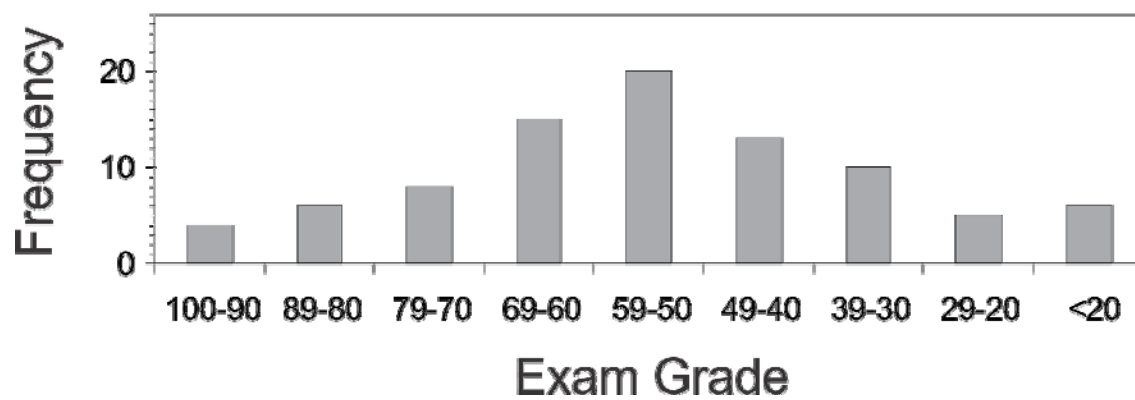
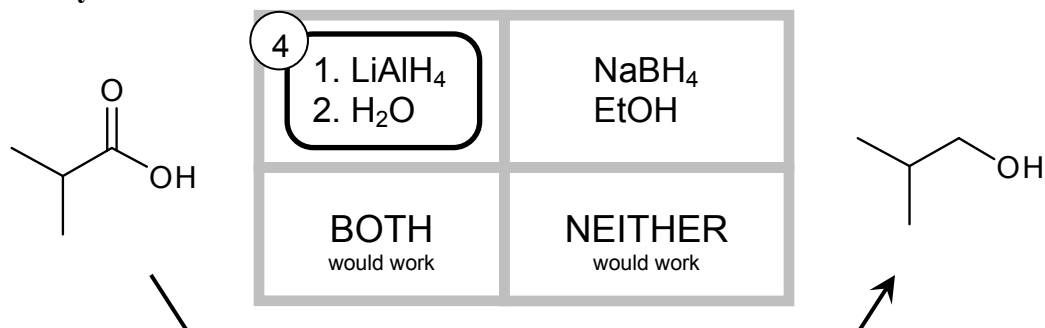


**Exam 2
Answer Key**

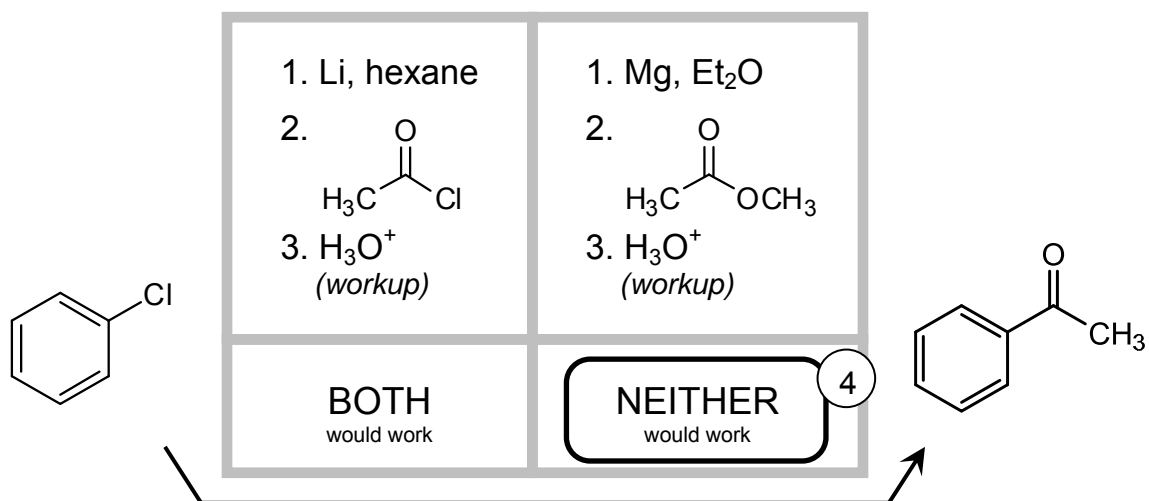
Exam 2 Mean: 53
Exam 2 Median: 53
Exam 2 St. Dev.: 19



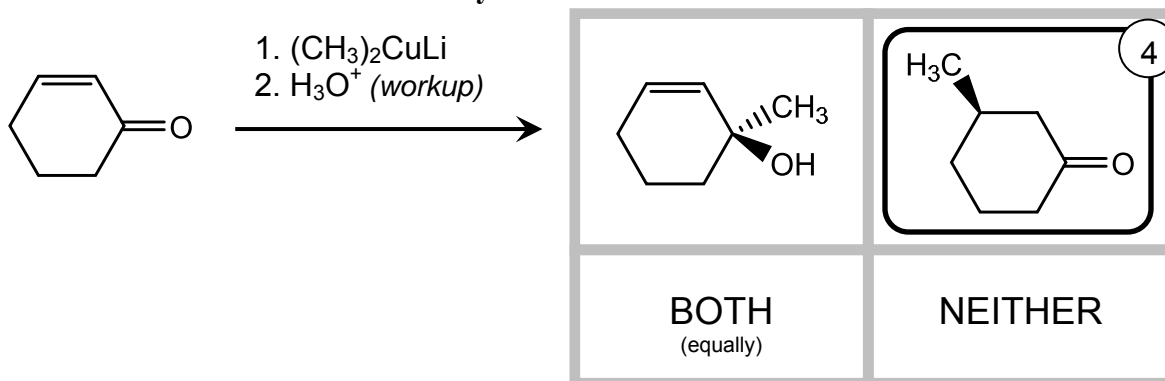
1. (8 pts) Each of the reactions below is drawn with two possible reaction conditions. If only one of the two reaction conditions would generate the given molecule as the major product, circle those conditions. If both sets of conditions would accomplish the reaction, circle "BOTH". If neither set of reaction conditions would succeed, circle "NEITHER". **Circle one answer only.**



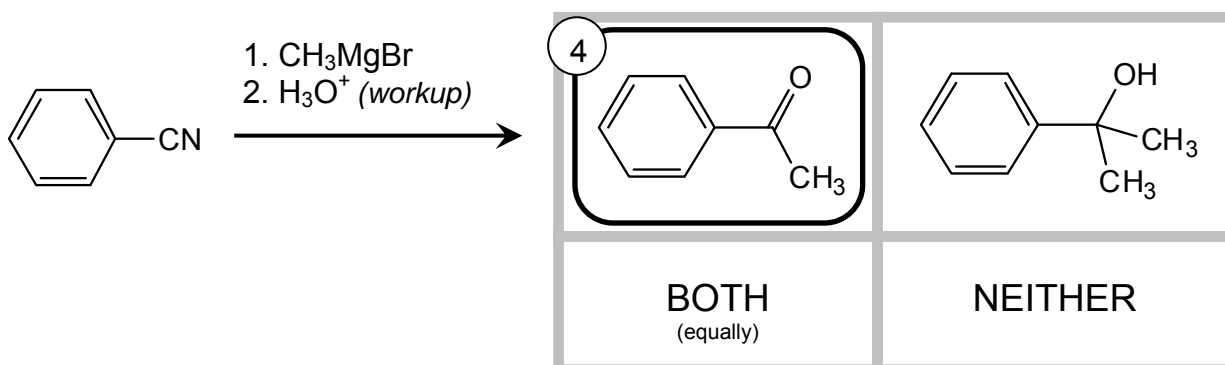
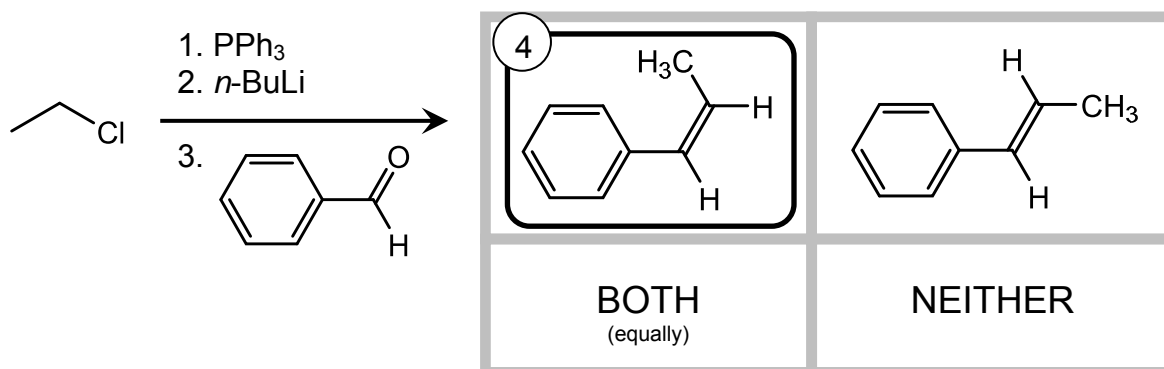
The reaction illustrated here is a reduction, and both LiAlH_4 and NaBH_4 are reducing agents. But NaBH_4 is a relatively mild reducing agent, and will only reduce aldehydes and ketones. Only the stronger LiAlH_4 will reduce carboxylic acids to alcohols.



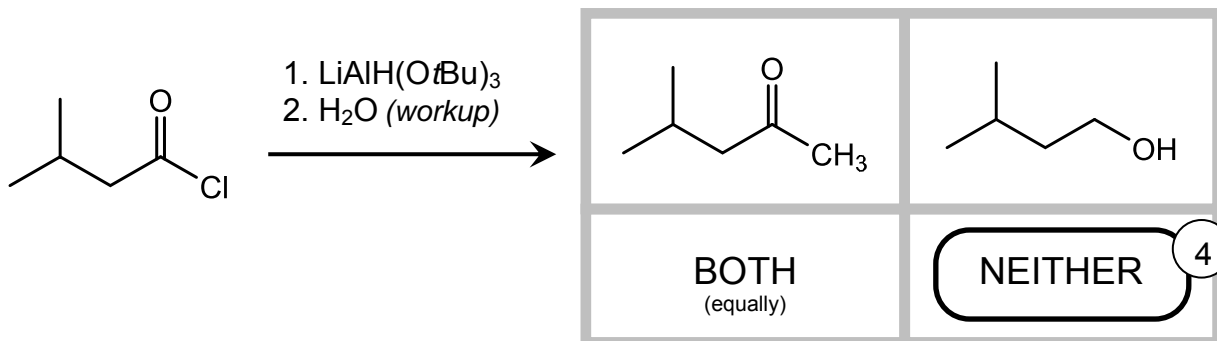
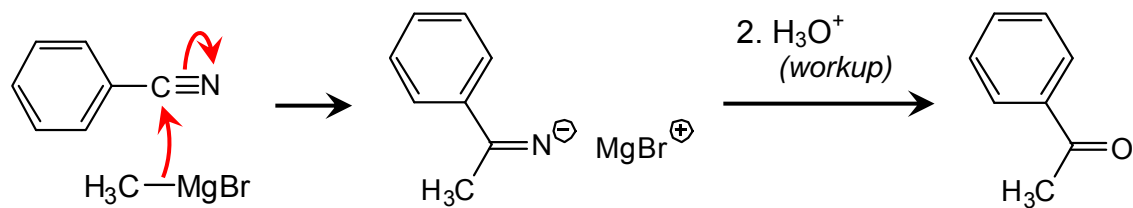
2. (16 pts) Each of the reactions on the next page is drawn with two possible products. If one of the two products predominates, circle that preferred product. If the two products are produced equally, circle "BOTH". If neither product would result from the reaction, circle "NEITHER". **Circle one answer only.**



Here we're asked to distinguish between 1,2- and 1,4-addition to an α,β -unsaturated carbonyl compound. Different nucleophiles have different preferences in this reaction; R_2CuLi alkylcuprates characteristically add 1,4. The " CH_3^- " will add to the 4-position to yield the product on the right.

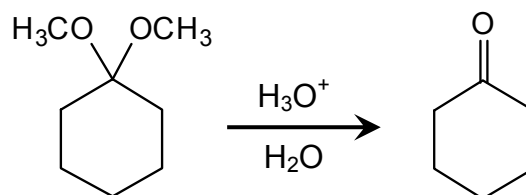


Nitriles add Grignard reagents only once to form an imine anion, which can't add again. In acid workup, this protonates and hydrolyzes to form the ketone.

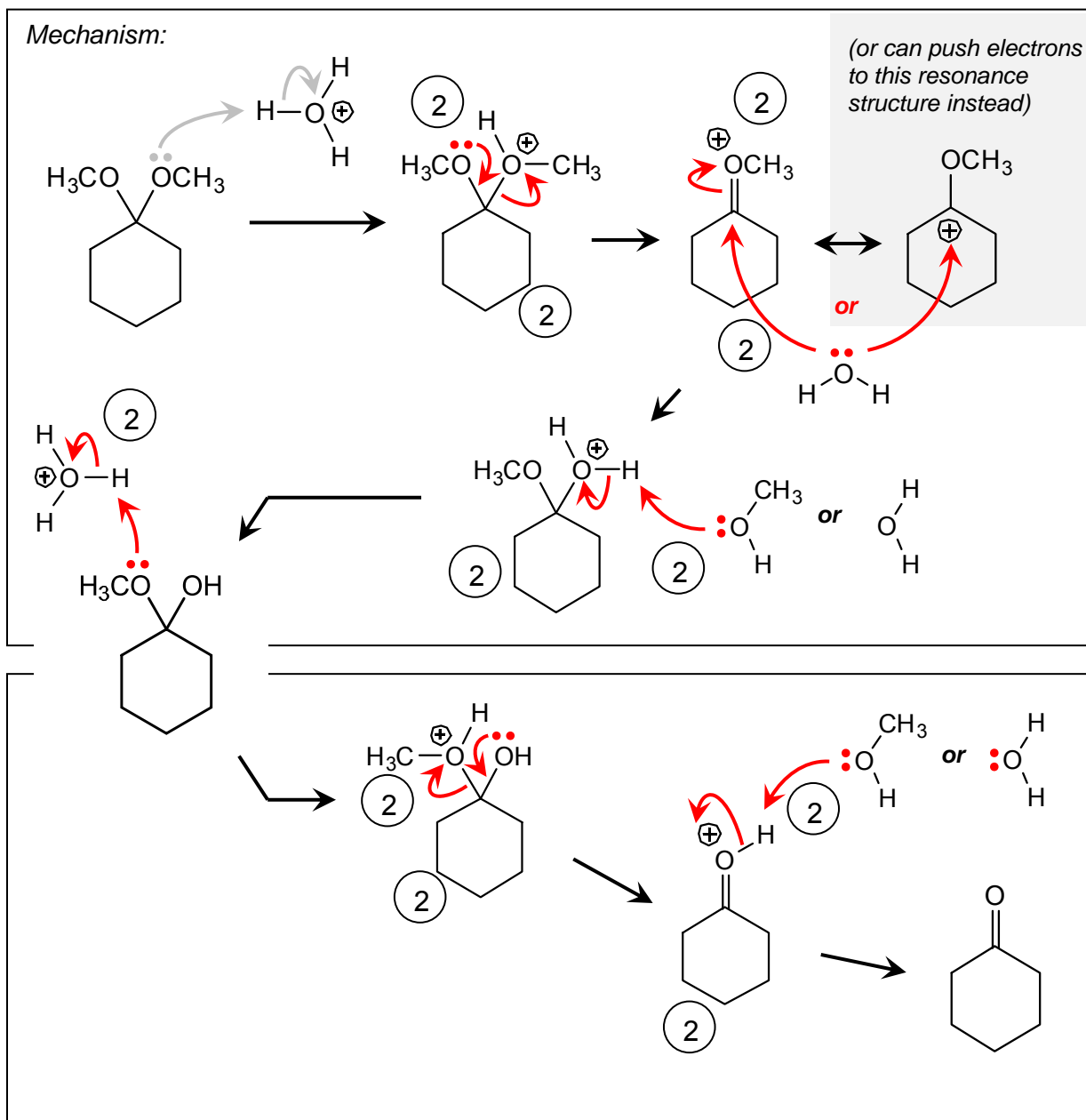


3. (22 pts) For the reaction shown on the next page, draw a mechanism that explains how the product is generated from the starting material, via the intermediate I've provided. In your answer, make sure that you:

- Draw each step of the mechanism separately;
- Use "electron pushing" to show where the electrons in each step go;
- Use only the molecules that you are given; do not invoke reactants or solvents that aren't in the problem.



I have drawn the first step of the mechanism for you; begin with this step.



Rubric: 22 points total.

Overall notes:

Overall, the minimum score for each item is zero; errors in a step cannot earn you negative points that count against another, correct step.

Spectators (e.g., H_2O in any step it isn't used) may be omitted.

Resonance is NOT a mechanistic step; it is just multiple ways of drawing the same intermediate. As a result, we did not evaluate electron-pushing that showed resonance—you can push electrons for resonance, or not, your choice. In addition, resonance does not have to be shown as an explicit "step"—it can be combined with adjacent steps, for full credit.

If you combine steps that can't be combined, you can get points for arrows that are in the rubric, but not for the intermediate you skipped.

2 points for each correct intermediate structure in your mechanism.

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

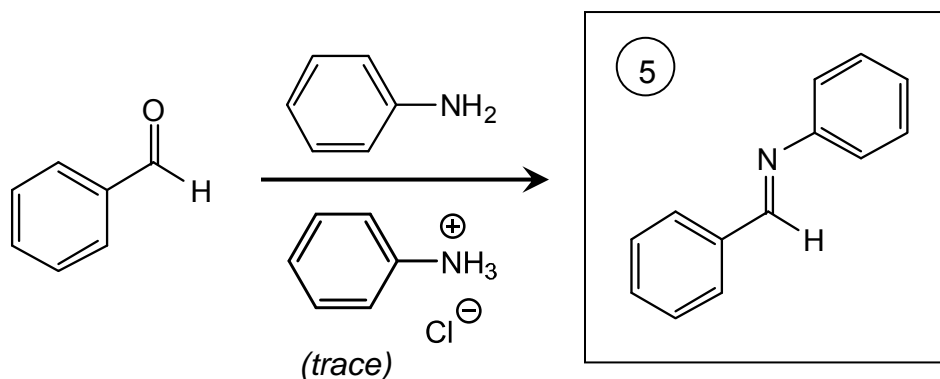
Any molecule can be depicted in any resonance state; no points are lost for drawing a molecule as a minor resonance contributor.

2 points for each electron-pushing step in your mechanism.

Arrow must start at an electron pair, and end at nucleus or bond where electrons will newly interact. If error is minor, grader may assign partial credit (1 point).

No credit for arrows that involve a generic or incorrect base/acid. For example, "H-A" couldn't be used to protonate anything here.

4. (20 pts) For each of the reactions on the following pages, fill in the empty box corresponding to product. Give only one answer in each box. For reactions that you expect to yield multiple products, draw one major product. For reactions that yield multiple enantiomers, draw only one enantiomer in the box, and include the note "+ enantiomer".



Rubric for this part:

5 points for correct structure.

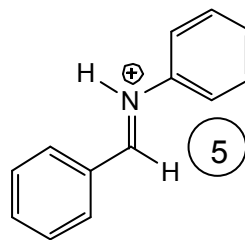
Full credit for protonated trans-iminium.

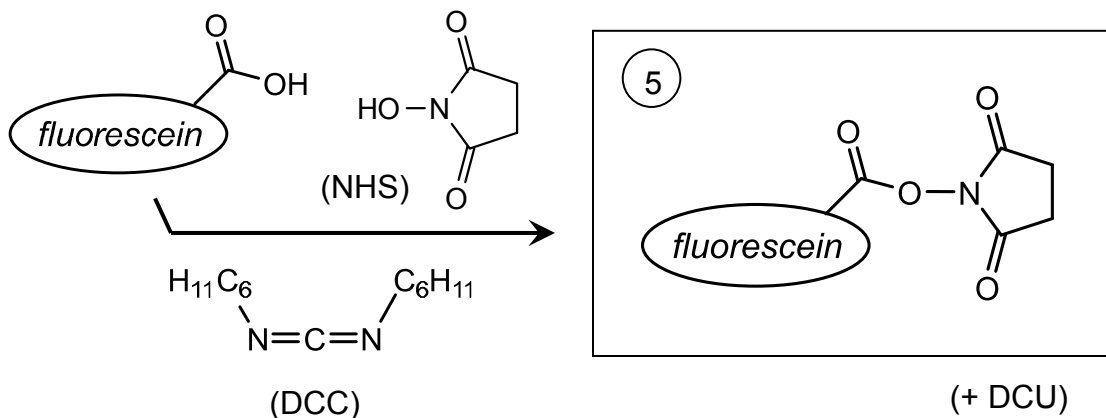
4 points partial for cis-imine or protonated cis-iminium.

3 points partial for carbinolamine (loses H₂O).

2 points for amide.

-2 points for each clearly trivial structure mistake.



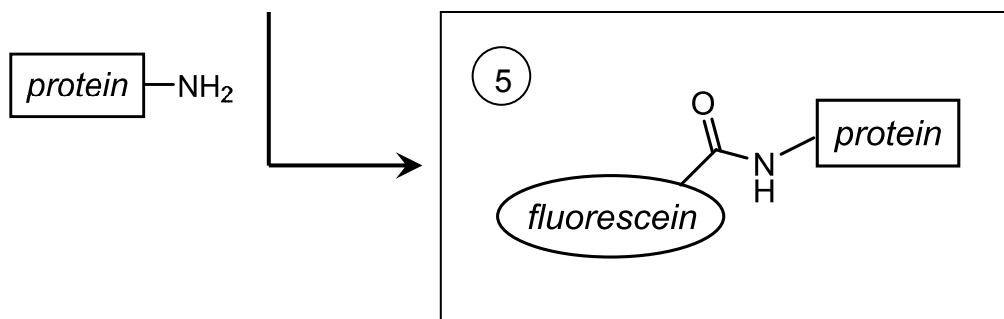


Rubric for this part:

5 points for correct structure.

3 points for amide.

-2 points for each clearly trivial structure mistake.

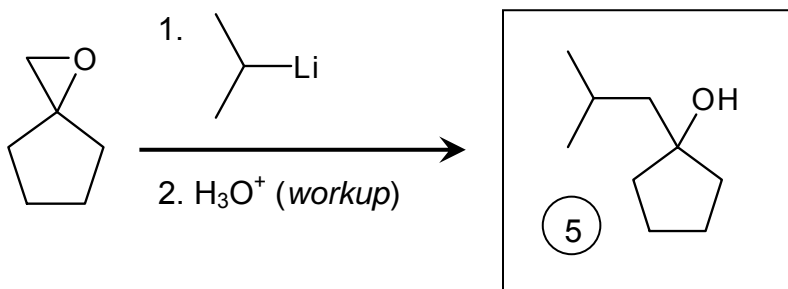


Rubric for this part:

5 points for correct structure.

2 points for any connection between protein and fluorescein.

-2 points for each clearly trivial structure mistake.



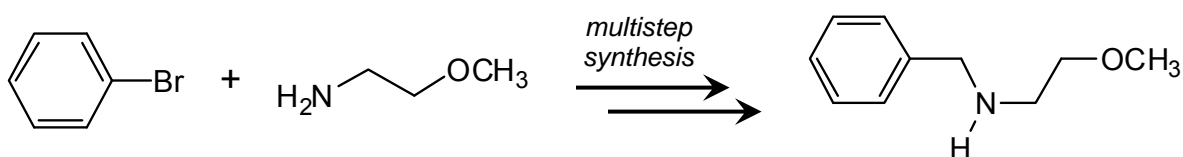
Rubric for this part:

5 points for NHS ester.

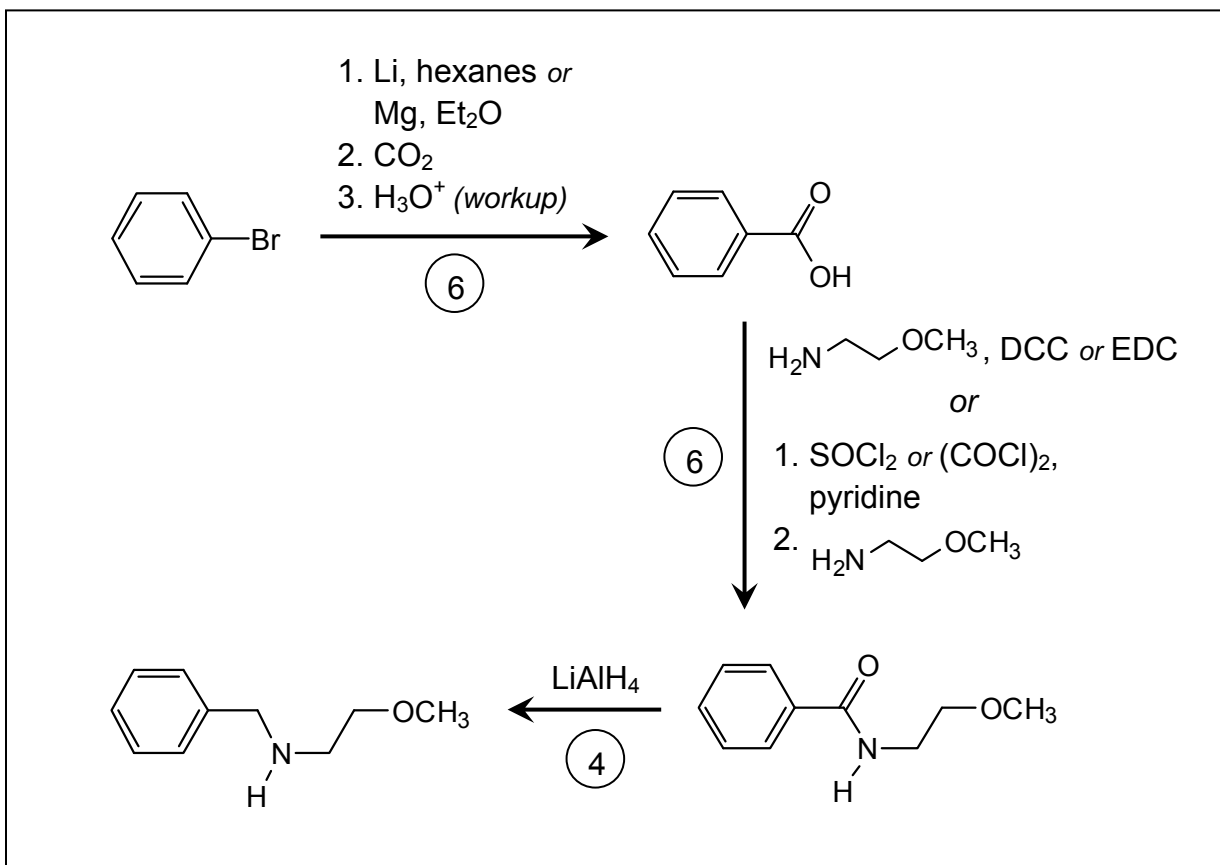
3 points partial for product of attack at more substituted carbon.

-2 points for each trivial structural mistake, including omitting a carbon from the sidechain.

5. (16 pts) Propose a multistep synthesis of the product below, beginning with the starting materials given. In addition to those organic starting materials, 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.



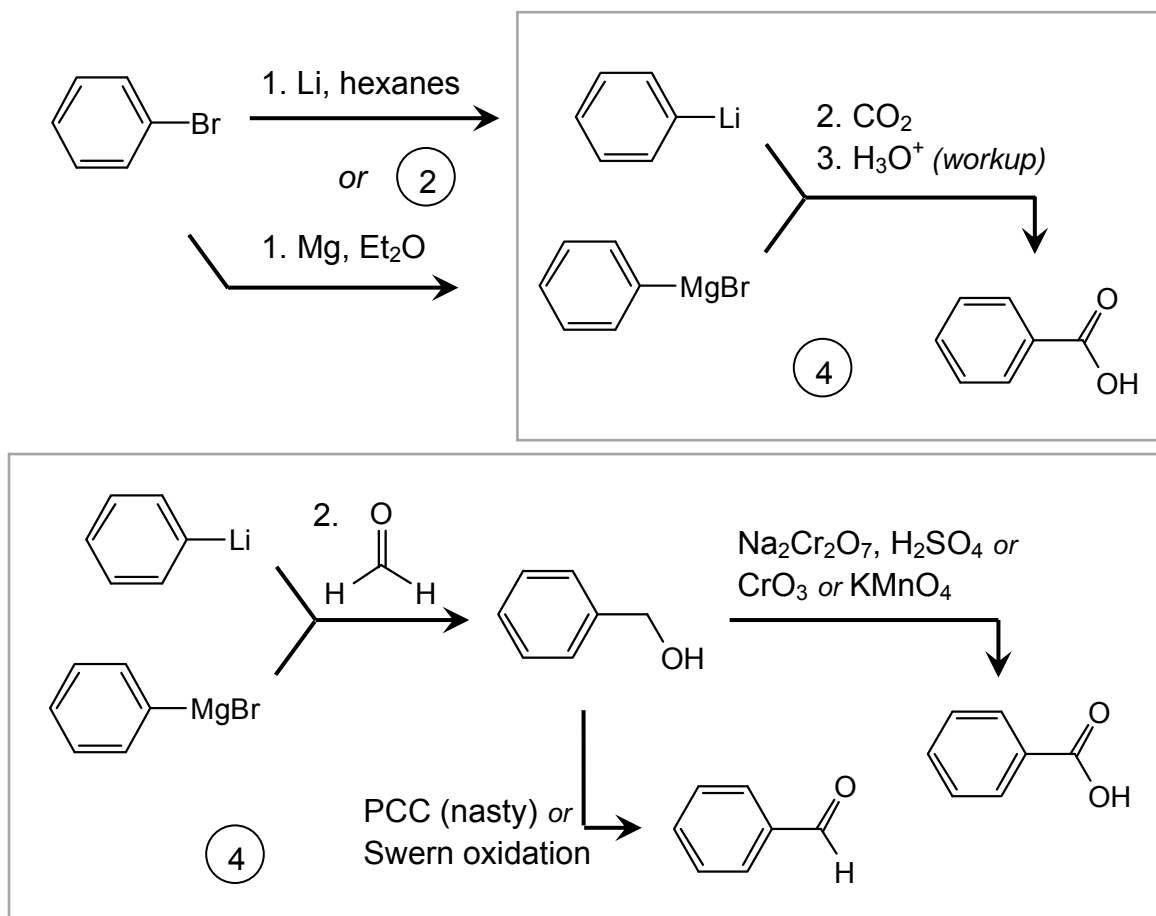
Many possible answers to this problem. One example:

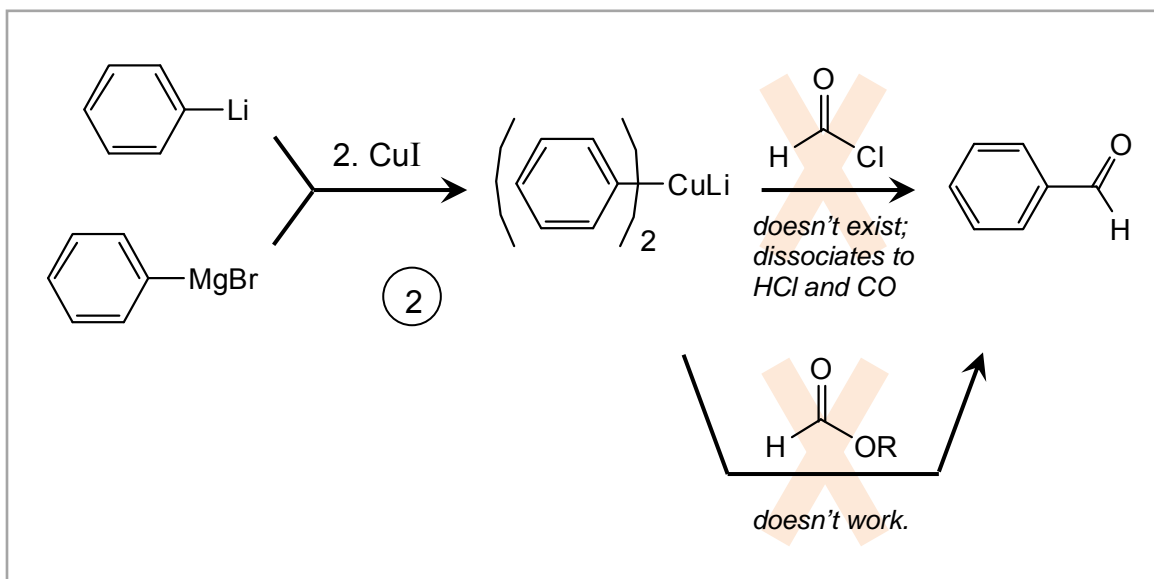


Overall, successful synthesis needed to accomplish three things:

1. Use the aryl bromide to add a single, electrophilic carbon to the benzene ring. (6 points.)

This sets up the molecule to accept the nucleophilic amine in a subsequent step. I have shown above how this might be done via addition of an alkylmetal (Grignard or alkyllithium) reagent to CO_2 , but it might also be accomplished with addition of an alkylmetal to formaldehyde, followed by oxidation to an aldehyde or ester. A couple things that wouldn't work, but have the right idea, include: alkylcuprate addition to "formyl chloride" (which doesn't exist); or cuprate addition to an ester (which doesn't happen). We also gave partial to full credit for anything more complicated than this, but still successful. (This was especially true for the aldehyde; I think the successful routes to this were all a little complicated.)

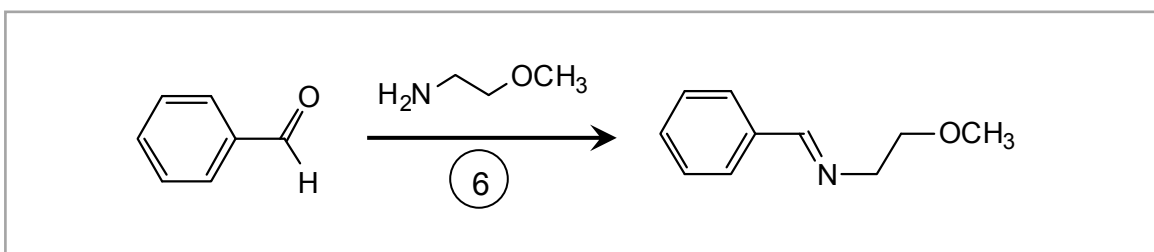
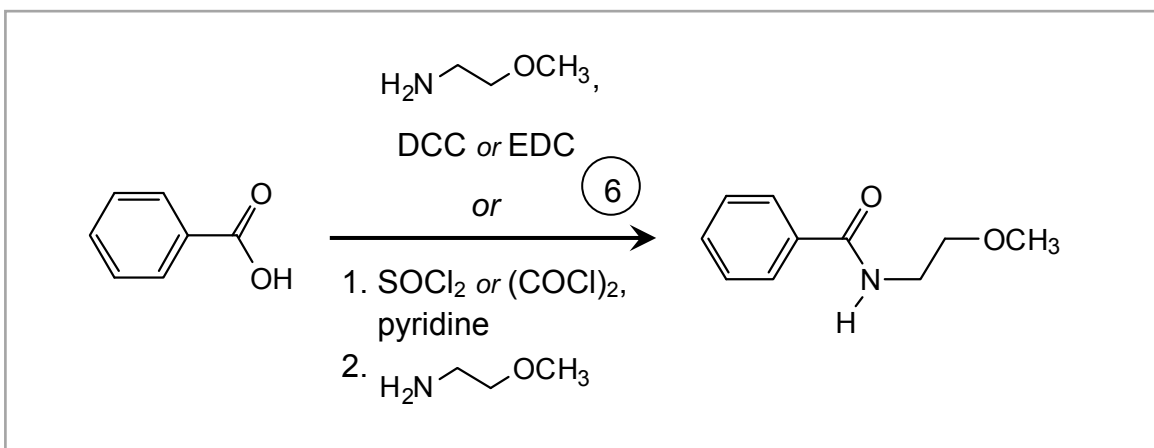




In the above, the cuprate would be used to avoid double addition of the alkylmetal to the acyl halide or ester (but neither would work in this case).

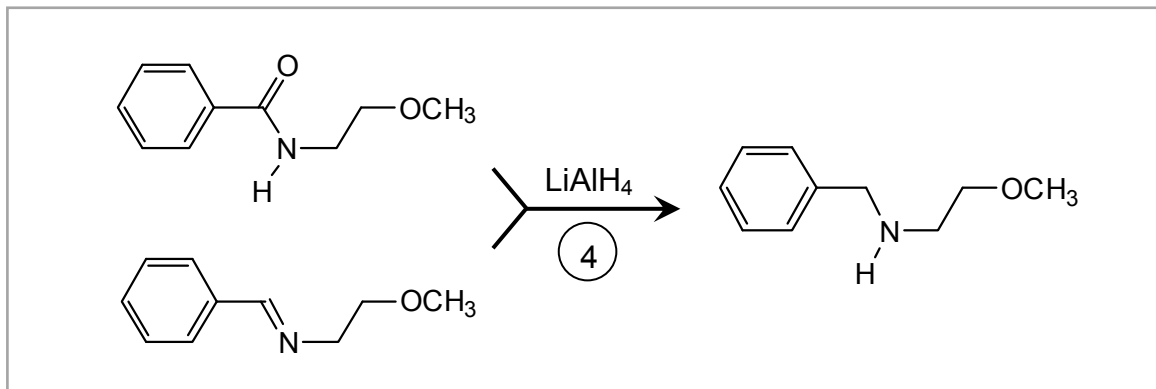
2. Combine the starting amine with the electrophile from step 1. (6 points.)

The best way to do this depended on the product you made in the first part above; we gave full credit to any valid combination. One clear way was to form an amide from the starting amine and a carboxylic acid or acid derivative. Another was to combine an aldehyde and the amine to form an imine; because the aldehyde is substituted with an aromatic group, the imine will be stable.



3. Reduce the amide or imine to an amine. (4 points.)

There are actually not a lot of ways to do this; both of these starting materials require LiAlH_4 to reduce them.



Rubric:

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

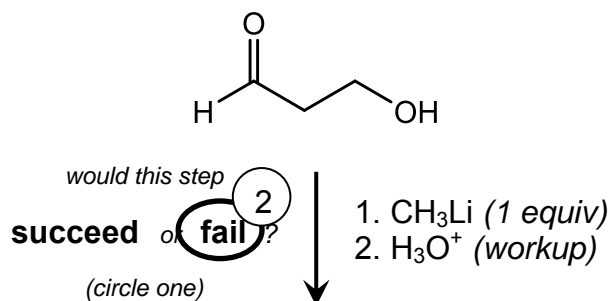
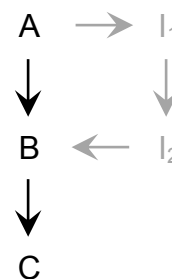
-1 point for each minor error in structures or reagents; if error propagates, points are taken off only for initial error.

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

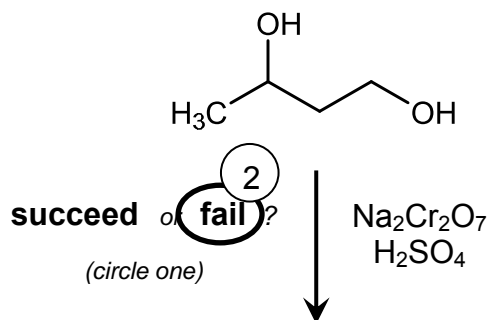
Graders had discretion on determining how successful your proposed synthesis would be and assigning points to your synthesis.

6. (18 pts) In the three-step synthesis below, at least one of the steps would fail as drawn. In your failed step(s), using a protecting group in the synthesis would help.

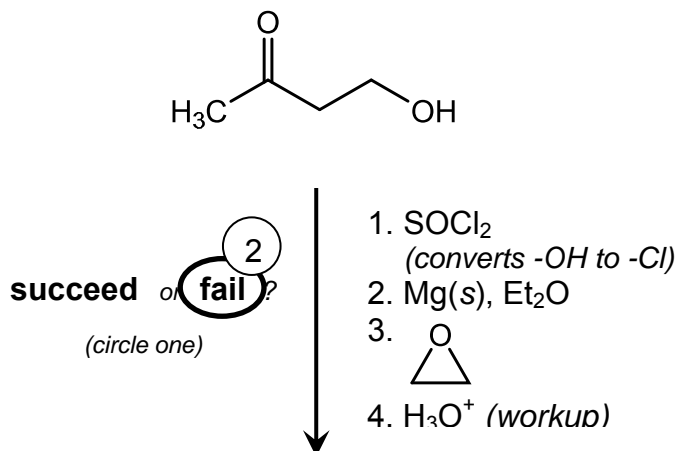
- Which steps do you think would succeed, and which would fail?
- For each step you predict would fail, draw a synthetic detour (like the scheme illustrated on the right) that incorporates protection and deprotection steps that would allow the synthesis to succeed.



CH₃Li is a very strong base; it will remove the proton from the -OH group before it gets the chance to add to the C=O bond.



Chromate is a strong oxidizing agent, and it will oxidize *both* of the -OH groups in the starting material. But if we keep the protecting group from the first step attached....



Once the Grignard is formed on the right-hand side of the molecule, it will attack the C=O bond on the same molecule (or on another copy of the same molecule).

