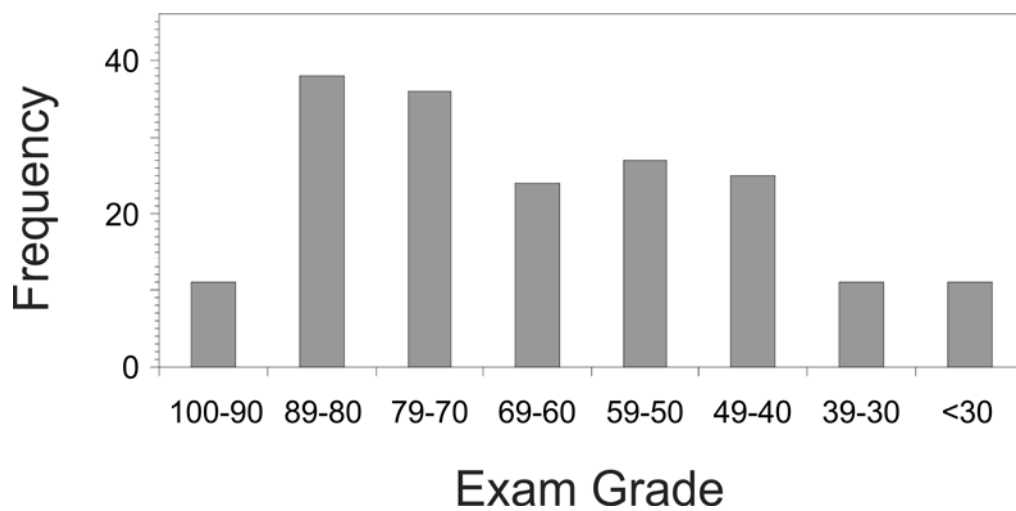
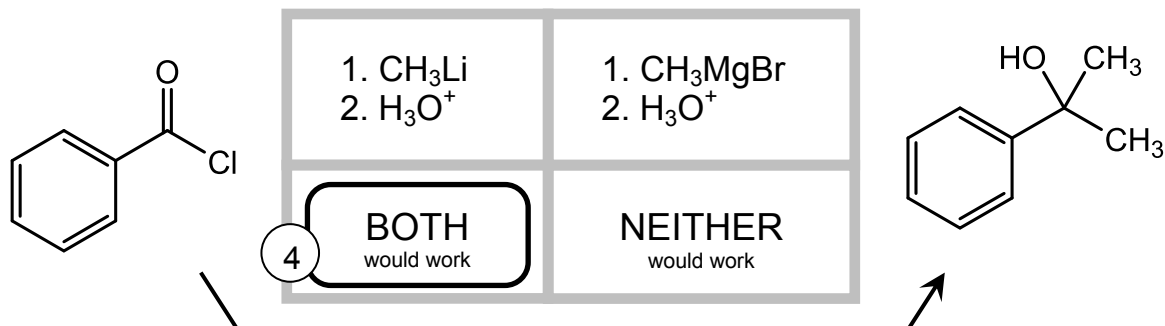


**Exam 2  
Answer Key**

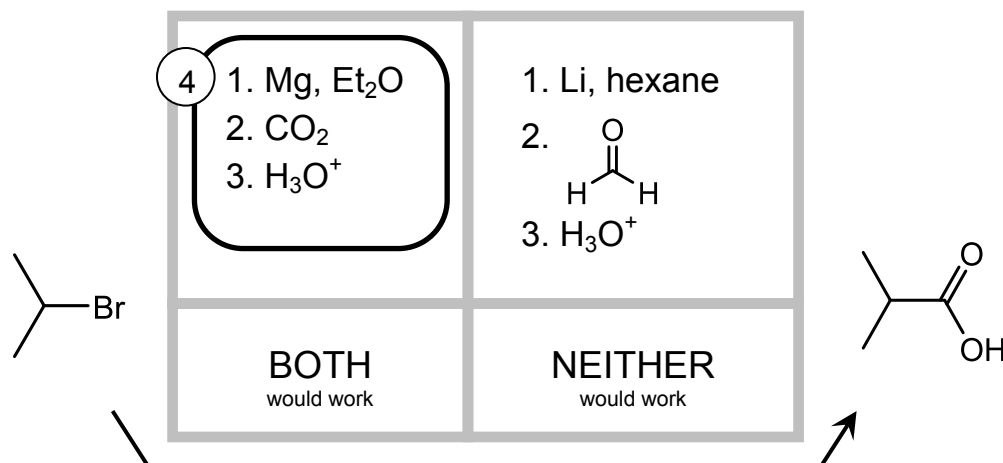
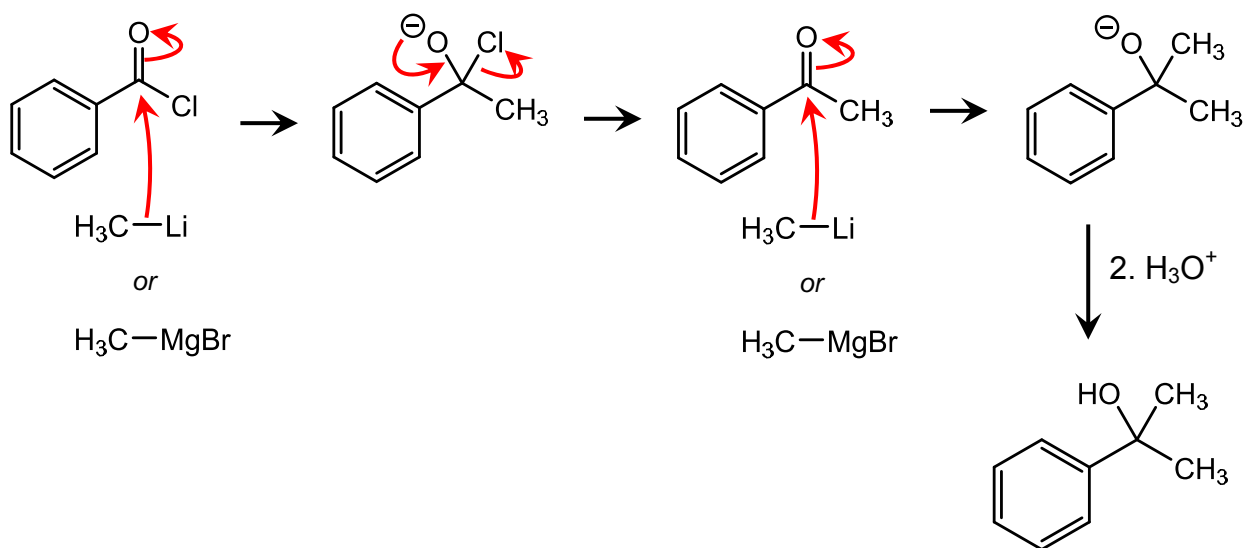
Exam 2 Mean: 66  
Exam 2 Median: 68  
Exam 2 St. Dev.: 20



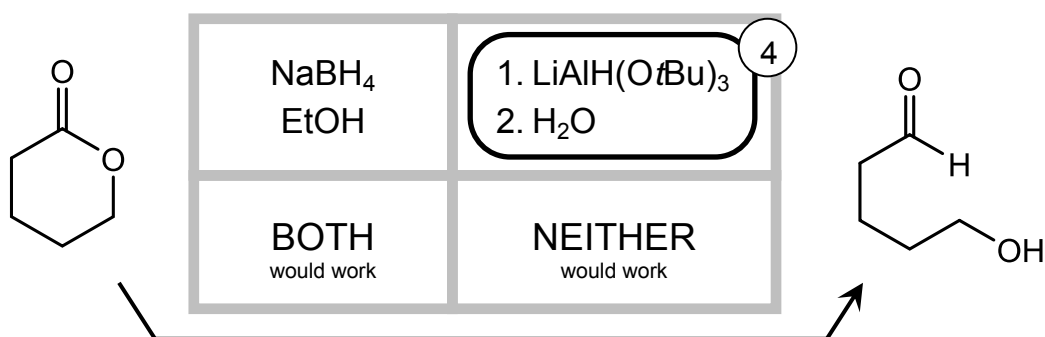
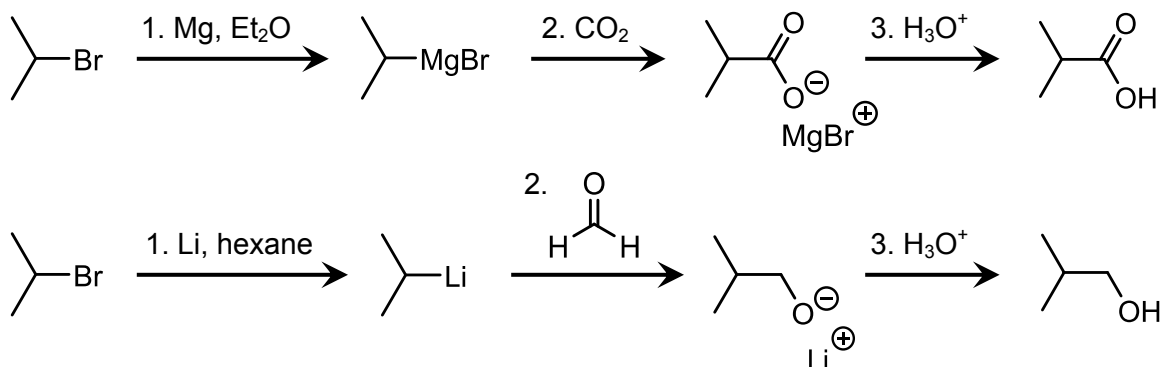
1. (12 pts) Each of the reactions below is drawn with two possible reaction conditions. If only one of the two reaction conditions would generate the given molecule as the major product, circle those conditions. If both sets of conditions would accomplish the reaction, circle "BOTH". If neither set of reaction conditions would succeed, circle "NEITHER". **Circle one answer only.**



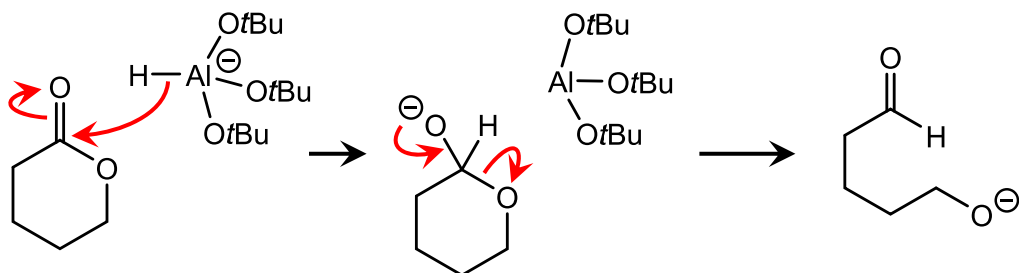
Both alkyllithium and Grignard (organomagnesium halide) reagents add twice to acyl halides:



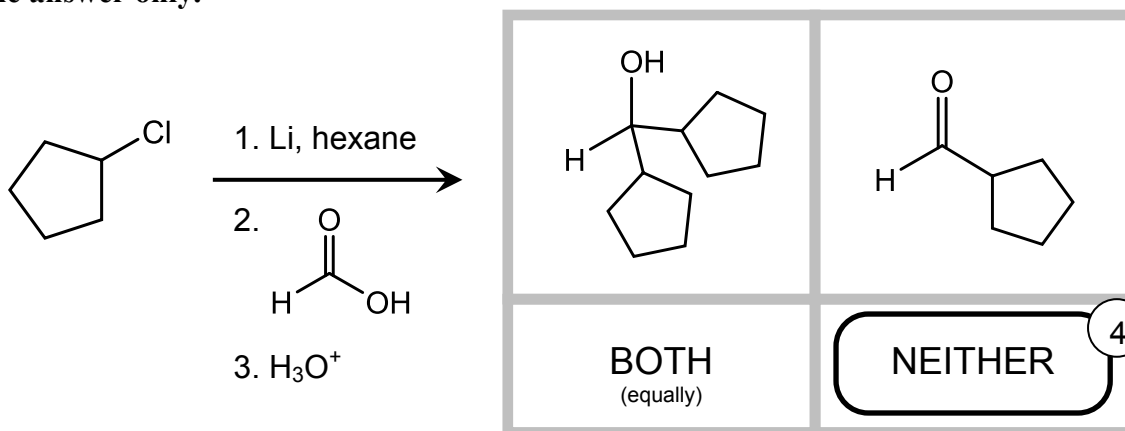
The first set of reagents generates the expected carboxylic acid. The second set generates an alcohol instead.



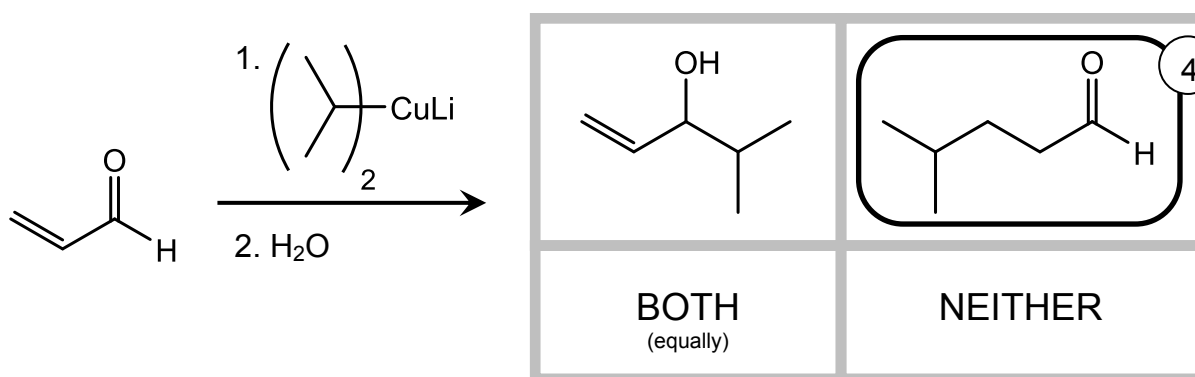
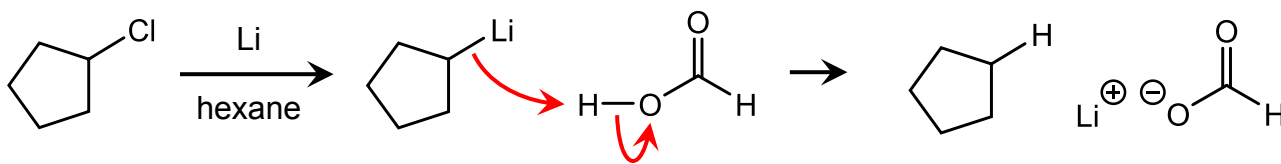
The starting material in this reaction is an ester, and the reaction shows a reduction of that ester. Esters won't react with weak reducing agents like  $\text{NaBH}_4$ ; they will only be reduced by stronger, aluminum hydride reductants. The second box contains a sterically hindered aluminum hydride reductant that reduces the ester, but only has one hydride equivalent, and will stop at just one addition of hydride:



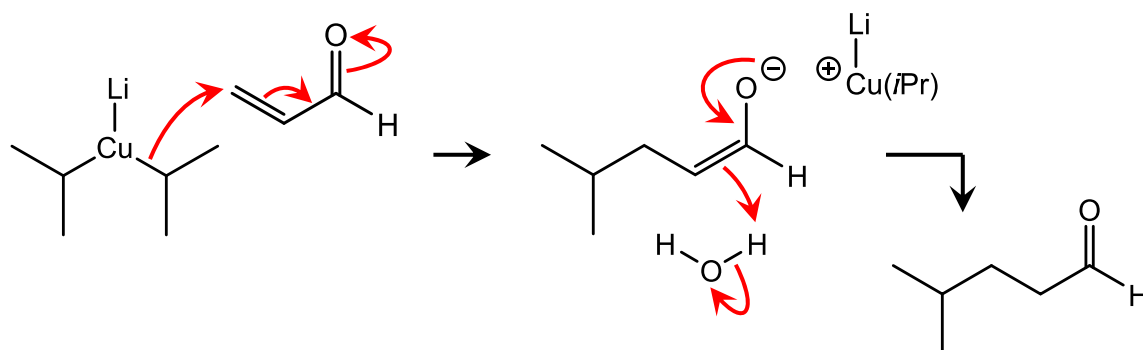
2. (12 pts) Each of the reactions below is drawn with two possible products. If one of the two products predominates, circle that preferred product. If the two products are produced equally, circle "BOTH". If neither product would result from the reaction, circle "NEITHER". **Circle one answer only.**



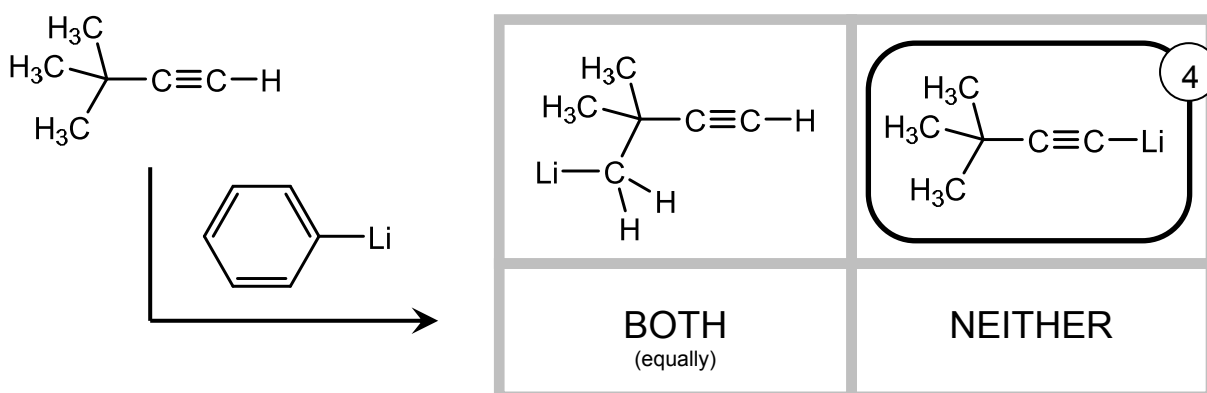
This problem illustrates initial formation of an alkyl lithium, followed by reaction with formic acid. Alkylmetals are voracious bases, and will react with acidic N-H and O-H protons before they get a chance to react with anything else. In this way, alkylmetals react differently with carboxylic acids than they do with esters or acyl halides.



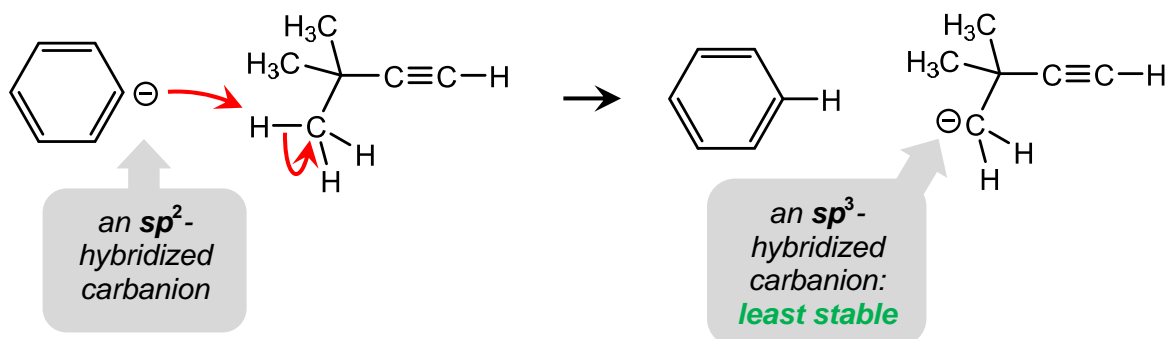
Our starting material is an  $\alpha,\beta$ -unsaturated aldehyde, and  $\alpha,\beta$ -unsaturated carbonyl compounds can react with nucleophiles via 1,2-addition to the carbonyl, or 1,4- (Michael) addition to the  $\beta$ -carbon. Organocuprates, like our first reagent, add 1,4:

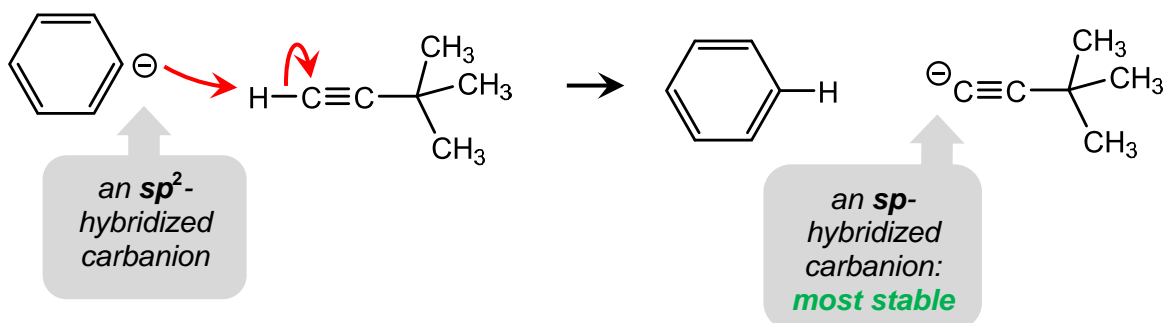


Actually, the real mechanism is a bit more complicated than this, because it involves some coordination gymnastics between the copper and the C=C double bond in the starting material. But this is the general idea.



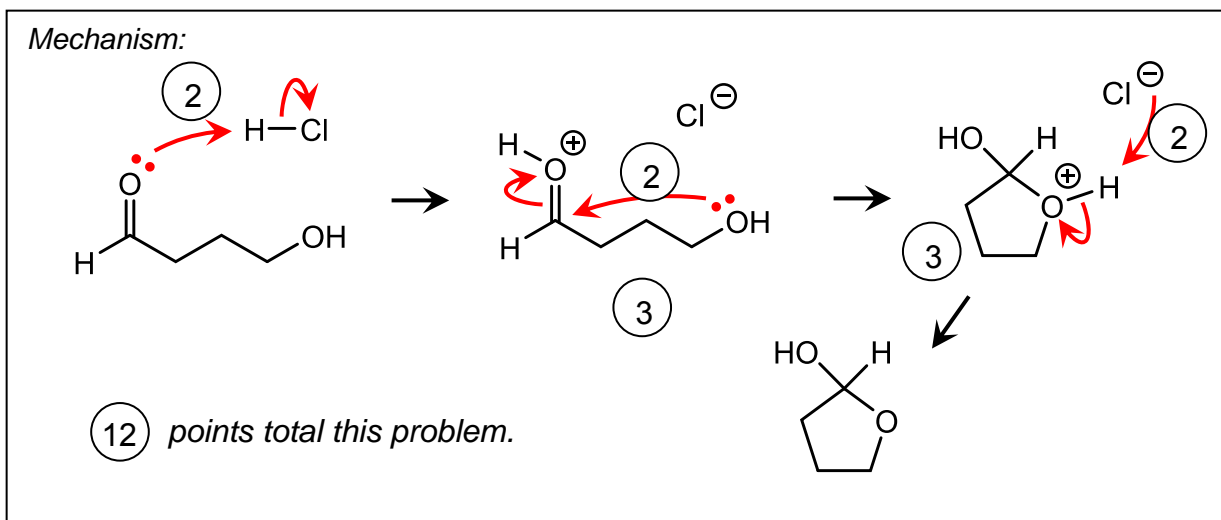
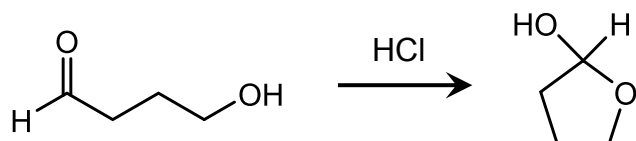
As we discussed in class, and Smith describes in the text, alkylmetals behave as if they were free carbanions. This problem illustrates two possible acid-base reactions, in which the starting alkylmetal (carbanion) deprotonates the starting material to produce two possible carbanion products:





Out of the three carbanions shown here and on the previous page, the  $sp$ -hybridized (alkynyl) carbanion will be the most stable, and the  $sp^3$ -hybridized carbanion will be the least stable. So the reaction will generate the alkynyl anion. But of course, the product won't really be an anion; it will be an alkylmetal, with the metal attached at carbon.

3. (26 pts) For each of the reactions shown on the next page, draw mechanisms that explain how the product is generated from the starting material. 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.



Rubric:

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., Cl in the middle step where 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. Any molecule can be represented in any resonance form; for example, there were a couple of ways that you could have drawn the first intermediate. In addition, resonance does not have to be shown as an explicit “step”—it can be combined with adjacent steps, for full credit.

3 points for each correct intermediate structure in your mechanism.

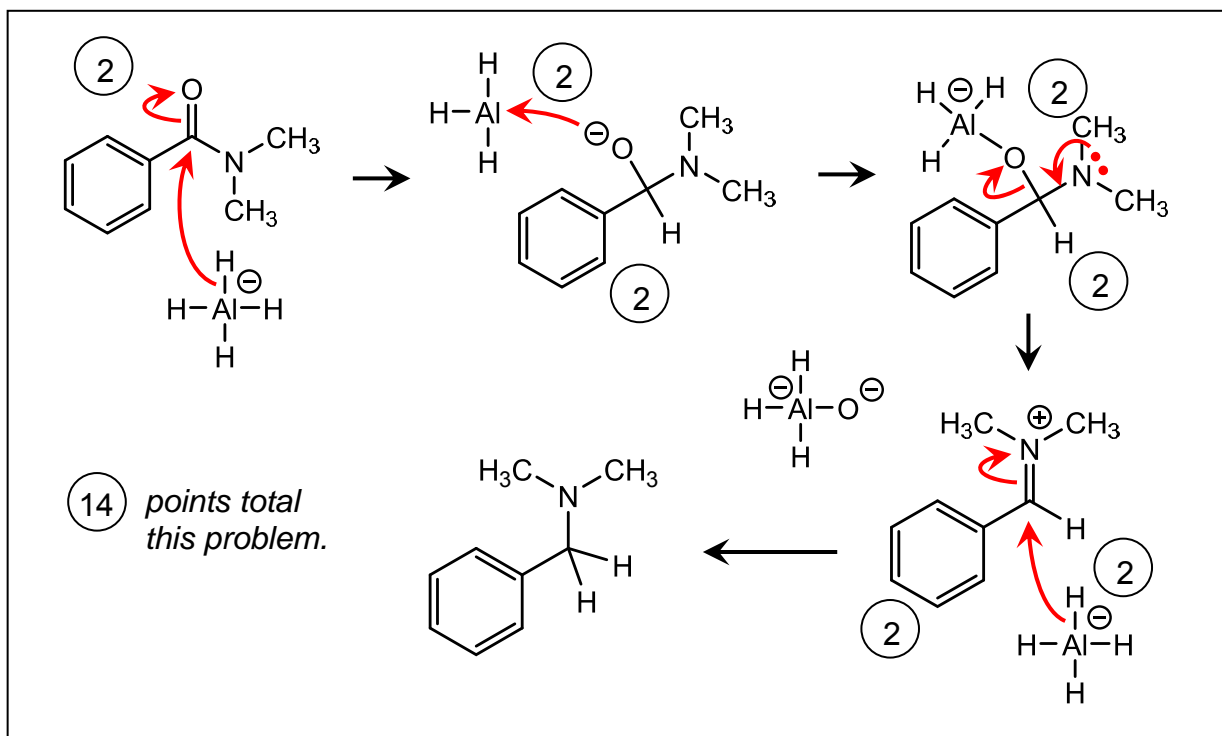
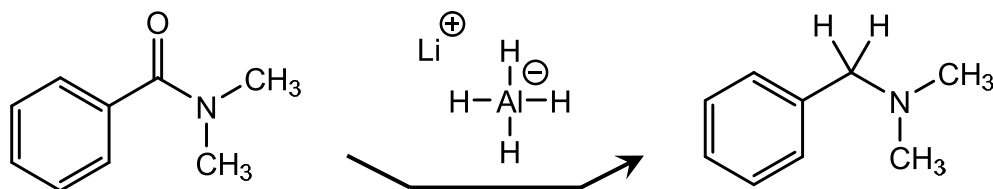
-1 point for each minor error in charge, valency, structure, etc.; if error propagates, points are taken off only for initial error.

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

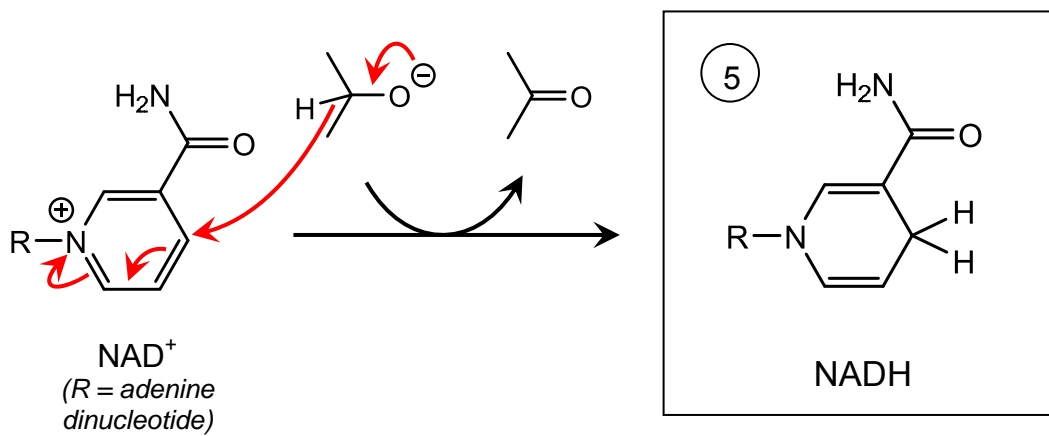
Arrow must start at an electron pair, and end at nucleus or bond where electrons will newly interact. If error is minor, grader may assign partial credit (1 point).

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

If you combined the two steps into one—say, addition and proton transfer—you can get points for arrows that are in the rubric, but not for the intermediate you skipped.



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".



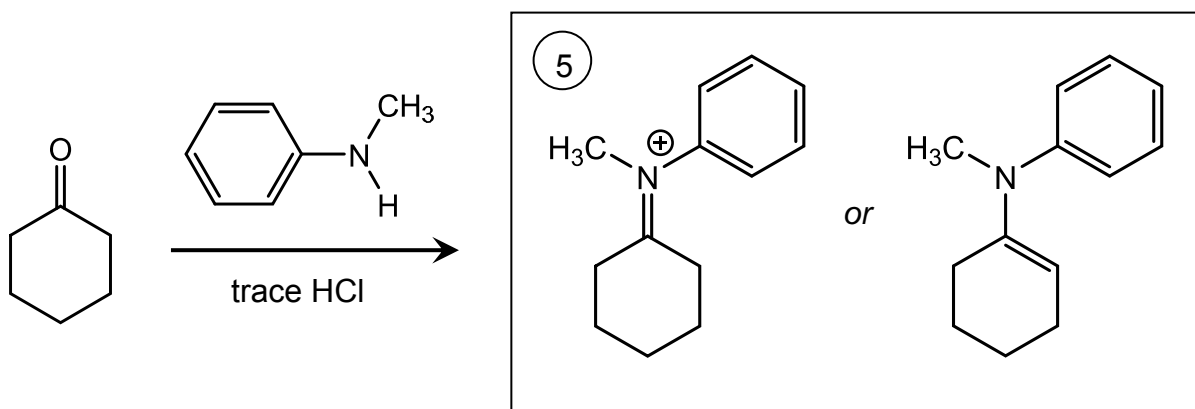
NADH is a biological reducing agent, and acts by donating hydride to form  $\text{NAD}^+$ . As we discussed in class, this reaction also works in reverse, with  $\text{NAD}^+$  accepting hydride as an oxidizing agent to form NADH.

Rubric for this part:

5 points for correct structure.

*It was not necessary to draw the C-H bonds in the product, like I did.*

*-2 points for each clearly trivial structure mistake. This includes omitting the amide group, or including a charge at nitrogen. However, the carbon on the right had to be  $\text{sp}^3$ -hybridized for credit on this problem.*



When combined with a primary or secondary amine, aldehydes or ketones can swap their  $\text{C}=\text{O}$  double bond for a  $\text{C}=\text{N}$  double bond, to form an imine (in the case of a primary amine) or an iminium ion (in the case of a secondary amine). Here we have a secondary amine, so an iminium ion is formed.  $\text{C}=\text{N}$  bonds are generally less



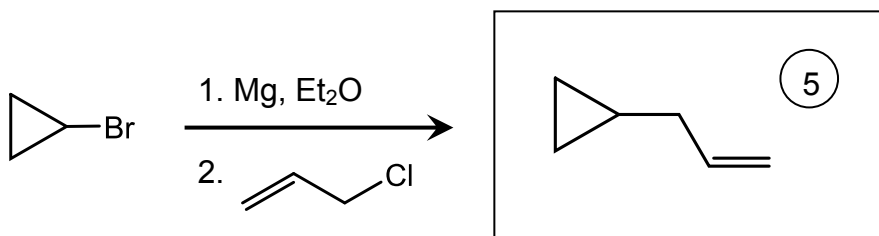
stable than C=O bonds, except when the imine/iminium product is more conjugated than the starting materials. That is indeed the case here, so our product would be stable relative to the ketone.

In the presence of a base—including an excess of the amine that made the iminium ion in the first place—iminium ions that have protons  $\alpha$  to the C=N equilibrate with enamines. This is something that Smith explains at the end of Chapter 21, but that I have delayed talking about in class until we discuss structurally similar enolates in Chapters 23 & 24. We gave full credit for enamine answers.

Rubric for this part:

5 points for either the iminium or enamine structure.

-2 points for each clearly trivial structure mistake. This includes omitting the charge at nitrogen.



Alkylmetals—reacting like carbanions—can serve as S<sub>N</sub>2 nucleophiles with alkyl halides when there is no opportunity for competing E2. That is the case here; our allyl chloride electrophile has no sp<sup>3</sup>-hybridized C-H bonds adjacent to the leaving group, and so it cannot do E2.

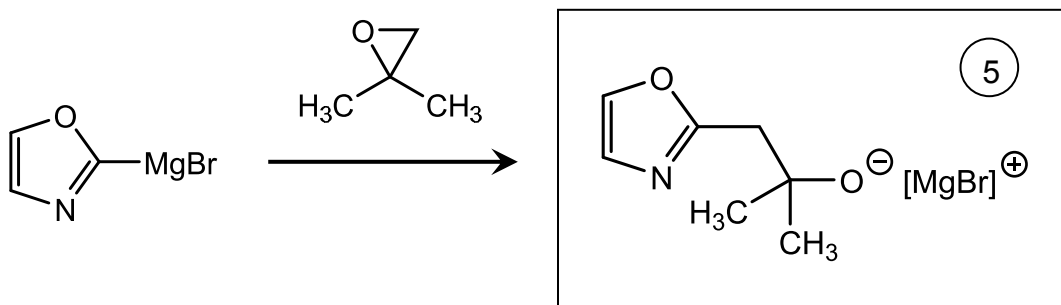


Rubric for this part:

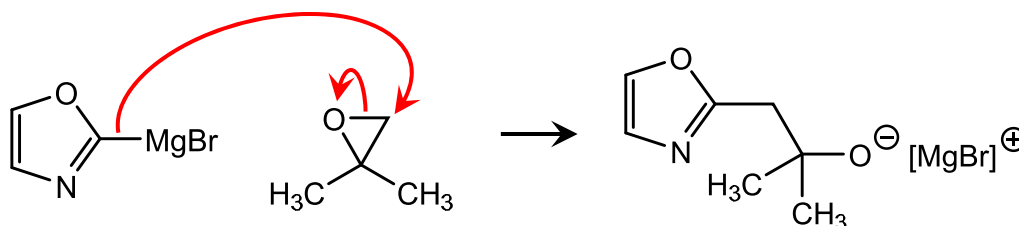
5 points for the correct structure.

2 points partial for answers that connect the cyclopropyl group to a new, unfunctionalized carbon chain with the wrong number of carbons, or lacking the double bond. (We did not consider these trivial mistakes.)

-2 points for each clearly trivial structure mistake.



Alkylmetals add to epoxides at the less substituted carbon:



There was no workup step shown, so the reaction ends there.

Rubric for this part:

5 points for correct structure.

*Okay to omit  $[MgBr]^+$  counterion.*

*4 points partial for drawing protonated alcohol as the product. The reaction recipe did not include a workup step, so the oxygen would not be protonated.*

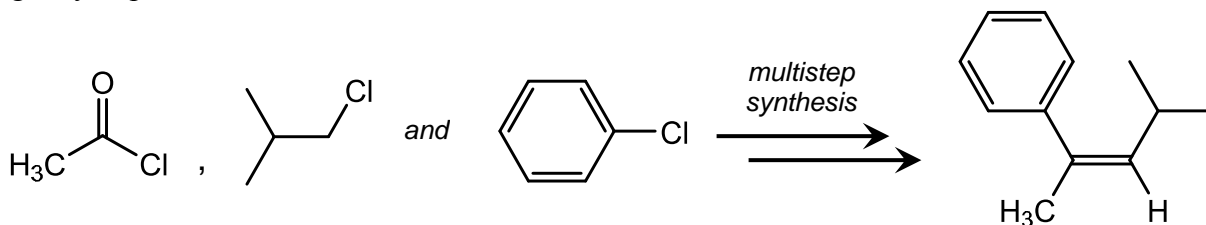
*2 points partial for attack at more substituted carbon (placing methyl groups at the other carbon).*

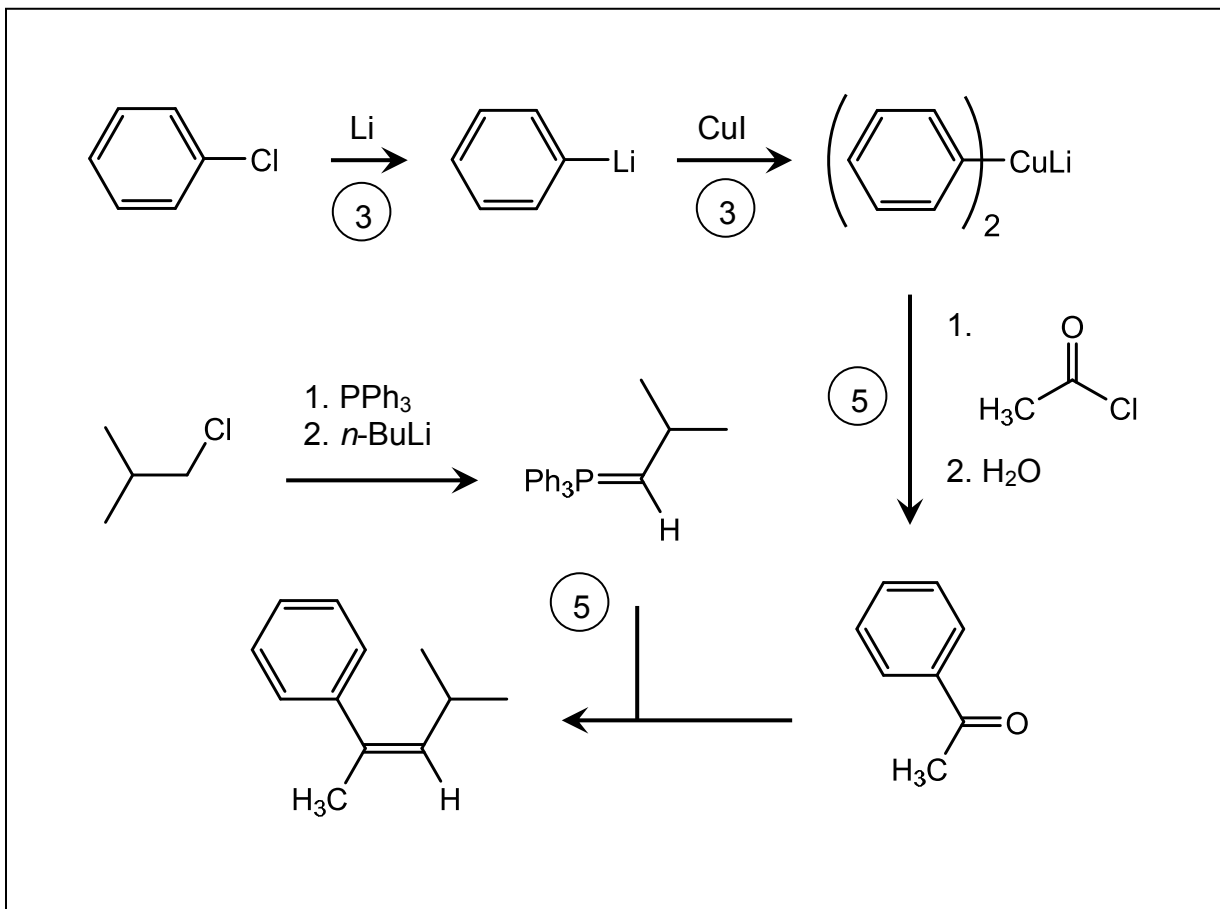
*No partial credit for placing oxygen at the carbon adjacent to the nucleophile.*

*This mistake was not considered trivial.*

*-2 points for each clearly trivial structure mistake.*

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.





### 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, trivial* 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, just writing a change in the starting material, by itself, isn't worth any points.

### Tasks:

1. Metalation of phenyl chloride. (3 points.)

Any metalation ( $\text{Mg}/\text{Et}_2\text{O}$ , lithiation) receives these points.

Solvent not required, just the metal.

- Conversion of phenyllithium to cuprate. (3 points.)
- Successful, single addition of cuprate to acyl halide. (5 points.)  
2 points partial for addition of alkyl lithium or Grignard to acyl halide. This will undergo double addition.
- Combination of isobutyl chloride and ketone in a Wittig reaction. (5 points.)  
2 points partial for adding isobutylmetal to ketone, followed by elimination to alkene. This will yield the incorrect (E)-alkene.

6. (14 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.

