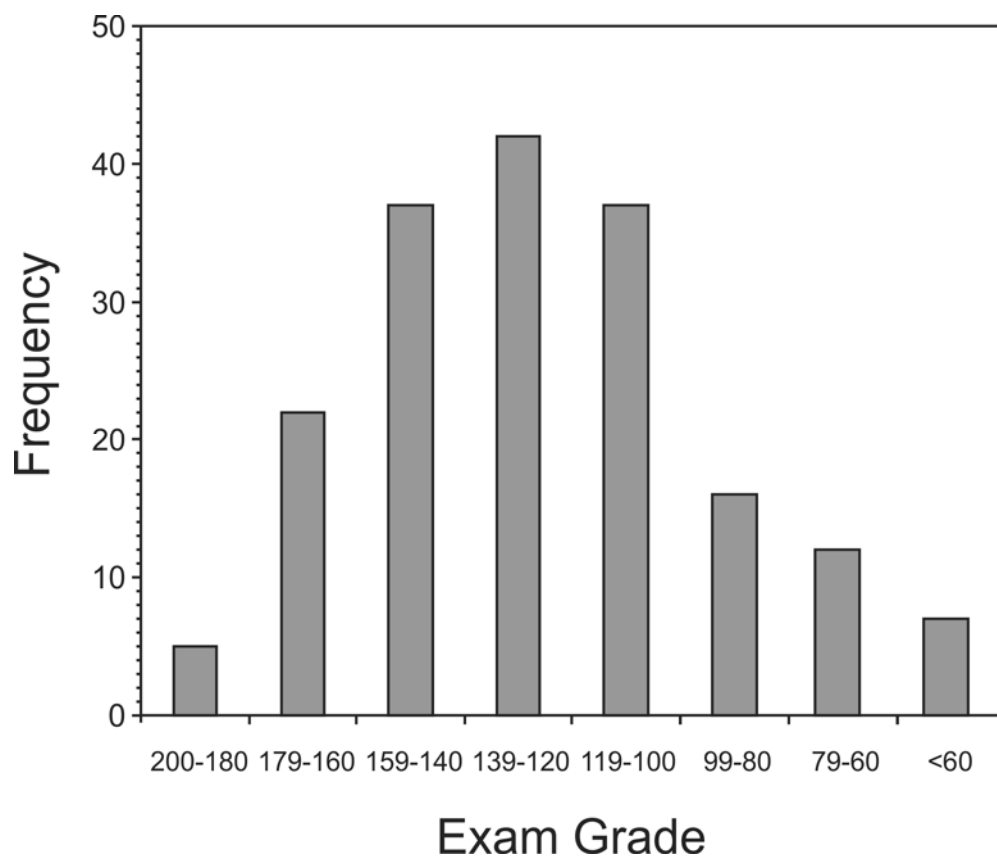
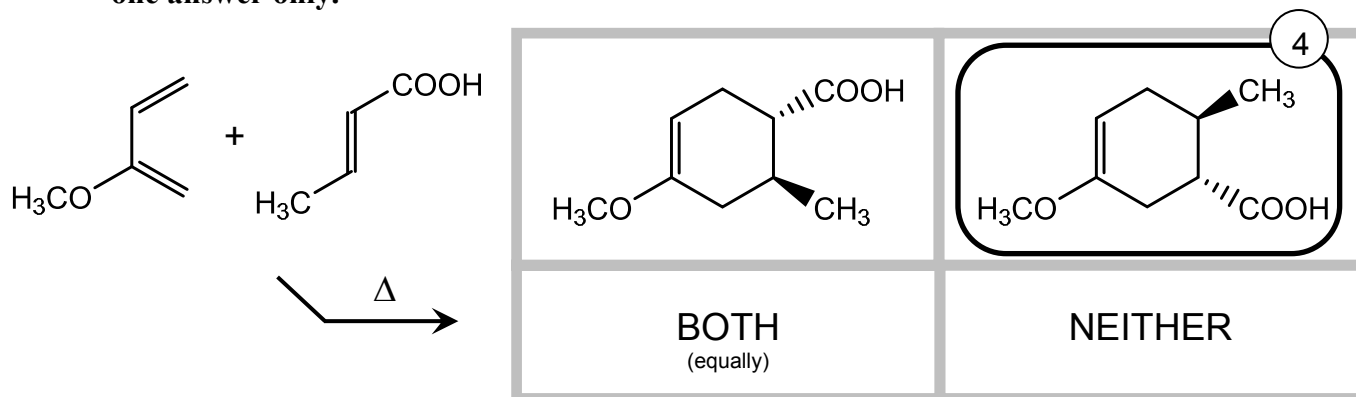


**Final Exam
Answer Key**

Final Exam Mean: 124
Final Exam Median: 127
Final Exam St. Dev.: 32

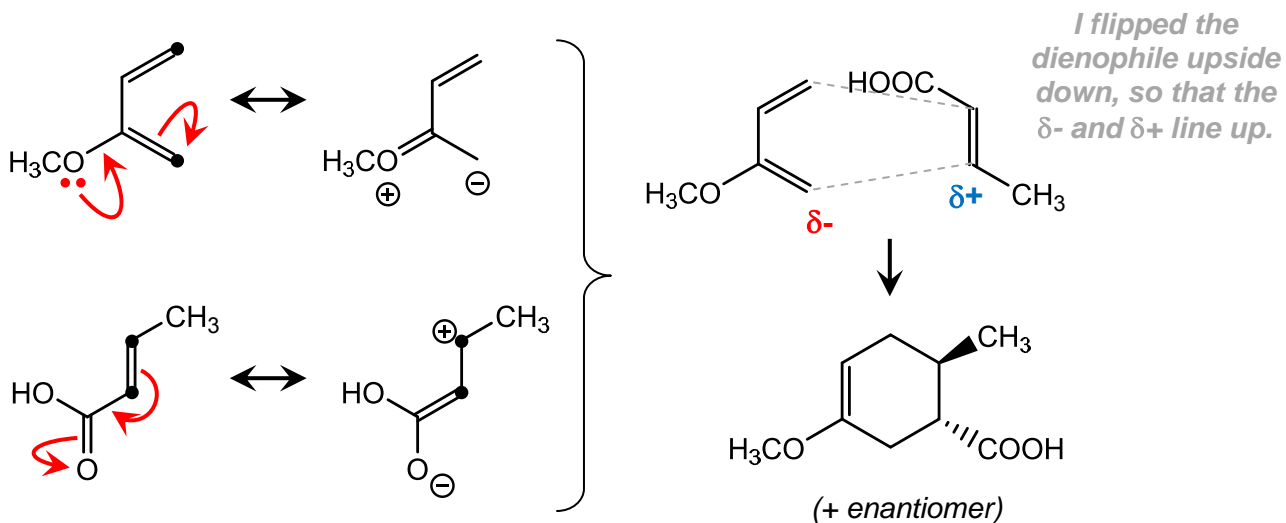


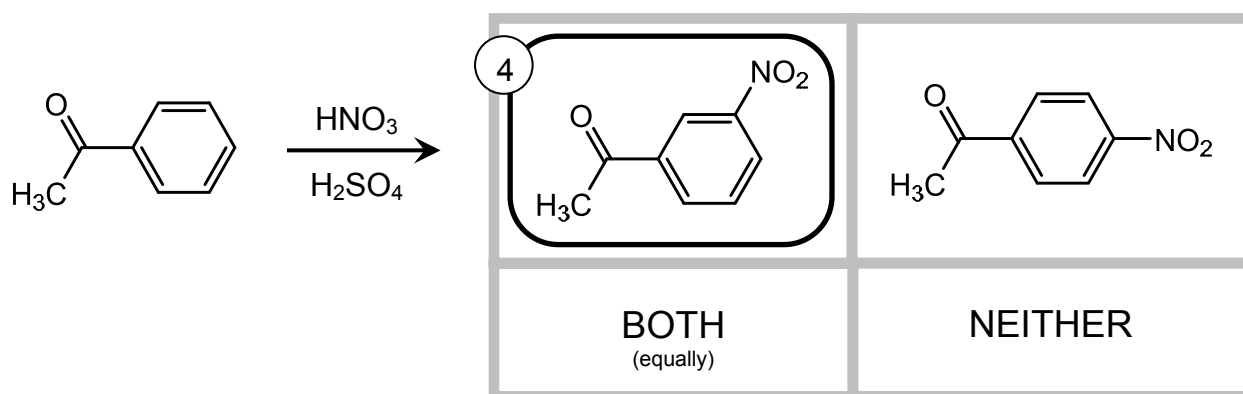
1. (32 pts) Each of the reactions below is drawn with two possible products. If one of the two products predominates, circle that preferred product. If the two products are produced equally, circle "BOTH". If neither product would result from the reaction, circle "NEITHER". **Circle one answer only.**



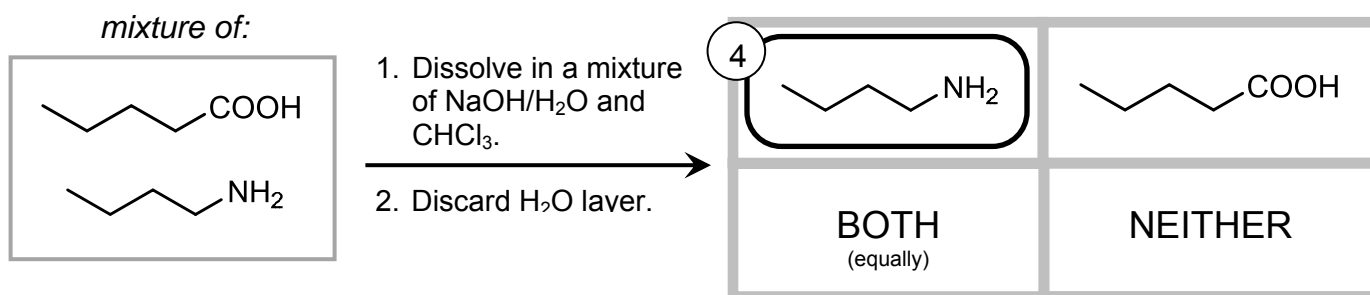
In all Diels-Alder reaction problems, we have to do three things: (i) identify the (*s-cis*) diene and the dienophile; (ii) line up partial charges to determine regiochemistry in the product; and (iii) put π -substituents *endo* and steric substituents *exo*, to determine stereochemistry in the product. Occasionally, either step (ii) or (iii) won't matter, but it's nearly always a good idea to do them anyway.

- Pretty simple: The starting material on the left is the diene, and the one on the right is the dienophile. They are even modified with the best kind of substituents to help the Diels-Alder reaction, in that the dienophile is electron-poor (because of the attached C=O bond) and the diene is electron-rich (because of the π -donating oxygen atom).
- In order to line up partial charges in our starting materials, we need to draw all of the resonance structures for each reactant, and see how those resonance structures affect the carbon atoms that will be connected with new bonds (which I've labeled with black dots).

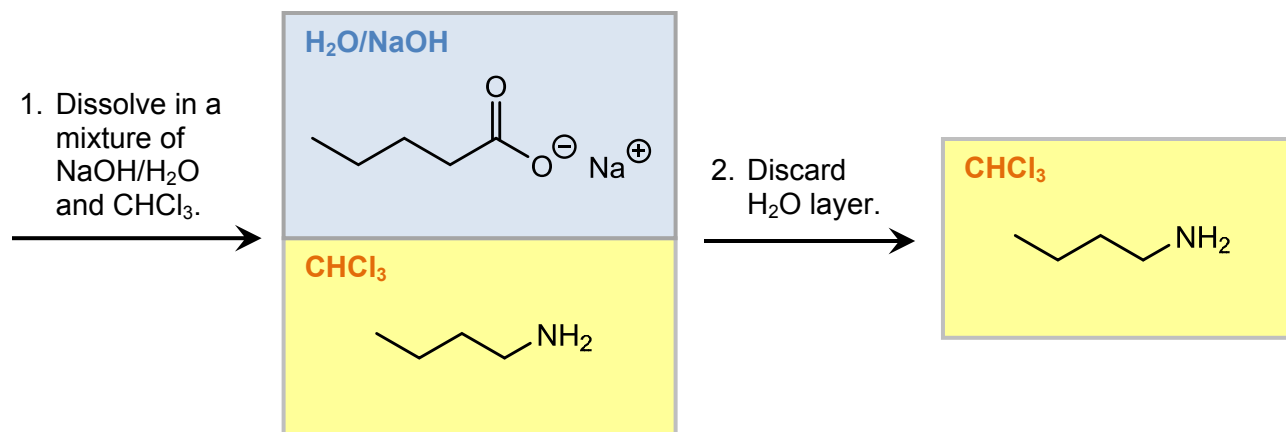


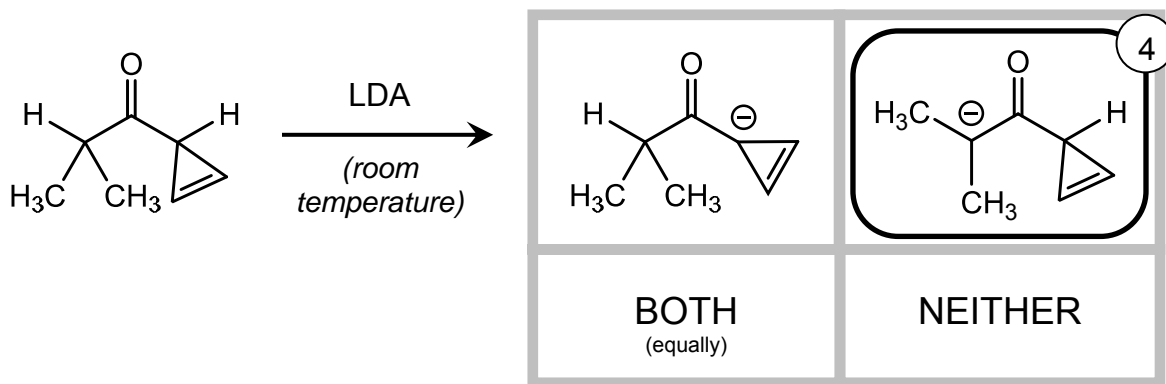


The carbonyl (C=O) group in the starting material is electron-withdrawing, because it has a partial positive charge at carbon, and is thus *meta*-directing. Electrophilic aromatic nitration occurs at the *meta*-position.

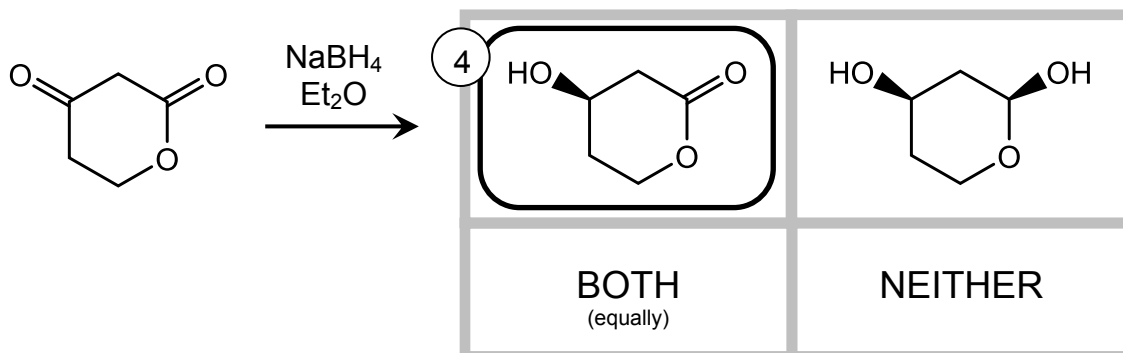


Dissolving the initial mixture in base deprotonates the carboxylic acid, and turns it into an ion, which is soluble in water:

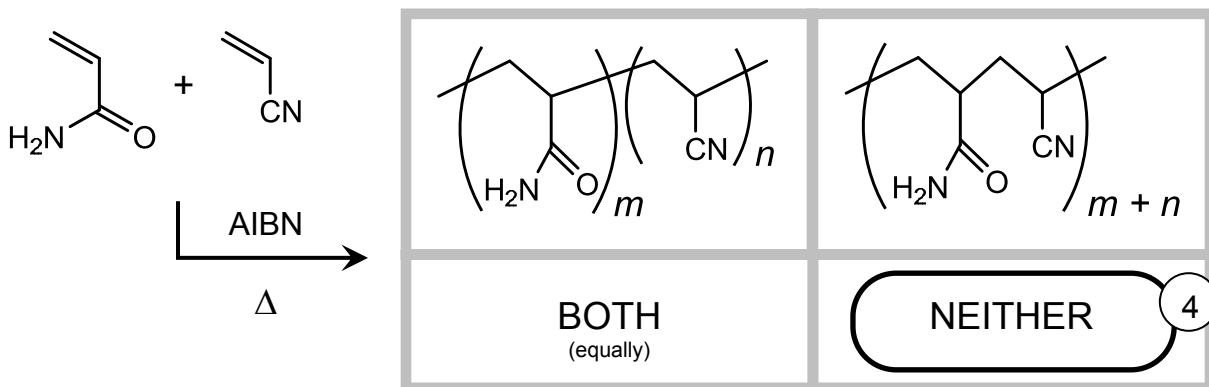




LDA is a strong base, and at room temperature, it will remove a proton from a carbonyl-containing starting material to yield the most stable enolate. This starting material has removable protons on either side of the carbonyl, with an identical substitution pattern. But the anion that is generated on the left has a number of 4- π -electron, anti-aromatic resonance structures—including the one drawn above—and, as a result, the anion isn't stabilized by resonance like it should be. (Put differently, the carbanion resonance structure on the right helps the anion on the right, but the carbanion resonance structure on the left doesn't help the anion on the left.) So, there will be a thermodynamic drive to form the anion on the right.



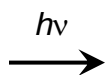
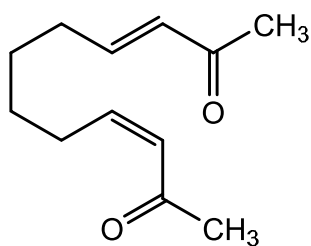
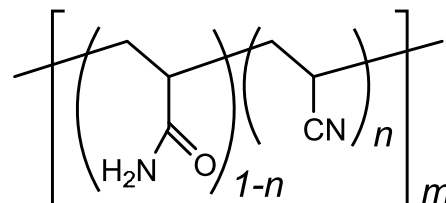
NaBH_4 is a mild reducing agent, and only reduces aldehydes and ketones. Our starting material has a ketone and an ester; only the ketone gets reduced.



This problem was a bit tricky, in that it involved all the different ways to illustrate the arrangement of monomers in a copolymer—a polymer that incorporates two different monomers into one chain. (As we discussed in class, copolymers are often useful because they can combine the physical properties of two different homopolymers into one uniform polymer material.) Looking at our two products, the product on the left illustrates a *block copolymer*—a polymer that has a stretch of one monomer, m repeat-units long, followed by a stretch of another monomer, n repeat-units long. Each polymer chain in the left-hand product would look like AAAAAABBBBBB. But our polymerization conditions involve our starting materials mixed together randomly at the beginning of the polymerization, and I would expect random incorporation of these monomers into the polymer chains. I certainly wouldn't expect all of the first monomer to polymerize first, before the second monomer gets involved. So the left-hand product doesn't match our expectations for the polymer chain structure.

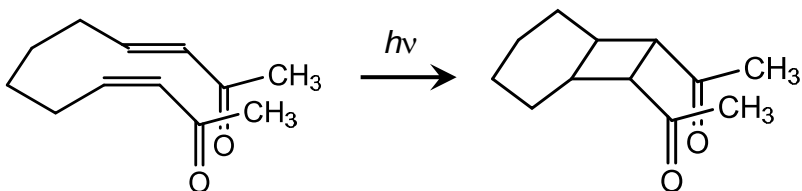
The right-hand product illustrates an *alternating copolymer*—a polymer that looks like ABABABABAB, in which A and B alternate. (Remember that the brackets represent a structure that repeats, so “-[AB] $_n$ ” means “AB repeats over and over”.) Once again, we wouldn't expect our randomly incorporated monomers to perfectly alternate, so this isn't the correct structure either. The correct answer was “NEITHER”.

Okay then, if neither of these structures is appropriate, what structure is? We didn't draw a random (or “statistical”) copolymer in bracket notation in class this term, but if we had, it would illustrate our two monomers as fractional components of the polymer whole, as shown at right. Here, $0 < n < 1$, and m is the total number of monomer units. You didn't need to know this to answer the problem, but there it is.

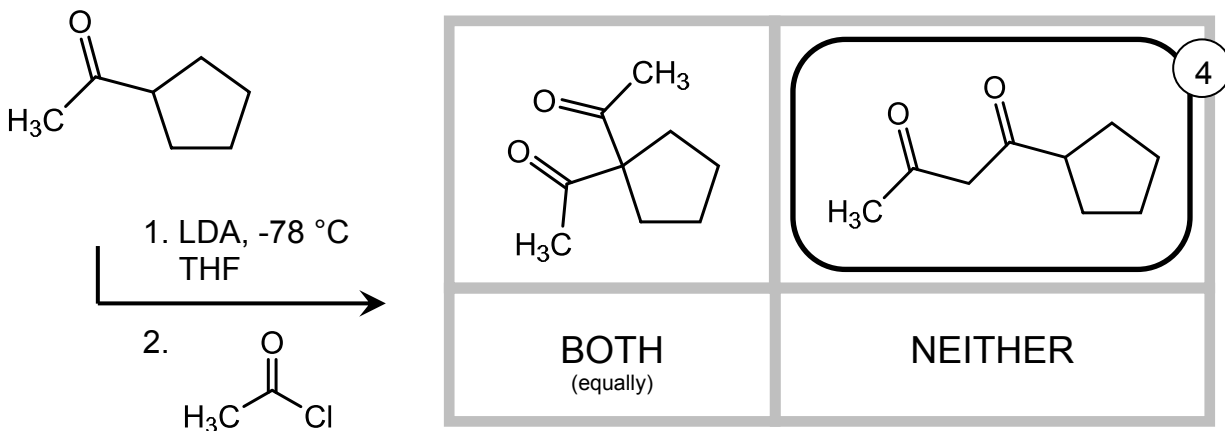


<p>BOTH (equally)</p>	<p>NEITHER</p>

Our starting material has two C=C double bonds, drawn right next to each other. Ordinarily, under thermal (heat) conditions, reaction of these two double bonds with each other via [2,2]-cycloaddition would be forbidden according to the Woodward-Hoffman rules for cycloaddition. But in the presence of light (and particularly UV light), [2,2]-cycloaddition is allowed under the Woodward-Hoffman rules, and the two alkenes can form the four-membered ring on the right.



The left-hand product would be made by [4+2] (Diels-Alder) cycloaddition, but there are a number of problems with this reaction. First, the Diels-Alder reaction requires heat, and won't work with light, according to the Woodward-Hoffman rules. Second, the Diels-Alder reaction only works with C-C bonds, not C-O bonds. The left product would not be formed.



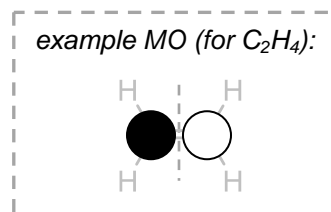
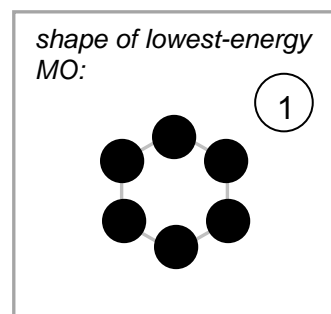
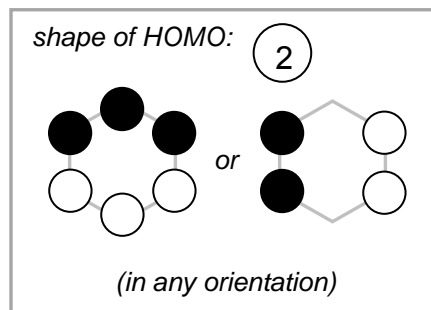
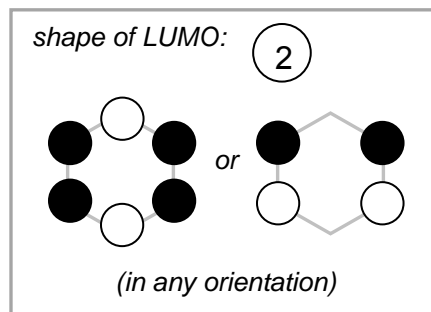
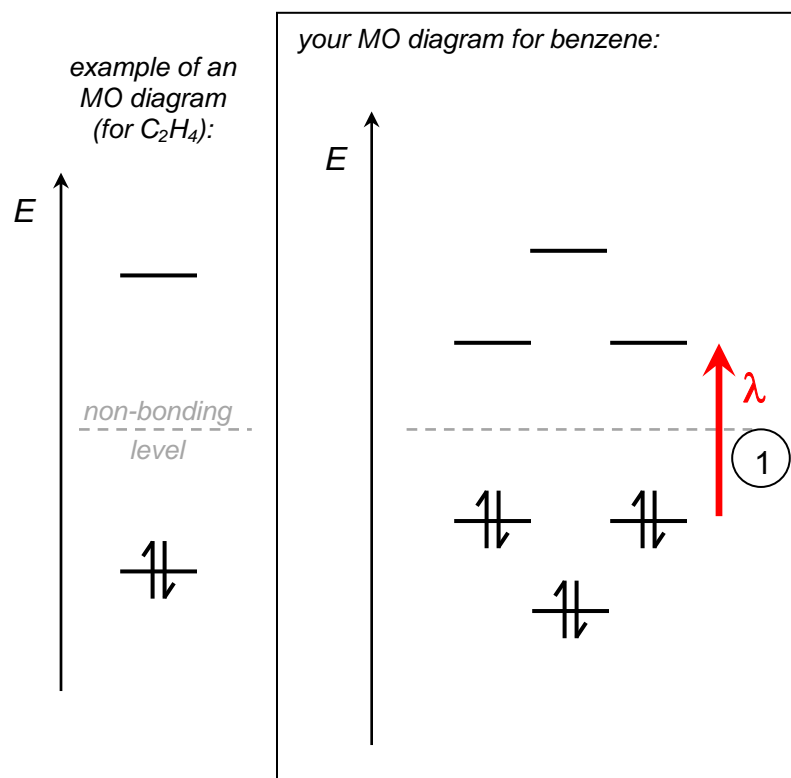
At low temperature, and in a polar, aprotic solvent like THF, LDA deprotonates the ketone starting material at the less-substituted α -carbon on the left. Nucleophilic acyl substitution on the acyl chloride then takes place on this side.

2. (17 pts) Benzene is a prototypical aromatic molecule. Benzene's aromaticity has sometimes been explained by using a molecular orbital diagram.

a. On the energy diagram below, **draw a molecular orbital (MO) diagram** for the conjugated π orbitals in benzene.

- Draw all orbital energy levels as horizontal lines;
- Fill your orbitals with the appropriate number of electrons.

b. In the boxes on the right, draw the shapes of benzene's LUMO, HOMO, and lowest-energy molecular orbital as combinations of atomic orbital lobes, viewed from the top of the molecule. If there is more than one LUMO, HOMO or lowest-energy orbital, just draw one. I have drawn the framework of benzene in each box; draw each orbital right on top of that.



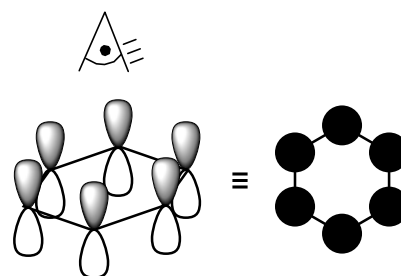
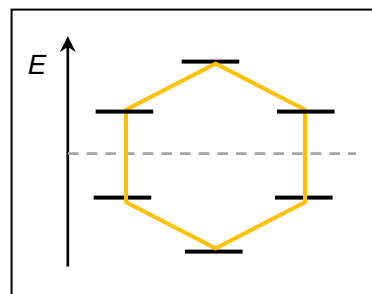
- (1) for 6 orbitals, in any order
- (2) for inverted polygon (any number of orbitals)
- (2) for filling with 6 e^- from bottom up

This question asks us to draw a molecular orbital diagram of a conjugated π system. To solve the problem, we have to ask some basic questions first:

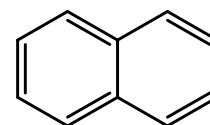
- Is the conjugated system of p orbitals linear or cyclic?** There is a p orbital on each sp^2 -hybridized carbon all the way around the ring, with no breaks. This is a cyclic system.
- How many p orbitals are there?** Six sp^2 -hybridized carbons, so six p orbitals. And thus six molecular orbitals, because the number of molecular orbitals in a conjugated π system is equal to the number of p orbitals that combine to create it.
- How many π electrons are there?** This is a different question than (ii); sometimes the answer to (ii) and (iii) will be the same, sometimes not. Within the ring, benzene has three double bonds that contribute 6 π electrons.

This means we need to draw a molecular orbital diagram for a cyclic system of 6 molecular orbitals that contains 6 electrons. *Cyclic* conjugated systems are drawn using the “inverted polygon method”. To do this:

- On the energy diagram, draw a big polygon with the same number of vertices as the number of MO's, pointed downward. We have six MO's, so we draw a big hexagon, point down.
- Draw a horizontal energy level at each vertex of the polygon.
- Each energy level corresponds to a MO shape that is a combination of the six atomic p orbitals, in which the mathematical phase of each orbital lobe is either matched or mismatched with its neighbor. The bottom-most, lowest-energy orbital has all of its component p orbitals in-phase (matched). All of the orbital interactions in this lowest-energy orbital are bonding.
- Higher-energy orbitals have nodes that represent mismatched phase between neighbors. Each level above the first has one more node. This problem asked you to draw a Highest-Occupied Molecular Orbital (HOMO), which is one level above the first, so it has one node; and a Lowest-Unoccupied Molecular Orbital (LUMO), which is two levels above the first, so it has two nodes.



- c. On your MO diagram on the previous page, draw a vertical arrow to illustrate an electronic transition that could be observed as an absorption peak in the UV/vis spectrum of benzene. Label the arrow " λ ".



naphthalene

- d. How would you expect the optical absorbance of benzene to compare to that of naphthalene (shown at right)? Would you expect

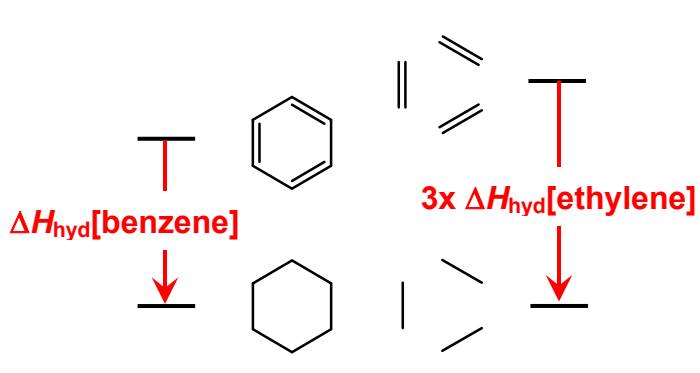
$\lambda_{\max}(\text{naphthalene})$ to be $>$ $<$, or $=$ $\lambda_{\max}(\text{benzene})$? (Circle one.)

In general, the more conjugated a molecule is, the closer in energy the HOMO and LUMO are, and the longer λ_{\max} is (because λ_{\max} is inversely proportional to energy). Naphthalene is more conjugated than benzene, so it should absorb light at longer wavelengths.

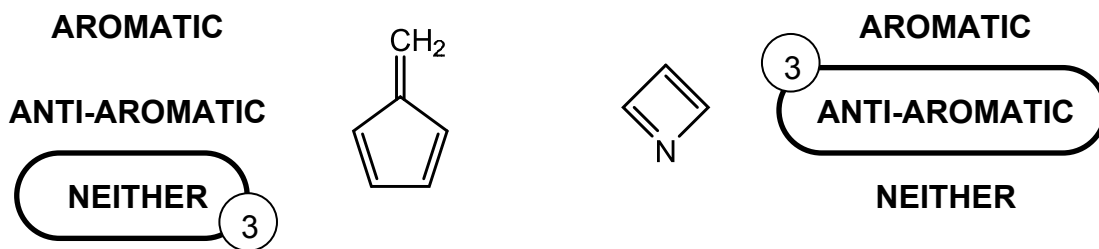
- e. Double bond hydrogenation is always exothermic—or, put another way, ΔH_{hyd} is always negative. The Lewis structure of benzene is drawn with three double bonds, and exhaustive hydrogenation of benzene would involve three consecutive additions of H_2 . How does $\Delta H_{\text{hyd}}[\text{benzene}]$ compare to hydrogenation of a three typical alkenes, like ethylene? Is

$\Delta H_{\text{hyd}}[\text{benzene}]$ $>$ $<$, or $=$ $3 \times \Delta H_{\text{hyd}}[\text{ethylene}]$? (Circle one.)

Benzene is a lot more stable than it would be if it were a simple triene. As a result, it gives off a lot less energy when it is hydrogenated than we otherwise might expect. Mathematically speaking, $\Delta H_{\text{hyd}}[\text{benzene}]$ is larger because it's less negative.



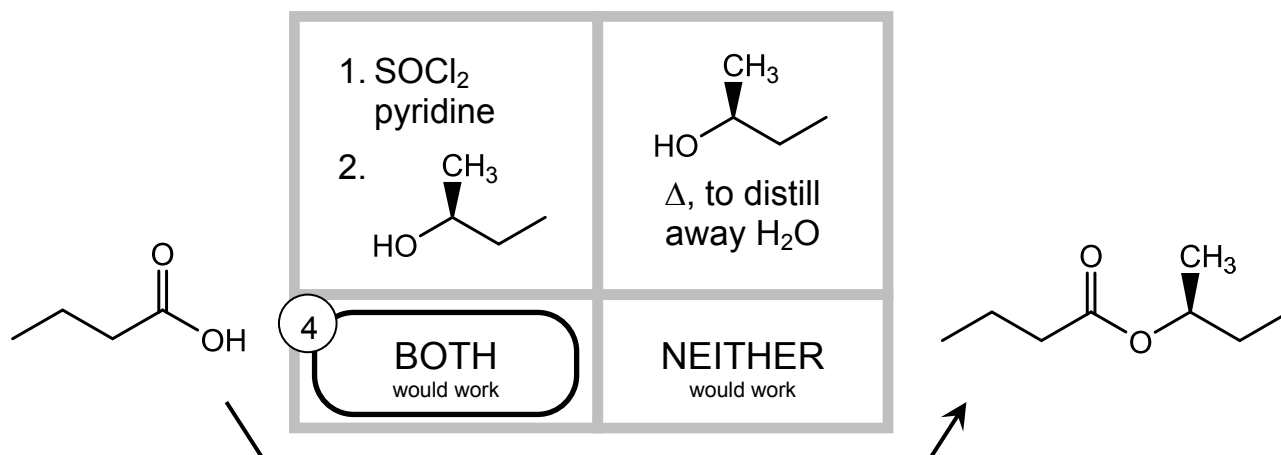
3. (6 pts) For each of the following molecules, circle whether the molecule is aromatic, anti-aromatic, or neither.



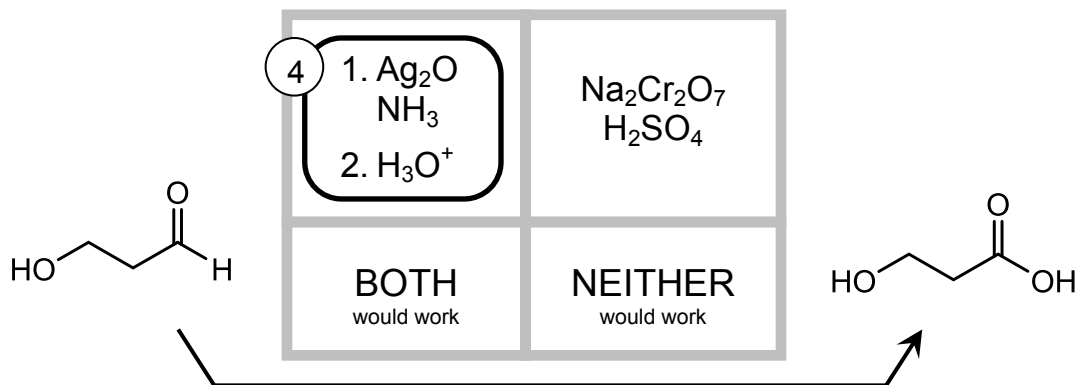
Has 5 π electrons in the ring—4 from the two double bonds in the ring, and 1 from the exocyclic C=CH₂ bond (which is half in the ring, half out). Non-aromatic.

4 π electrons from the two double bonds in the ring. The lone pair on nitrogen is in an sp² hybrid orbital, not a p orbital, so it doesn't contribute.

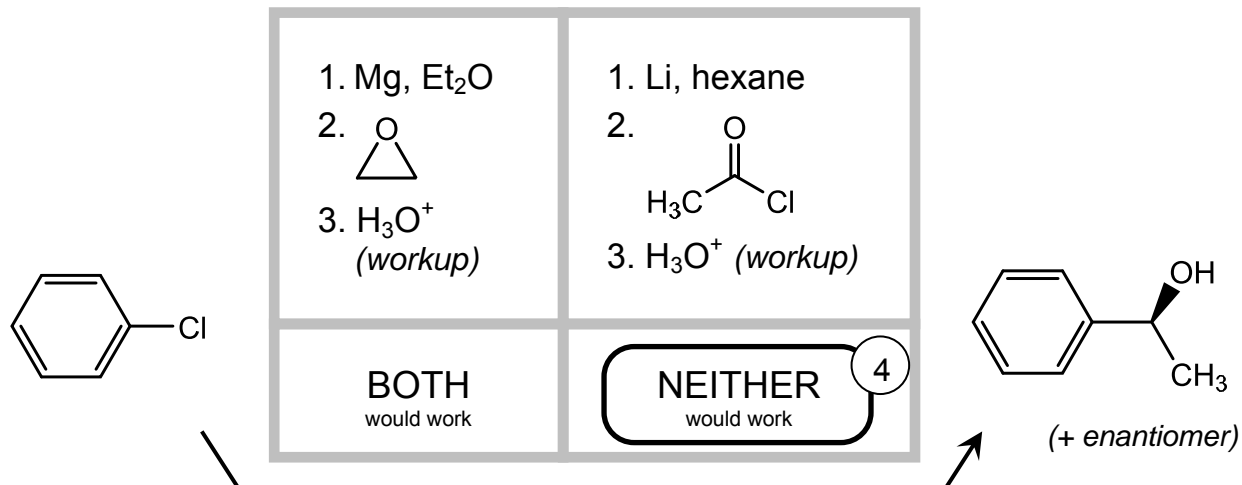
4. (16 pts) Each of the reactions below is drawn with two possible reaction conditions. If only one of the two reaction conditions would generate the given molecule as the major product, circle those conditions. If both sets of conditions would accomplish the reaction, circle "BOTH". If neither set of reaction conditions would succeed, circle "NEITHER". **Circle one answer only.**



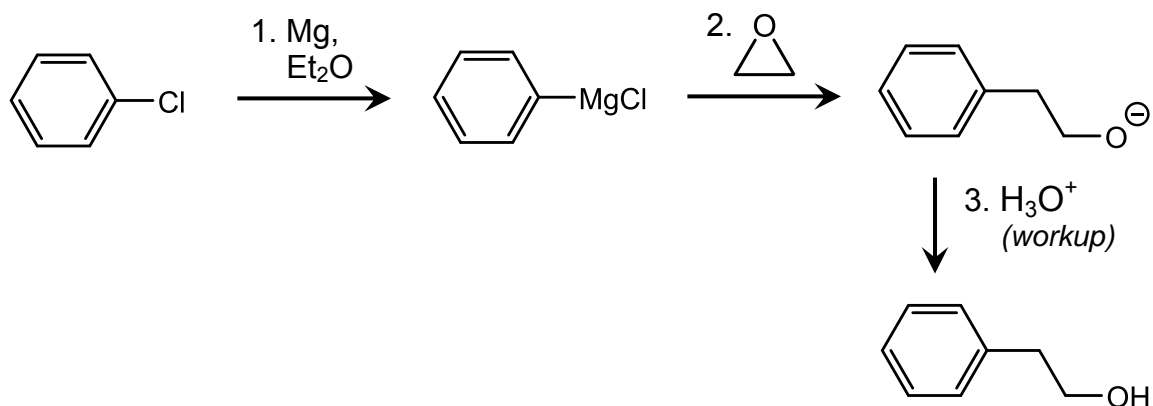
I will admit, the first method will work much better than the second, especially without any acid to catalyze the reaction. But both will work.

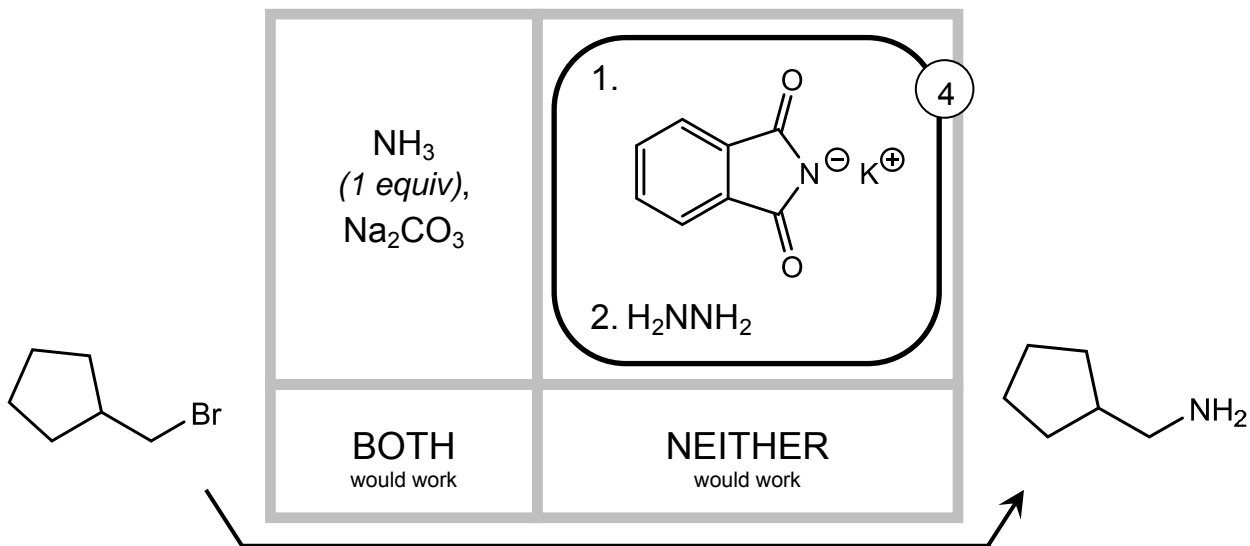
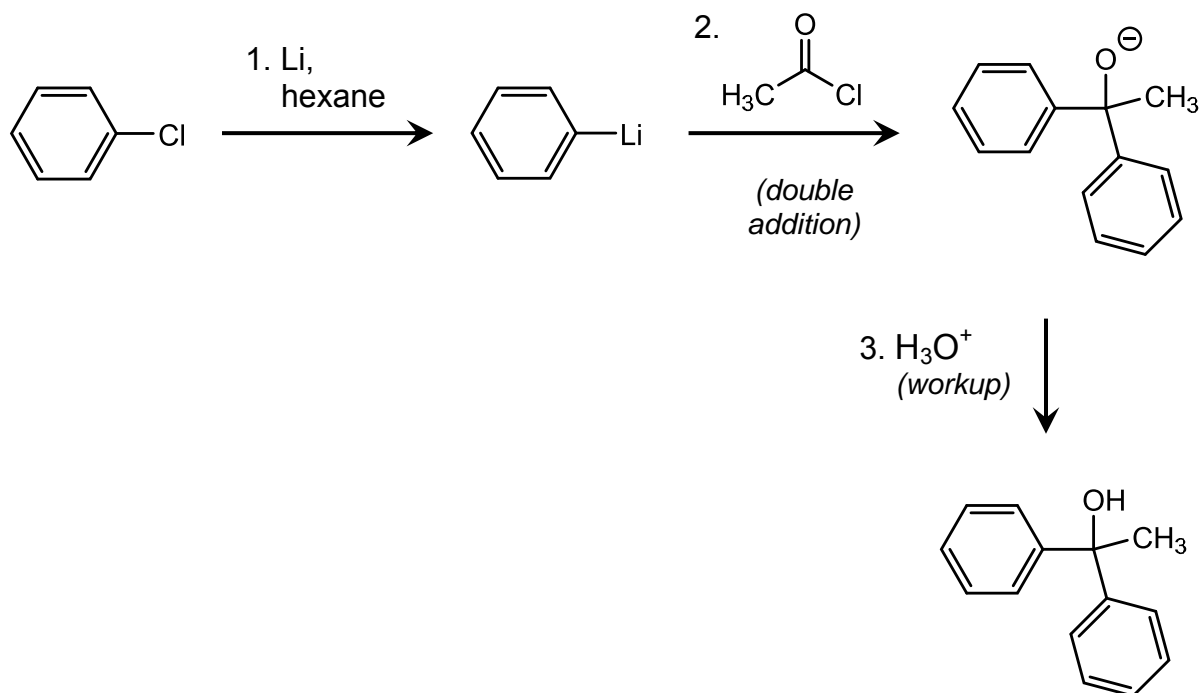


Tollens' oxidation selectively oxidizes the aldehyde to a carboxylic acid. Chromate, by contrast, would oxidize everything—including the alcohol on the left.



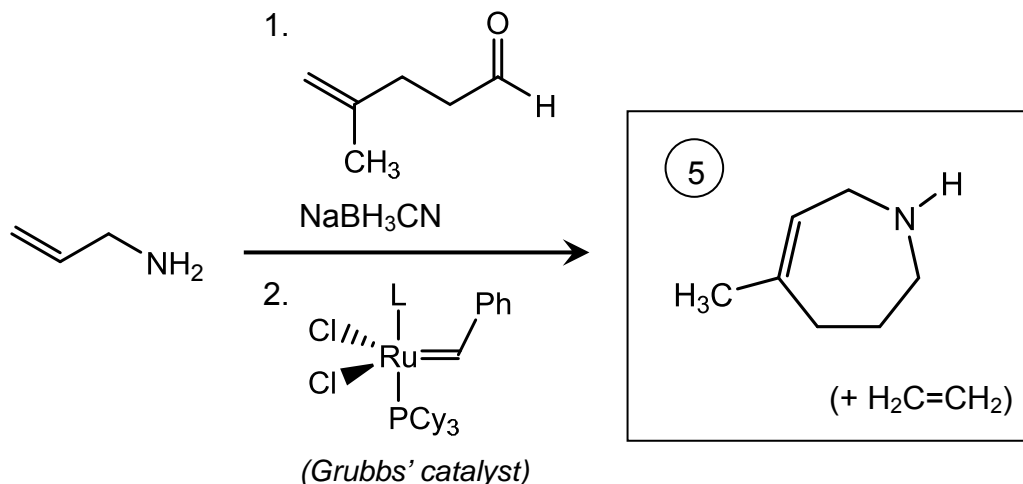
Both of these reaction conditions result in addition of an alkylmetal to an electrophile, but neither of them yield the product shown:





The conditions on the left will lead to poly-alkylation of the ammonia nitrogen; once ammonia reacts once, to form the amine product, that amine will react again and again because it becomes more nucleophilic with each addition. Gabriel synthesis—the conditions on the right—solves this problem and yields the primary amine product.

5. (20 pts) For each of the reactions below, fill in the empty box corresponding to reagents or 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”.



The first step in this reaction sequence is a reductive amination; it turns the primary amine into a secondary amine, attaching the aldehyde to the amine group. The second step is a ring-closing metathesis reaction.

Rubric for this part:

5 points for correct structure.

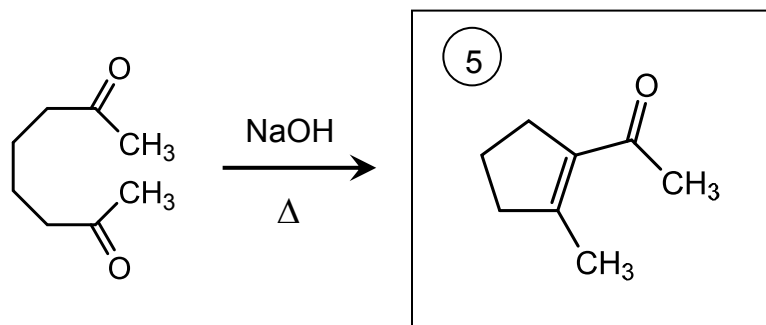
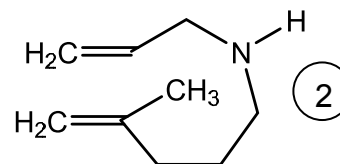
2 points partial for stopping at reductive amination.

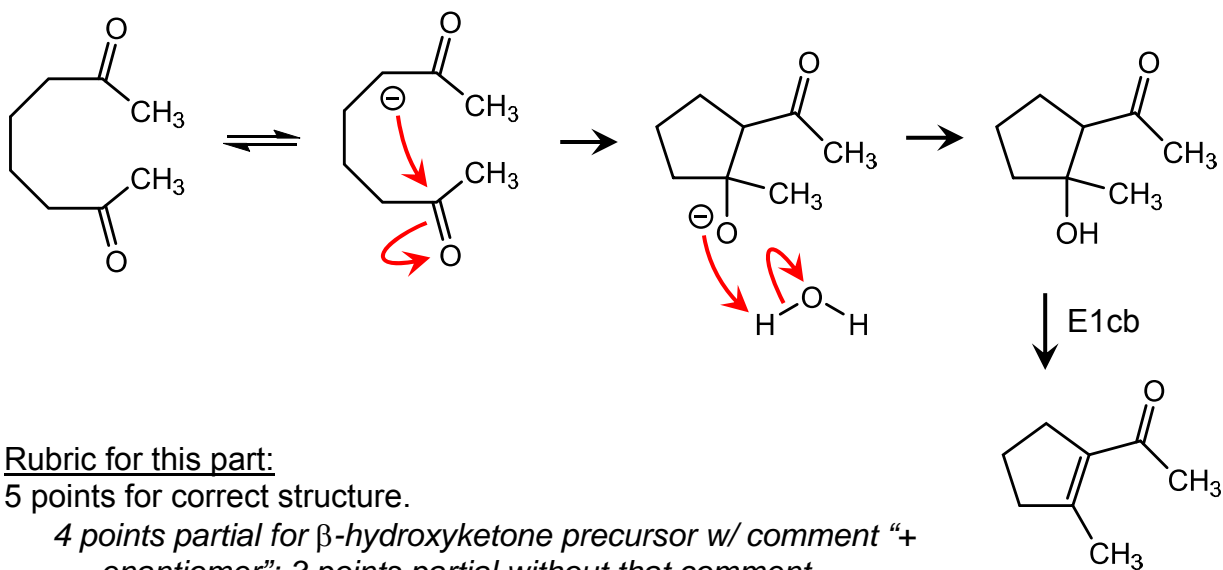
-2 points for omitting exocyclic $-\text{CH}_3$ group.

-2 points for incorrect number of carbons in the ring.

-2 points for omitting double bond, or having extra double bonds.

-2 points for each other, clearly trivial structure mistake.





Rubric for this part:

5 points for correct structure.

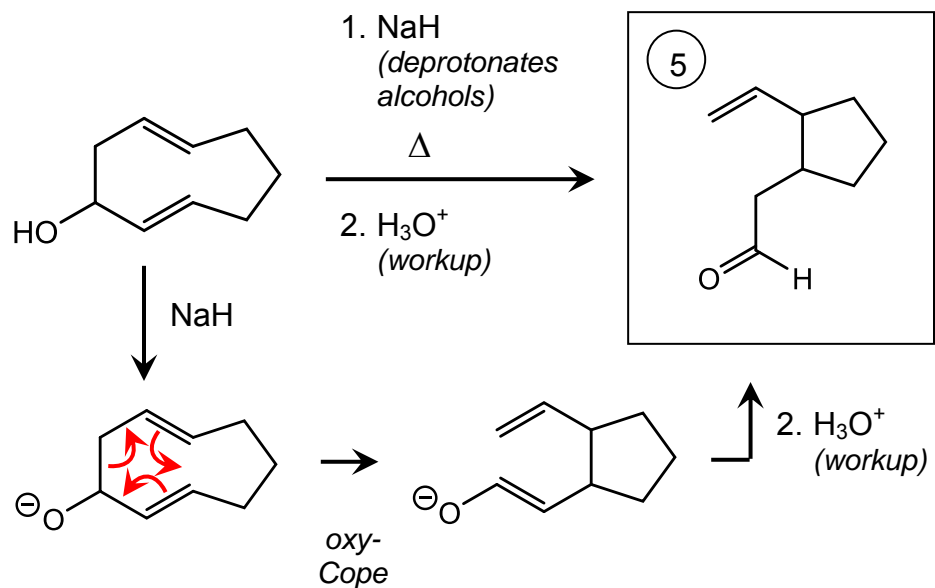
4 points partial for β -hydroxyketone precursor w/ comment "+ enantiomer"; 3 points partial without that comment.

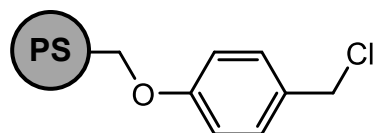
-2 points for omitting exocyclic -CH₃ group.

-2 points for incorrect number of carbons in the ring.

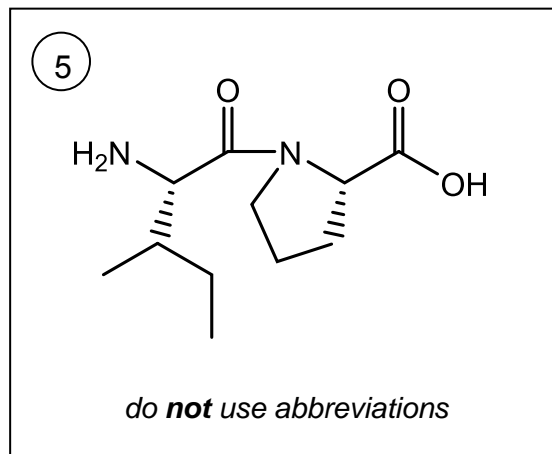
-2 points for omitting double bond, or having extra double bonds.

-2 points for each other, clearly trivial structure mistake.





1. Fmoc-Pro, base
2. piperidine
3. Fmoc-Ile, DCC
4. piperidine
5. CF_3COOH



Rubric for this part:

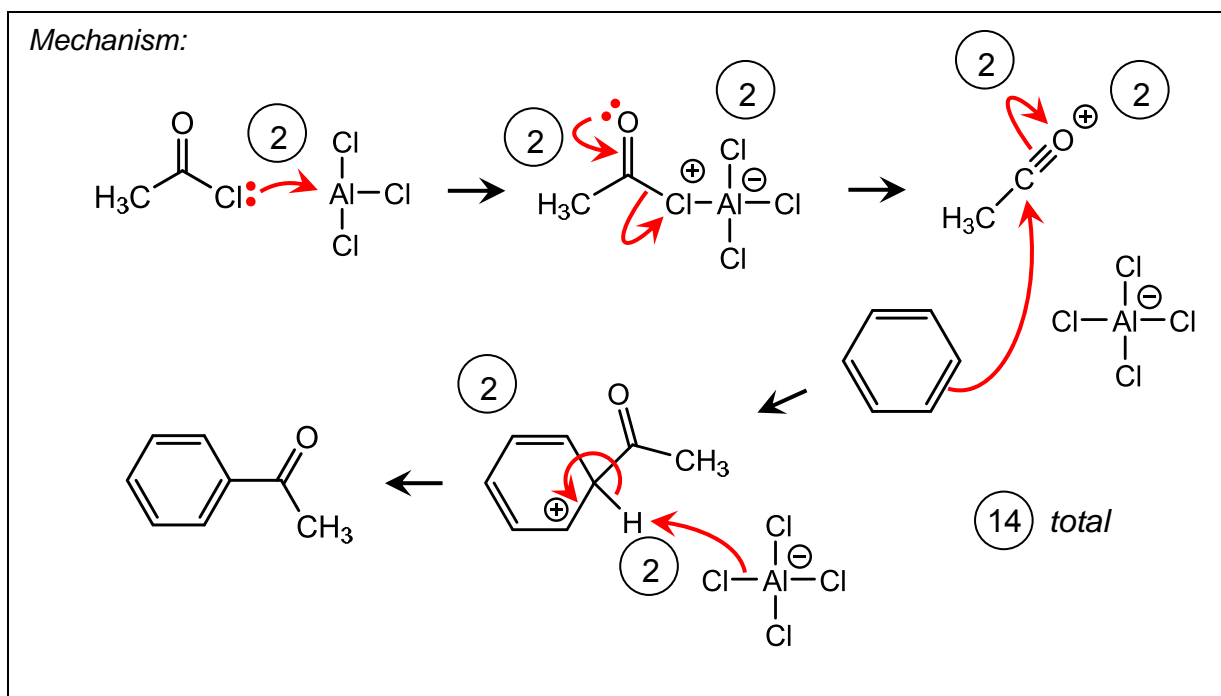
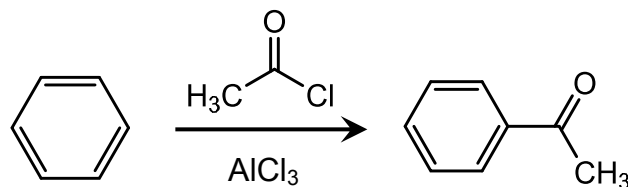
5 points for correct structure.

3 points partial for switching order of amino acids.

-1 point for each stereochemistry error.

-2 points for each clearly trivial structure mistake.

6. (38 pts) **Draw a mechanism** (using “electron pushing”) for each of the reactions shown below. Draw each mechanistic step explicitly; don’t cheat by combining multiple processes in a single step, or by taking shortcuts. Use only the molecules shown in the problem.



Rubric:

2 points for each arrow-pushing step.

2 points for each intermediate.

Overall notes:

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

Things that have left for good (e.g., AlCl_3 & HCl at the end) and spectators may be omitted.

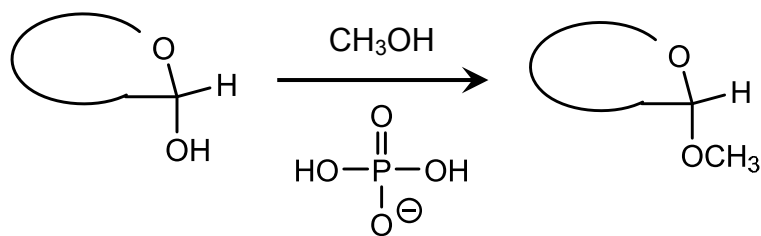
Resonance is NOT a mechanistic step; it is just multiple ways of drawing the same intermediate. As a result, we did not evaluate electron-pushing that showed resonance—you can push electrons for resonance, or not, your choice. Any molecule can be represented in any resonance form. In addition, resonance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

-1 point, for each arrow in each step, for errors in drawing arrows, unless the step has only one arrow. Arrow must start at an electron pair, and end at nucleus where electrons will newly interact. Can only lose points if you get them.

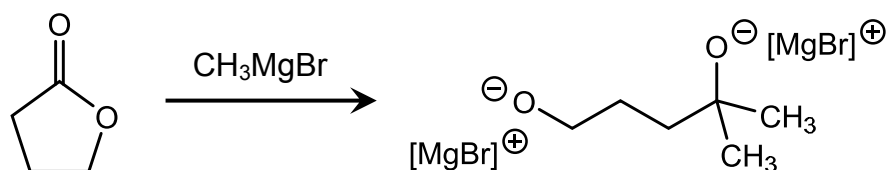
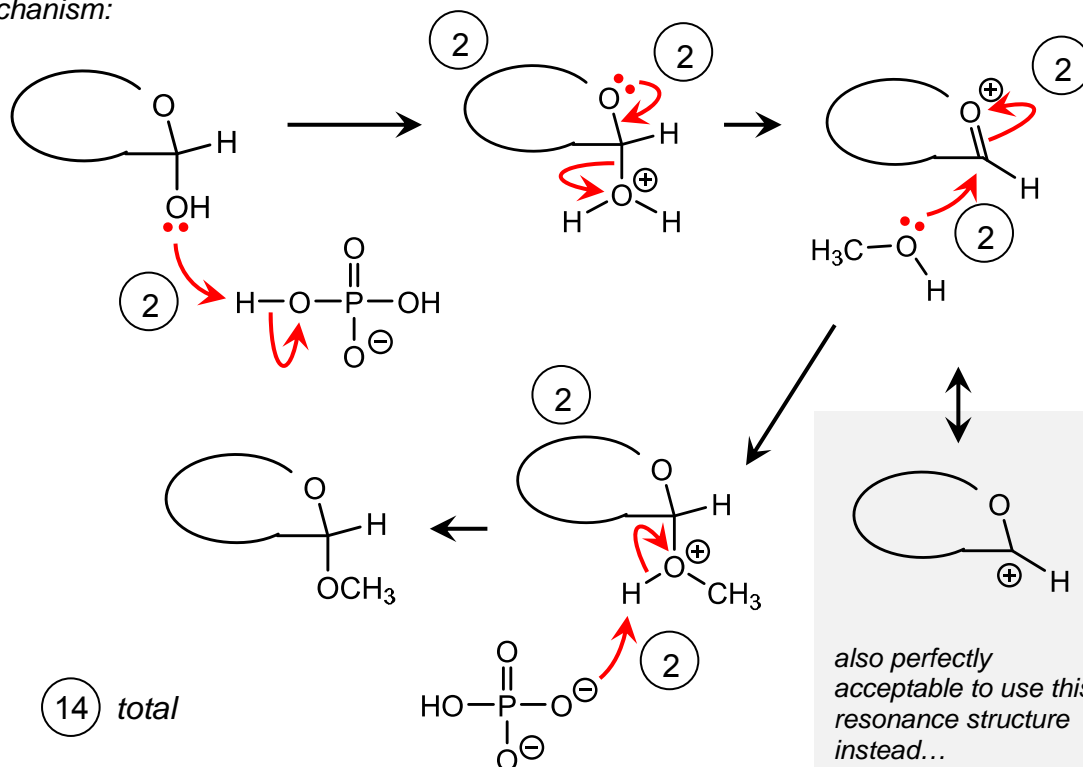
-1 point for each minor error in charge, valency, structure, etc.; if error propagates, points are taken off only for initial error.

-1 points for each use of a generic or incorrect acid/nucleophile/base. For example, in the last step you couldn't invoke H_2O or base other than AlCl_4^- that you may have used in other problems.

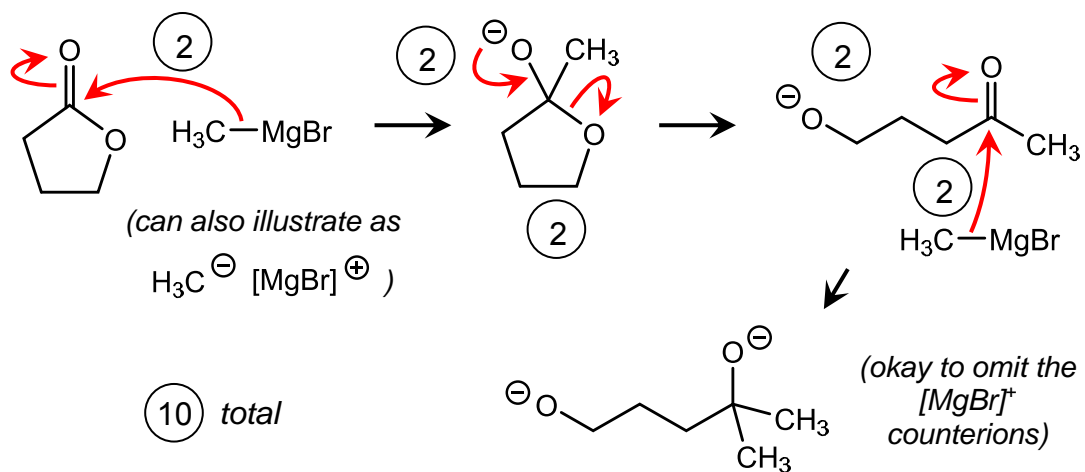
Half credit for each step combined with another, taken off each step. (So, you would get 2 points total for combining two 2-point steps.) You will also lose the 2 points for omitting the intermediate between the two steps.



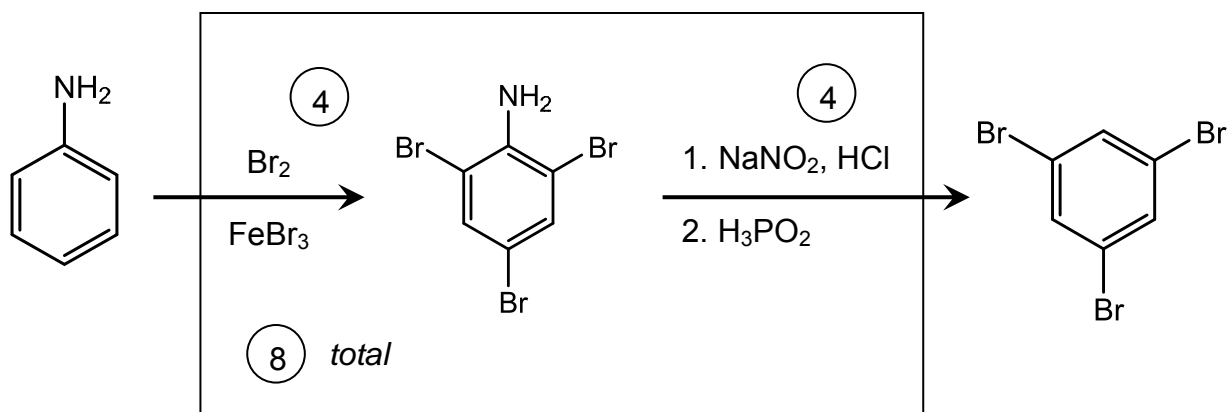
Mechanism:



Mechanism:



7. (32 pts) Each of the syntheses shown below can be accomplished in a few steps. For each synthesis, fill in the empty boxes with any appropriate reagents (or sets of reagents) and synthetic intermediates.



General rubric for synthesis problems:

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

4 points for each task/step.

-1 point for each trivial error in structures or reagents; if error propagates, points are taken off only for initial error. What you intended must be clear from what you wrote for this to apply.

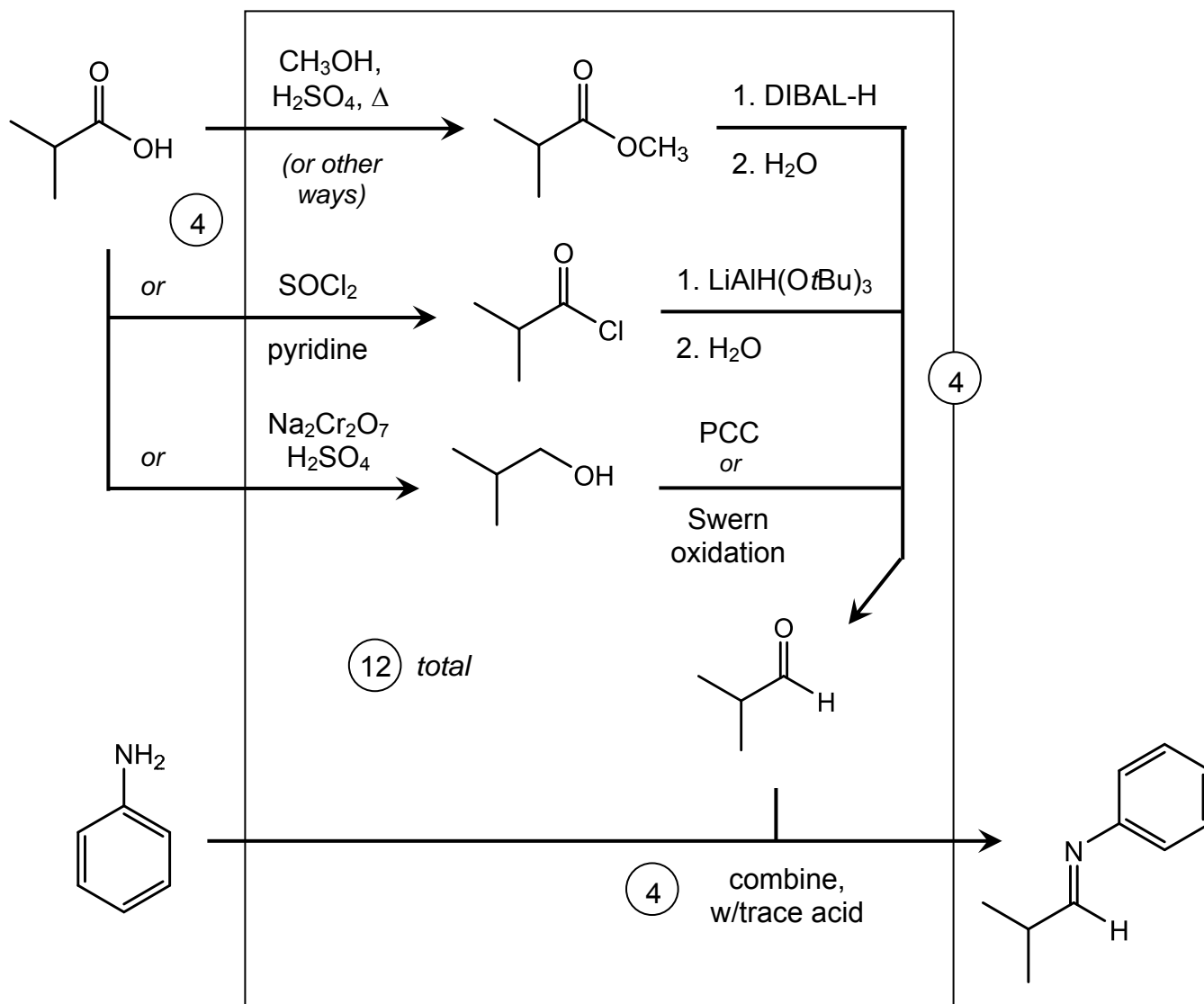
-2 points if step reagents are incorrect, but reaction could otherwise be accomplished with correct reagents.

-2 points if step reagents are correct, but lead to an incorrect intermediate. This could also cause you to lose points on later steps (because now you are working with a molecule you could not otherwise make).

If your alternative synthesis was valid, but considerably longer than the one above, graders had latitude to take points away for length.

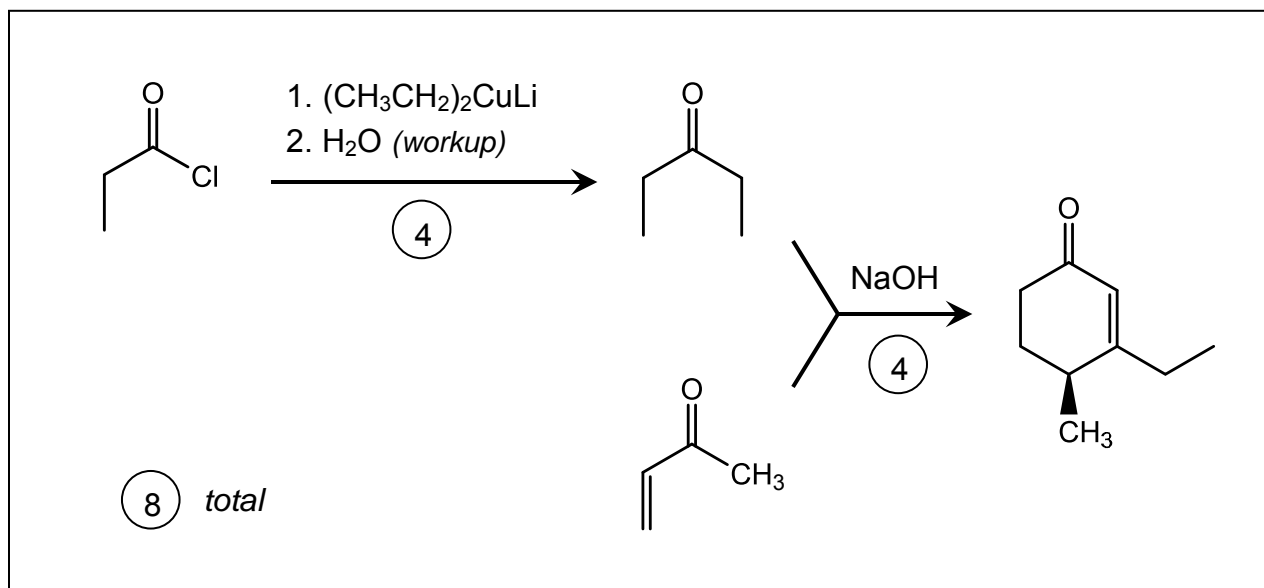
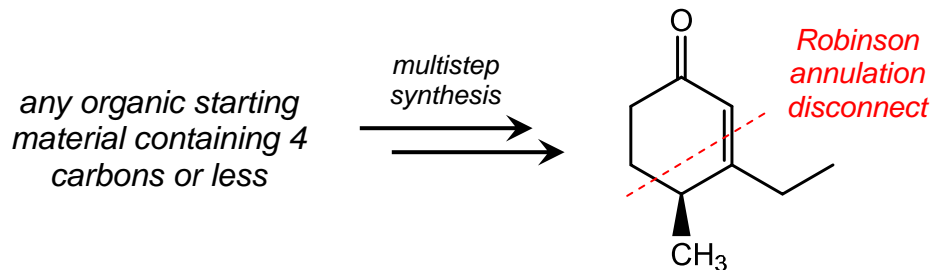
Special notes on this synthesis:

- In the final, Sandmeyer reaction step, "NaNO₂/HCl" is the reagent combination used to generate HNO₂ *in situ*. If you wrote "HNO₂" instead, that was fine.



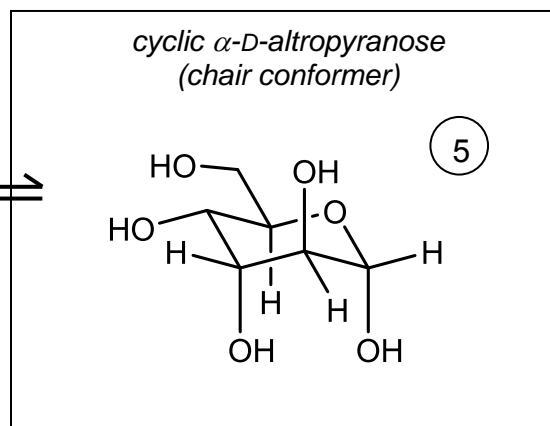
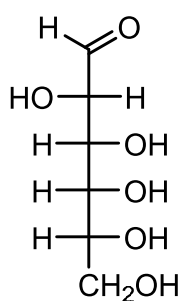
Special notes on this synthesis:

- In the final, Sandmeyer reaction step, "NaNO₂/HCl" is the reagent combination used to generate HNO₂ *in situ*. If you wrote "HNO₂" instead, that was fine.



8. (11 pts) The acyclic structure of D-altrose, an epimer of glucose, is shown below as a Fischer projection.

- a. Acyclic D-altrose equilibrates with a cyclic, 6-membered-ring, α -anomer altropyranose form. Draw the cyclic α -anomer as a chair conformer in the box at right.



Rubric for this part:

5 points for sugar structure.

-1 point for each incorrect functionality or stereochemistry at each carbon.

b. What is the timescale of this equilibrium? Does it take place spontaneously over

minutes? ³ **weeks?** or **decades?** (Circle one.)

c. The equilibrium above is responsible for **mutarotation**—the process by which α and β anomers in a monosaccharide equilibrate with each other. By comparison, how quickly do disaccharide, C1 glycosides of altrose undergo mutarotation? Do altrose glycosides exchange α and β anomers

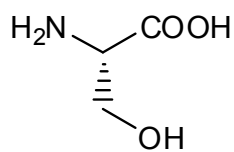
faster , **slower** ³ , or **at the same rate**

compared to monosaccharides? (Circle one.)

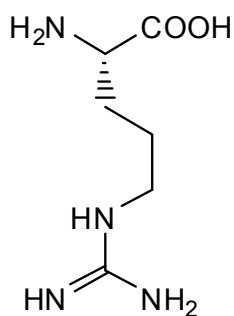
In fact, so much slower we can't even measure it.

9. (8 pts)

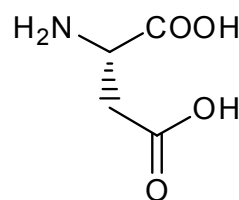
a. Sort the three amino acids serine (Ser), arginine (Arg), and aspartic acid (Asp) in order of increasing isoelectric point (pI). Write their three-letter abbreviations in the appropriate boxes below.



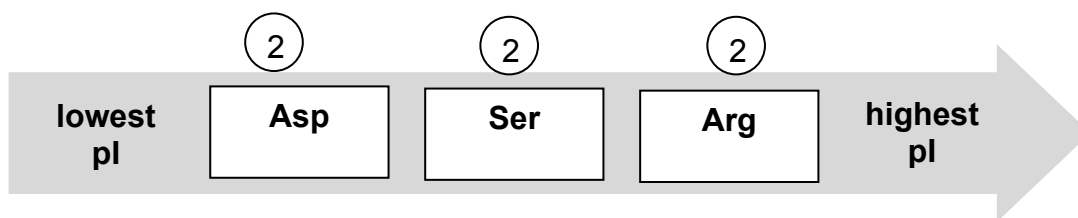
serine (Ser)



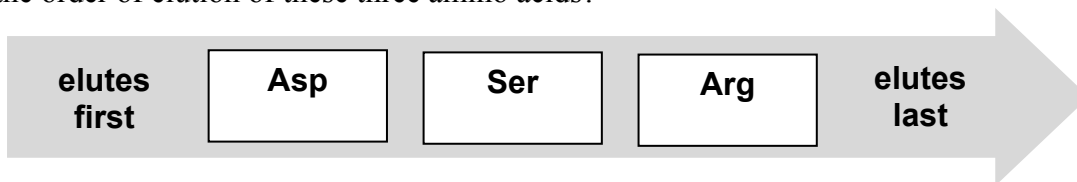
arginine (Arg)



aspartic acid (Asp)



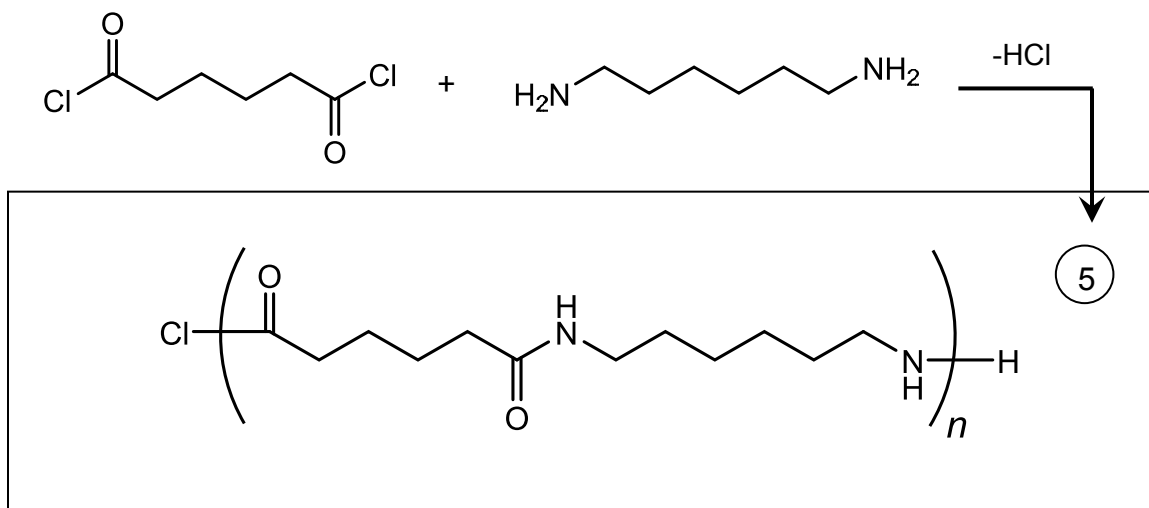
- b. If these three amino acids were analyzed by ion exchange chromatography, using an anionic column subjected to a solvent gradient of gradually increasing pH, what would be the order of elution of these three amino acids?



2 for either all three correct, or for answer the same as the student wrote for part (a)

10. (20 pts)

- a. For each of the polymer syntheses proposed below, draw the polymer product using bracket notation (“[-M-]_n”). If *n* is known, define it. If there is a part of the polymer structure that isn’t known (e.g., the initiating or terminating group), draw this as a squiggle in your structure.



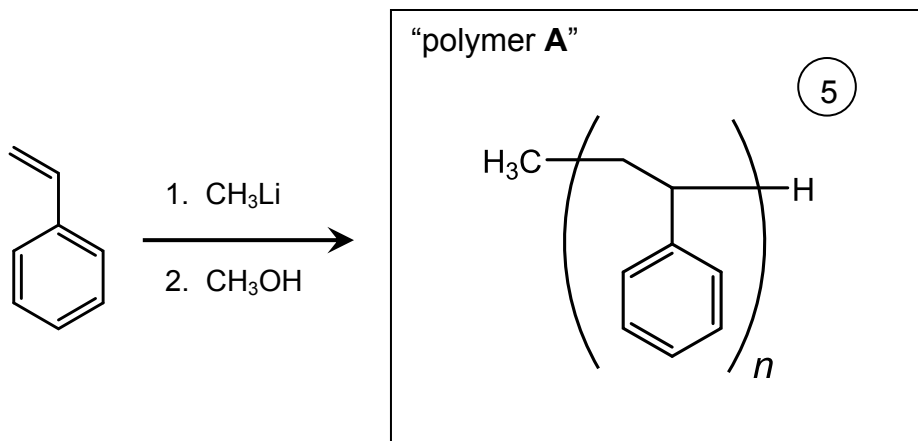
Rubric for this question:

5 points for correct structure.

-1 point for each incorrect terminus.

2 points partial for correct linkage between monomer units, but incorrect bracket arrangement.

-2 points for trivial structural mistake (including omitting or extra carbons).



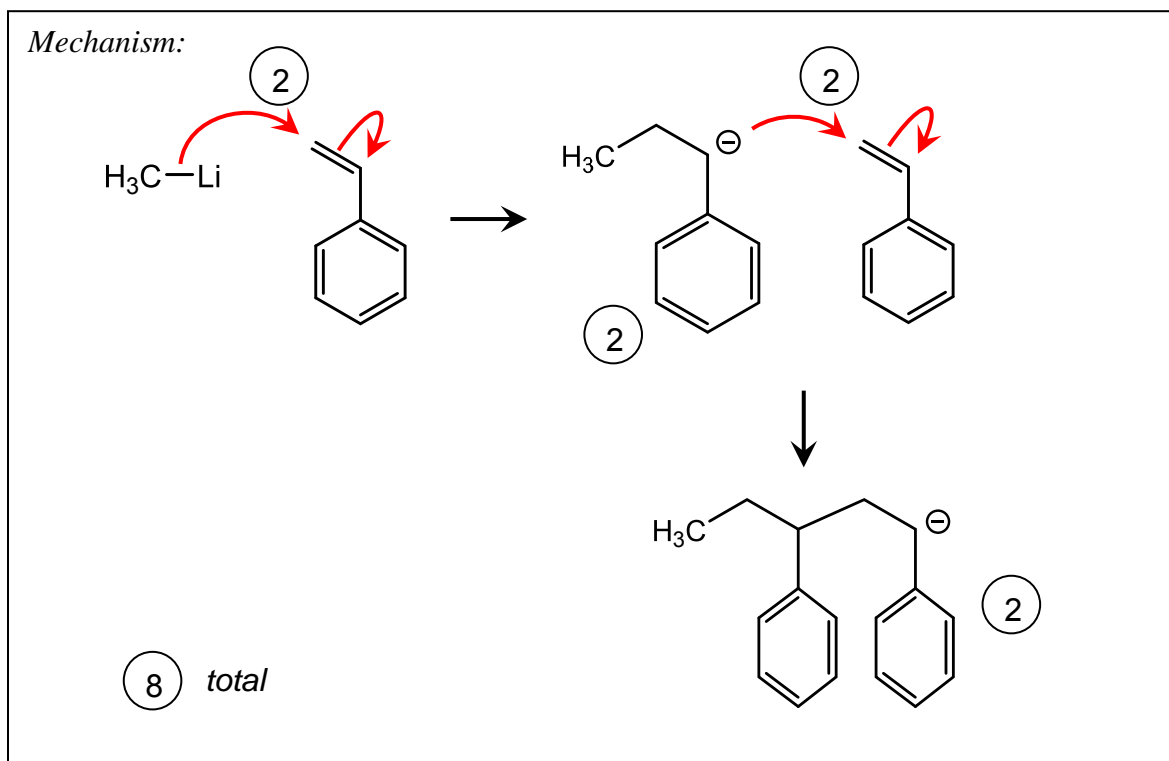
Rubric for this question:

5 points for correct structure.

-2 points for each incorrect terminus.

-2 points for trivial structural mistake (including omitting or extra carbons).

- b. In the box below, draw a mechanism for the initiation step and the first propagation step in the formation of polymer A above, using “electron pushing”.



Rubric for mechanism:

2 points for each arrow-pushing step.

2 points for each intermediate.

- c. If half as much styrene monomer were used in the synthesis above, the average product “polymer **B**” molecule would be half as long. How would the mobility of polymer **B** in gel permeation chromatography (GPC) relate to polymer **A**? Would polymer **B** elute

earlier than

,

later than

or

at the same time as

2