doesn't lose its nitrogen atom. The molecule gets substantially bigger, so something is clearly adding to this molecule. And our reaction conditions make it look like that something needs to come either from water, ethanol, or another molecule of starting material. (Given two carbons and an oxygen being added, my bet is on ethanol.)

- a. Based on the features in the IR spectrum below, what functional groups would you expect the unknown molecule to have? **Circle all answers that apply.**



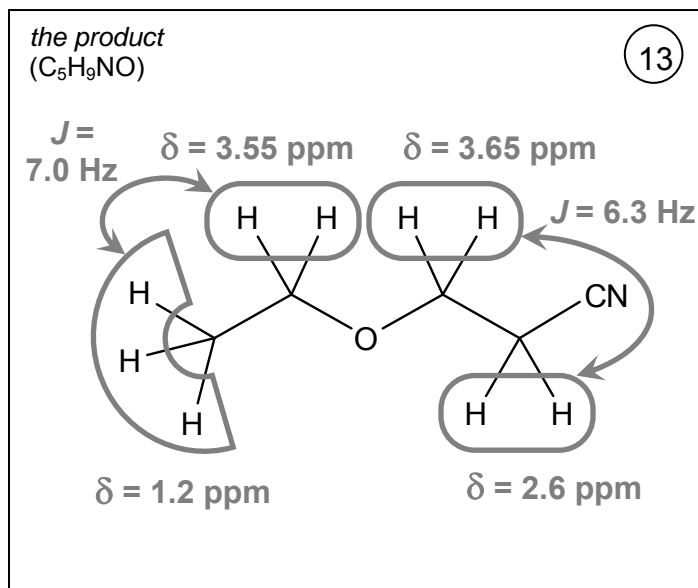
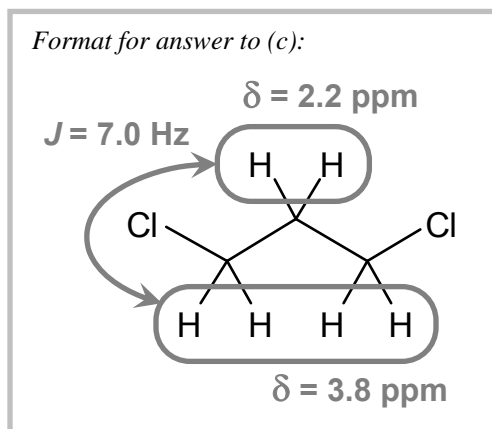
The IR spectrum really only has two important features: (1) no peaks above 2982 cm^{-1} , which indicates no $\text{C}(sp^2)\text{-H}$ or $\text{C}(sp)\text{-H}$ bonds; and (2) a peak at 2256 cm^{-1} , which the IR table tells us corresponds to either a $-\text{C}\equiv\text{N}$ or a $-\text{C}\equiv\text{C}-$ group. The starting material already has a $-\text{C}\equiv\text{N}$ group, so it seems likely that the reaction doesn't change the group that's already there. The starting material also has $\text{C}(sp^2)\text{-H}$ bonds which are gone in the product, so our reaction must be changing the alkene.

Rubric for part (a):

2 points for each correct circle.

-2 for each incorrect circle (up to 2; minimum score for this part is zero).

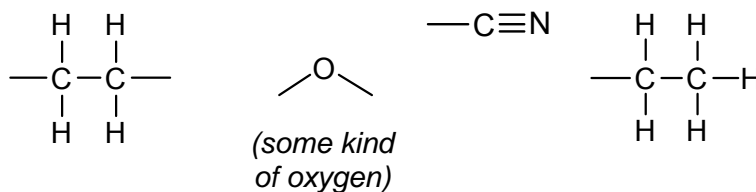
- c. **What is the structure of the product?** In the box on the next page, draw the molecule's structure, including all hydrogens. Then, considering the ^1H NMR spectrum,
- Circle each group of equivalent H's;
 - Assign a ^1H chemical shift (δ) to each circled group, within 0.05 ppm;
 - Connect any pair of coupled, inequivalent groups of H's with a double-headed arrow, and then label that arrow with the corresponding coupling constant (J).



The NMR spectrum tells us that our unknown molecule must have four different (inequivalent) types of H's, and the coupling constants tell us that two out of the four are adjacent to each other, and the other two out of four are also adjacent. Graphically, our molecule must look like this:



All of these H's must be $\text{C}(sp^3)\text{-H}$'s (from the IR data), and there are only 4 carbons to support them. (The fifth is in the $-\text{CN}$ group.) That means our molecule probably has these pieces:



I think the only way to put these together is in the product structure above, which is the ethanol adduct of acylonitrile.

Rubric for part (c):

Structure need not be correct to receive points in this problem.

1 point for the correct molecule.

2 points for assigning each δ value. (8 points total.) To get 2 points, circle must include all equivalent protons for your structure, match the integration intensity of the peak, and match the type of proton that would appear at that frequency.

3.65, 3.55 ppm: Must be CH_n protons adjacent to an O.

1 point partial for assigning each ppm value to the wrong number of H's, or with the wrong number of neighbors. If multiple inequivalent H's are labeled with the same δ value, you get maximum 1 point partial credit for each δ value.

2.6 ppm: Must be two protons adjacent to CH_2O protons.

1.3 ppm: $-\text{CH}_3$ group that is part of an ethyl fragment.

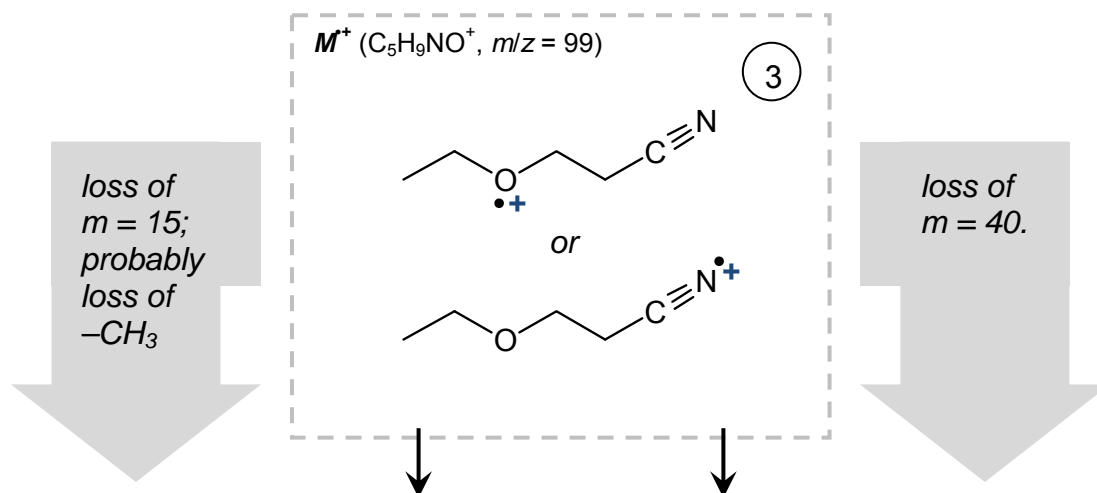
1 point partial if methyl group has no neighboring H's, or the wrong number.

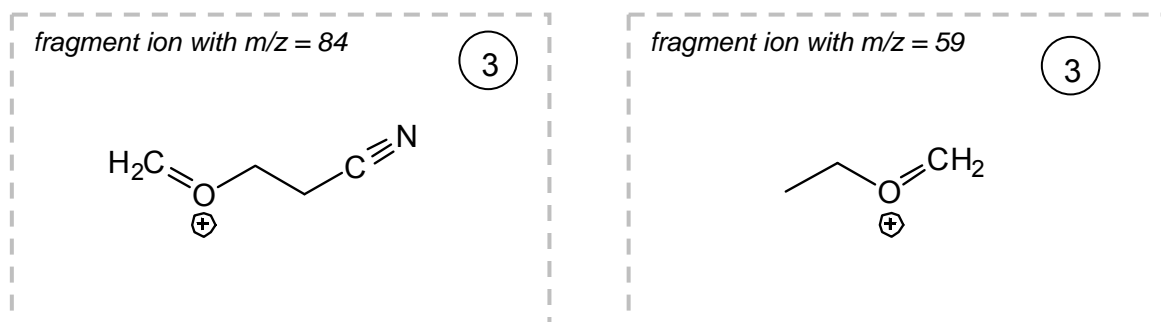
If you got the correct structure, but did not label δ values, you could receive 1 point partial for each correctly circled group of protons.

2 points for each J assignment (4 points total.)

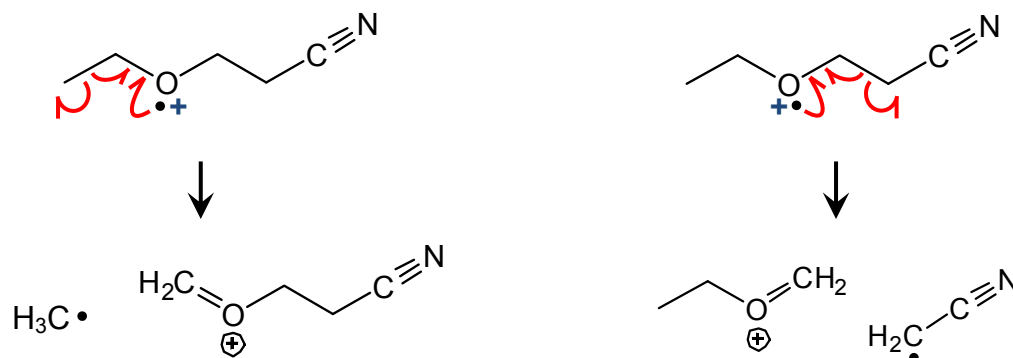
Circles need not be correct to get these points, but shift assignments of coupled protons must be. Curved arrow only needs to connect one proton with an adjacent partner.

- d. In an electron-ionization (EI) mass spectrometry experiment, parent ions often fragments into daughter ions that give information about the parent's molecular structure. In the EI mass spectrum below, the parent mass peak at $m/z = 99$ corresponds to a radical cation (M^+) that fragments into ions with mass 84 and 59. In the boxes below, draw the structures of these ions. *You do not need to do electron pushing to answer this question—just draw the cations.* On all ion structures, make sure to specifically illustrate where the formal charge lies.





These fragments make sense in terms of the first of the two parent ions above:



In each pair, only the cation is observed in the mass spectrum.

Rubric for part (d):

PARENT:

Structure need not be correct to receive points in this problem.

3 points for any molecule that (i) has formula $\text{C}_5\text{H}_9\text{NO}$ and (ii) has a lone-pair electron on oxygen or nitrogen removed (leaving a radical cation).

DAUGHTERS:

Structures need not be correct to receive points in this problem.

3 points for correct answer.

-or-

3 points for any fragments that are substructures of answer to (b), that have the right mass, and that are drawn as cations.

-2 points for omitting positive charge.