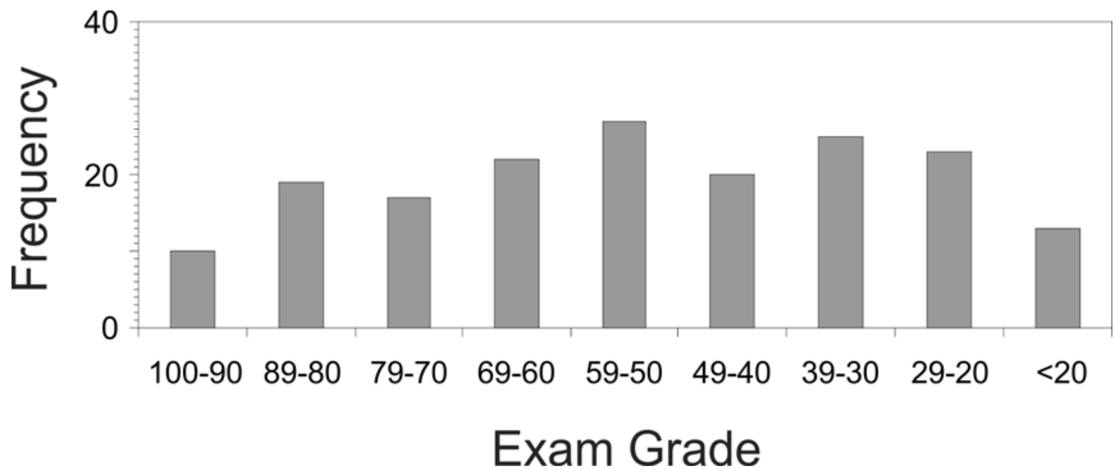
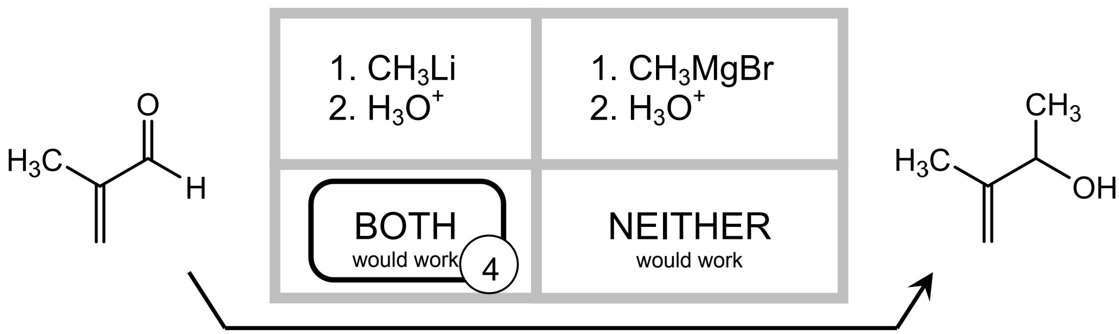
Exam 2
Answer Key

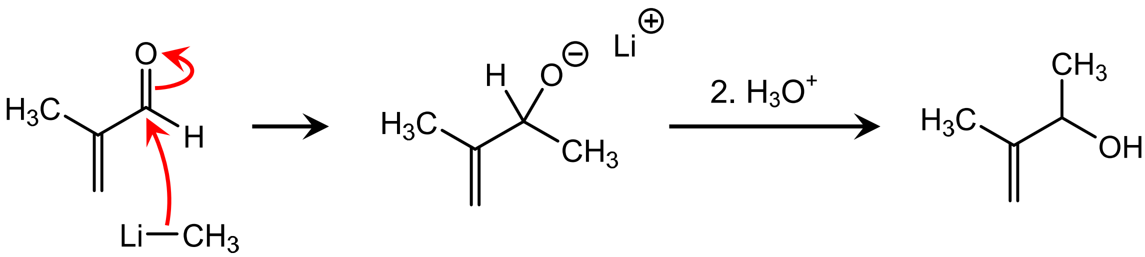
Exam 2 Mean:	53
Exam 2 Median:	52
Exam 2 St. Dev.:	22

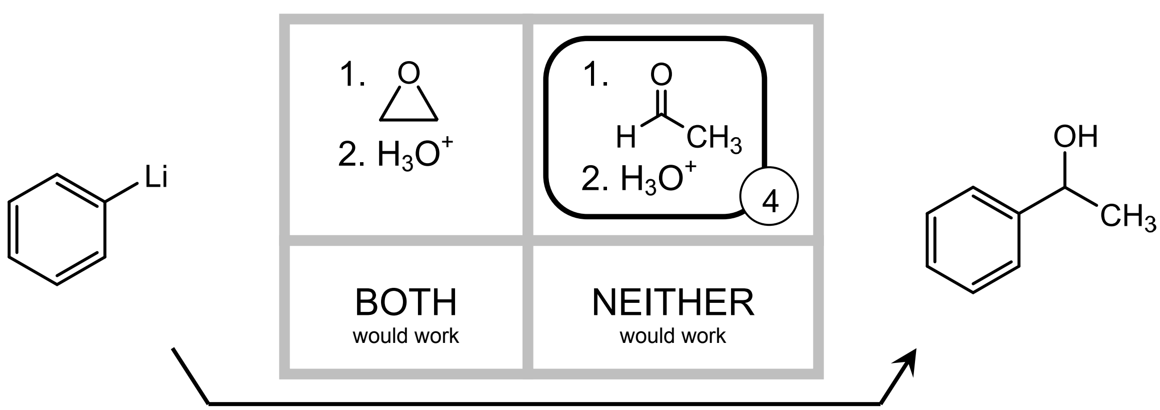


1. (12 pts) Each of the reactions below is drawn with two possible reaction conditions. If only one of the two reaction conditions would generate the given molecule as the major product, circle those conditions. If both sets of conditions would accomplish the reaction, circle "BOTH". If neither set of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

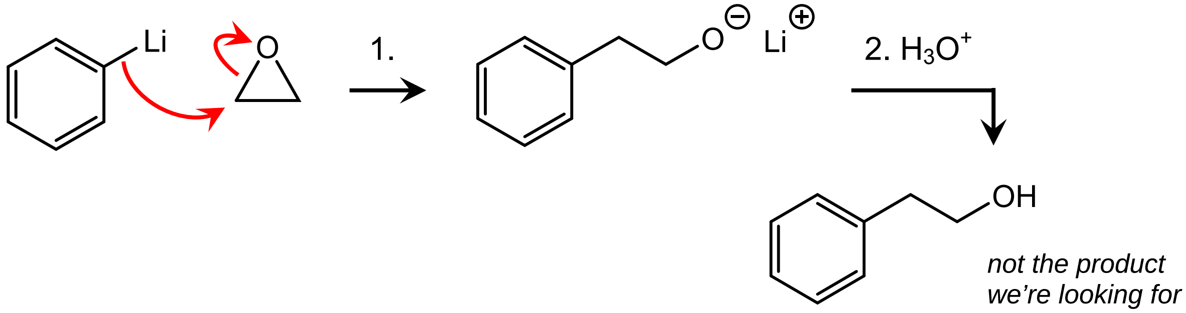


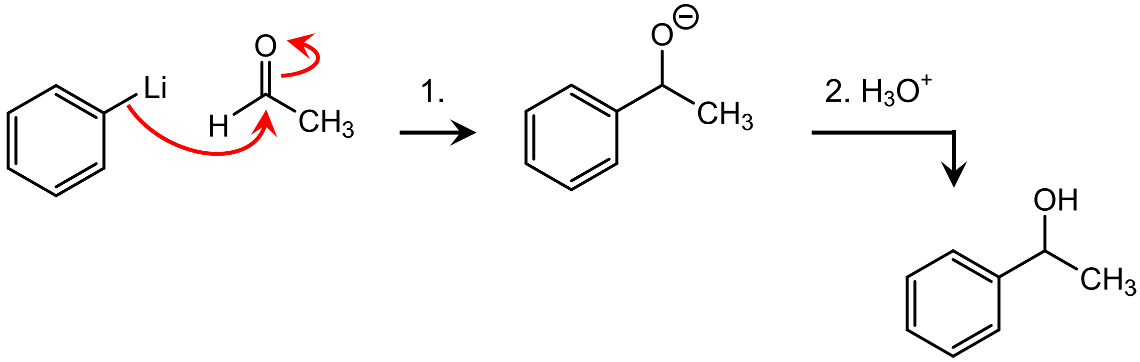
The starting material here is an α,β-unsaturated aldehyde, and nucleophiles can add either to the carbonyl carbon (sometimes called "1,2-addition") or the end of the conjugated double bond ("1,4-addition"). Heteroatom nucleophiles and lithium dialkylcuprates will do 1,4-addition, but other alkylmetal reagents (including the alkyllithium and Grignard reagents in these two boxes) will do 1,2-addition.

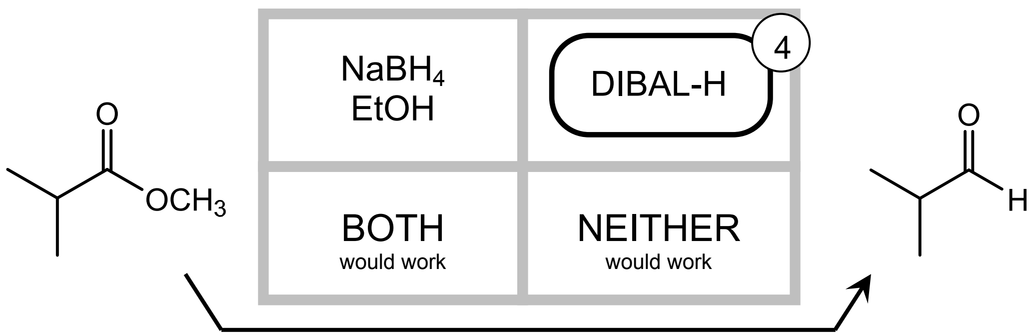




Each of these reactions generates an alcohol product, but only the aldehyde adduct has the alcohol group in the right place.

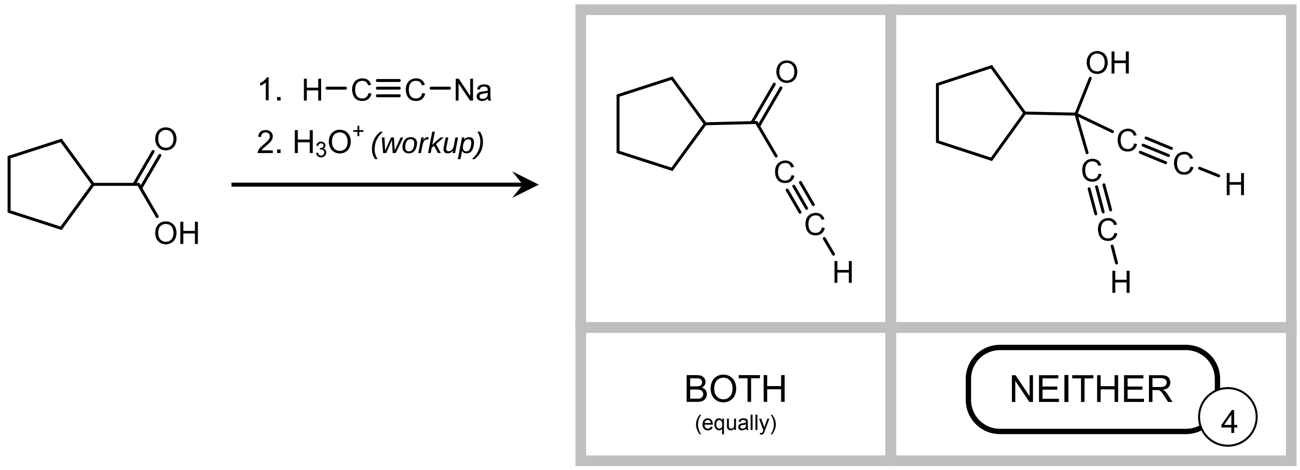




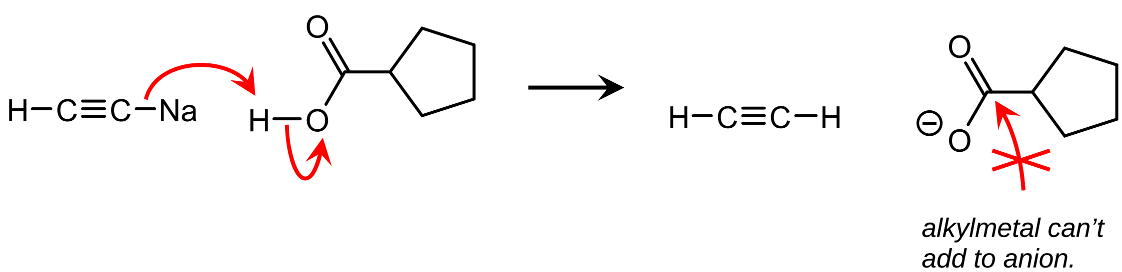


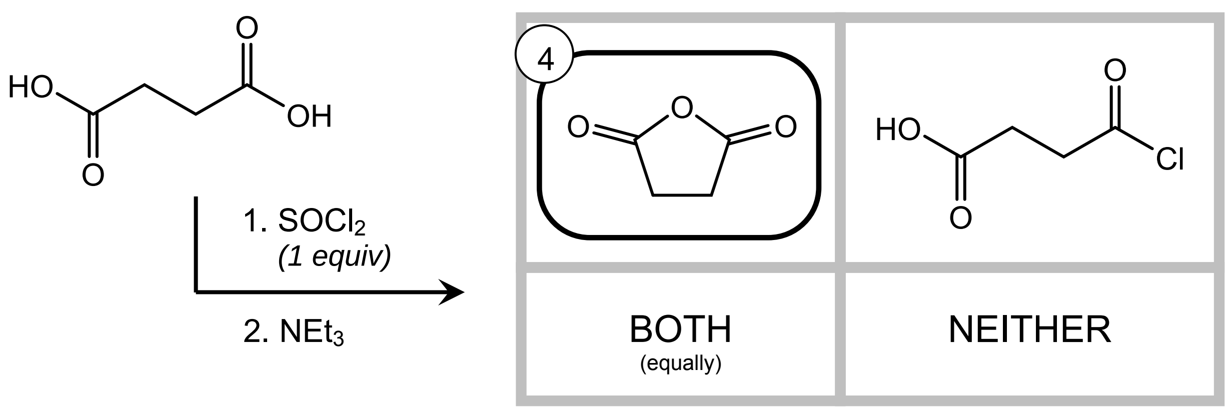
DIBAL-H reduces ester one step, to aldehydes. $NaBH_4$ is also a reducing agent, but it reduces aldehydes and ketones selectively to alcohols.

2. (16 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.**

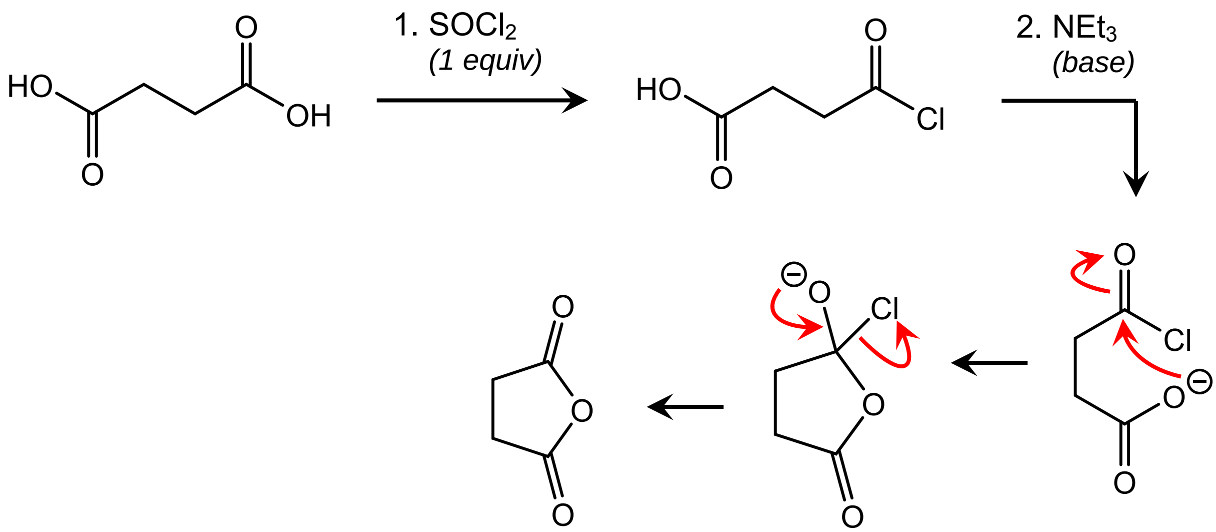


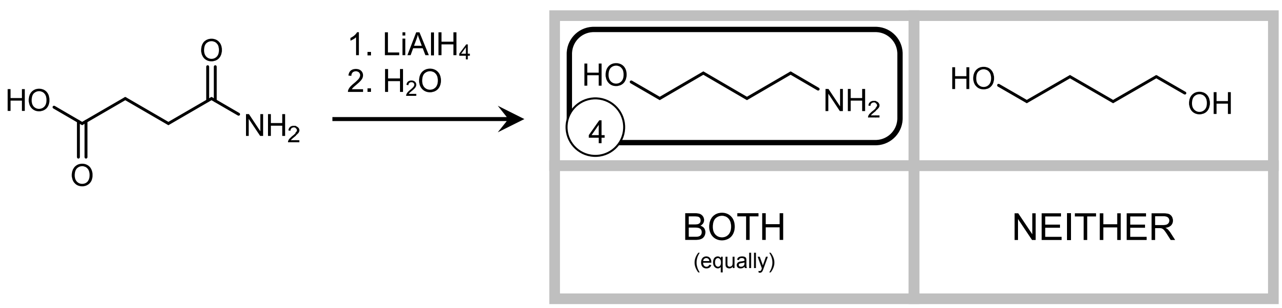
Alkylmetal reagents are voracious bases, and react with acids via acid-base reaction. Rather than add to the carboxylic acid carbonyl, the alkynylsodium will deprotonate it; then the resulting negative charge prevents the alkylmetal from adding to the carboxylate.



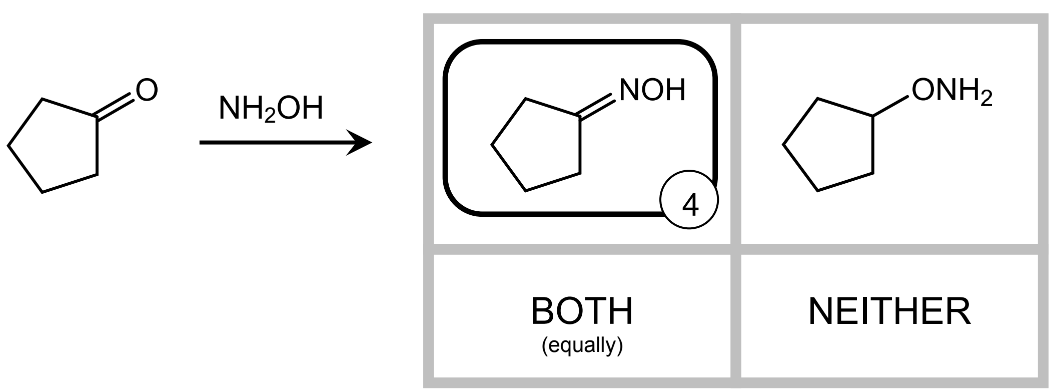


Anhydrides are formed by combining a carboxylate with an acyl halide. When those two components are in the same molecule, the result is a cyclic anhydride:





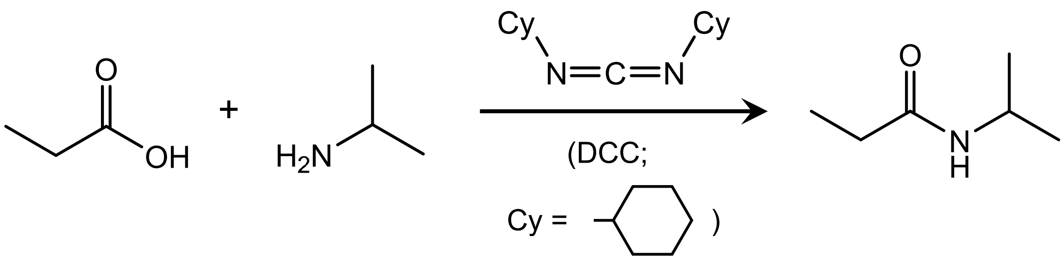
LiAlH$_4$ reduces nearly all carbonyl-containing functional groups, *except amides*, all the way to alcohols. Amides are reduced to amines.



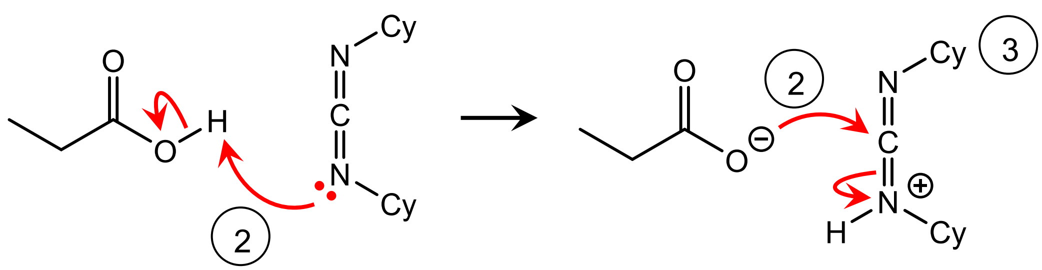
Here, HO-NH$_2$ adds to the carbonyl group just like any R-NH$_2$ would, to form a C=N double bond. As we discussed in class, the added oxygen atom makes oximes like the product here more stable than a typical imine would be.

3. (20 pts) For the reaction shown below, draw a mechanism that explains both steps of the two-step reaction below, via the intermediate I've provided. In your answer, make sure that you:

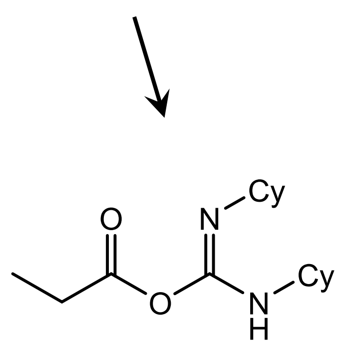
- Draw each step of the mechanism separately;
- Use "electron pushing" to show where the electrons in each step go;
- Use only the molecules that you are given; do not invoke reactants or solvents that aren't in the problem.



Mechanism:



As I explained in class, the Smith text has this mechanism wrong; the optimal rate for DCC activation is pH 5, and at this pH, the carboxylic acid is deprotonated, and DCC is protonated. We gave full credit that achieved this with a proton shuttle (like the amine) instead of via direct proton transfer. If you did nucleophilic addition first, followed by proton transfer, we gave credit for the electron pushing but not the intermediate (so, 4 points out of 7).



<u>Rubric:</u> *7 points total for this part.*

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 may be omitted.

Half credit for each arrow-pushing step combined with another. You lose the points on each step you combine; so two 2-point steps could be combined into a step that would be worth a maximum of 2 points total. You would also lose the points for the intermediate you skipped.

3 points for each correct set of intermediate structures in your mechanism.

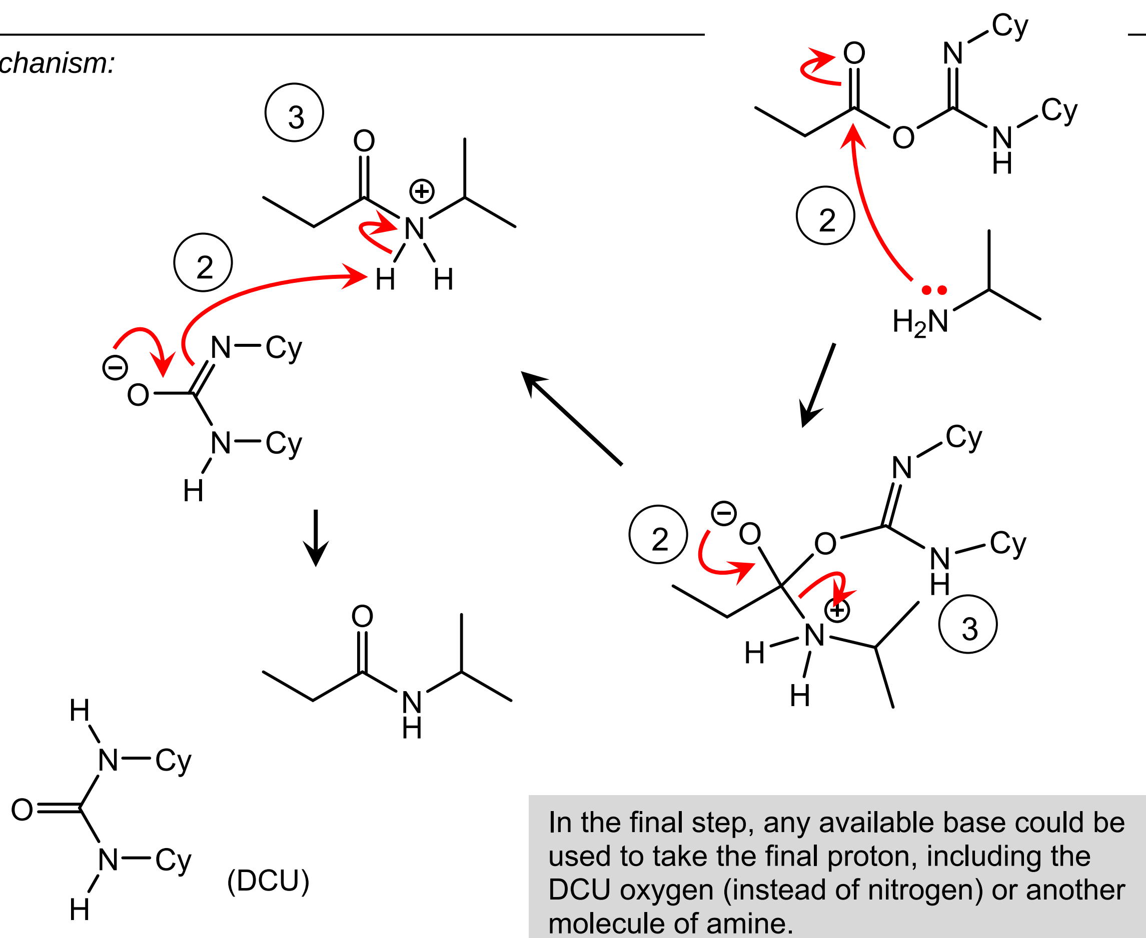
-1 point for each minor error in charge, valency, structure, etc.; if error propagates, points are taken off only for initial error.

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).

Mechanism:



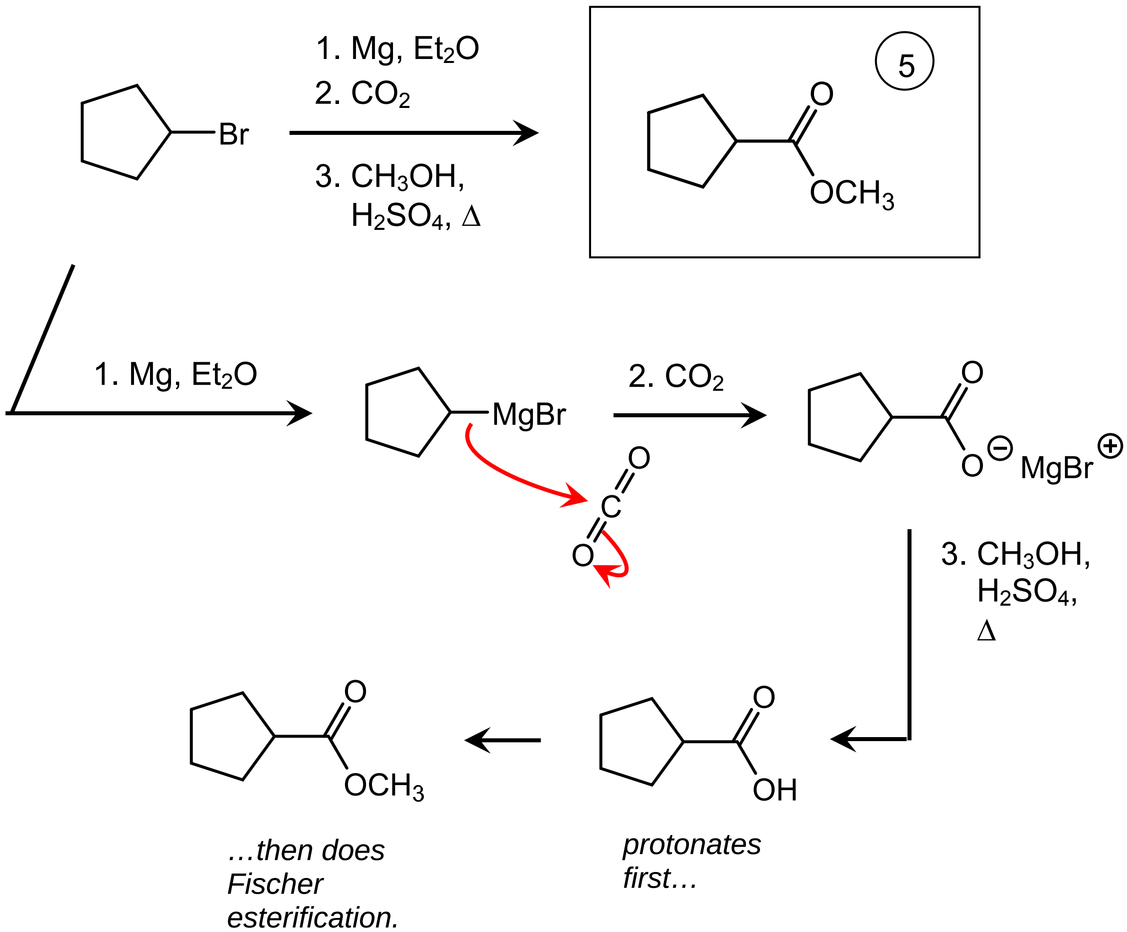
In the final step, any available base could be used to take the final proton, including the DCU oxygen (instead of nitrogen) or another molecule of amine.

Rubric: *13 points total for this part.*

Same as above.

12 points partial if you used the oxygen instead of nitrogen; your mechanism should show formation of DCU.

4. (20 pts) For each of the reactions below, 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".



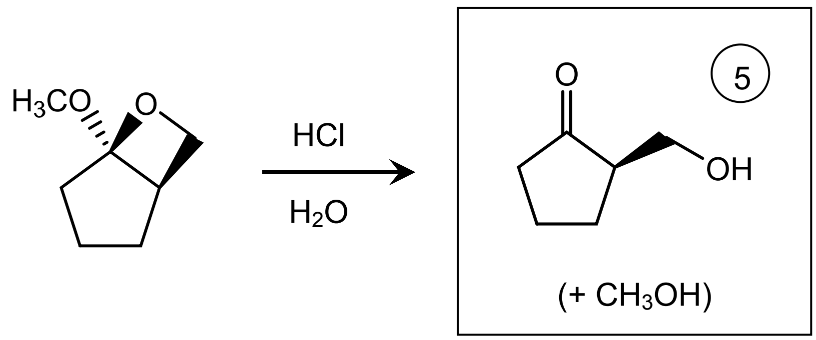
Rubric for this part:
5 points for correct structure.

3 points partial for carboxylic acid, or carboxylate.

1 point partial for product with addition of one carbon.

-2 points for each clearly trivial structure mistake. (E.g., adding an extra carbon.)

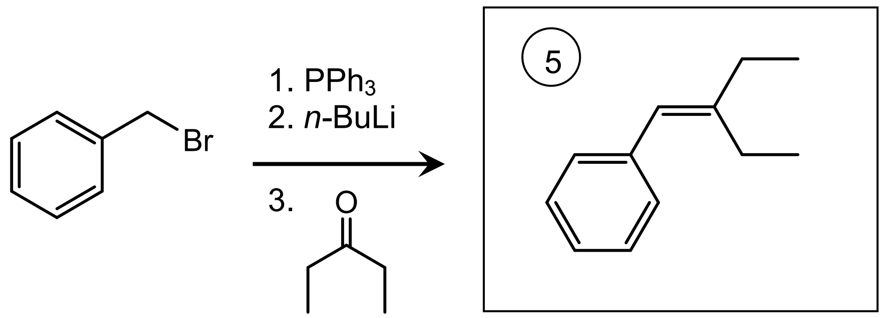
By "trivial", I mean your intent must be clear—it must be obvious that you meant to write the correct answer, but you accidentally made a minor change that keeps your intent clear.



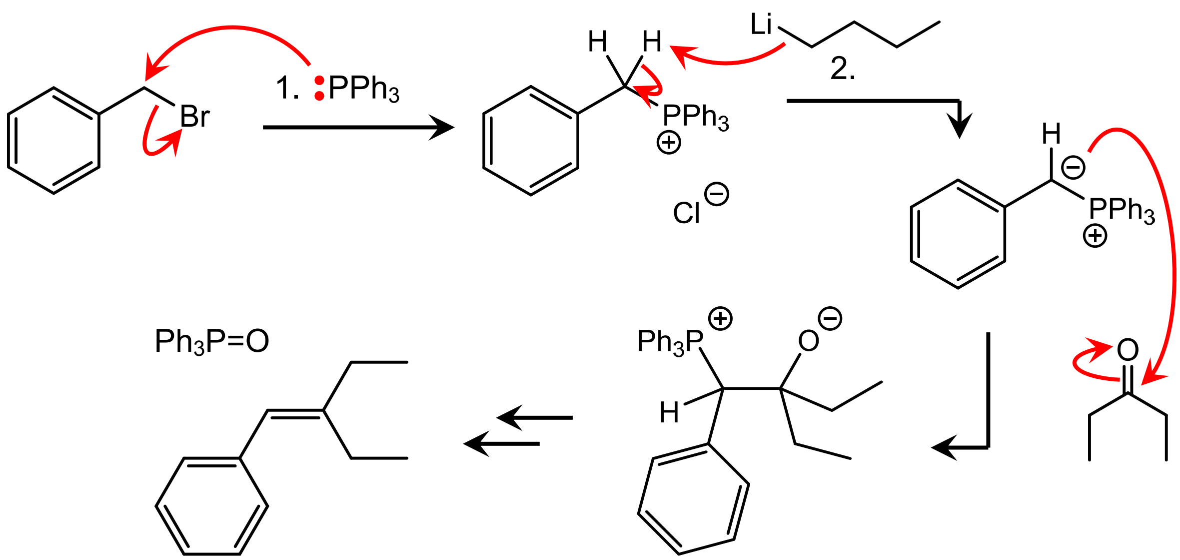
Our starting material is a ketal—a molecule with a carbon atom that has two C-OR single bonds. In general, ketals are thermodynamically less stable than ketones, (mainly because of reaction entropy), and this ketal is particularly unstable because of its strained, four-membered ring. In acid and water, ketals equilibrate with hemiketals, and then with ketones:

Rubric for this part:
5 points for correct structure.

2 points for hemiketal, where -OH replaces either -OR.
2 points for a cyclopentanone with an incorrect side-chain structure.
2 points for addition of -CH_2OH side chain, with incorrect ketone carbon.
-2 points for each clearly trivial structure mistake.

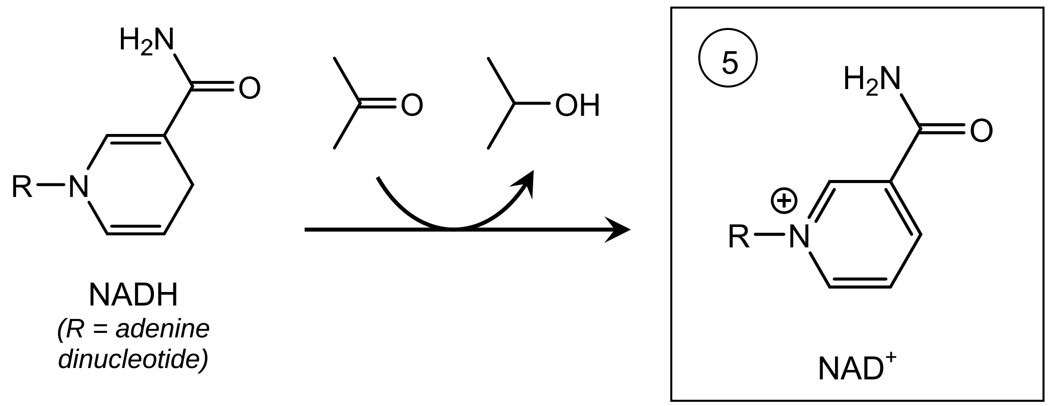


This is a standard Wittig reaction, in which an alkyl halide and an aldehyde or ketone are combined to form a double bond:



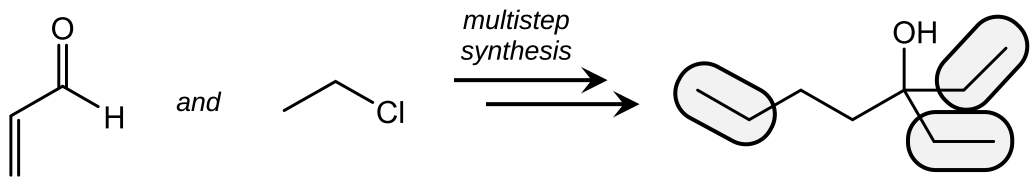
Rubric for this part:
5 points for correct structure.

1 point for an alkene.
-2 points for each clearly trivial structure mistake. This includes omitting a carbon.

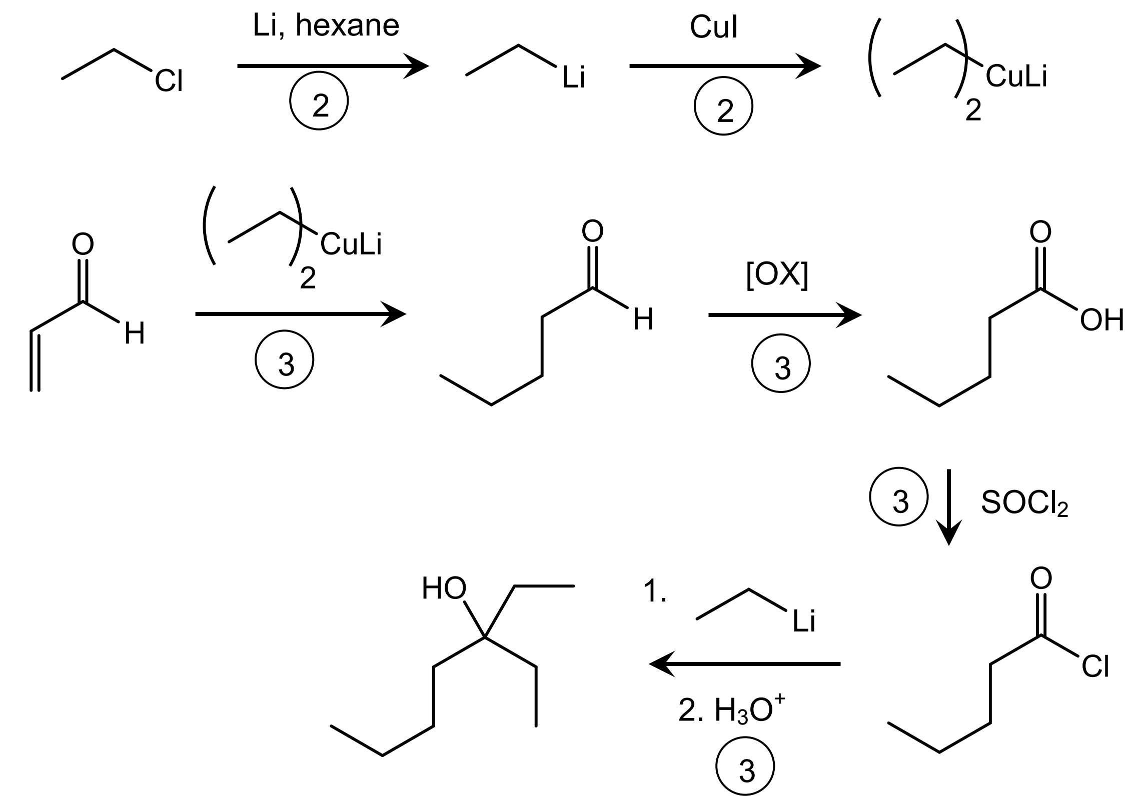


Rubric for this part:
5 points for correct structure.
- *-1 point for correct structure but omitting charge.*
- *-2 points for each clearly trivial structure mistake. Graders had latitude to decide what errors were trivial.*

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.



Our product has a number of two-carbon pieces that need to be added to our three-carbon starting material. One of these needs to be added via conjugate addition (at the 4-position), and the other two need to be added via direct addition to a C=O containing starting material (at the 2-position).



Rubric:

This synthesis requires six tasks, listed below. 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.

1. **Metalation of ethyl chloride (2 points).**
   Full credit for either lithiation or Grignard formation.

2. **Formation of lithiumdiethylcuprate from ethyllithium (2 points).**
   No credit for forming cuprate from Grignard.

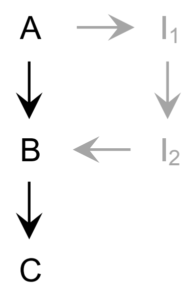
3. **Conjugate addition of cuprate (3 points).**
   Full credit for any oxidation.

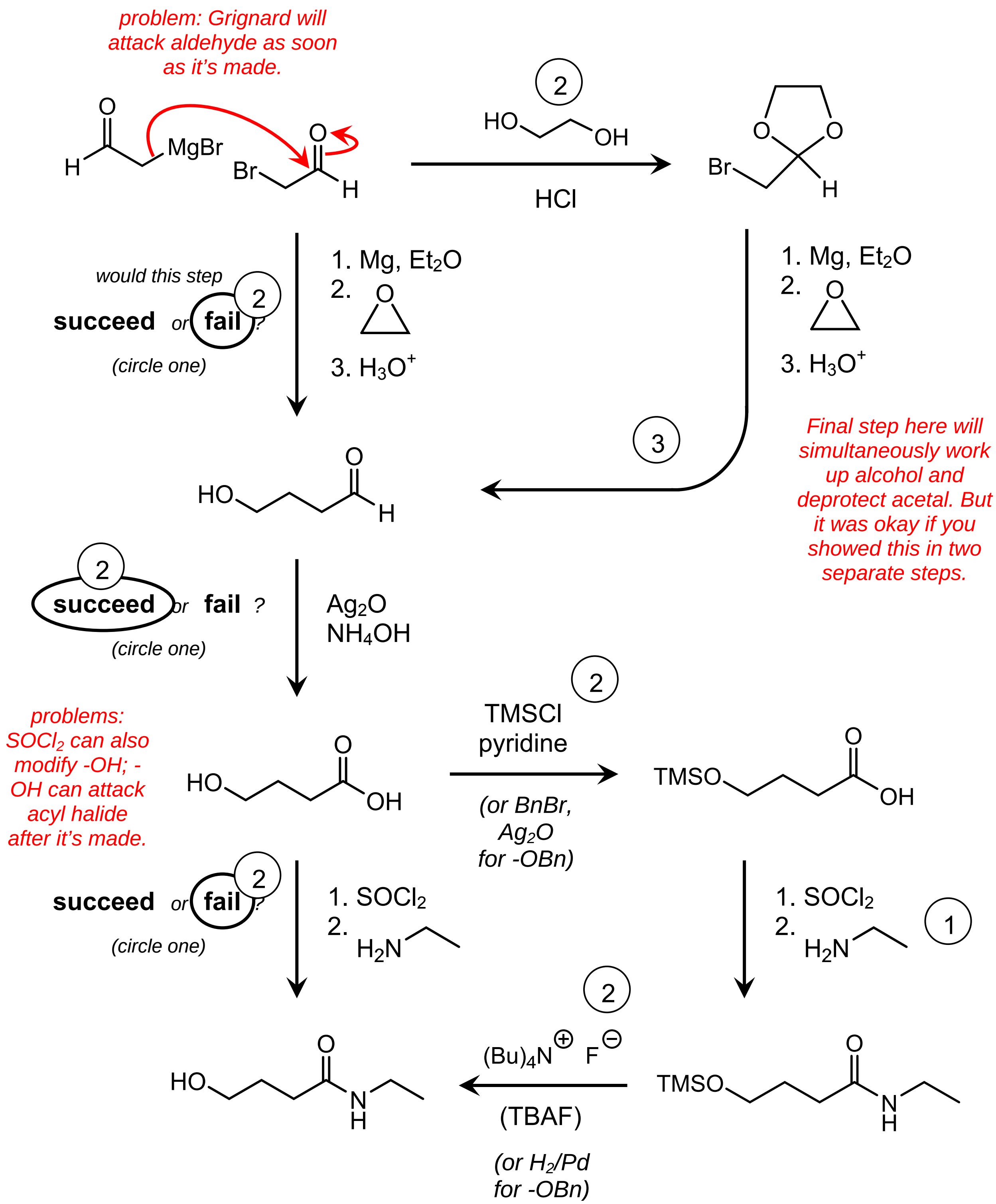
4. **Oxidation of aldehyde (3 points).**

5. **Conversion of carboxylic acid to an ester or acyl halide (3 points).**

6. **Double addition of ethylmetal to ester or acyl halide (3 points).**

6. (16 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.





Rubric:
2 points for each correctly circled "succeed" or "fail". (*6 points total for these.*)
2 points for each protection step. (*4 points total for two.*)
2 points for each deprotection step. (*4 points total for two.*)