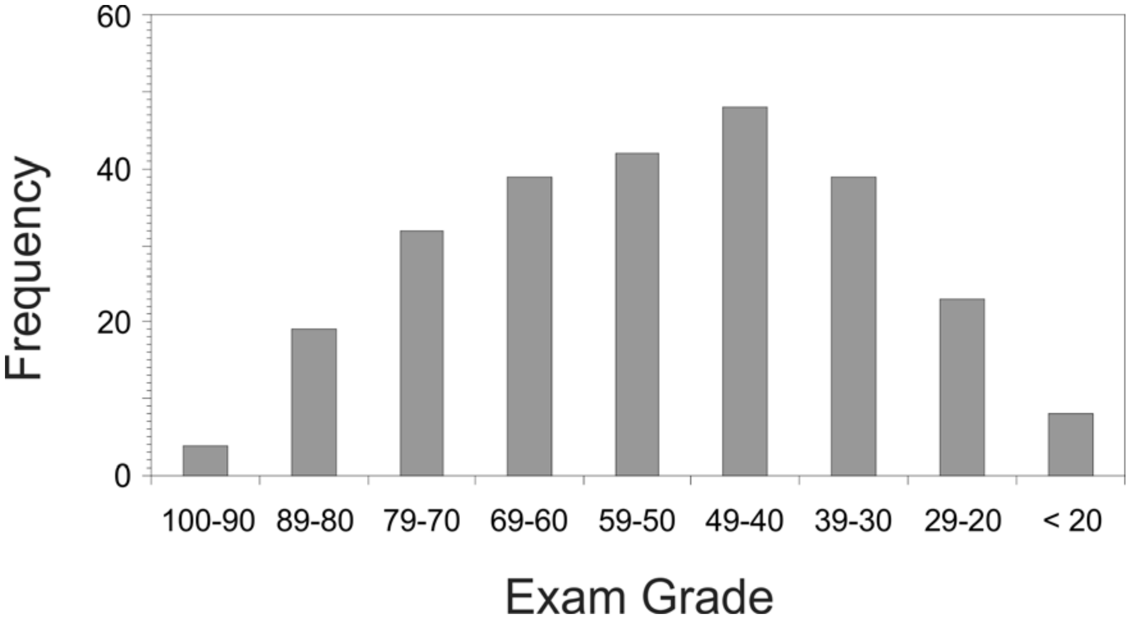
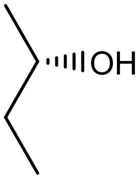
Chemistry 2301 Wednesday, November 19, 2014

Exam 3
Answer Key

Exam 3 Mean:	52
Exam 3 Median:	50
Exam 3 St. Dev.:	19

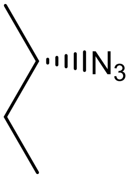


1. (16 pts) Each of the reactions below is drawn with two possible reaction conditions. If only one of the two reaction conditions would generate the given molecule as the major product, circle those conditions. If both sets of conditions would accomplish the reaction, circle "BOTH". If neither set of reaction conditions would succeed, circle "NEITHER". **Circle one answer only.**

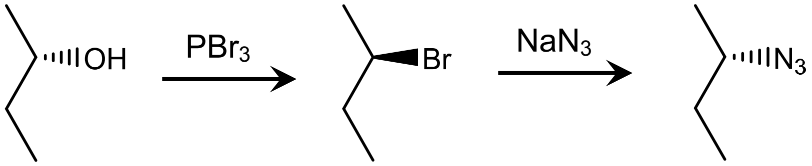


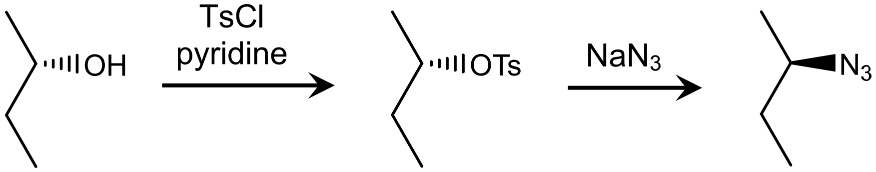
④

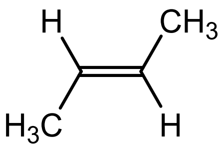
[✓ 1. PBr_3 2. NaN_3]	1. TsCl, pyridine 2. NaN_3
BOTH would work	NEITHER would work



Each of these recipes starts with a step that turns an -OH group into a good leaving group, and ends with an S_N2 reaction that substitutes that leaving group with an azide ($-N_3$) group. In the first box, both of these steps invert stereochemistry at the reacting carbon; PBr_3 inverts, and then N_3^- substitution inverts again. TsCl doesn't invert, so the result of the recipe on the right is just one inversion, to yield the opposite isomer from what's shown.







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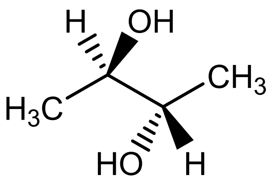
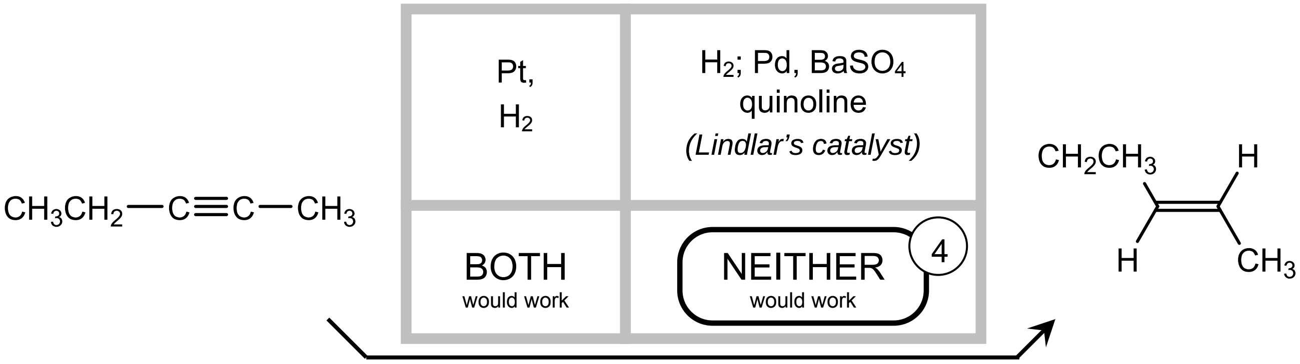
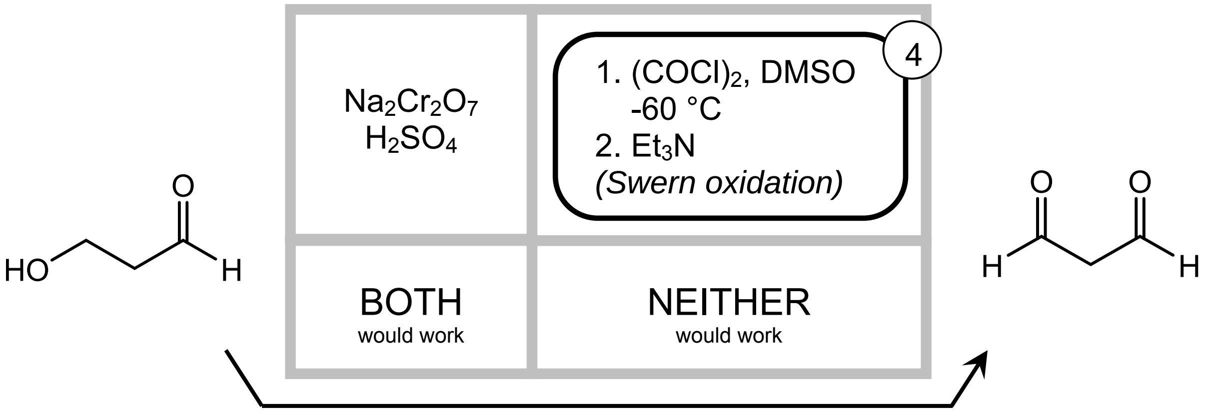
[✓ *m*CPBA H_2O]	$KMnO_4$ H_2O, ^-OH
BOTH would work	NEITHER would work



Both of the reagent sets listed in this problem perform dihydroxylation of alkenes; *m*CPBA/H_2O does *anti*-dihydroxylation, and $KMnO_4$ does *syn*-dihydroxylation. The product is *trans*, so we need *anti*-dihydroxylation.

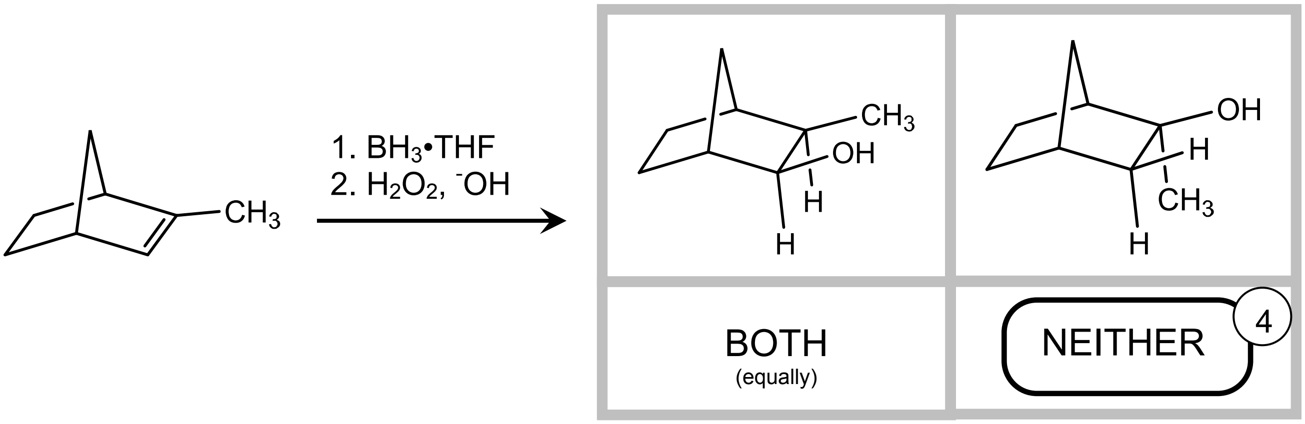


Both of these reagent sets perform hydrogenation of alkynes. Pt/H_2 hydrogenates alkynes all the way to alkanes, which is not what we want. Lindlar's catalyst does *syn*-hydrogenation to generate a *cis*-alkene, but our product is a *trans*-alkene. So neither of these work. (Na/NH_3 would though.)

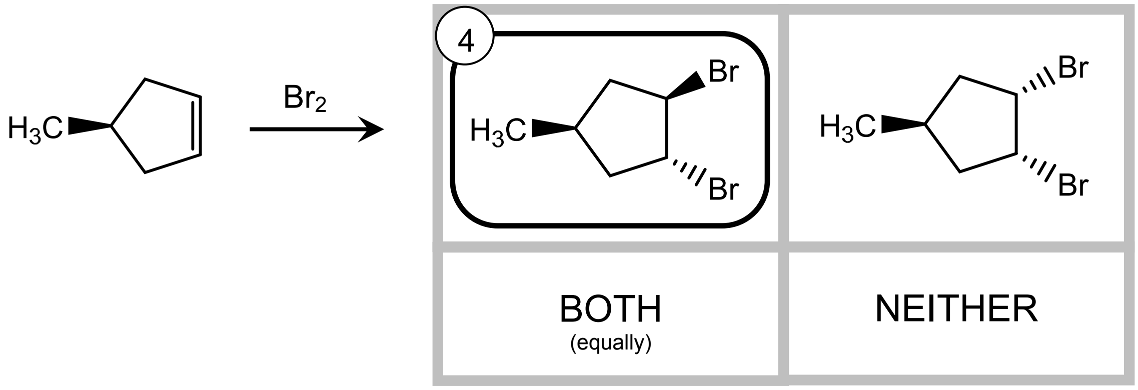


Chromate ($Cr_2O_7^{2-}$) is a strong oxidizing agent—it will oxidize any C-O bond as far as it can without breaking any C-C bonds. Chromate would oxidize the two primary carbons in our starting material all the way to carboxylic acids. Swern oxidation, on the other hand, is a mild oxidation method, and oxidizes these primary carbons to aldehydes only. (The carbon on the right is already an aldehyde, so it doesn't get oxidized any further.)

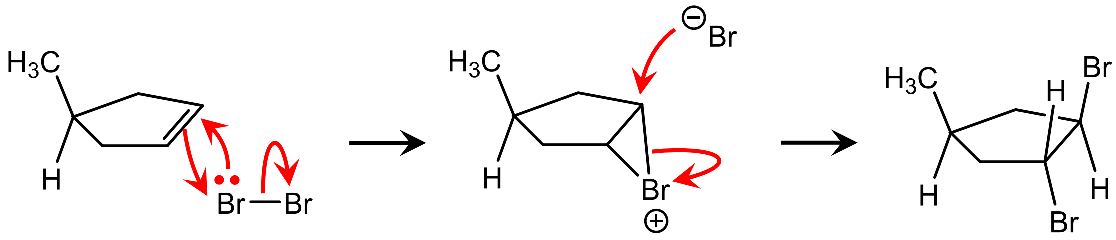
2. (12 pts) Each of the reactions below is drawn with two possible products. If one of the two products predominates, circle that preferred product. If the two products are produced equally, circle “BOTH”. If neither product would result from the reaction, circle “NEITHER”. **Circle one answer only.**



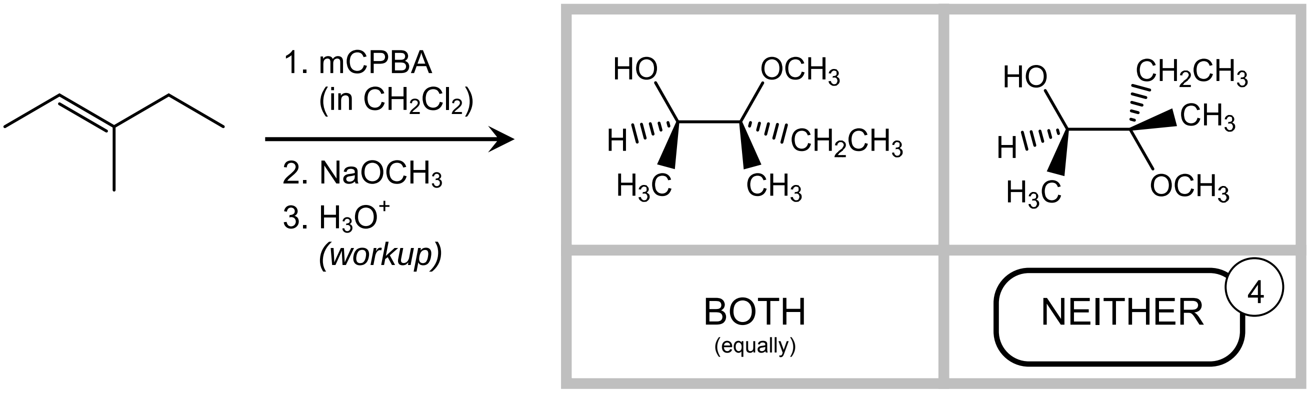
Hydroboration adds H-OH to alkenes with anti-Markovnikov regioselectivity, and does *syn*-addition. (In other words, it adds H and OH to the same face of an alkene, and puts the OH at the more substituted carbon.) The first product is anti-Markovnikov, but has H and OH added *anti*, not *syn*. The second product is Markovnikov. Neither of these is correct.



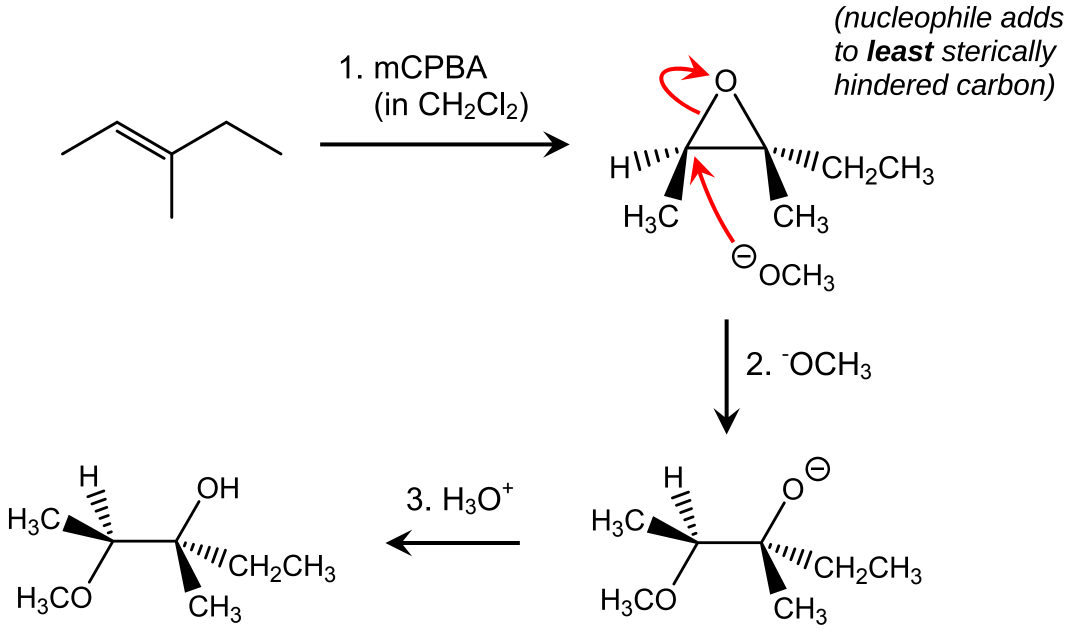
Bromination of alkenes is an *anti*-addition, via a bromomium ion:



This is the product in the left box. The reaction would also make the enantiomer of this product (not shown).

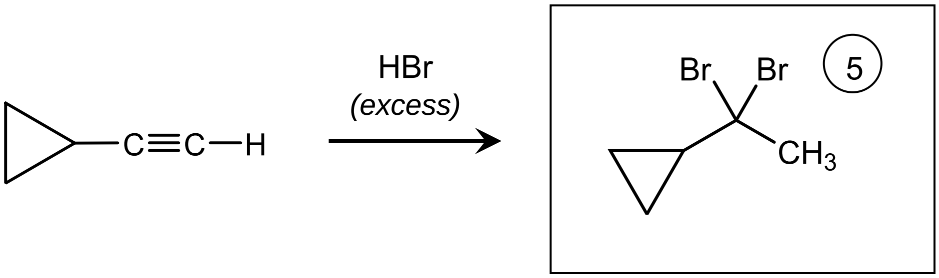


The three steps, in order:

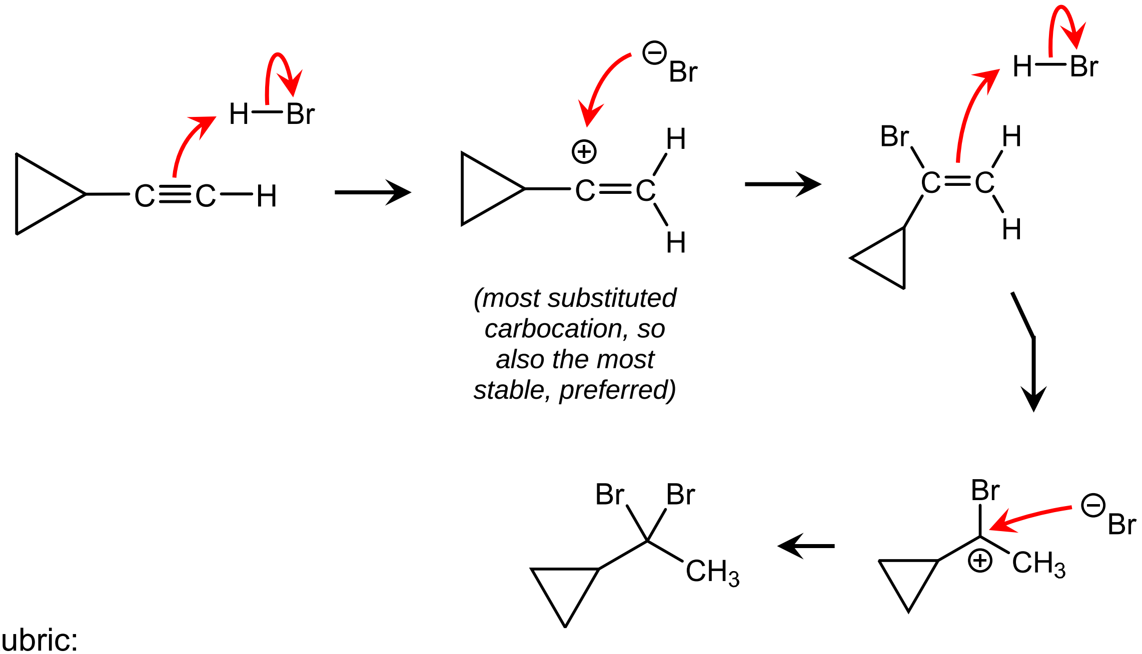


This product has the $^{-}OCH_3$ nucleophile attached to the less substituted carbon, but neither of the products in the boxes do.

3. (25 pts) For each of the reactions below, **fill in the empty box corresponding to reactants or products**. For reactions that you expect to yield multiple products, give the major product. For reactions that yield multiple enantiomers, draw only one enantiomer in the box, and include the note "+ enantiomer".



Alkynes undergo hydrohalogenation (an electrophilic addition reaction) in the presence of halogen acids HX. When excess HX is available, the alkyne will react twice, with Markovnikov regioselectivity (in which the halogen ends up at the more substituted carbon of the starting alkene, if there is one).



(most substituted carbocation, so also the most stable, preferred)

<u>Rubric:</u>

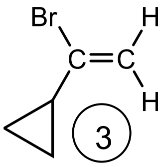
5 points for correct structure.

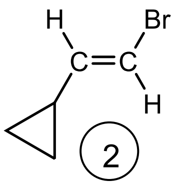
3 points partial for single, Markovnikov addition of HBr.

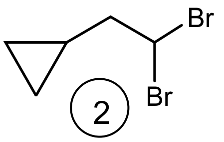
2 points for anti-Markovnikov addition of HBr, either once or multiple times, or for a combination of Markvnikov and anti-Markovnikov addition.

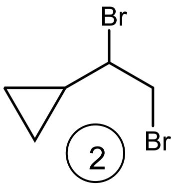
-1 point for writing "+ enantiomer". All of these products are achiral, they have no enantiomers.

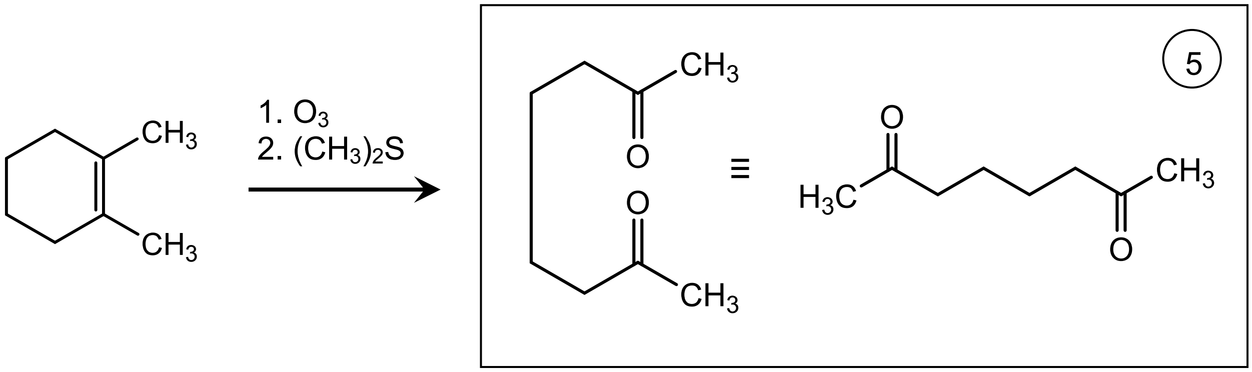
-2 points for a trivial structural error. The intent of your answer must be clear; if you make an error that makes it unclear which answer you meant, we can't give you the benefit of the doubt.











Ozonolysis cleaves double bonds, and replaces each double-bonded carbon with a carbonyl (C=O) group.

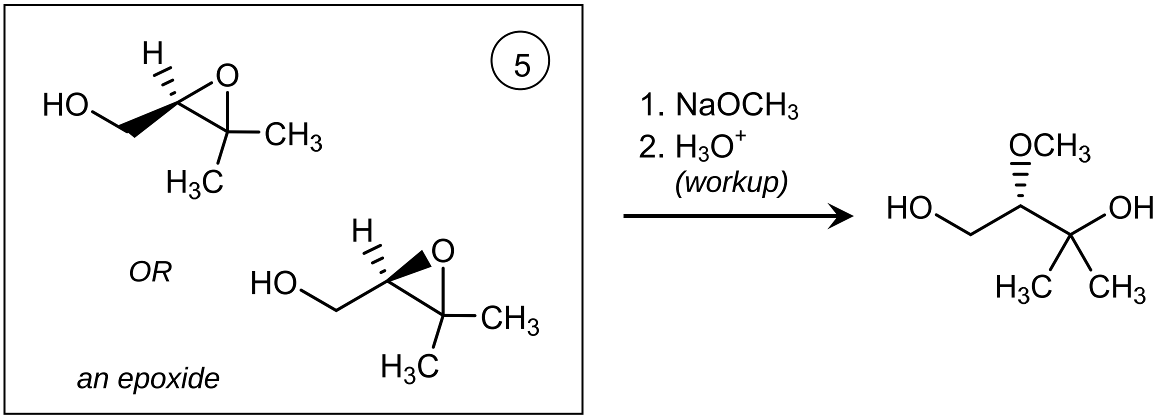
Rubric:

5 points for correct structure. *In general, you can draw correct structures any way you like, as long as they correctly identify the product.*

2 points partial for any product that cleaves C=C bond, but doesn’t have correct functional groups added.

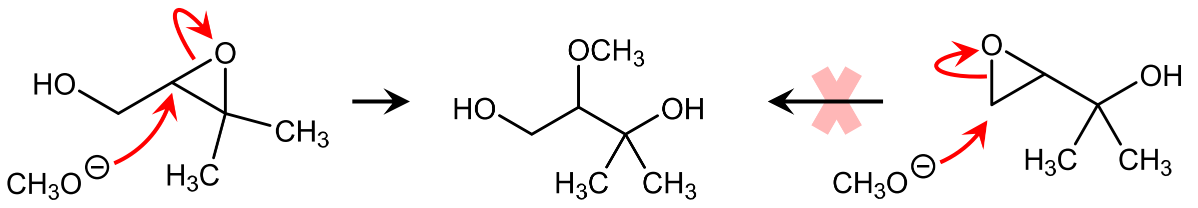
-2 points for any trivial error, including drawing too many or too few carbons in central alkyl chain.

-1 point for writing “+enantiomer”—this product is achiral.



Okay, this was a complex problem. The empty box tells us that our starting material is an epoxide, and reactions of nucleophiles (like the $^{-}OCH_3$ in recipe step 1) with epoxides generate products in which the nucleophile is adjacent to an -OH group. Our product here has two -OH groups; that must mean that our starting material must not only contain an epoxide, but also an alcohol group that isn’t made from that epoxide. So which alcohol comes from the epoxide, and which doesn’t?

We’ve got two options for starting materials that would make the expected product: one with an epoxide on the left, and one with an epoxide on the right.



CH_3O^- is only possible under basic conditions, and so here I show it adding to the less sterically hindered epoxide carbon. This makes sense.

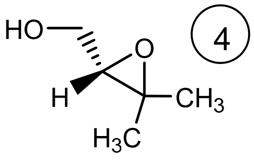
But that means that, when CH_3O^- adds to the less sterically hindered carbon in this epoxide, the wrong product would be formed. This can't be the starting material.

Stereochemically, the CH_3O- must approach the epoxide from behind. That means that the epoxide must be in front in the starting material, with a wedge.

<u>Rubric:</u>

5 points for correct structure.

- *-1 point for writing "+ enantiomer".*
- *-1 point for incorrect stereochemistry at central carbon, or for not illustrating stereochemistry. In this case, we did not also take a point for "+ enantiomer".*
- *3 points partial for epoxide on left-hand side of molecule, with any stereochemistry.*
- *1 point partial for drawing ANY epoxide.*
- *-2 points for any trivial error. If an alcohol group is missing from your answer, this is probably not trivial—it would need to be clear to graders where you would have put the alcohol if you had drawn it.*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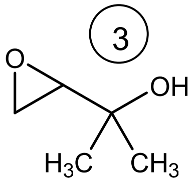
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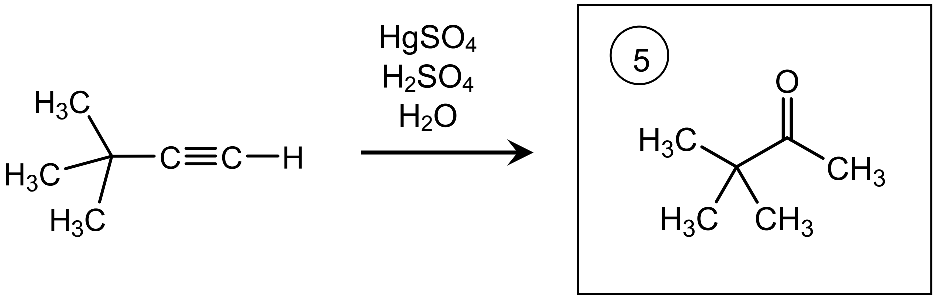
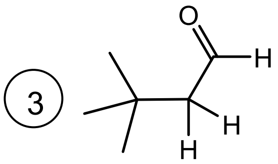
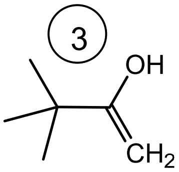
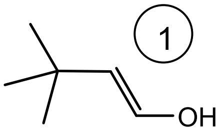


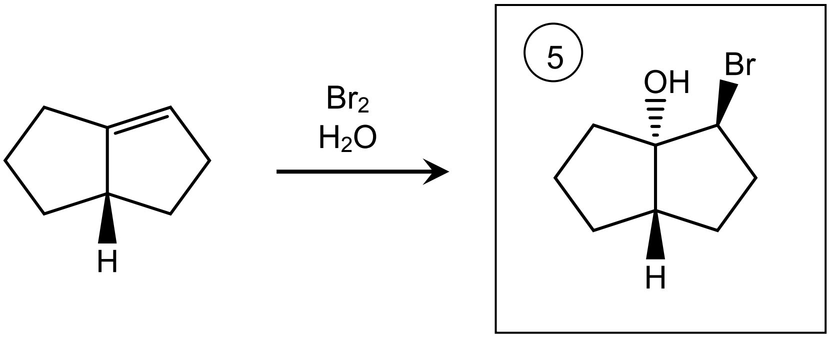
This is the standard recipe for Markovnikov hydration of an alkyne to an intermediate enol, which spontaneously tautomerizes to the product ketone. The ketone oxygen ends up at what used to be the more substituted carbon of the alkyne.

Rubric:
5 points for correct structure.
- *-1 point for writing "+ enantiomer". Product is achiral.*
- *3 points partial for anti-Markovnikov aldehyde.*
- *3 points partial for Markovnikov enol.*
- *1 point partial for anti-Markovnikov enol.*
- *-2 points for any trivial error.*

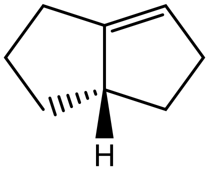




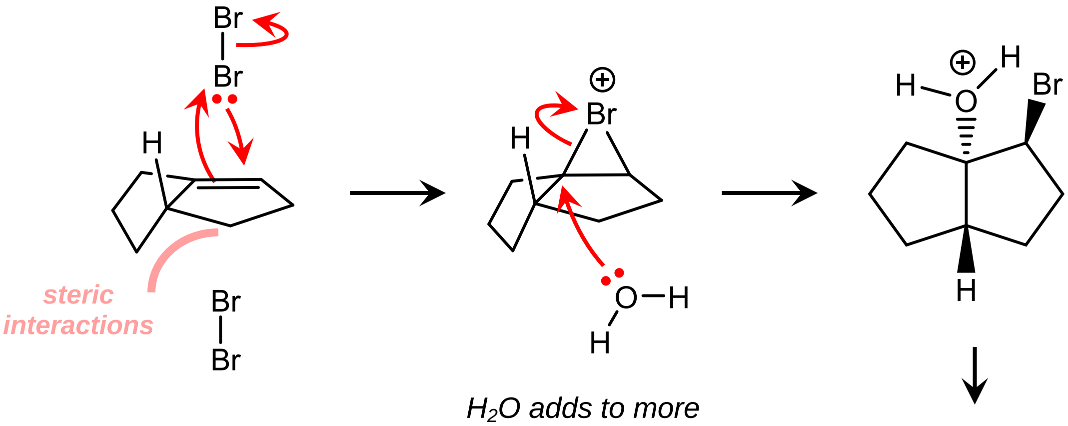




The reaction conditions convert alkenes into halohydrins—molecules that have a -Br and an -OH group where the double bond used to be. And the reaction adds these groups *anti*-, to opposite faces of the starting alkene. But which carbon of our starting material gets which group, and in which direction?



I've drawn the starting material as if it's flat, but it's not; the ring on the left is pointed downward, in the opposite direction from the H. That downward ring will sterically block access to the bottom face when Br_2 approaches to form the initial bromonium ion:



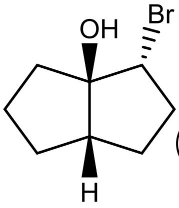
H_2O adds to more substituted carbon, with bigger δ+

product

Rubric:

5 points for correct structure.

- *-1 point for writing "+ enantiomer". Reaction would make this enantiomer only.*
- *4 points partial for correct regiochemistry, but incorrect anti-stereochemistry.*
- *3 points partial for anti-Markovnikov regiochemistry, anti, either direction.*
- *2 points partial for any syn-adduct (either regiochemistry).*
- *3 points partial for trans-dibromide with matching stereochemistry.*
- *2 points partial for mismatched trans-dibromide.*



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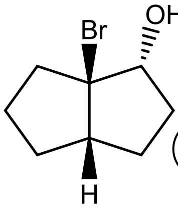

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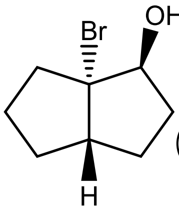

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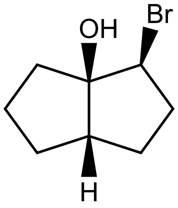

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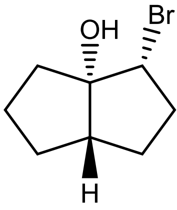

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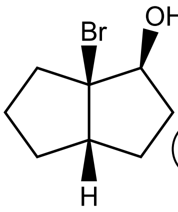

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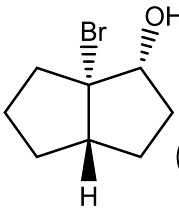

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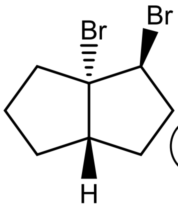

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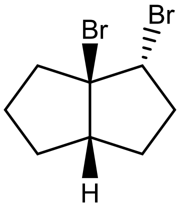

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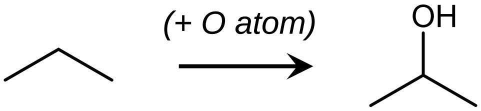
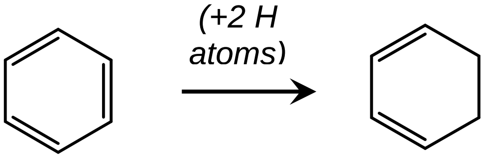
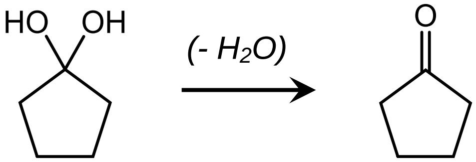
4. (9 pts) Identify each of the transformations shown as a reduction, an oxidation, or neither. **Circle only one answer for each transformation**.



REDUCTION *or* [✓ **OXIDATION**] ③ *or* **NEITHER**

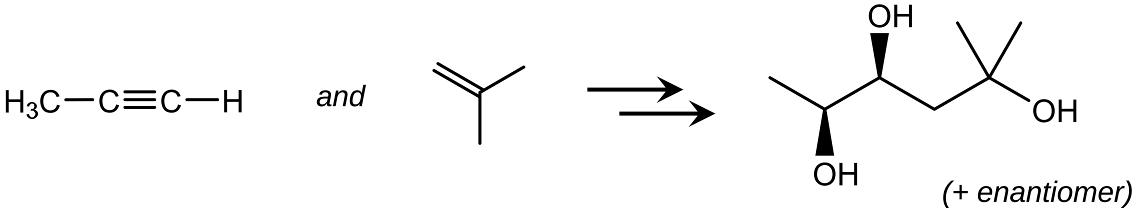


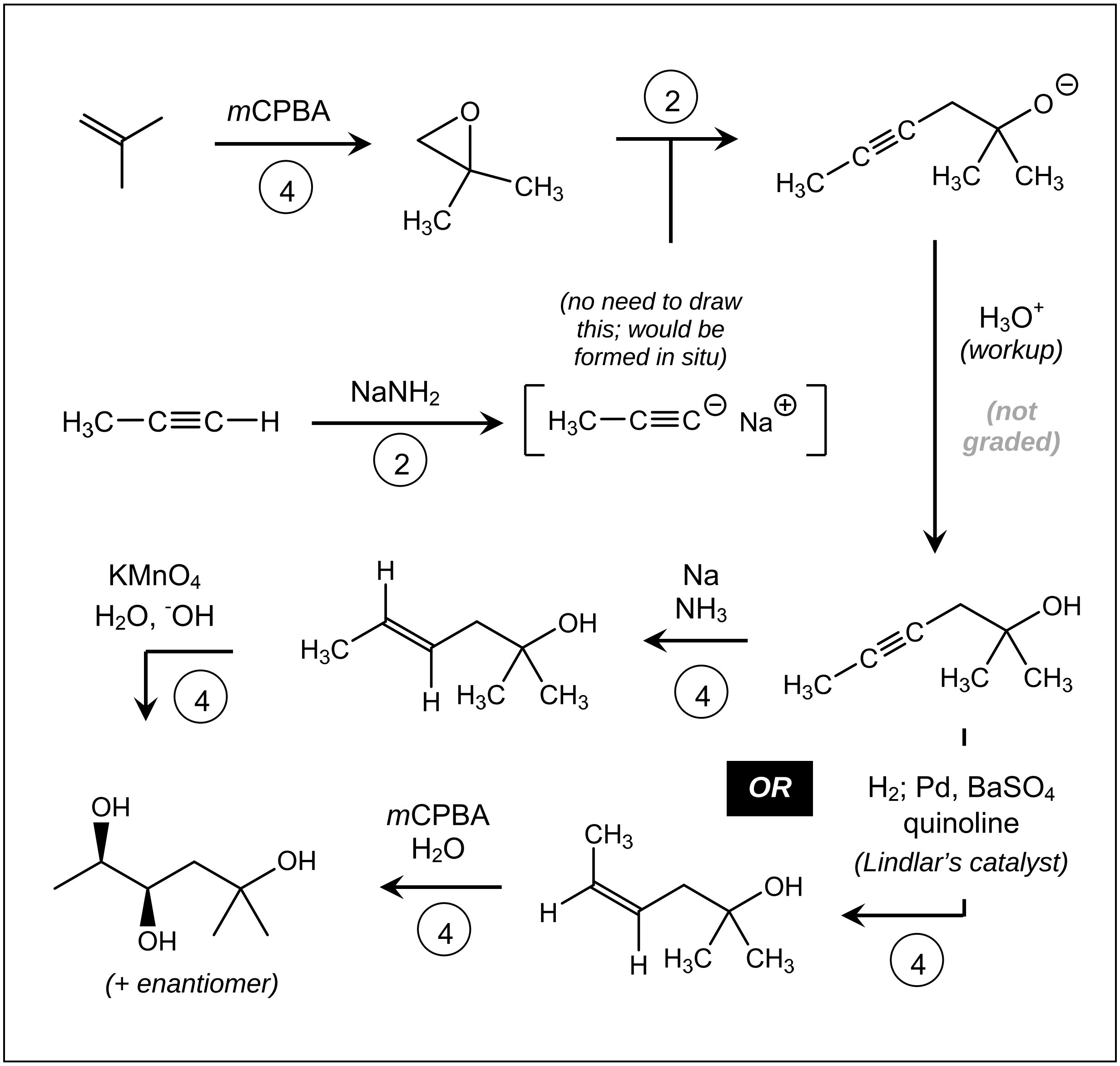
[✓ **REDUCTION**] ③ *or* **OXIDATION** *or* **NEITHER**



REDUCTION *or* **OXIDATION** *or* [✓ **NEITHER**] ③

5. (16 pts) For the starting materials and product 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:*

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

-1 point for each clearly accidental error in structures or reagents; if error propagates, points are taken off only for initial error, as long as synthesis still works toward target presented in the problem. (So, for example, if you wrote "mCBPA" instead of "mCPBA". Or if you accidentally add a carbon in a way that doesn't affect future steps.)

-2 points if step reagents are incorrect, but reaction could otherwise be accomplished with correct reagents. ("Right reaction, wrong reagent.")

-2 points if reagents are correct/reasonable, but wrong step product. ("Wrong reaction, right reagent.")

We only gave points for correct reagents if they connected a starting material and a product in an understandable way. So, for example, just writing the names of chemicals in that big empty box ("$NaNH_2$") was not enough; they need to connect starting materials and products in a mechanistically meaningful way.

We required that your synthesis have four elements, each of which was worth 4 points:

(1) The alkene needs to be prepared to accept an alkynyl anion, preferably in a way that will lead directly to a product alcohol or ether. There are a couple of ways to do this:

Epoxidation (mCPBA) gets 4 points.

Bromination (Br_2), and halohydrin formation also get 4 points; these will fail in a subsequent step, but work at the beginning.

(2) The alkyne needs to be deprotonated to make an alkynyl anion, and this alkynyl anion needs to be combined with the electrophile from element 1 to yield an alcohol.

2 points partial for deprotonation w/ $NaNH_2$ or NaH alone.

Other 2 points depend on no side reactions. Halohydrin fails here (protonation), as well as bromination (elimination). Even though these fail, subsequent steps in synthesis can be judged as if they succeed, wherever appropriate.

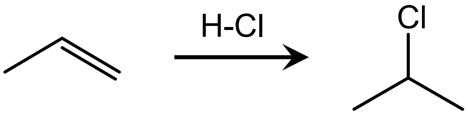
(3) The alkyne needs to be reduced to an alkene, either *syn* or *anti*.

Remember: If a student does a reduction to an alkene, but uses the wrong reagent, that's good for 2 points. (Right reaction, wrong reagent.)

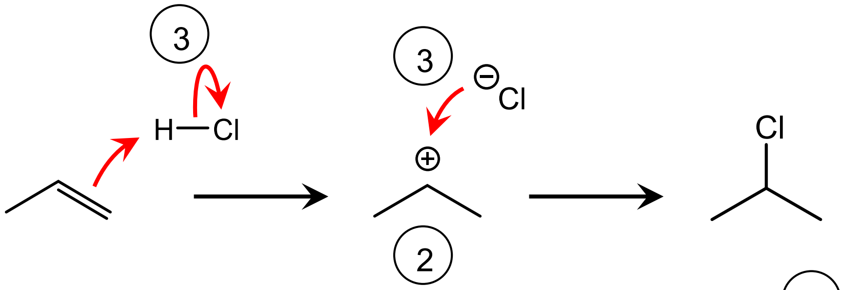
(4) The alkene needs to be dihydroxylated, either *syn* or *anti*, in a way that matches the alkene stereochemistry.

If the student matches things incorrectly, keep in mind that this may still be worth 2 points. (Right reaction, wrong reagent.)

6. (22 pts) **Draw a mechanism** (using "electron pushing") for each of the 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.)



Mechanism:



⑧ *points total.*

<u>Rubric:</u> *(8 points total for this box)*

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 and spectators may be omitted.

Proton transfer must be shown explicitly, with two arrows (one to proton, one from proton-acid bond). It's not okay to just write "proton transfer" or "+H^+".

-2 points, for each arrow in each step, for errors (including omission) in drawing arrows. Arrow must start at an electron pair (either a bond or a lone pair), and end at nucleus or bond where electrons will newly interact.

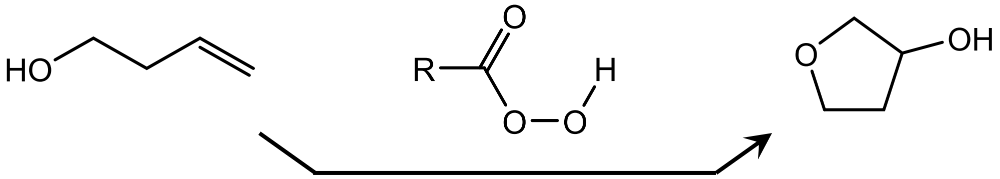
-2 points for each error in charge, valency, structure, base, etc.; if error propagates, points are taken off only for initial error.

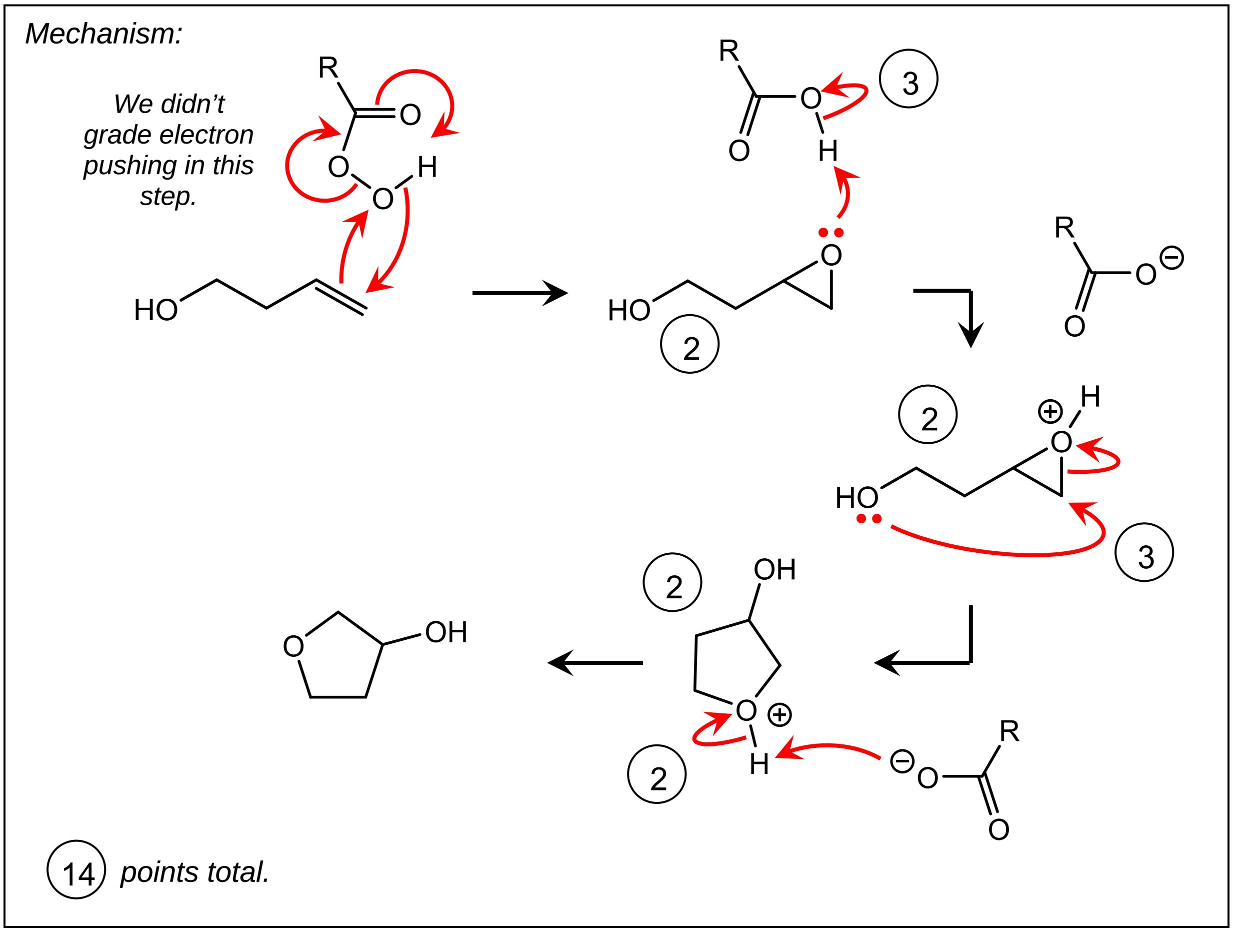
-2 points for each step combined with another, taken off each step.

-2 points for each use of a generic or incorrect acid/base. Only HCl can be used as the acid—that's it.

3 points for each set of curved arrows.

2 points for cation intermediate.





Rubric: *(14 points total for this box)*

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 and spectators may be omitted.

Proton transfer must be shown explicitly, with two arrows (one to proton, one from proton-acid bond). It's not okay to just write "proton transfer" or "+H$^+$".

-2 points, for each arrow in each step, for errors (including omission) in drawing arrows. Arrow must start at an electron pair (either a bond or a lone pair), and end at nucleus or bond where electrons will newly interact.

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

- *-2 points for each step combined with another, taken off each step.*
- *-2 points for each use of a generic or incorrect acid/base. Only “RCOOH” or peracid can be used as the acid, and “$RCOO^-$“ as the base—that’s it.*

3 points for each set of curved arrows. (2 points for the last step.)
2 points for each intermediate.

This mechanism involved a sequence of four steps—epoxidation, protonation of the epoxide oxygen, intramolecular attack, and deprotonation. Epoxidation really had to happen first, but if you did the other three steps in a different order, you lost points for the intermediates, but you could still get credit for the electron pushing steps if you pushed electrons correctly.