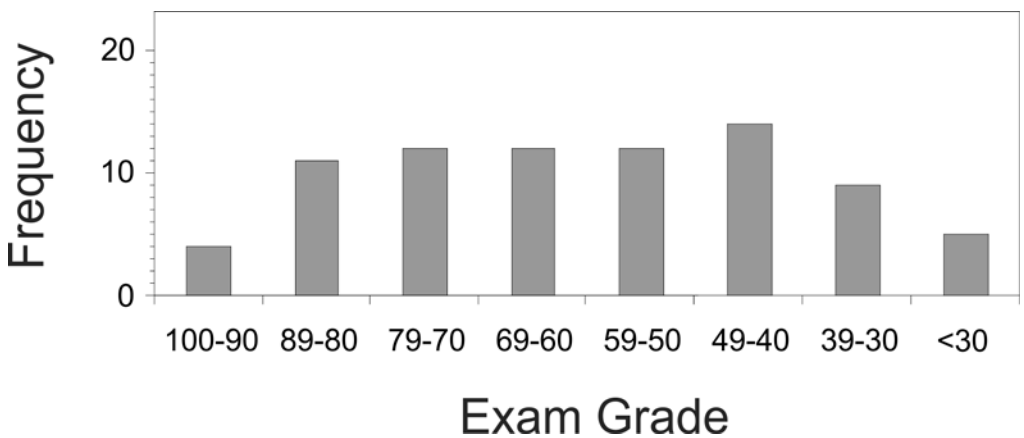
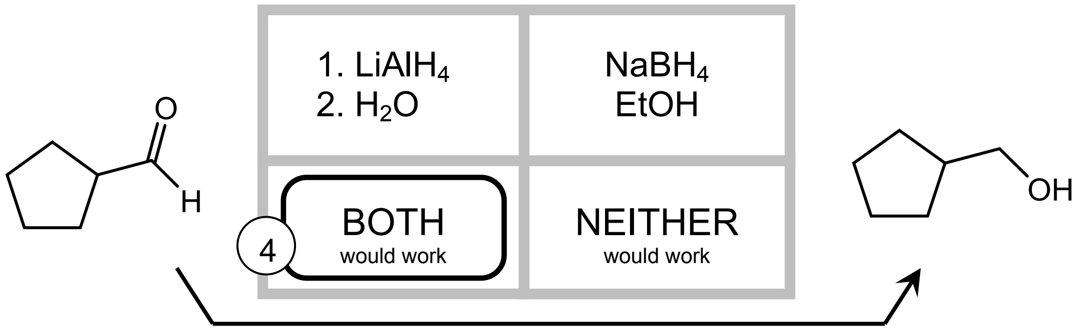
Exam 2
Answer Key

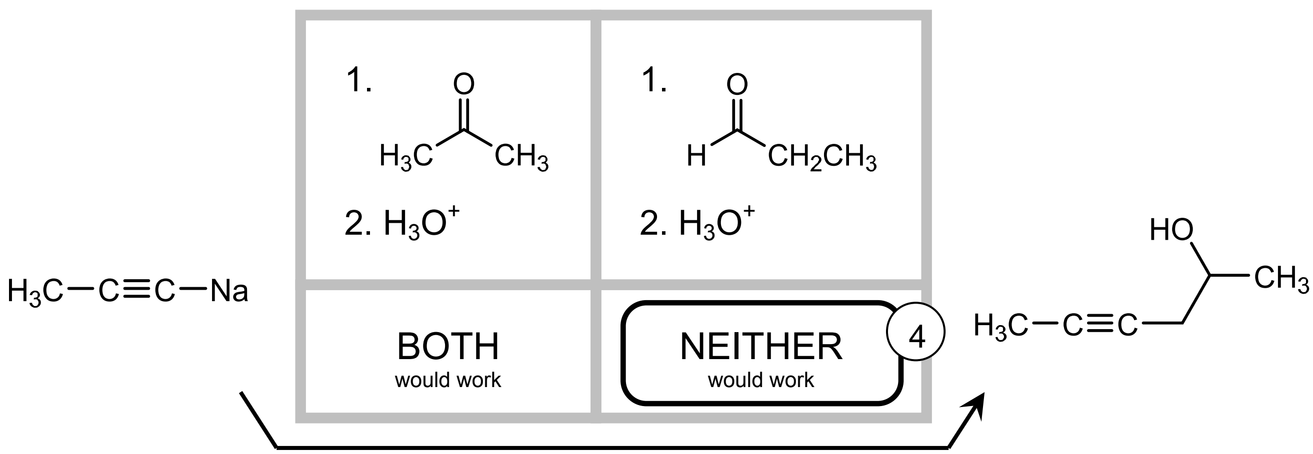
Exam 2 Mean:	60
Exam 2 Median:	60
Exam 2 St. Dev.:	19



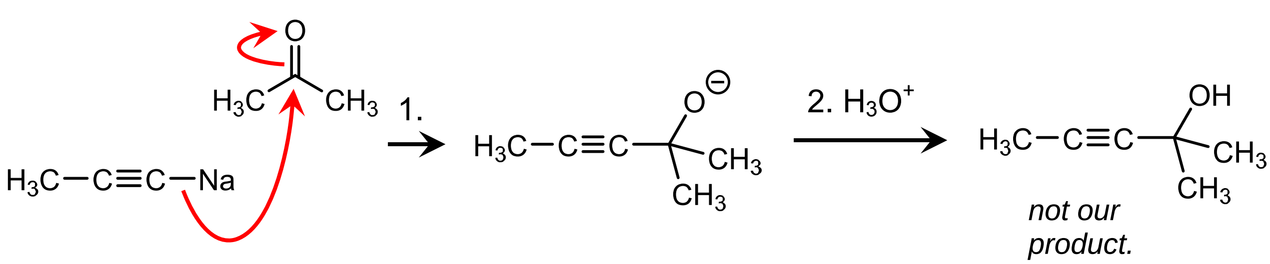
1. (12 pts) Each of the reactions below is drawn with two possible reaction conditions. If only one of the two reaction conditions would generate the given molecule as the major product, circle those conditions. If both sets of conditions would accomplish the reaction, circle "BOTH". If neither set of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

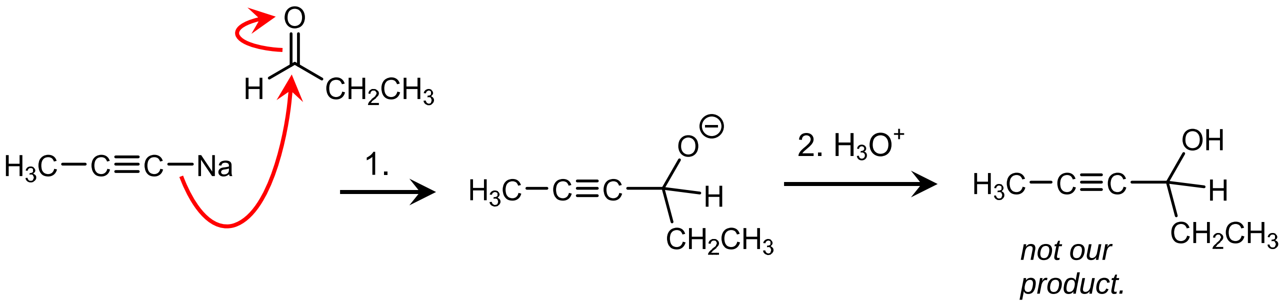


$LiAlH_4$ and $NaBH_4$ are both reducing agents, and add hydride ("H^-") to C=O bonds. $LiAlH_4$ is a strong reducing agent, and will reduce almost anything (including the aldehyde here) to an alcohol. $NaBH_4$ is choosier, and will only reduce ketones and aldehydes—but that's exactly what we've got here. So both work.

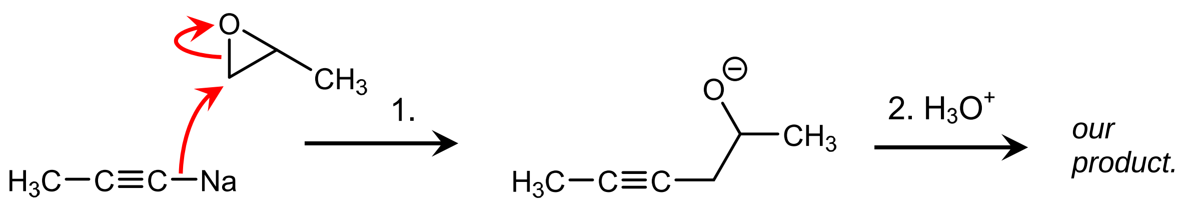


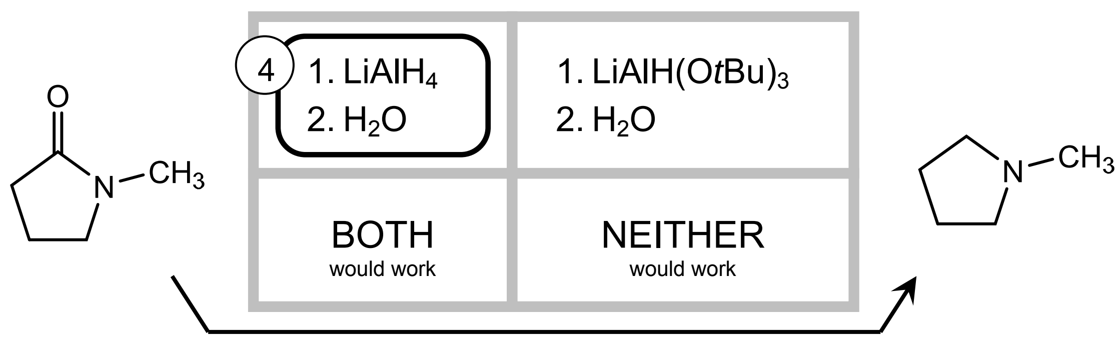
Both of these reactions illustrate addition of an alkylmetal to a three-carbon electrophile. But do either of the additions produce the product on the right? Let's find out:





Neither of these conditions yield our product—they both generate products in which the alcohol -OH is one carbon too close to the triple bond. I think the electrophile we're looking for is not a C=O bond, but an epoxide:

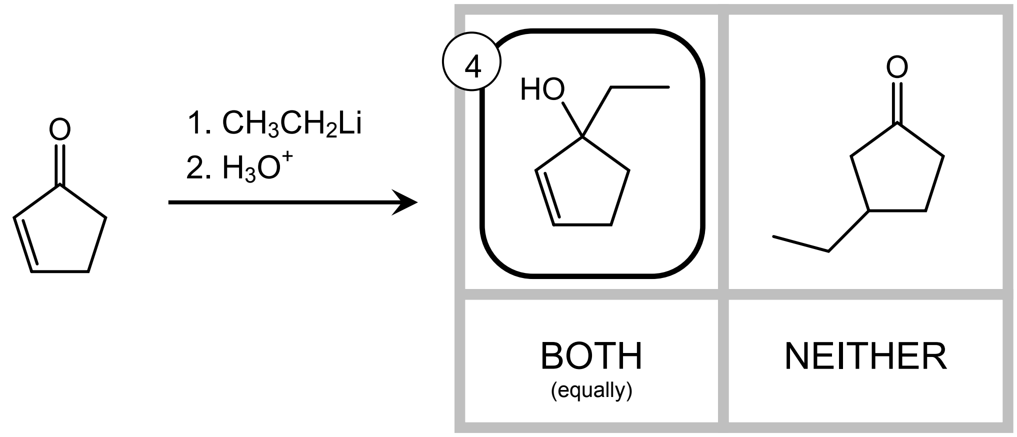




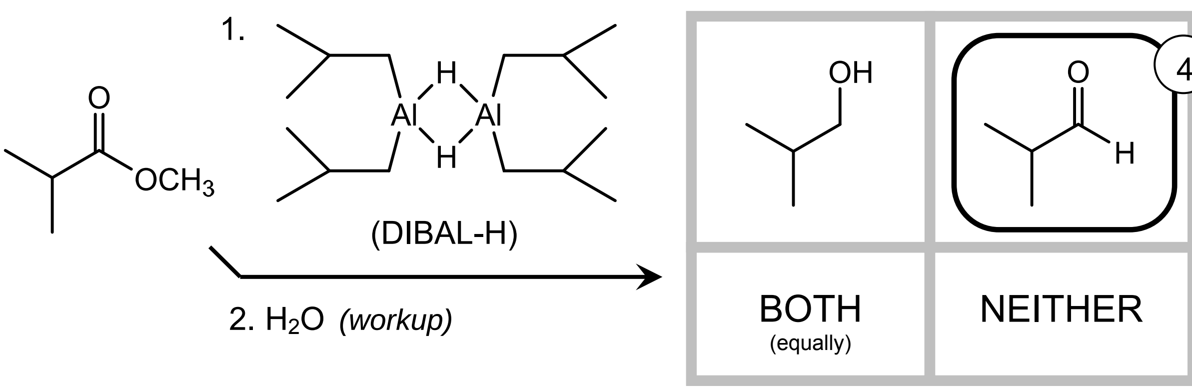
$LiAlH_4$ reduces amides, by adding two hydride equivalents to the C=O bond and converting it to a CH_2; this converts our amide into an amine. We didn't talk in class about whether $LiAlH(OtBu)_3$ will reduce amides or not. (It won't.[1] But let's assume we don't know that.) We *do* know that $LiAlH(OtBu)_3$ will only supply only one hydride equivalent to a C=O containing functional group, and our amide needs two to make an amine. So regardless of whether $LiAlH(OtBu)_3$ adds or not, it certainly won't make an amide.

[1] One authoritative resource on the reactivity of different reagents is *Organic Reactions*, a refereed publication that now has a website. Its [site on metal alkoxyhydride reductions] says $LiAlH(OtBu)_3$ won't reduce amides at all.

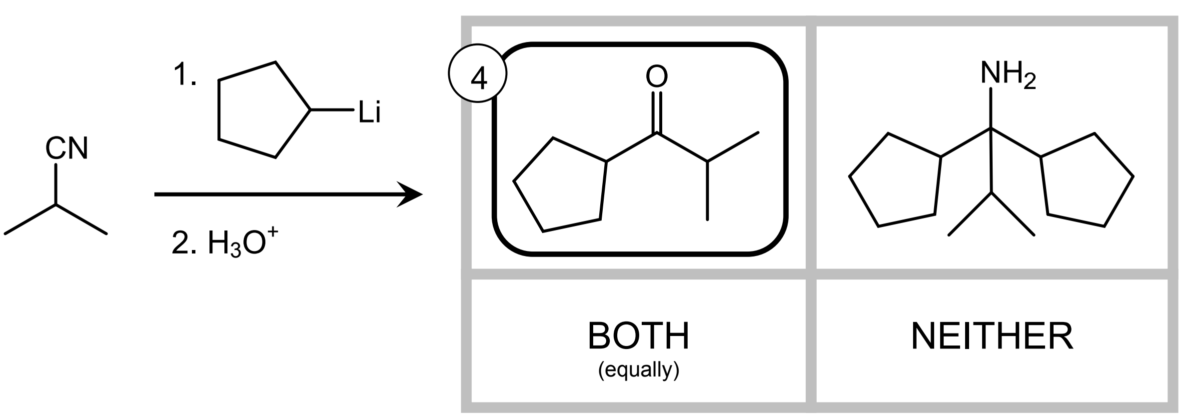
2. (20 pts) Each of the reactions below is drawn with two possible products. If one of the two products predominates, circle that preferred product. If the two products are produced equally, circle "BOTH". If neither product would result from the reaction, circle "NEITHER". **Circle one answer only.**



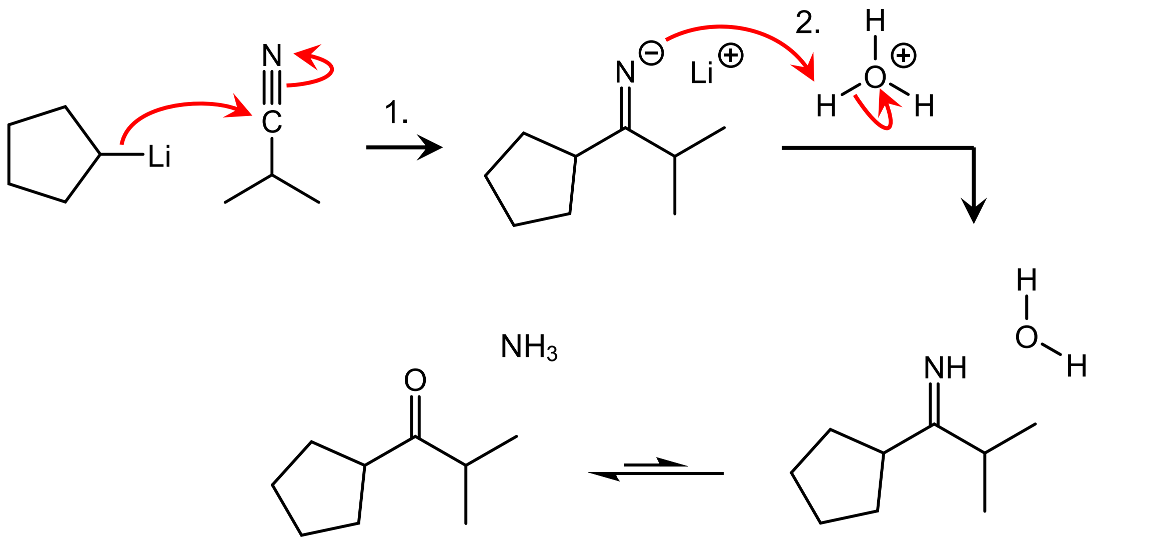
Our starting material is an α,β-unsaturated ketone, and will undergo either 1,2-addition (to yield the left-hand product) or conjugate addition (to yield the product on the right). Alkyllithium reagents are strong, irreversible nucleophiles, and so they add 1,2.

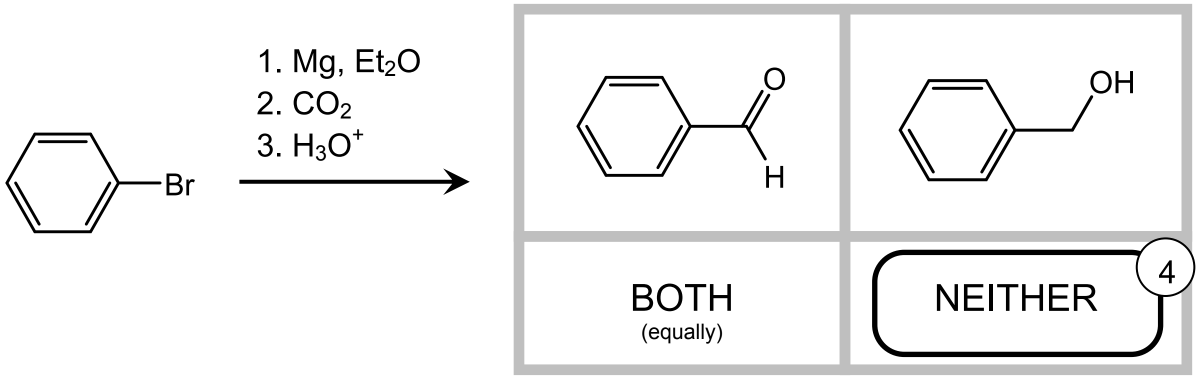


DIBAL-H will reduce esters just once, to aldehydes.

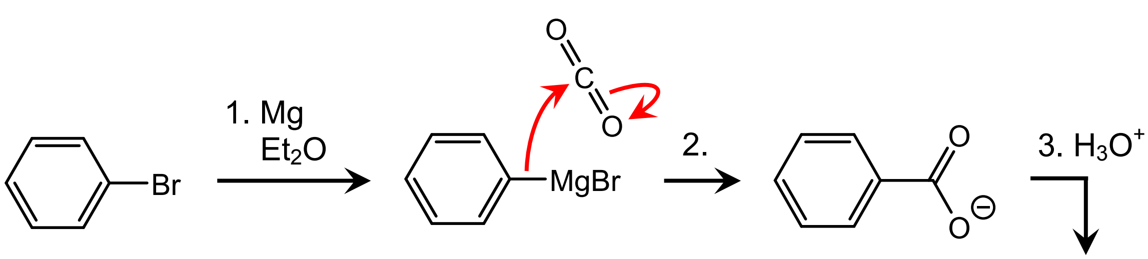


Alkylmetals add just once to nitriles to yield an imine. This imine is converted into a ketone during acid workup.

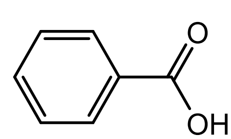


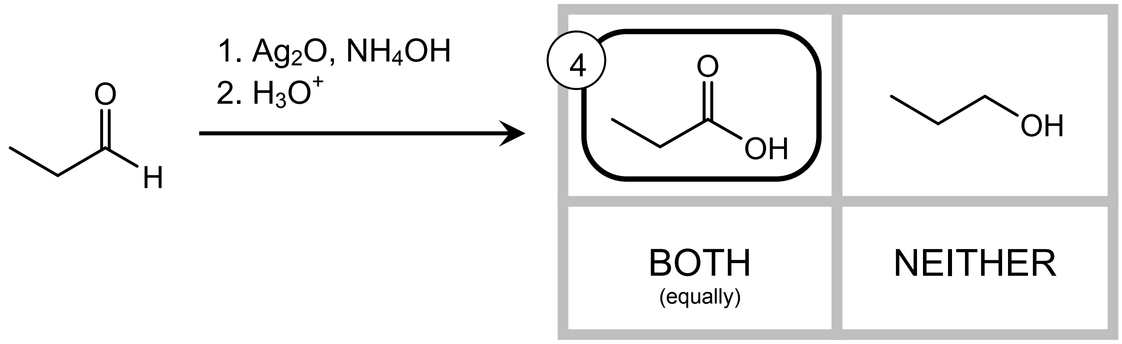


Grignard reagents add to CO_2 to yield carboxylic acids (after workup):



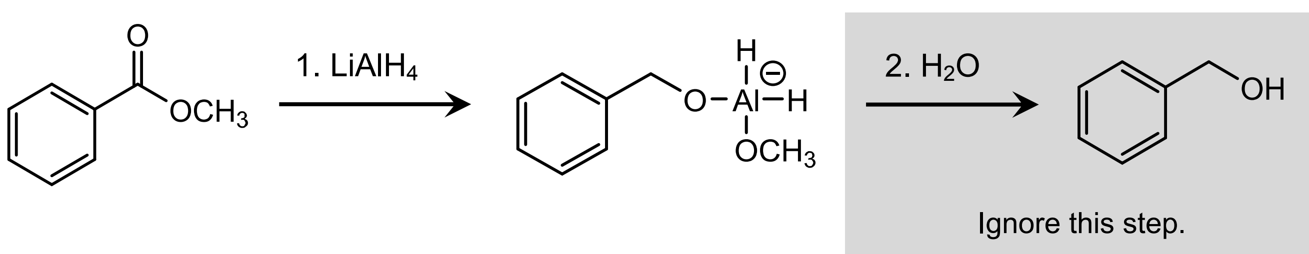
Neither of our products is this carboxylic acid.

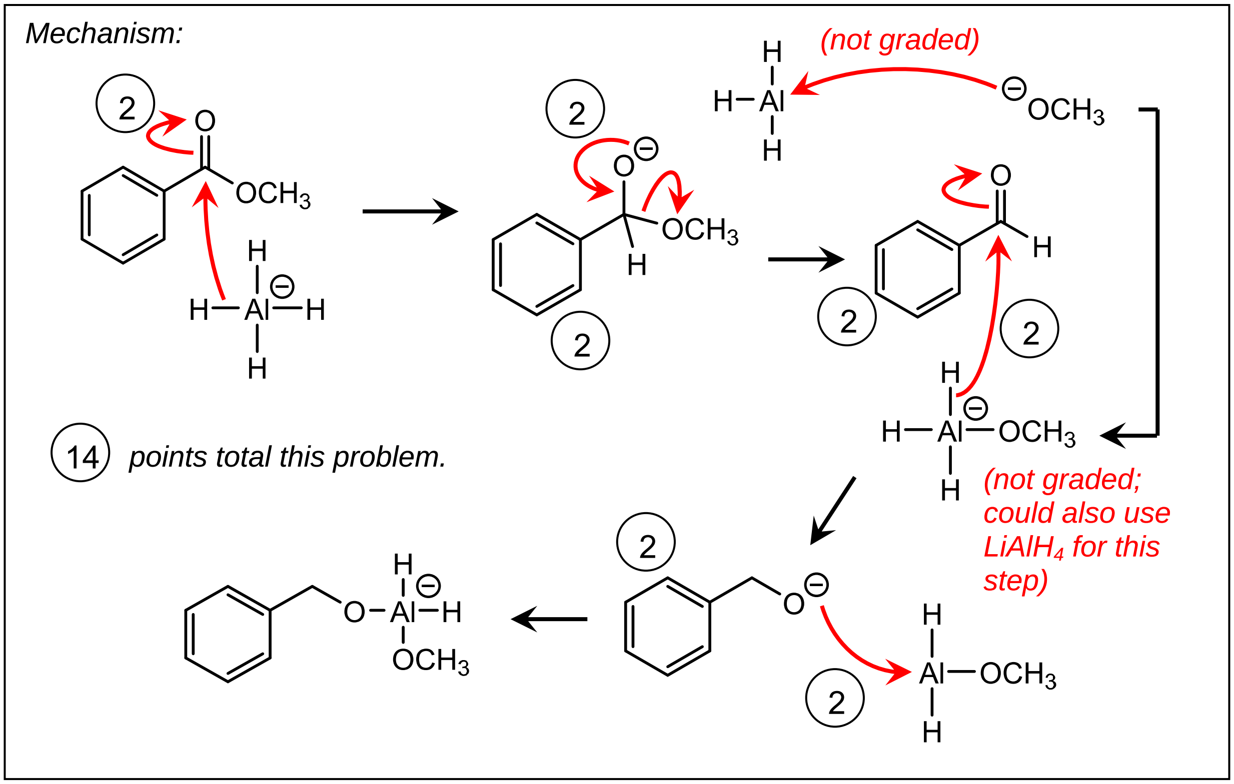




Ag_2O treatment of aldehydes (Tollens oxidation) converts them selectively to carboxylic acids.

3. (28 pts) For each reaction shown below, draw a mechanism that explains how the product is generated from the starting material. (For the first reaction, draw a mechanism that explains the first step; ignore the second step in the gray box.) In your answers, 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: *14 points total for this first problem.*

Overall notes:

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, and then brought back into the mechanism later. For example, AlH_3 is generated in step 1, but isn't needed until step 3; you could leave it out of the mechanism until you needed it.

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 (out of 4). You will also lose the full points for omitting the intermediate you would have drawn.

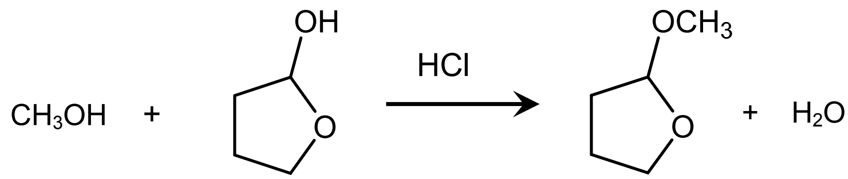
2 points for each correct intermediate structure in your mechanism.

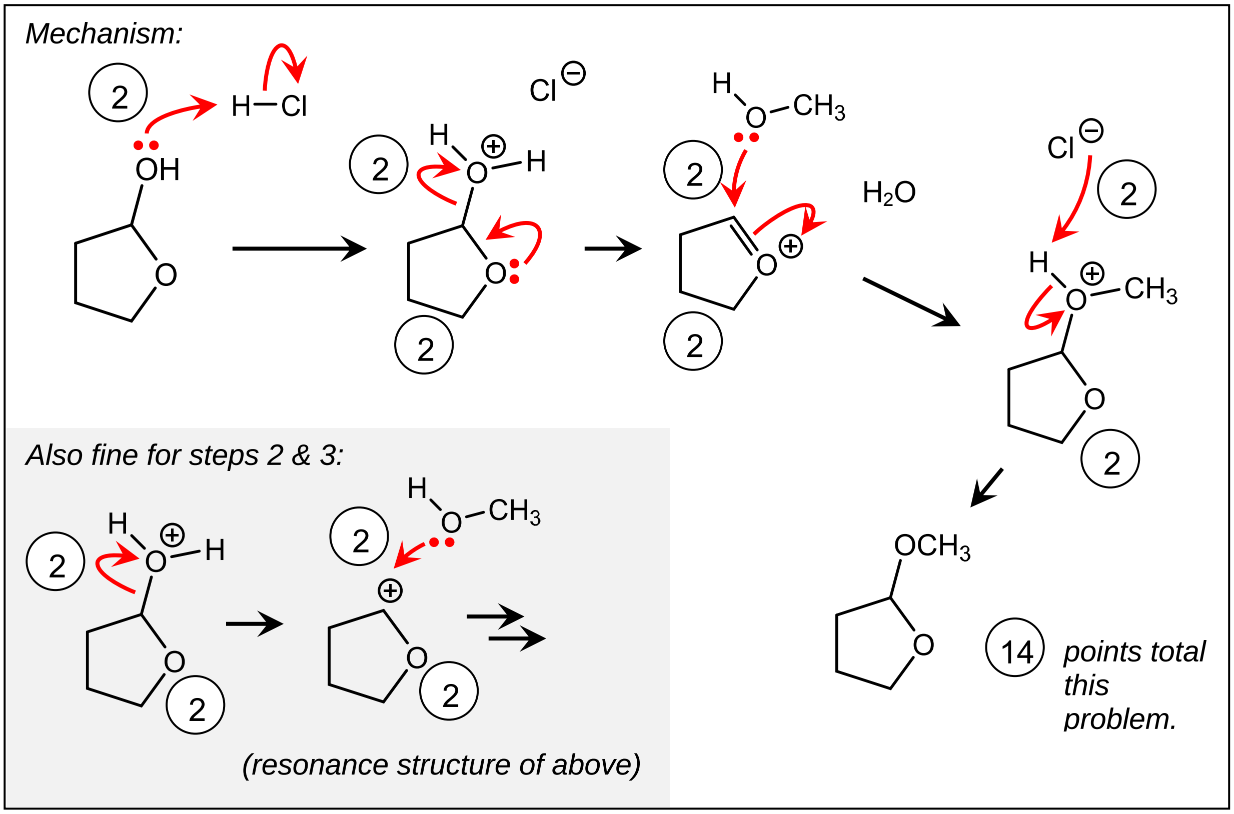
-1 point for each minor error in charge, valency, structure, etc.; if error propagates, points are taken off only for initial error.

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).

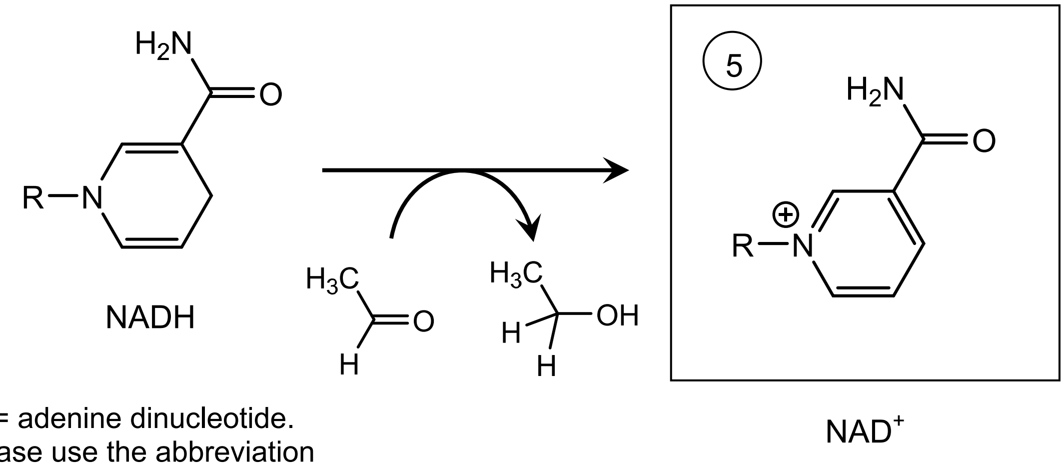




Sometimes, students combine steps 2 and 3 into an S_N2 reaction. This isn't what happens; the nearby oxygen atone makes S_N1, with its stabilized carbocation, more likely.

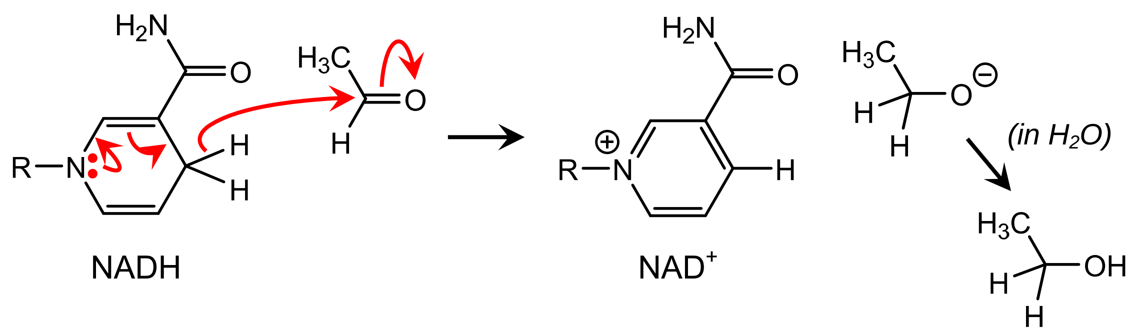
Rubric: *Same as above. 14 points total for this second problem.*

4. (12 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".



(R = adenine dinucleotide. Please use the abbreviation "R" in your answer.)

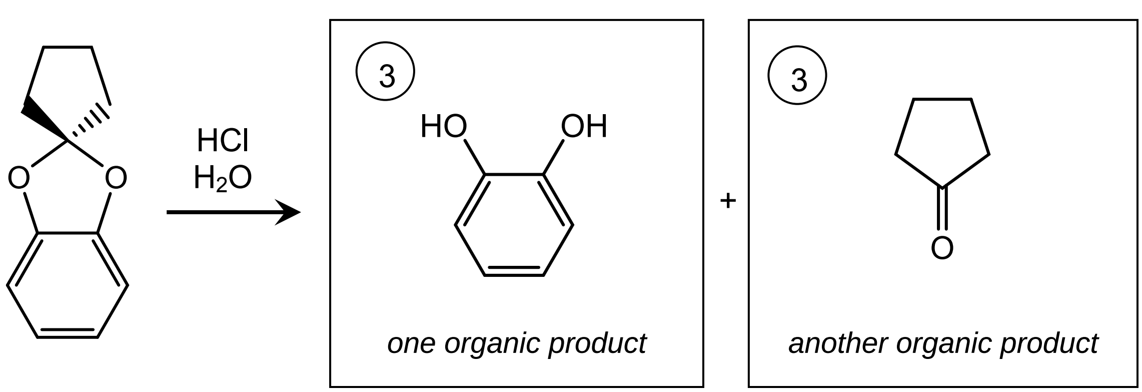
NADH is a reducing agent that donates hydride ("H-") to C=O bonds in biological reductions. NADH is motivated to do this because its central, six-membered ring is almost aromatic—if it could just get rid of an H atom, and a pair of bonding electrons, it would be aromatic. And so, in the presence of a C=O bond, it does just that:



Rubric for this part:

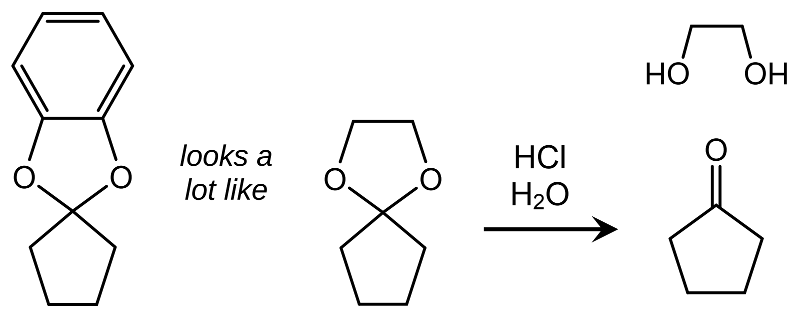
4 points for correct structure.

-1 point for each clearly trivial structure mistake. 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. In this problem, that might include omitting the amide group, or the positive charge.



+ (1) *for getting both correct*

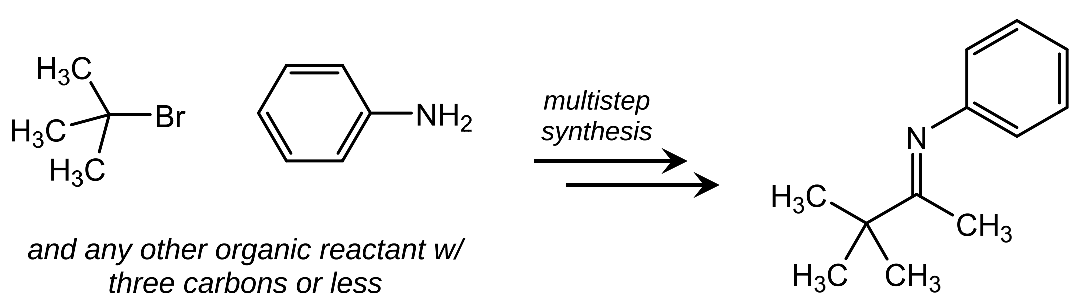
The starting material in this problem is a ketal, and looks very similar to the structure formed by using the cyclic ketal protecting group we talked about in class:

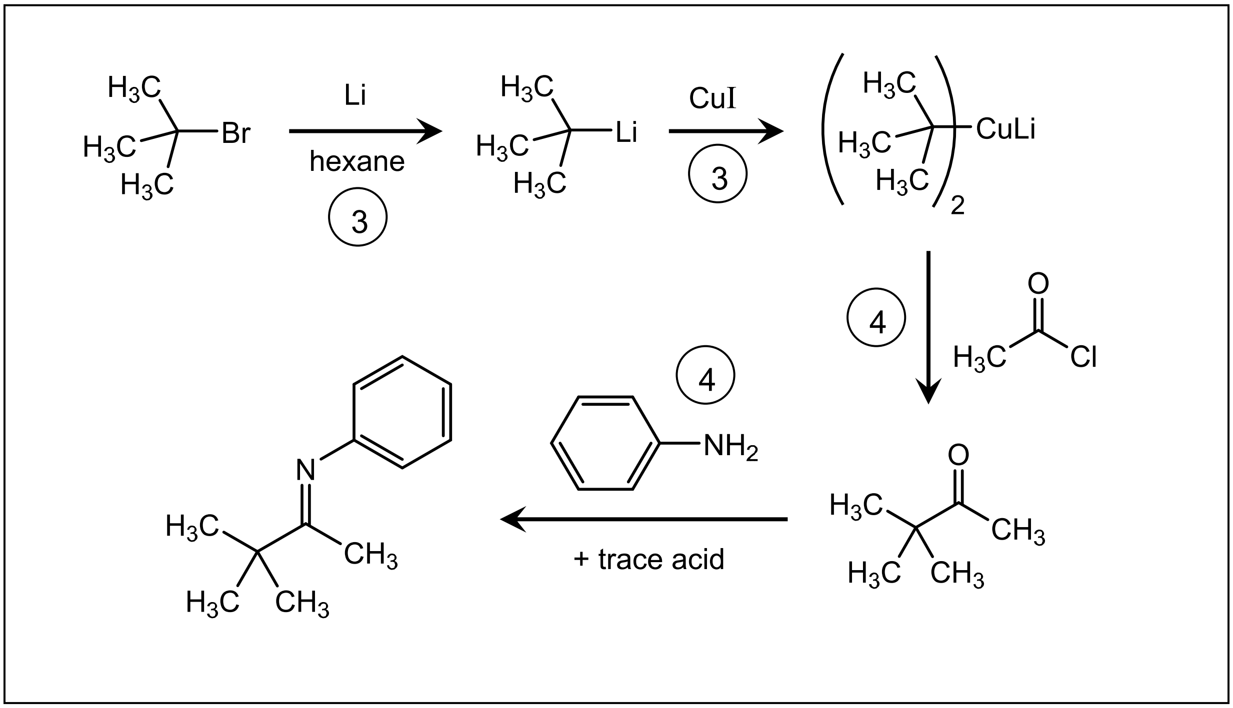


As I've shown above, in acid and water the cyclic ketal is converted (deprotected) to a ketone and ethylene glycol, by adding an O to the central carbon, and one H to each of the singly bound oxygens. In principle, the exact same thing should happen to our molecule in acid and water, with the benzene ring along for the ride with the diol.

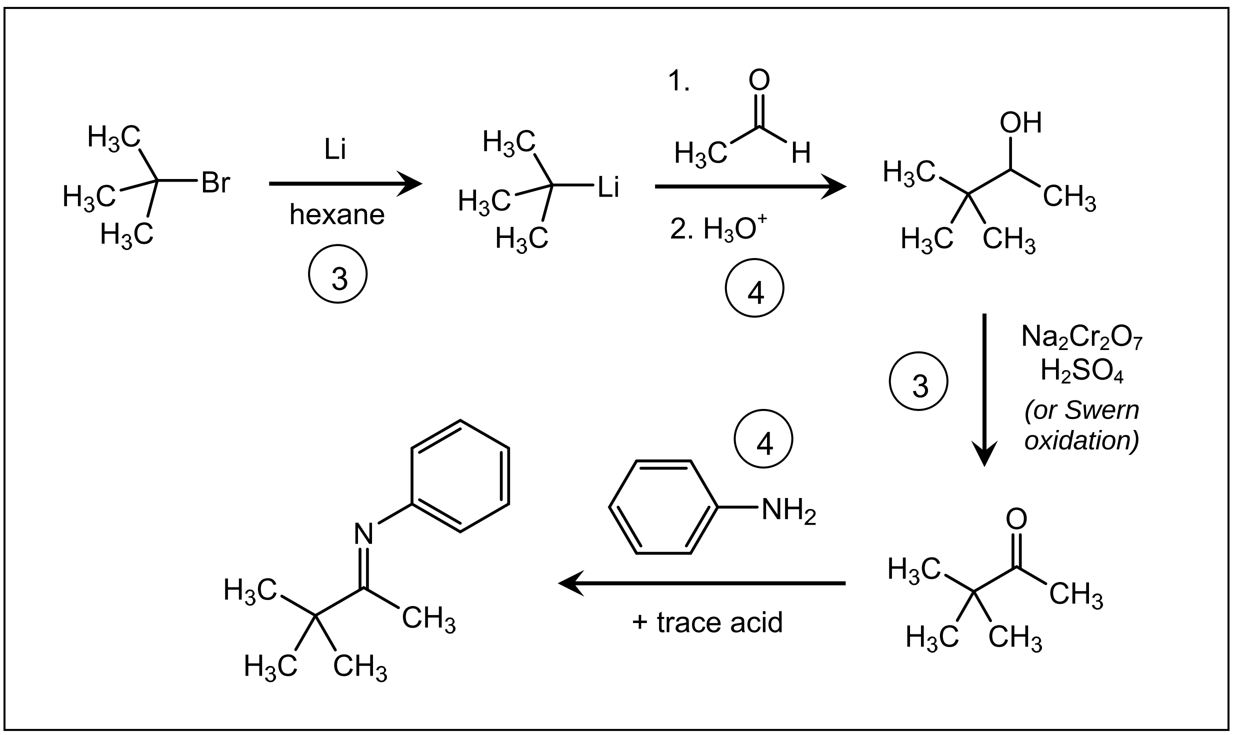
<u>Rubric for this part:</u>
Either molecule can be in either box.
3 points for diol.
3 points for cyclohexanone.
- *-1 point for each clearly trivial structure mistake (includes omitting a carbon from backbone).*

5. (14 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.





OR



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 <u>minor</u>, <u>trivial</u> 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.

<u>Tasks:</u>

1. **Metalate *t*-BuBr.** (3 points.)
   Either Li or Mg received full credit here. (RMgBr can't be converted to a cuprate, but we penalized you for that later.)

2. **Convert alkyllithium to an lithium dialkylcuprate.** (3 points.)

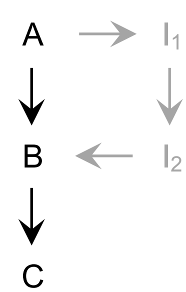
OR

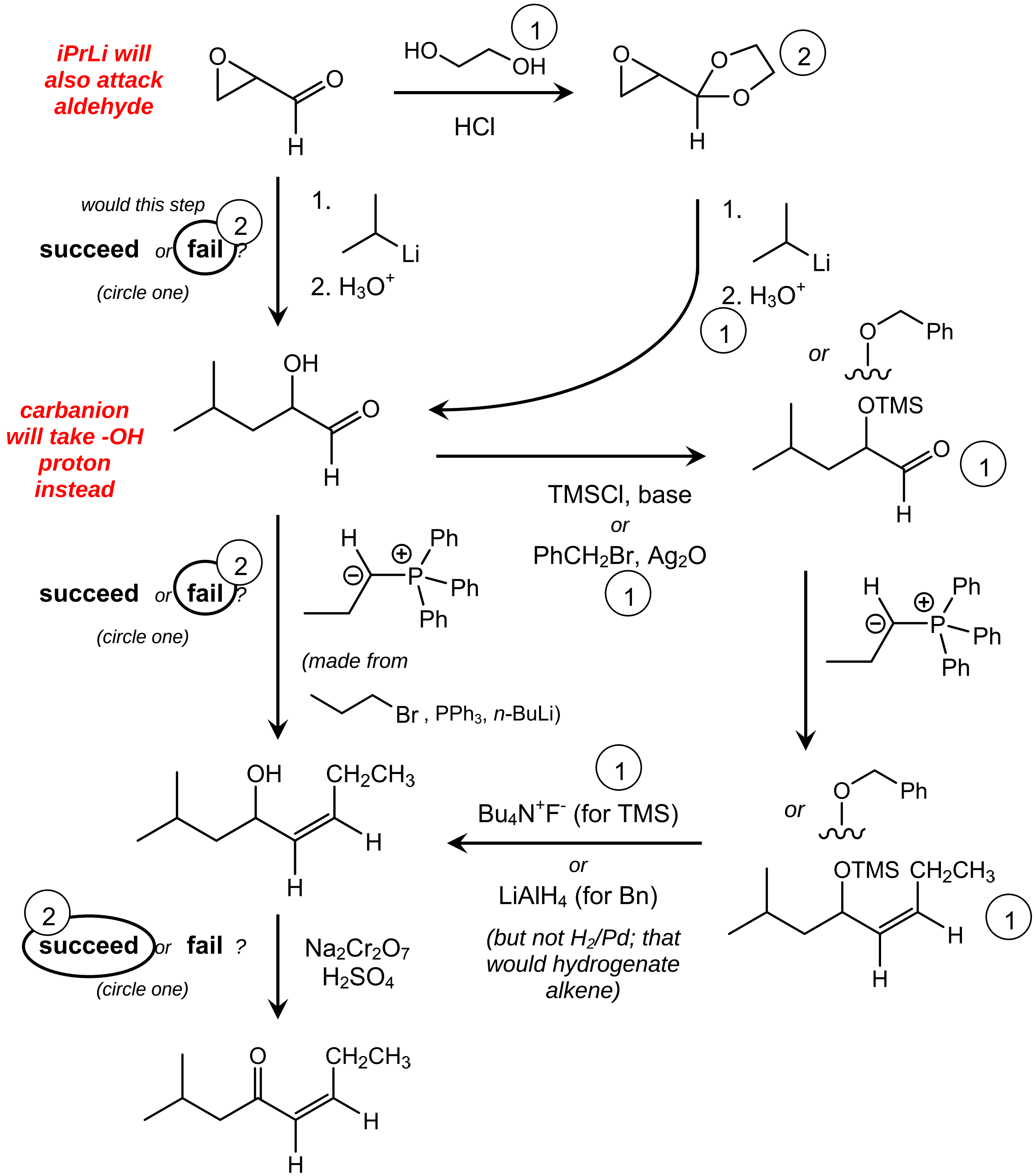
2. **Oxidize/reduce molecule to final ketone.** (3 points.)

3. **Form a single carbon-carbon bond between *tert*-butylmetal and a two-carbon electrophile.** (4 points.)
   Any successful such reaction gets these points. This would include not just reactions shown above, but also those that couldn't connect with a successful synthesis—such as alkyllithium addition to an epoxide (alcohol ends up at wrong carbon).

4. **Form imine from final ketone.** (4 points.)

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.





Rubric:
2 points for each circled succeed/fail.
4 points for each protection/deprotection cycle.
1 point for using correct reagents in each protection/deprotection;
2 points for drawing correct molecules on the right.