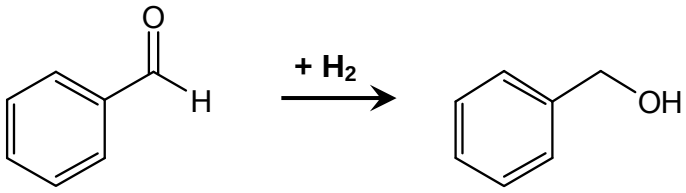
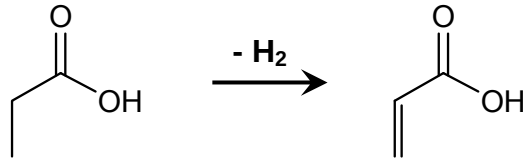
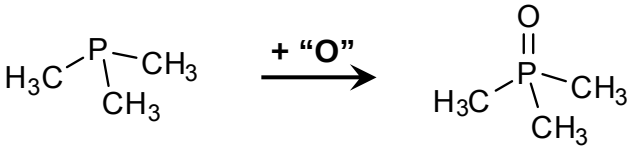
1. (9 pts) Identify each of the transformations below as a reduction, an oxidation, or neither. **Circle only one answer for each transformation**.



3 **REDUCTION** *or* **OXIDATION** *or* **NEITHER**



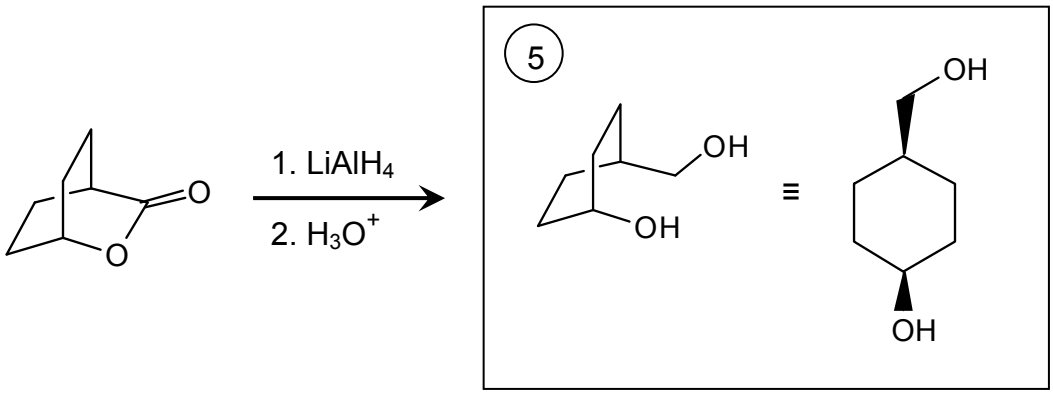
REDUCTION *or* **OXIDATION** *or* 3 **NEITHER**



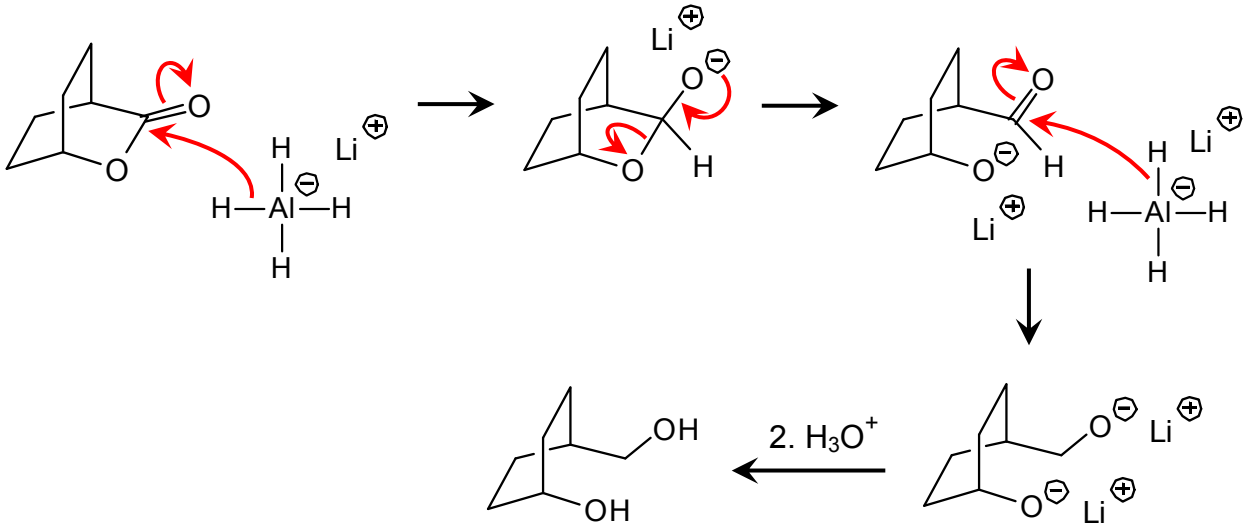
REDUCTION *or* **OXIDATION** *or* 3 **NEITHER**

Rubric:
3 points each answer. (9 points total.) *No partial credit.*

2. (10 pts) For each of the reactions below, **fill in the empty box corresponding to 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".



$LiAlH_4$ is a strong reducing agent, which will not only reduce the ester group in this molecule, but will also reduce the aldehyde intermediate formed by addition of the first hydride:



Rubric for this part:

5 points for correct structure.

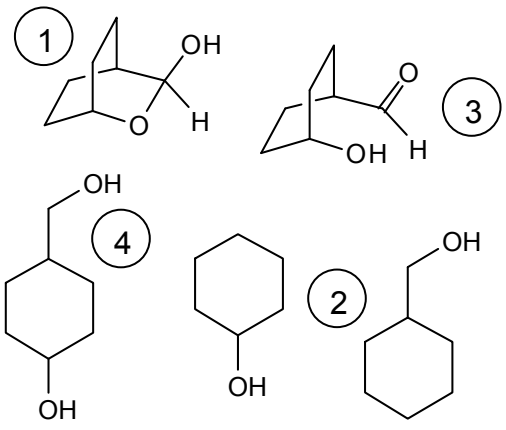
3 points partial for incomplete reduction.

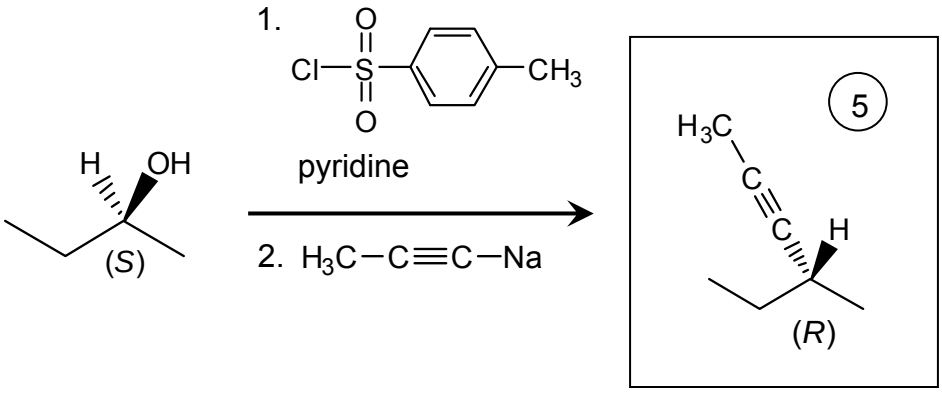
2 points partial for mono-alcohol.

-2 points for each clearly trivial structure mistake. (This includes leaving out or adding a carbon.)

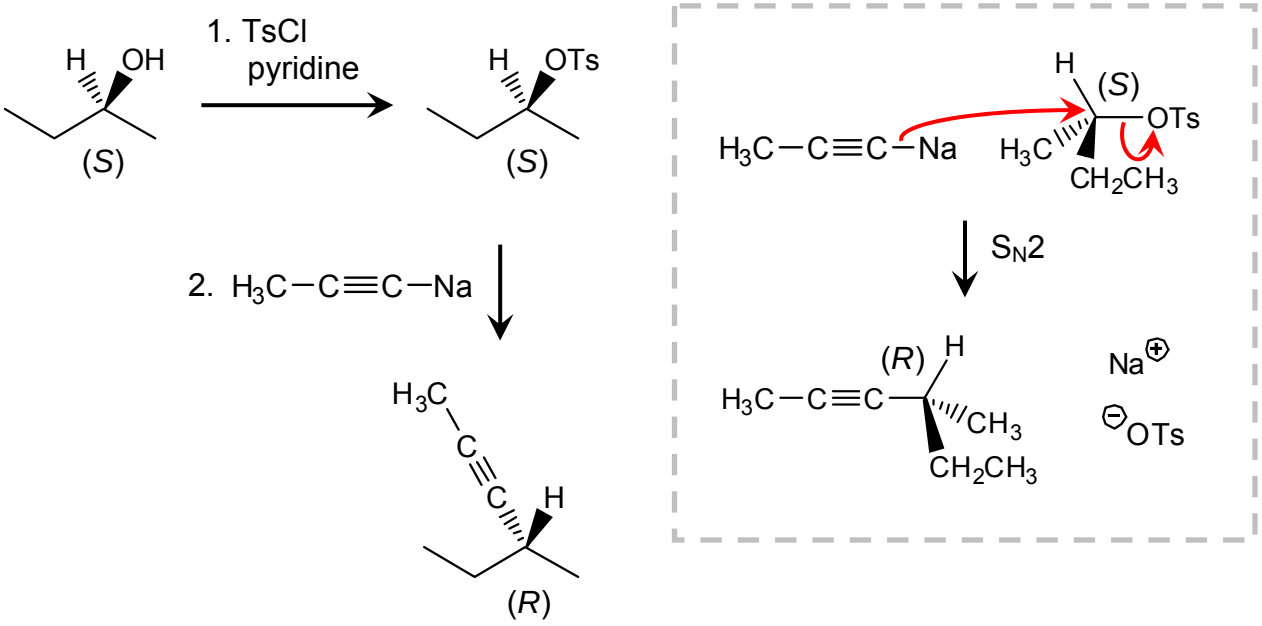
-1 for trans-disubstitution, or for di-substitution with no stereochemistry.

-1 point for not protonating alkoxides.





In the reagent sequence shown, the first step tosylates the alcohol (with retention of stereochemistry), and the second step substitutes the tosylate with an alkynylide (via S_N2, which inverts stereochemistry):



Rubric:
5 points for correct structure.

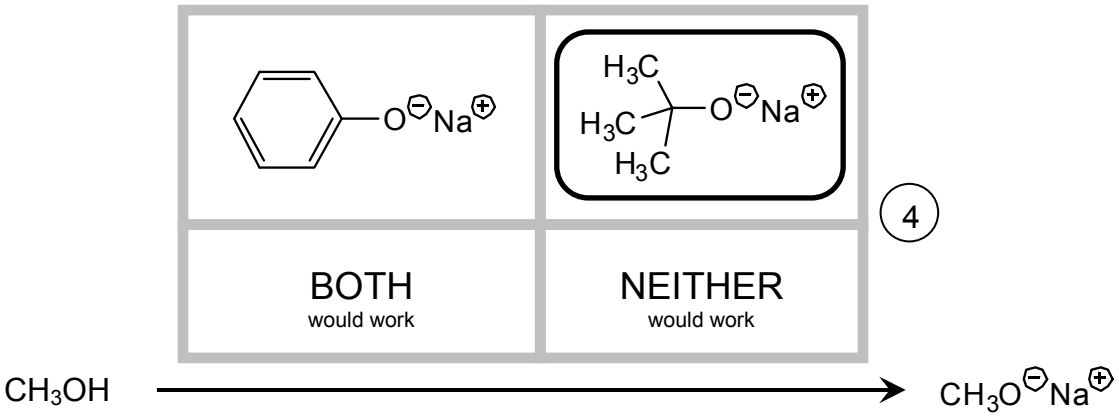
The answer doesn't have to be drawn like my answer, as long as it's correct and has (R) stereochemistry.

4 points for correct substitution product with incorrect or no stereochemistry.

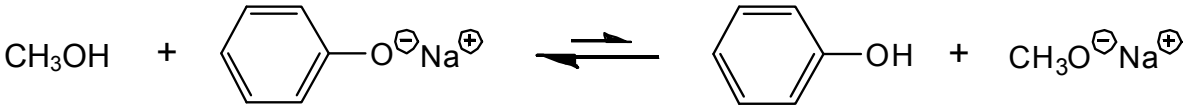
2 points partial for tosylate (any stereochemistry).

-2 points for each clearly trivial structure mistake.

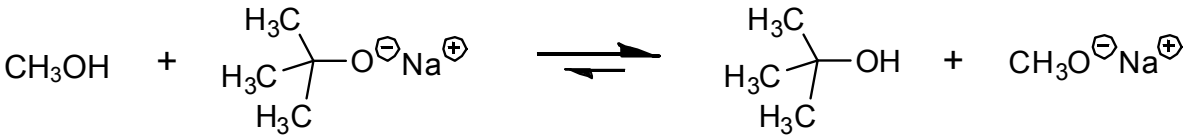
3. (16 pts) Each of the reactions below is drawn with two possible reaction conditions. If only one of the two reaction conditions would generate the given molecule as the major product, circle those conditions. If both sets of conditions would accomplish the reaction, circle "BOTH". If neither set of reaction conditions would succeed, circle "NEITHER". **Circle one answer only.**



Both of the alkoxides in the boxes could act as bases, but only *tert*-butoxide is basic enough to deprotonate methanol. Thinking in terms of acid-base reactions,

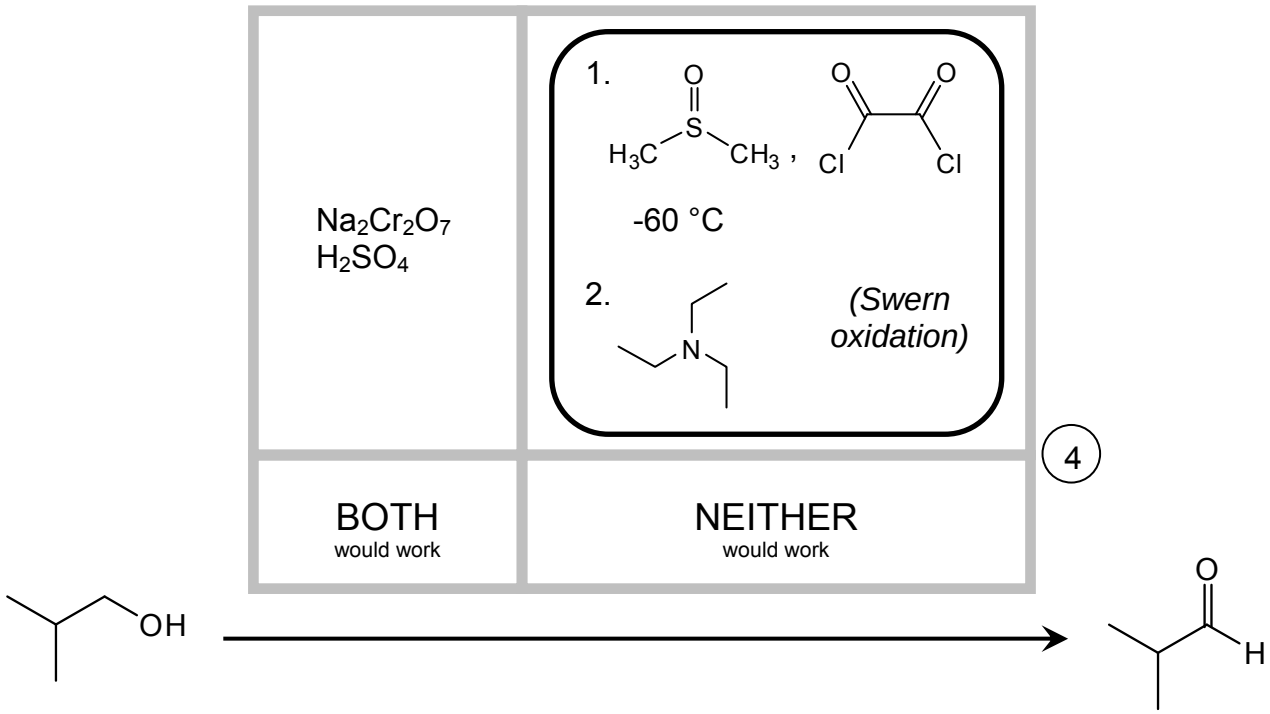


pK_a = 15.5 pK_a = 10.0

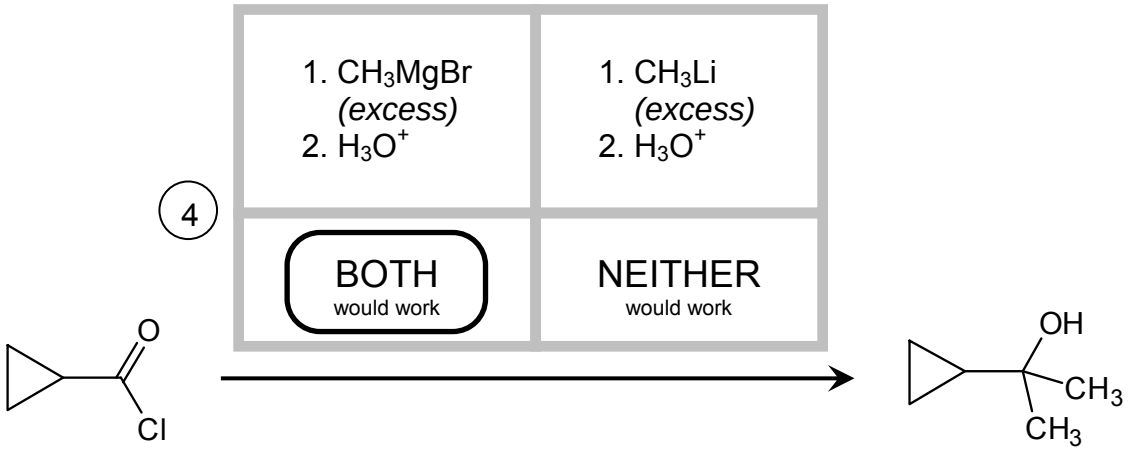


pK_a = 15.5 pK_a = 18.0

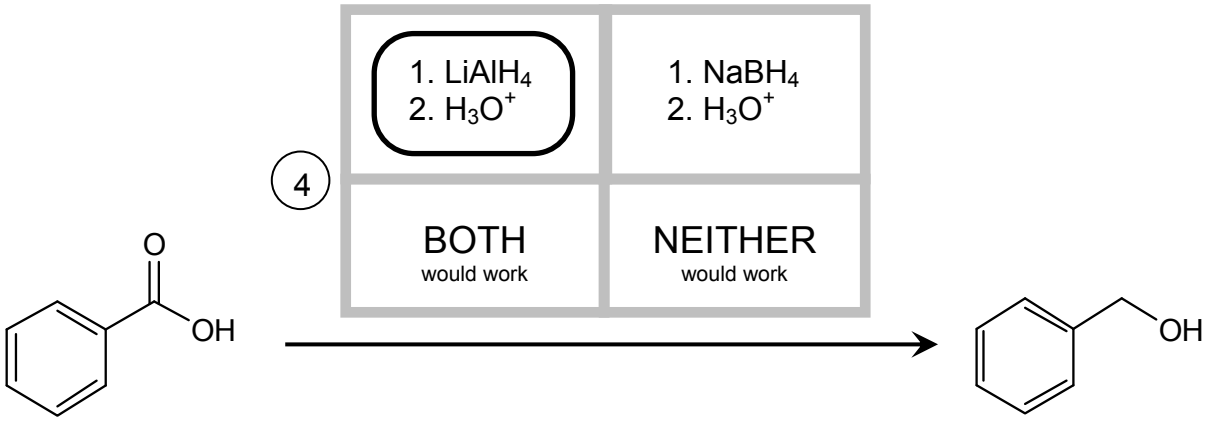
Of these two acid-base equilibria, only the second lies to the right (to products).



Both of these reagent systems are for oxidation. Chromate ($Cr_2O_7^{2-}$) is a strong oxidant, and will oxidize alcohols all the way to carboxylic acids. Swern oxidation, on the other hand, is a mild oxidation protocol that will oxidize alcohols only to aldehydes.

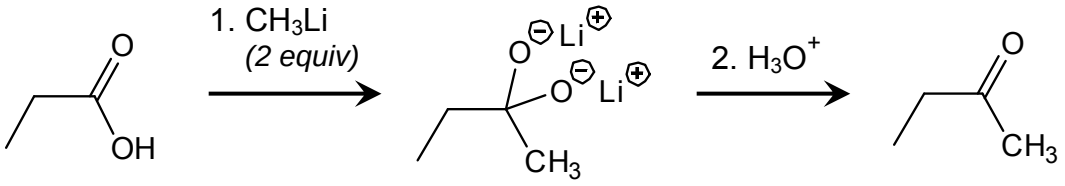


Both alkyllithium reagents and Grignard reagents will add twice to acyl halides: the first time to generate a ketone intermediate; and then the second time, unavoidably, to generate the alcohol.

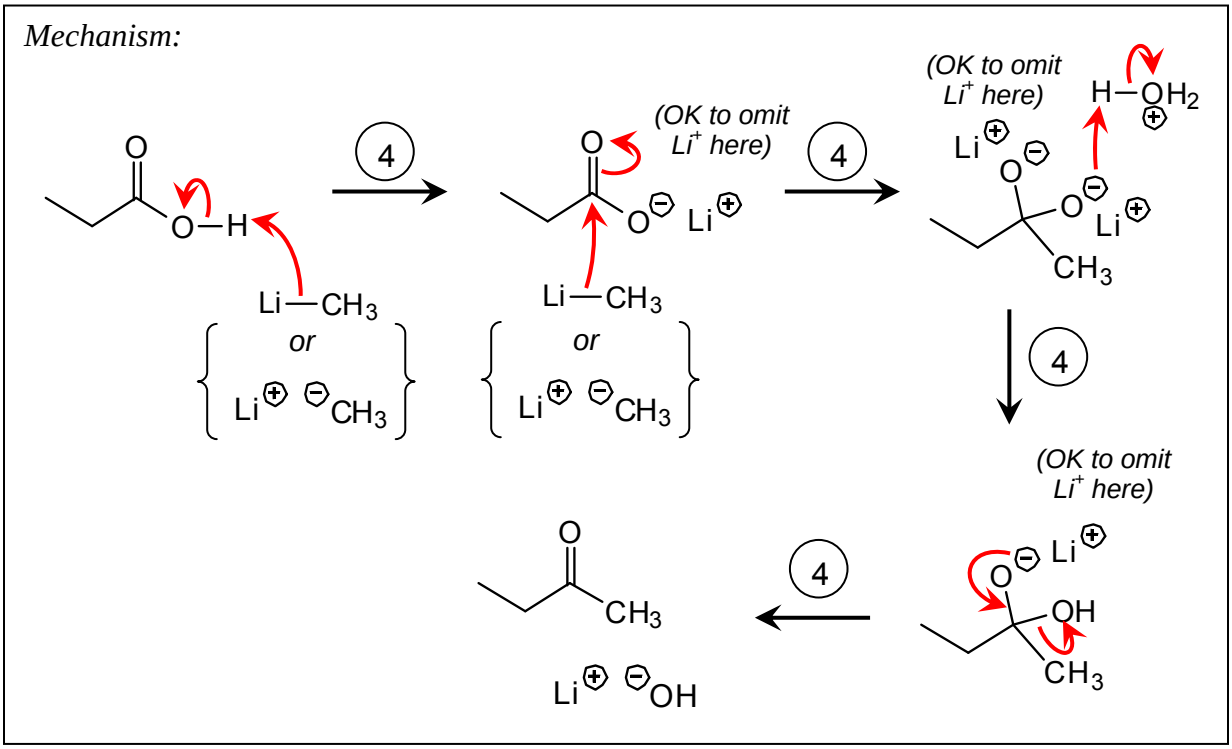


Both $LiAlH_4$ and $NaBH_4$ are reducing agents. $LiAlH_4$ is strong enough to reduce aldehydes, ketones, carboxylic acids, esters, just about anything to an alcohol. $NaBH_4$ is milder, and is capable of reducing aldehydes and ketones, but not carboxylic acids, to alcohols.

4. (16 pts) Draw a mechanism (using "electron pushing") for both of the reaction steps 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.)



Mechanism:



Rubric:

4 points for each of the four steps. (16 points total.) Must be these steps, in this order.

Electrons from CH_3Li can come from C-Li bond, or from an explicit carbanion. The carbon is technically bound to Li, but you can draw it as a separated ion.

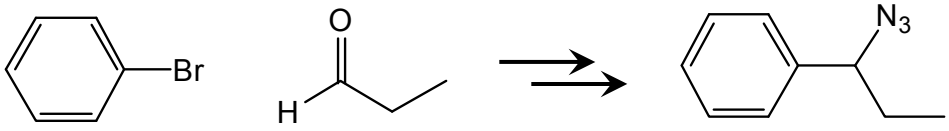
No need to keep track of Li^+, or to draw ^-OH after it is gone.

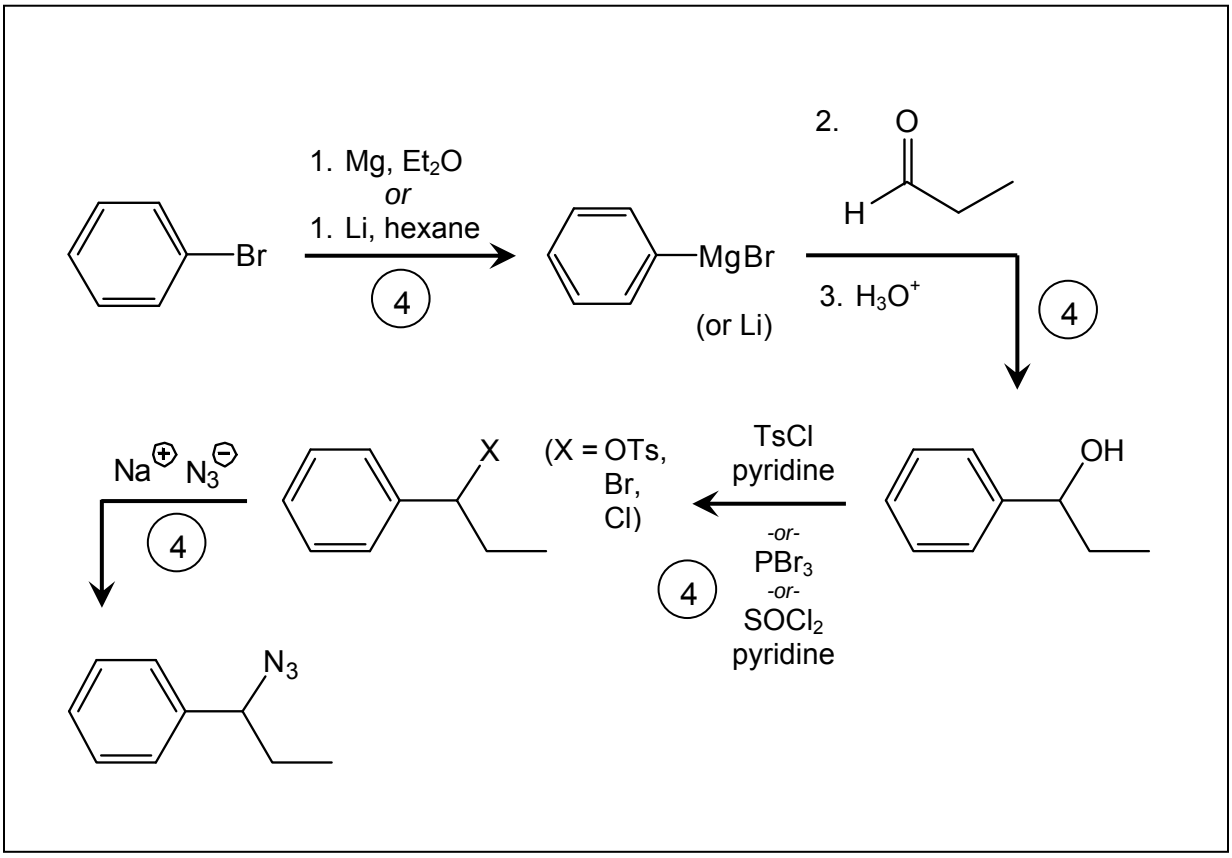
-2 points, for each arrow in each step, for errors in drawing arrows. Arrow must start at an electron pair (or a charge that indicates a pair), and end at nucleus where electrons will newly interact. Can only lose points if you get them.

-2 points for each minor 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. This is counted off of each of the combined steps.

5. (16 pts) Propose a multistep synthesis of the product shown below from the given starting materials, along with any reagents we have covered 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.





This synthesis has four requirements:

(**a**) Preparing an alkylmetal from phenyl bromide;
(**b**) Combining the alkylmetal with the aldehyde;
(**c**) Converting the alcohol into a good leaving group;
(**d**) Replacing the leaving group with azide by S_N2.

Rubric: *(General notes)*

This synthesis requires the five tasks **a-d** shown above. Each task is worth 4 points. 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/reasonable, but wrong step product, except for the last step (where the step product is obviously the final product).

We only gave points for correct reagents if they connected a starting material and a product in an understandable way.

4 points for generating alkylmetal from phenyl bromide.

Can use Mg, Li, or tBuLi (halogen-metal exchange). No need to show solvent.

I've drawn the alkylmetal intermediate explicitly, but in an actual synthesis, the alkylmetal would be generated in situ and would not be isolated or purified. (This is why I used the numbers 1., 2. for this and the following step. You didn't need to, but now you know why I did.) There is no need for you to draw the alkylmetal intermediate for this step. But, if you didn't, the following step needs to make sense. If it doesn't, you don't get credit for this step either.

4 points for combining alkylmetal with ethyl reactant in a way that works.

Can omit H_3O^+/H_2O workup.

2 points partial for alkylmetal + alkyl halide/tosylate. (Let's face it—this would be the hard way to do this problem.)

4 points for converting product alcohol to a good leaving group.

Tosylation or any halogenation works.

"TsCl" alone or "$SOCl_2$" alone is fine; these require pyridine, but we didn't grade on it.

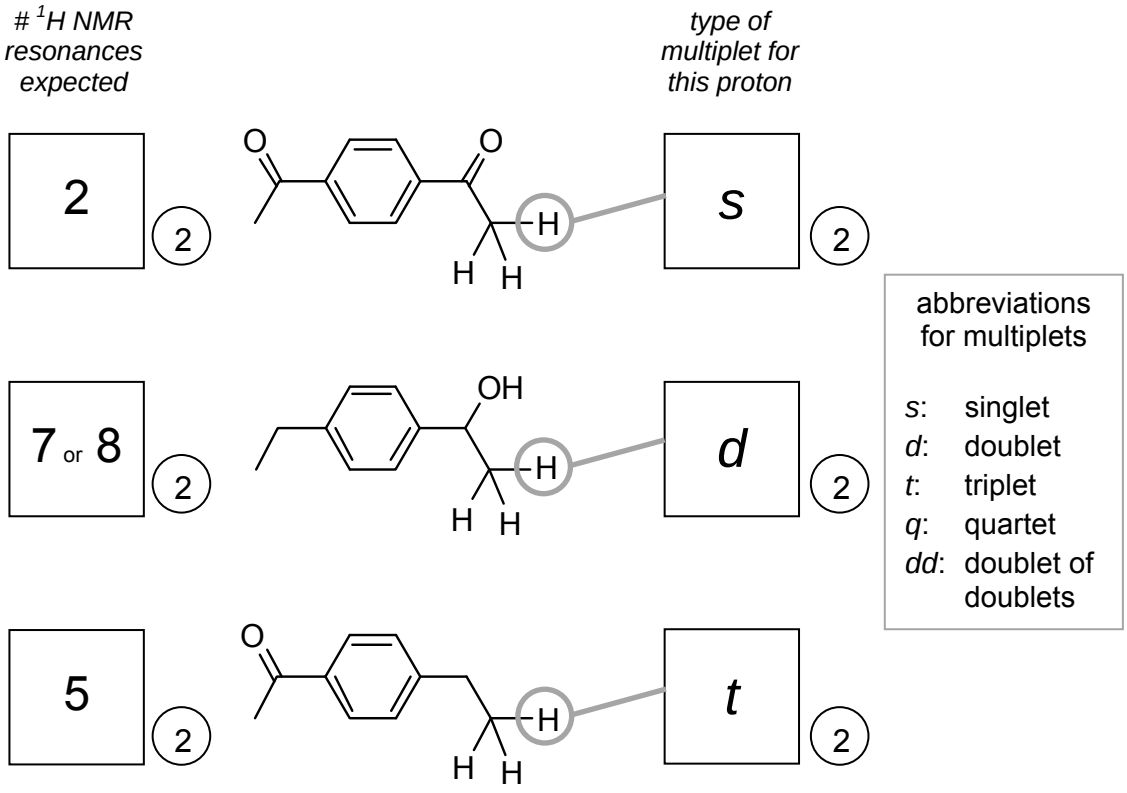
4 points for substituting leaving group for N_3^- nucleophile.

Just "N_3^-" is fine.

6. (**33 pts**) The test form says this problem is worth 32 points, but it's actually worth 33.

(a) How many resonances would you expect to see in the ^{1}H NMR of each of the potential oxidation products? In other words, how many inequivalent sets of protons are there in each structure? Write your answers in the boxes in the *left-hand* column below.

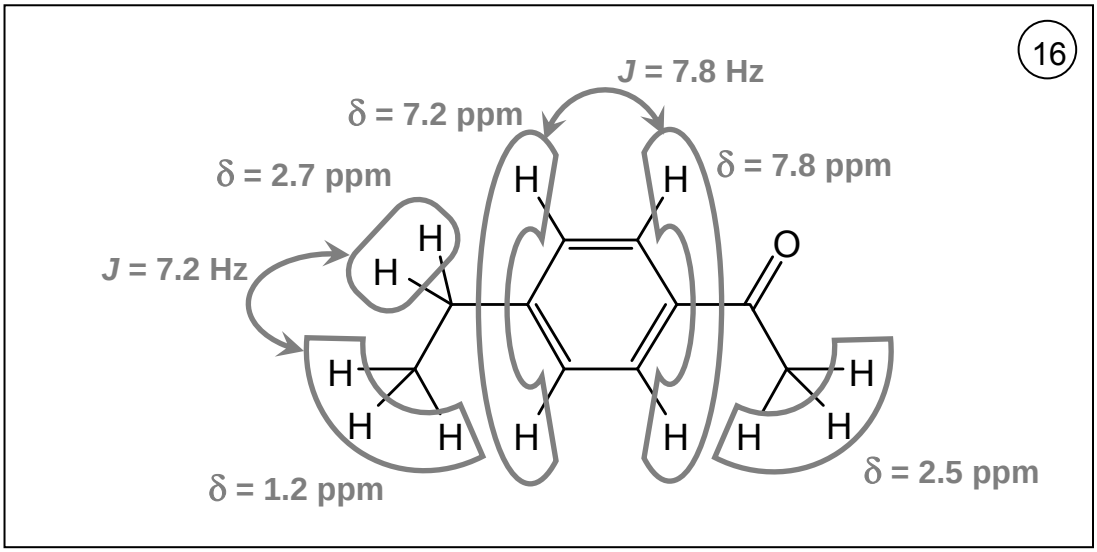
(b) Each proton highlighted in the structures below could be split by neighboring protons. What kind of multiplet should each proton produce in a ^{1}H NMR spectrum? (Assume that there is no long-range coupling in these molecules.) Use the abbreviations on the chart on the right, and write your answers in the boxes in the *right-hand* column below.



These answers are justified in the explanation for part (c) below.

Rubric for parts (a) and (b):
2 points each box. (12 points total this part.) *No partial credit.*

(c) The number of points you received in this section depended, in part, on what molecule you chose as the contaminant. Some of the ^{1}H and ^{13}C assignments were inconsistent with incorrect contaminant structures, and as a result your maximum possible score was reduced for these other choices.



Rubric for part (c), assuming this answer:

2 points for choosing the correct contaminant structure.

2 points for each pair of circled protons and δ values. (**10 points total for chemical shift assignments.**) To get 2 points, the circle must be perfect (include all the right hydrogens, no less, no more), and the δ value must be correct within 0.1 ppm.

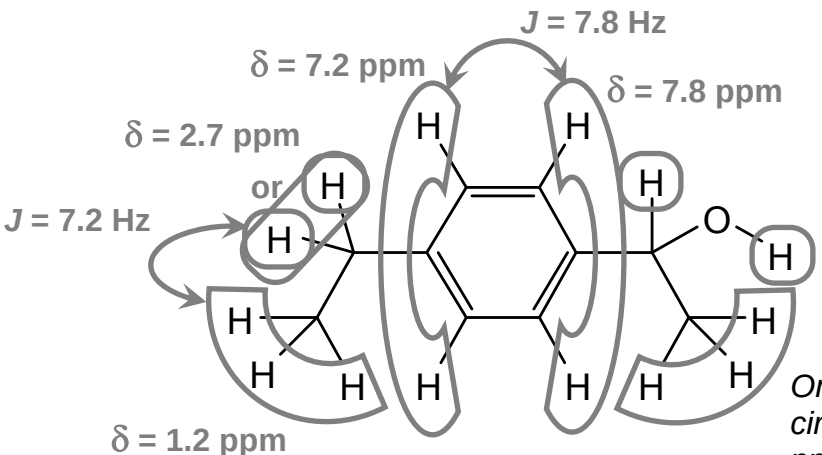
1 point partial for each δ assigned correctly to one correct proton. You get this if circle is incorrect, but δ is correctly associated with one of the protons in the circle.

1 point partial for each circle that is correct but has incorrect δ assignment.

2 points for each *J* assignment. (**4 points total for J's.**) Circles need not be correct to get these points; curved arrow only needs to connect one correct proton with one correct partner. But, both partners need to be correct to get points.

1 point partial if arrow is correct but J value is not.

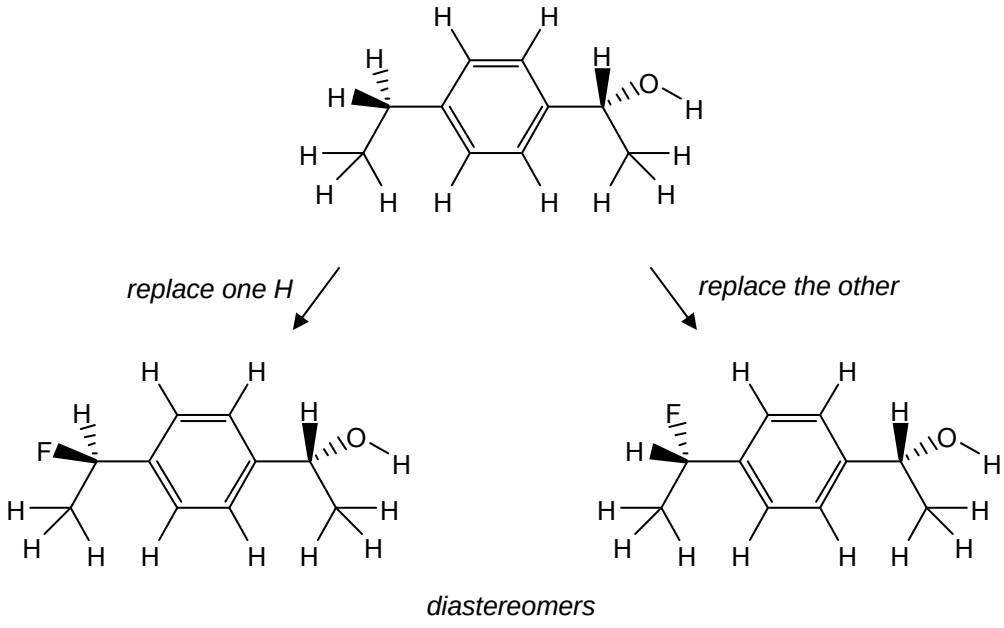
For other answers, only elements that make sense are graded. So:



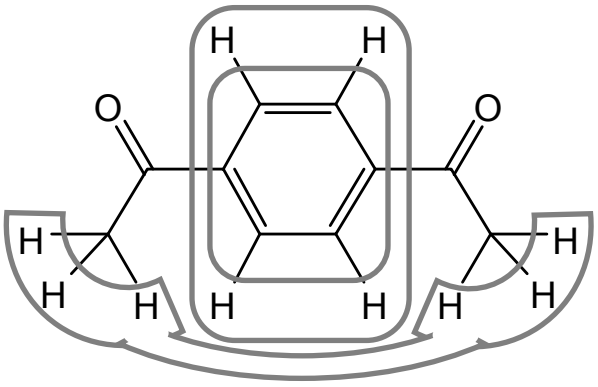
13 points can be earned here. Graders will ignore alcohol, HCO protons.

Only 1 point for this circle. (Because 2.5 ppm singlet makes no sense.)

Why have I drawn the $–CH_2–$ on the left as having one or two circles? The two protons on that $–CH_2–$ are technically not equivalent, because they are "diastereotopic"—meaning, if each one were replaced with a different atom, they would generate diastereomers, which are different molecules:



However, even though these protons are inequivalent, they are likely to have nearly identical electronic environments, and thus nearly identical chemical shift. It won't be possible to tell them apart.

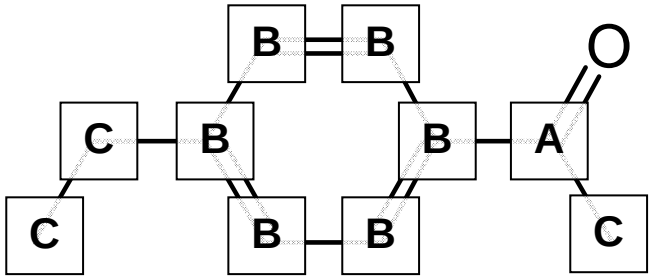


(2) points

can be earned here, for correct circles only. Spectrum is very inconsistent with this structure.

(d)

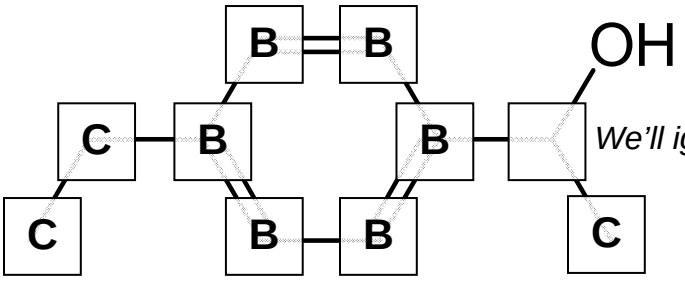
5



Rubric for part (d), assuming this answer:
1 point for letter **A** in the right place.
2 points for each letter **B**, **C**. To get 2 points, the letter must be perfect (in all the right boxes, no fewer, no more).
1 point partial for the letter appearing correctly in <u>one</u> box.

For other answers, only elements that make sense are graded. So:

4



We'll ignore this box.

5