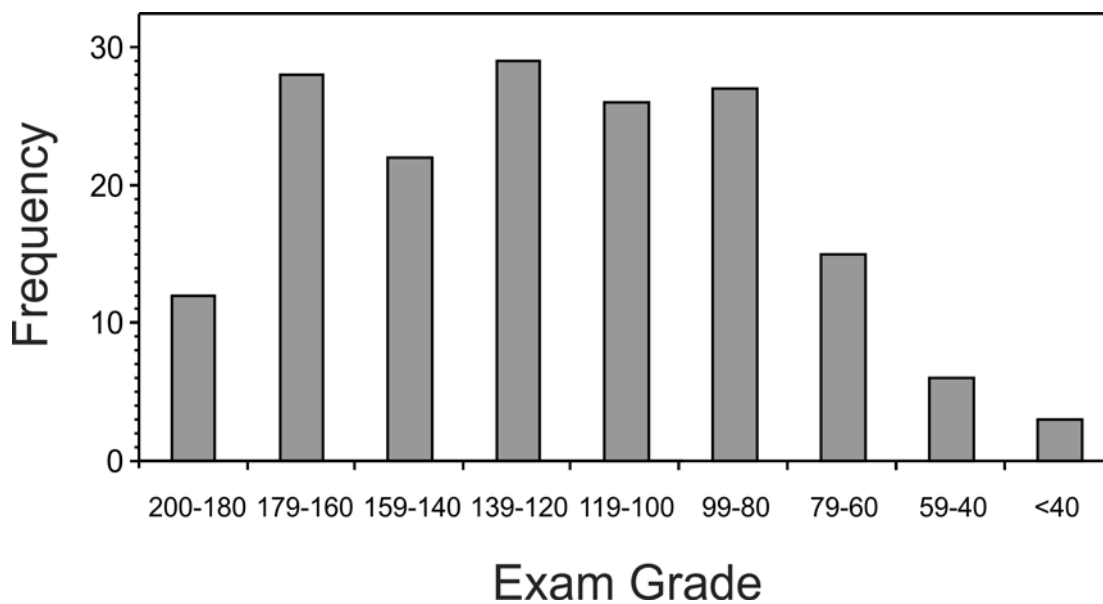


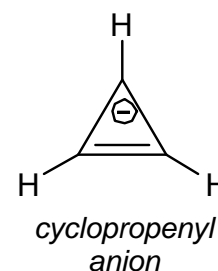
**Final Exam
Answer Key**

Final Exam Mean: 123
Final Exam Median: 123
Final Exam St. Dev.: 39



1. (16 pts) For cyclopropenyl anion,
- How many molecular orbitals describe the conjugated π -system?

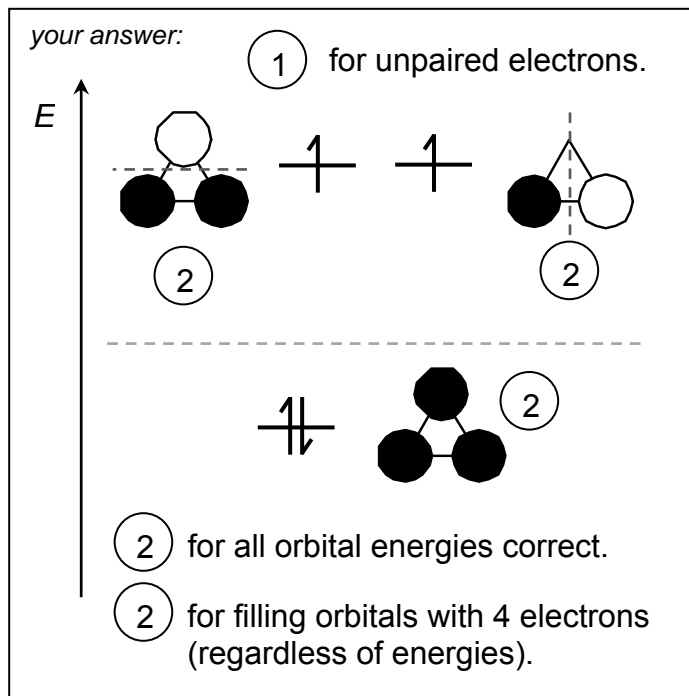
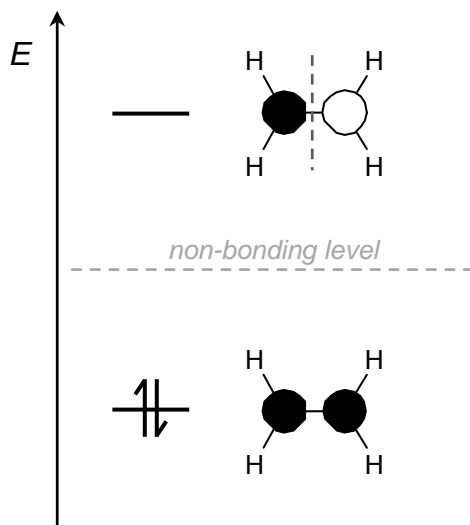
3
of π MO's



The number of molecular orbitals in a molecule is always the same as the number of atomic orbitals used to build those molecular orbitals. The cyclic π -system in this molecule is built from atomic p orbitals. Our molecule has three sp^2 -hybridized carbon atoms in the cycle, each of which also has an available p orbital. So, our ion will have 3 π molecular orbitals, coming from the 3 p orbitals in the circle of 3 atoms. (The number of *electrons* is **not** used to determine how many orbitals there will be.)

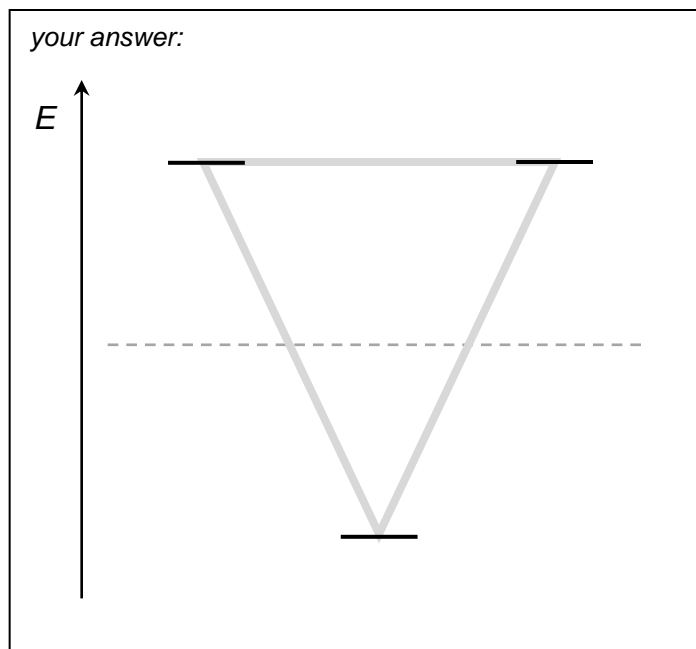
- Draw all of these molecular orbitals on the energy diagram below. Draw both the shapes of the orbitals (as viewed from the top) and their energies, and fill the orbitals with the appropriate number of electrons.

example of answer format (for C_2H_4):



In the case of a cyclic set of p orbitals, we construct a molecular orbital diagram using the “inscribed polygon method” (explained in class, and in Smith 17.10). We need 3 MO's, so we take a big polygon with 3 sides—yep, that's a triangle—and put it point-down inside the energy diagram. We will be constructing a molecular orbital at each of the vertices of that giant triangle.

Each of the three molecular orbitals corresponds to a different combination of the three atomic p orbitals. The lowest-energy orbital will be all-bonding (or all in-phase), and the two orbitals at the next level up will each have one node running through the middle. There are a number of ways that you could draw the top two levels, with only two rules: (i) the node has to pass through the middle; and (ii) the two orbitals can't be the same, or exact opposites.



When you fill this diagram with the 4 p electrons in the anion, you get the answer on the previous page.

Rubric (11 points total for diagram):

3 points for writing "3" π MO's. *No partial credit.*

2 points for each correct orbital drawing, regardless of position on the diagram. (6 points total.)

No partial credit. Grade on lobes only, not nodes.

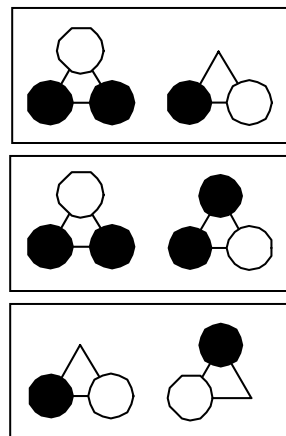
Can only draw each orbital once. However, two antibonding orbitals can be any mathematically orthogonal combination. So, any combination shown on right is correct.

2 points for drawing one bonding, two equal antibonding energies.

2 points for filling energy levels with four electrons.

1 point for top two orbitals containing one electron each.

some possible antibonding combinations:



• Is the ion

AROMATIC

or

2

ANTIAROMATIC

? (Circle one.)

There are two ways that you know this anion is anti-aromatic:

- 1) There are two unpaired electrons near the non-bonding level in the diagram. These unpaired electrons act like radicals, making the anion extremely reactive and unstable.

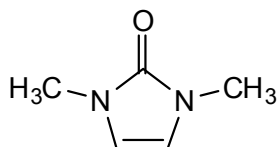
2) There are an even number of pairs of p electrons in the cyclic π system. Hückel's rule says that an even number of pairs of electrons— $4n$ electrons, where n is an integer—makes a cyclic π system anti-aromatic.

2. (6 pts) For each of the following molecules, circle whether the molecule is aromatic, anti-aromatic, or neither.

AROMATIC (3)

ANTI-AROMATIC

NEITHER

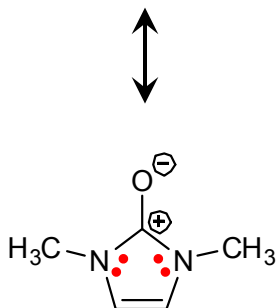


AROMATIC

ANTI-AROMATIC

NEITHER (3)

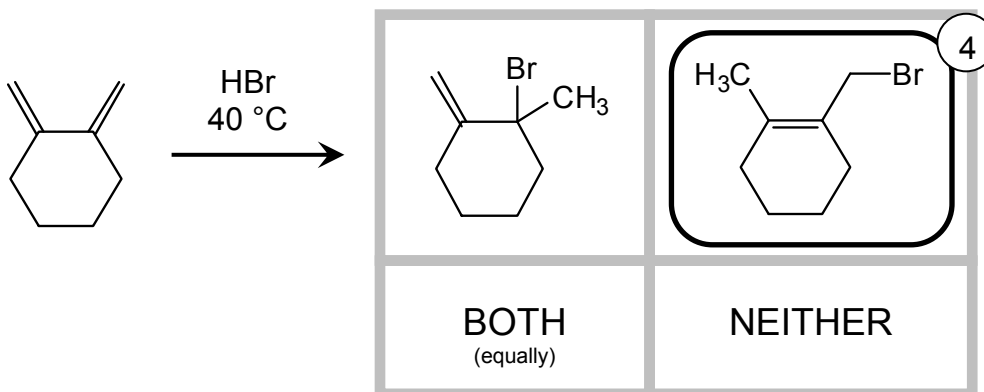
This resonance structure has 6 π electrons in the cycle. Because the molecule has an aromatic resonance structure, it is aromatic.



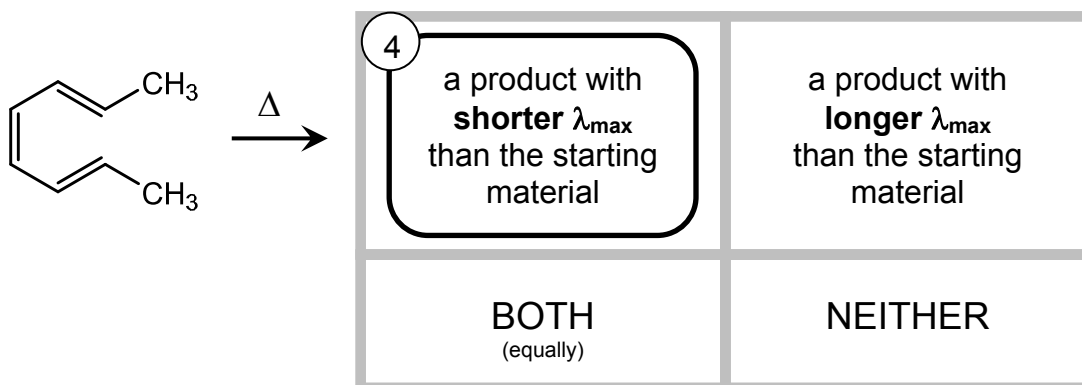
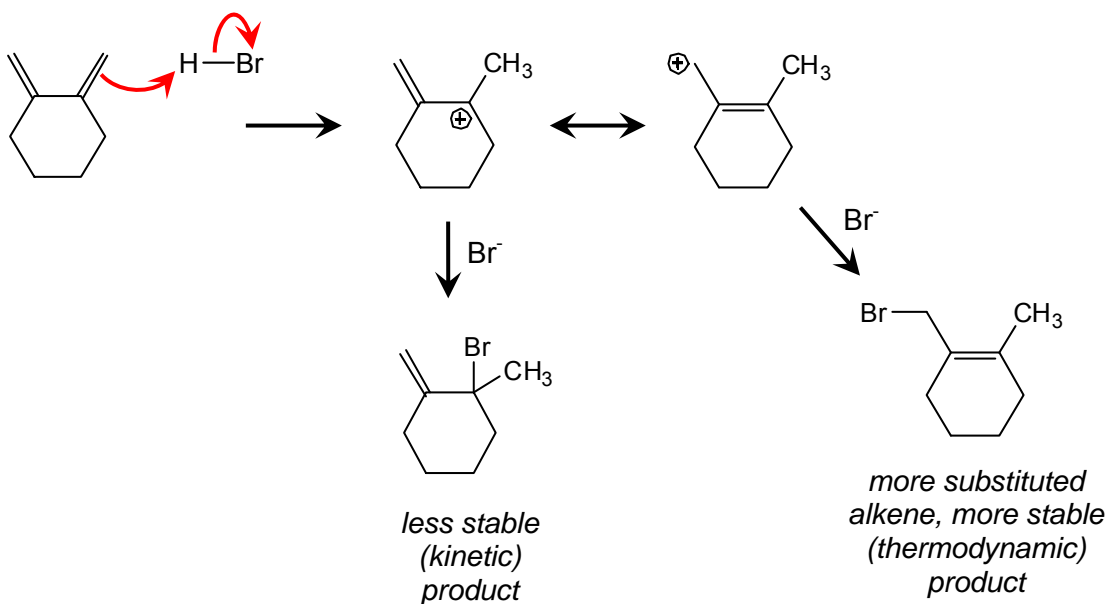
This ring has one saturated $-\text{CH}_2-$ carbon, so the ring of p orbitals is not continuous. Therefore, it's not aromatic or antiaromatic.

Rubric (6 points total): 3 points each circle. No partial credit.

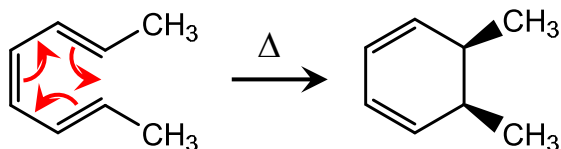
3. (52 pts) Each of the reactions below is drawn with two possible products. If one of the two products predominates, circle that preferred product. If the two products are produced equally, circle "BOTH". If neither product would result from the reaction, circle "NEITHER". **Circle one answer only.**



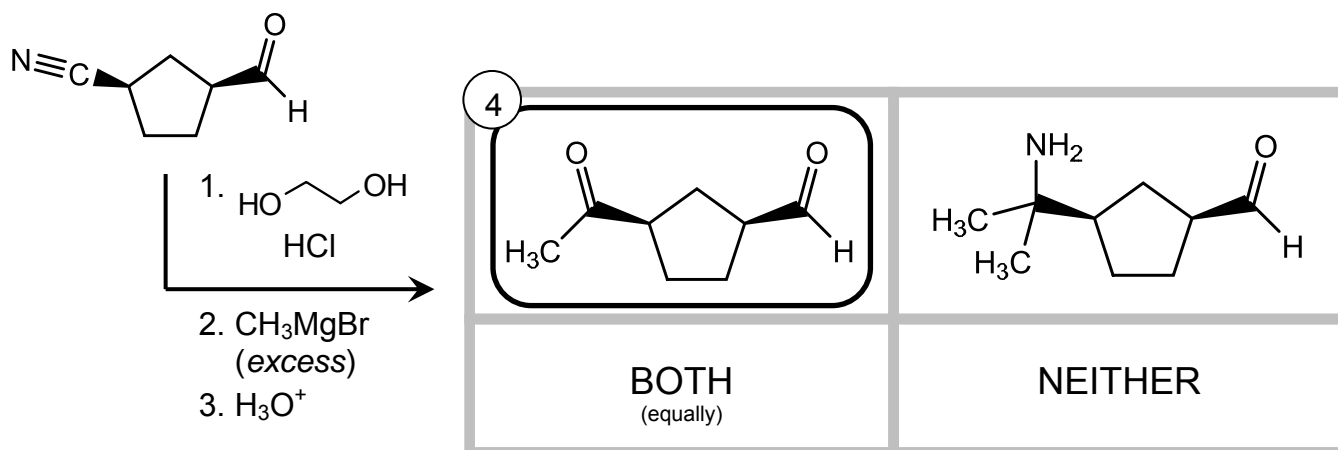
HBr can undergo either 1,2-addition or 1,4-addition to dienes, like this starting material, depending on reaction conditions. At higher temperatures (like 40 °C), 1,4-addition is preferred and generates the thermodynamic product:



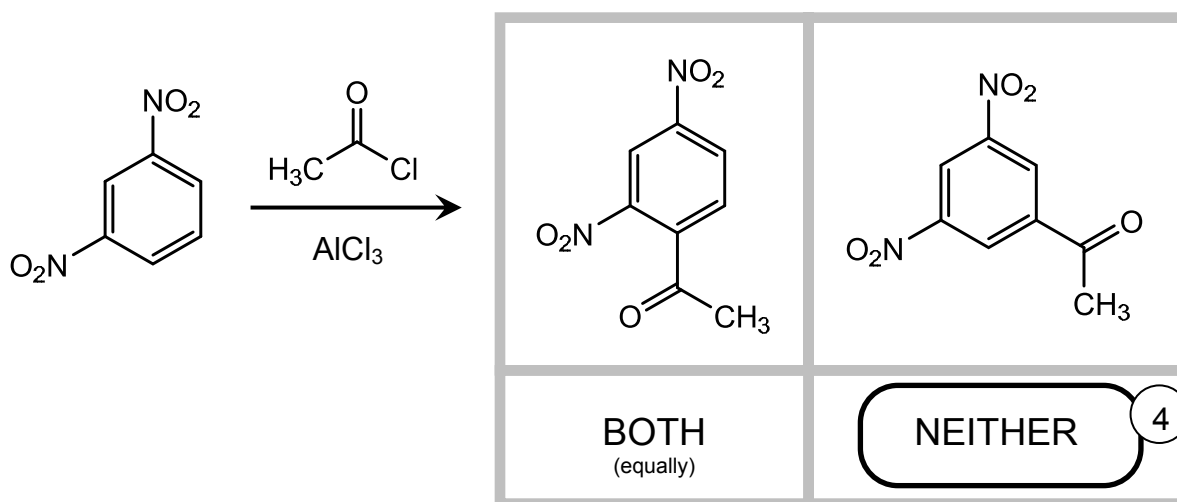
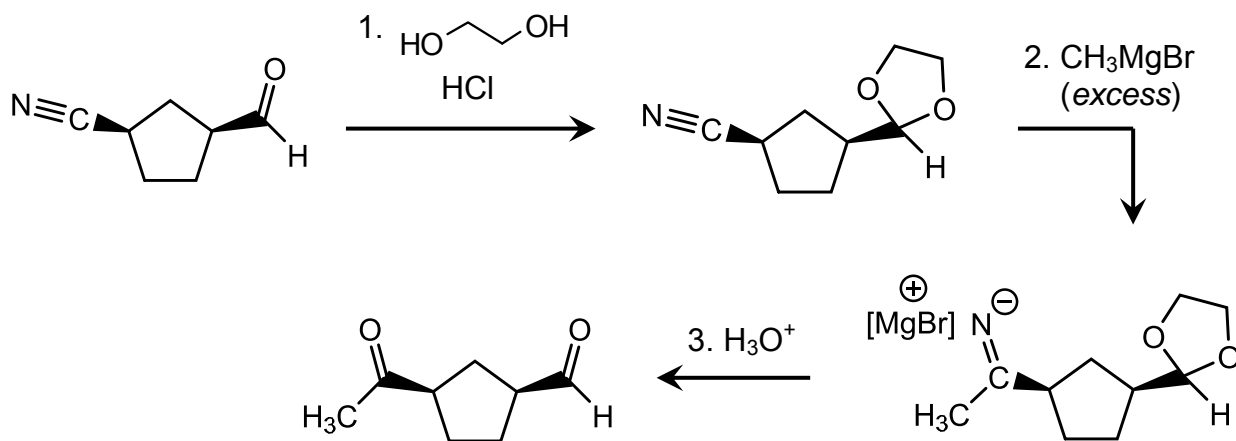
This illustrates an electrocyclic ring closure:



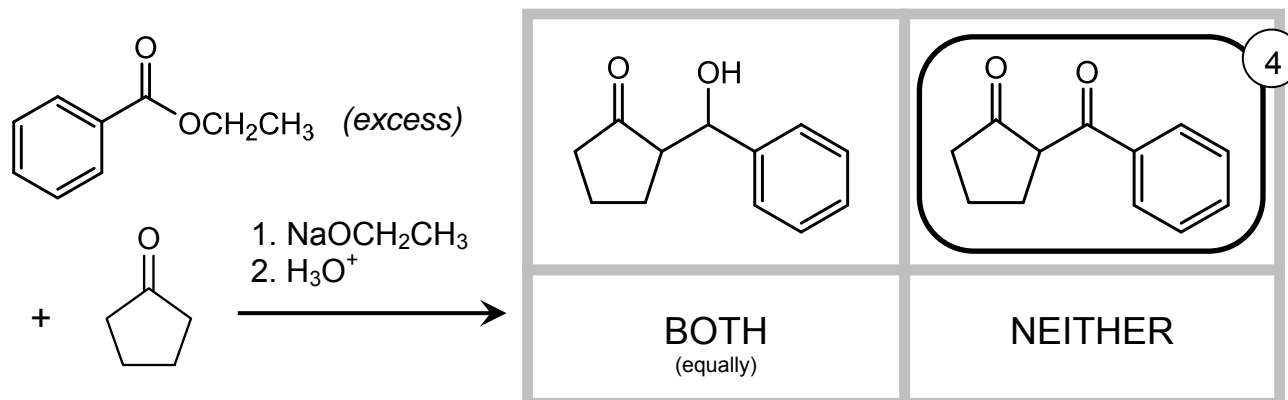
This reaction is disrotatory under thermal conditions, as shown above, but you really didn't need to know that to answer this problem. The starting material has three conjugated double bonds, but the product has just two. The more conjugated a molecule is, the longer the wavelength of light it will absorb (the longer λ_{\max} will be). So the product in this case will have the shorter λ_{\max} .



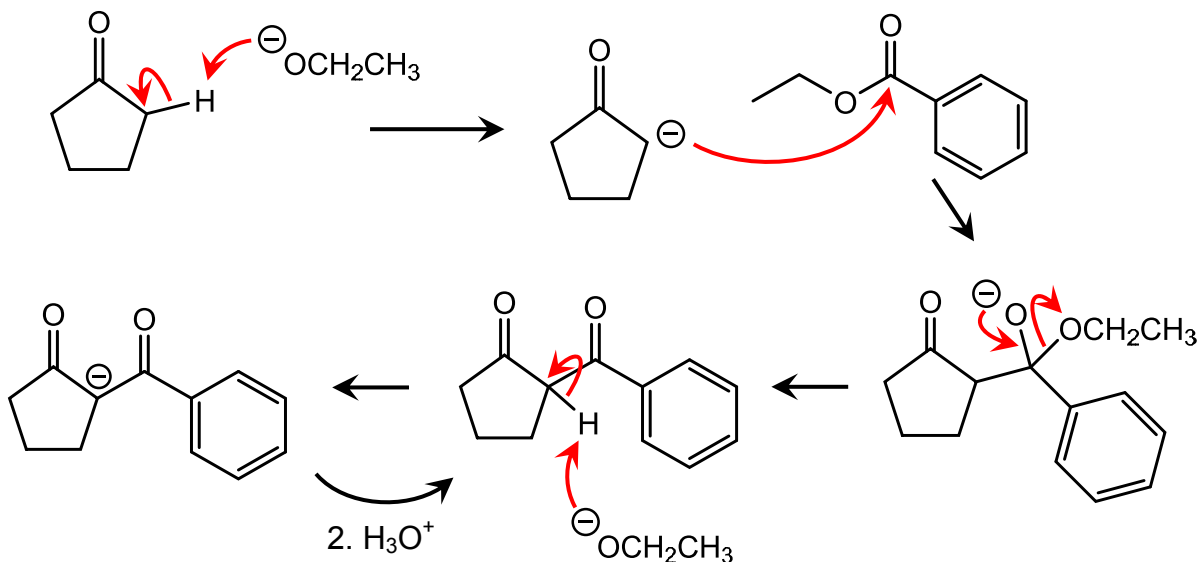
This question asked you to follow the starting material through a few stages of a multi-stage reaction. The first set of reagents converts the aldehyde to a cyclic acetal, which protects the C=O double bond against other reactions. The second reaction involves nucleophilic attack of a Grignard reagent on the nitrile triple bond. The Grignard adds just once, to produce an anion that can't accept another carbanion nucleophile. The third step hydrolyzes both the Grignard adduct and the cyclic acetal to yield C=O double bonds on either side.

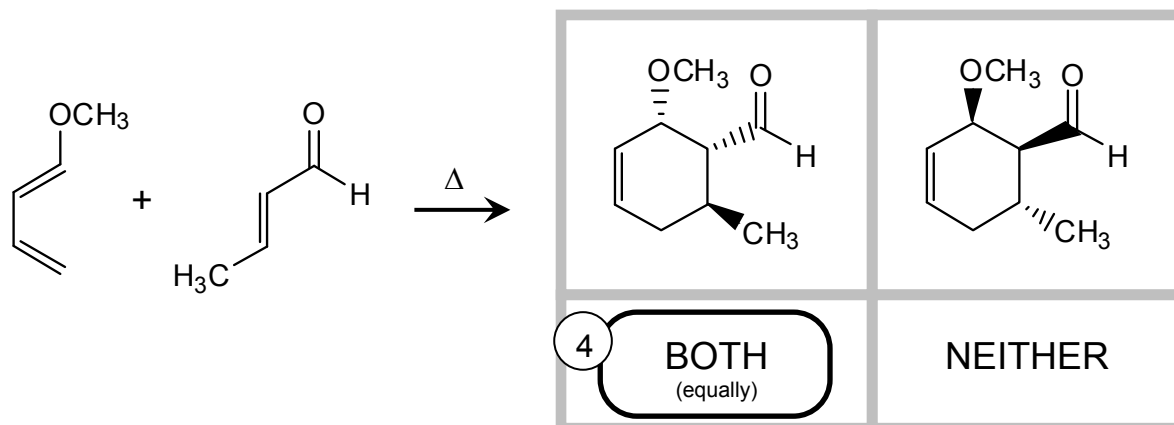


The $-\text{NO}_2$ groups are deactivating, and Friedel-Crafts acylation only occurs on benzene or on activated substrates. Under the conditions given, no reaction would occur.

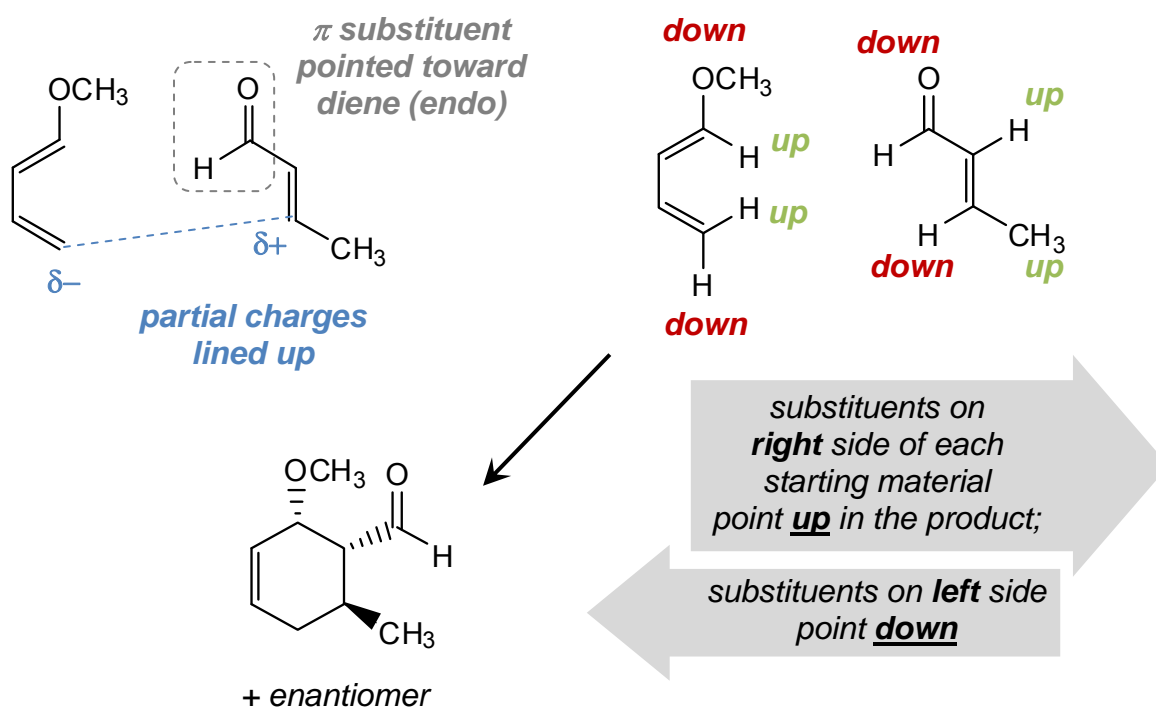


This is a mixed Claisen condensation. Out of our two starting materials, only one has an acidic α -proton, so only that molecule can form an enolate. That enolate will then attack the next electrophile it finds, which is the ester:

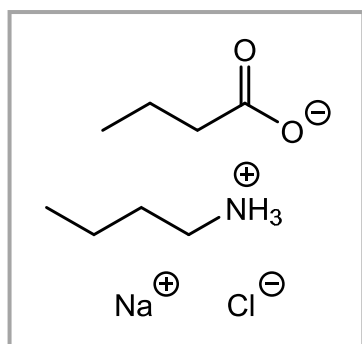




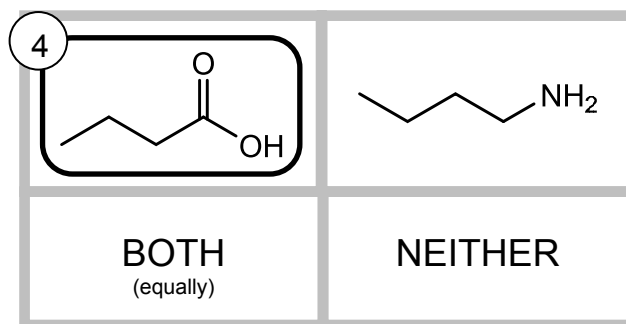
These products are enantiomers of one another, and from the achiral molecules on the left, there would be no chiral preference for making either one. So the question then becomes, would this Diels-Alder reaction generate both of the products shown, or neither? To answer this, we have to check both the regiochemistry (determined by partial charges) and stereochemistry (determined by endo approach of the dienophile):



a mixture containing:

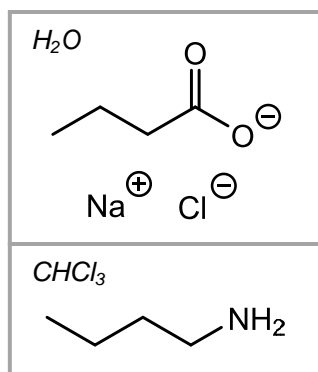


1. Dissolve in a mixture of aqueous base (NaOH/H₂O) and CHCl₃.
2. Discard CHCl₃ layer.
3. Add fresh CHCl₃, and enough HCl to make the H₂O solution acidic.
4. Discard H₂O layer.

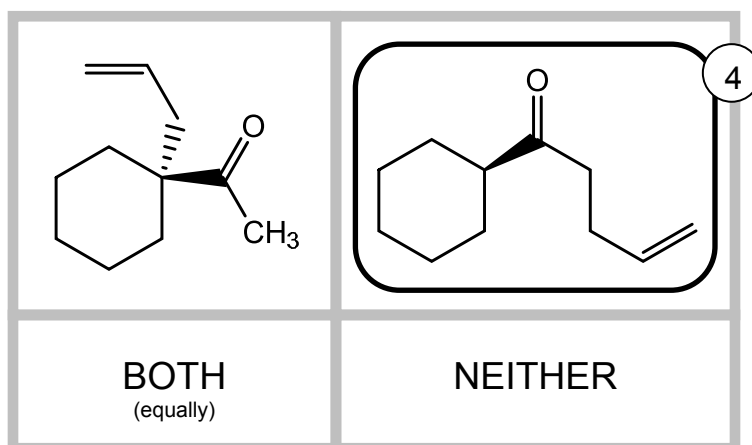
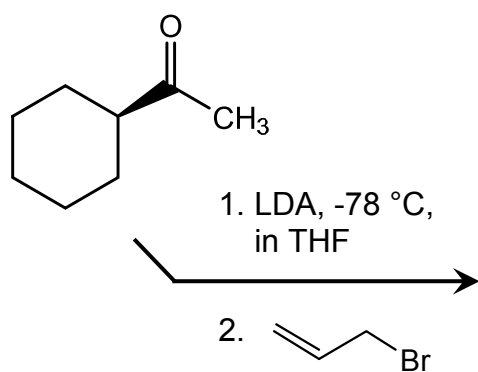
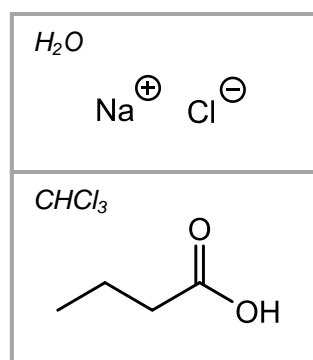


↓ 1. NaOH/H₂O and CHCl₃.

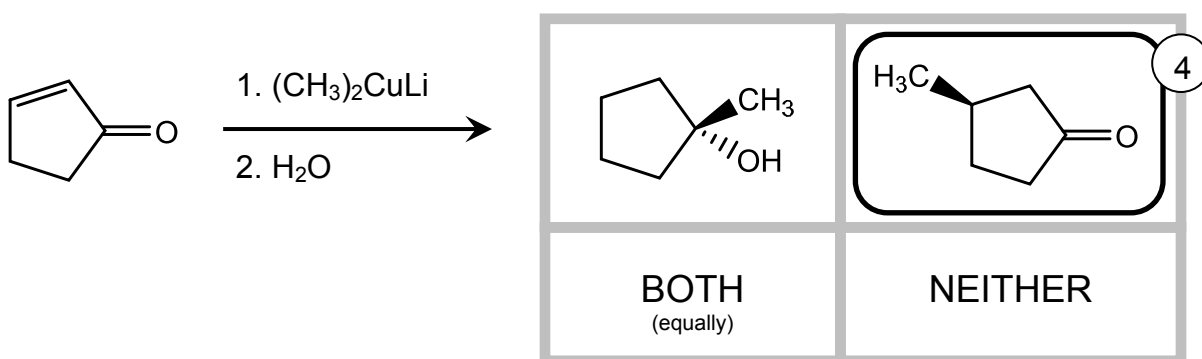
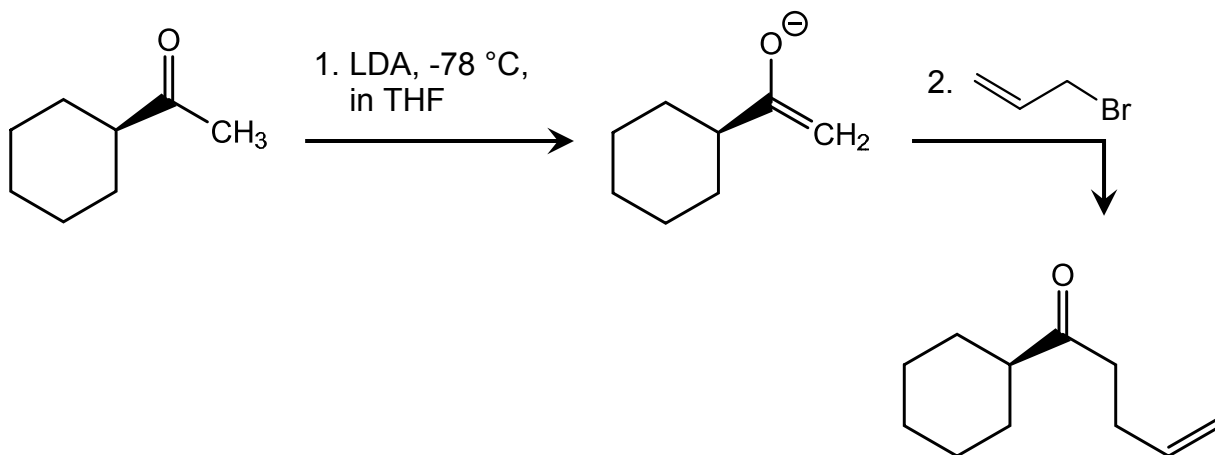
↑ 4. Discard H₂O layer.



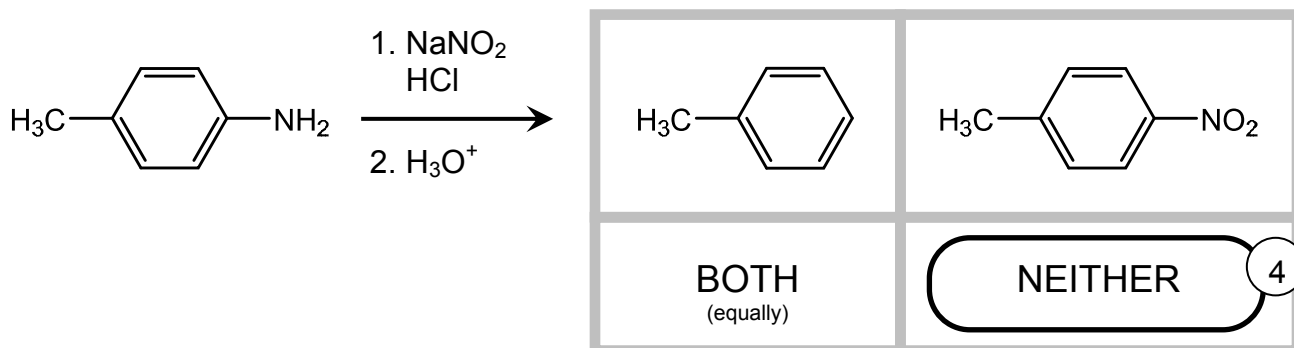
2. Discard CHCl₃ layer.
3. Add fresh CHCl₃ and HCl.



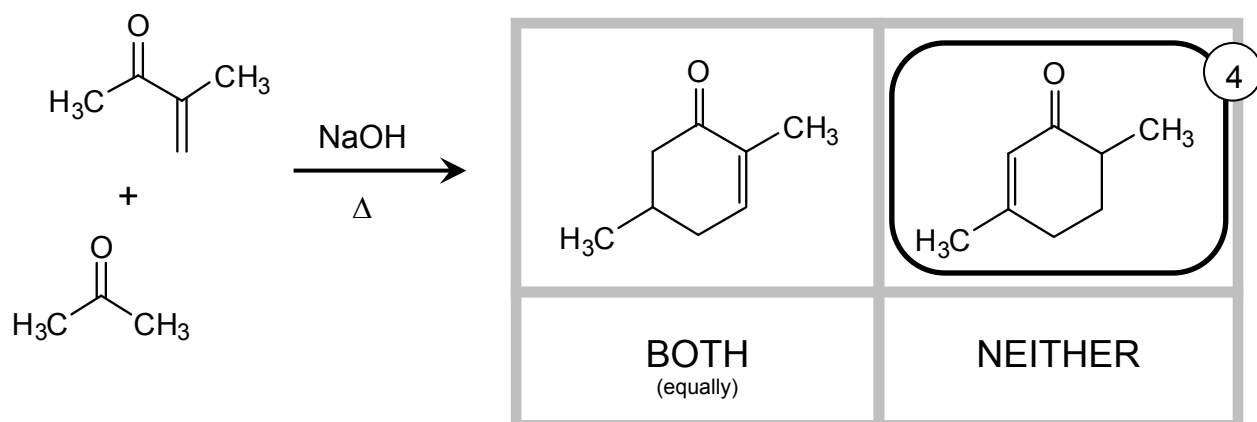
At very low temperature, and in a polar aprotic solvent like THF, LDA deprotonates the starting ketone at the less-substituted α -carbon, to generate the kinetic enolate. This enolate is then alkylated to generate the product on the right:



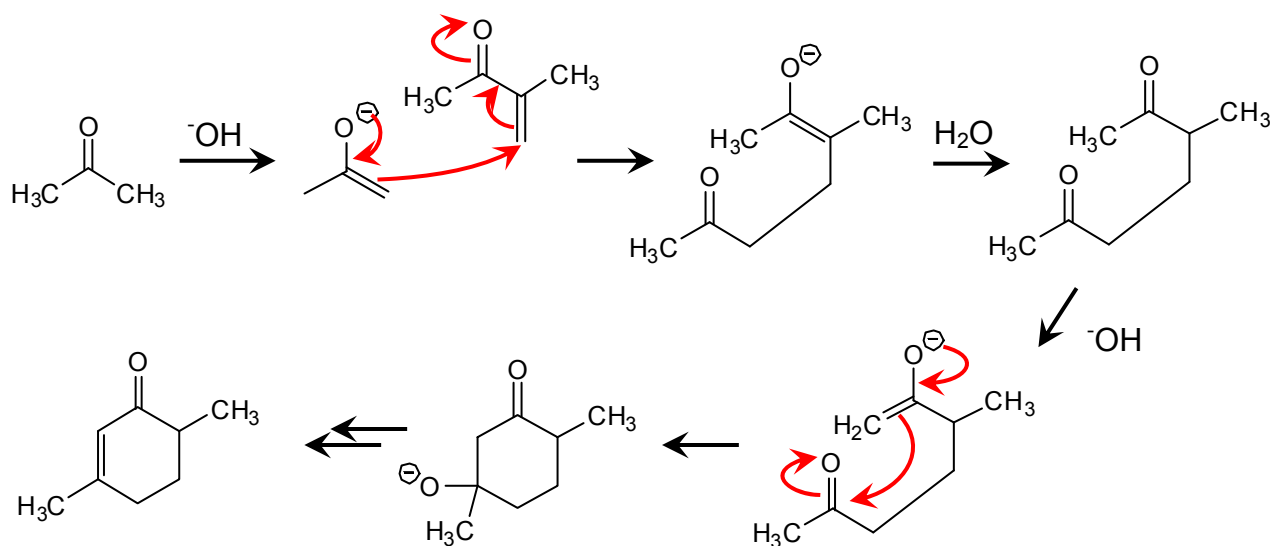
Dialkylcuprates add to α,β -unsaturated carbonyls via conjugate addition, at the β -position.



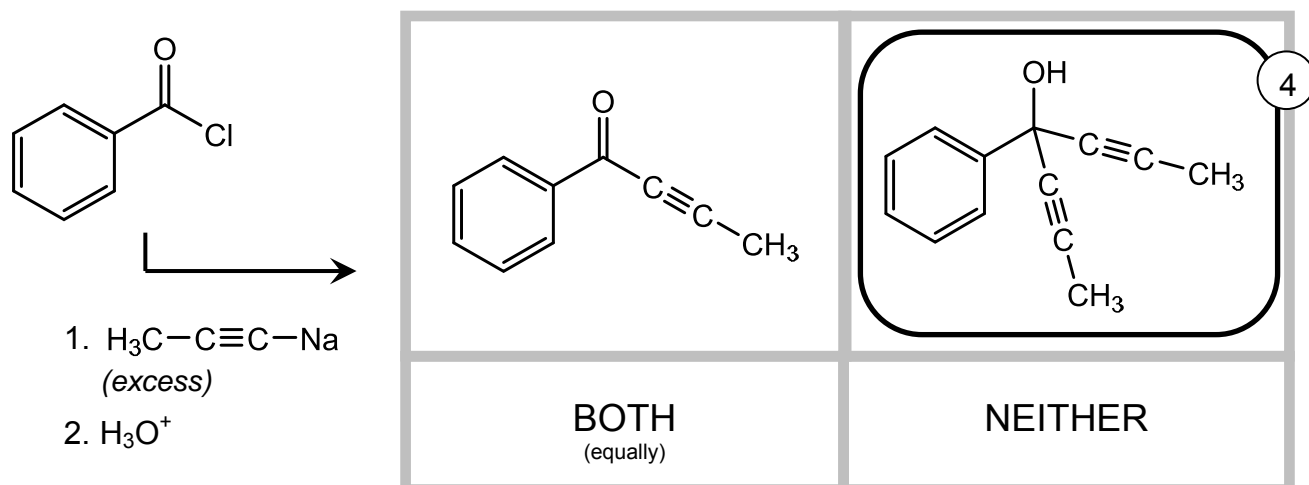
This problem illustrates a Sandmeyer reaction, in which the aromatic amine is first oxidized to a diazonium salt, and then reacted with a nucleophile. In this case, the nucleophile is water, and so the group that replaces the $-\text{NH}_2$ group should be an $-\text{OH}$.



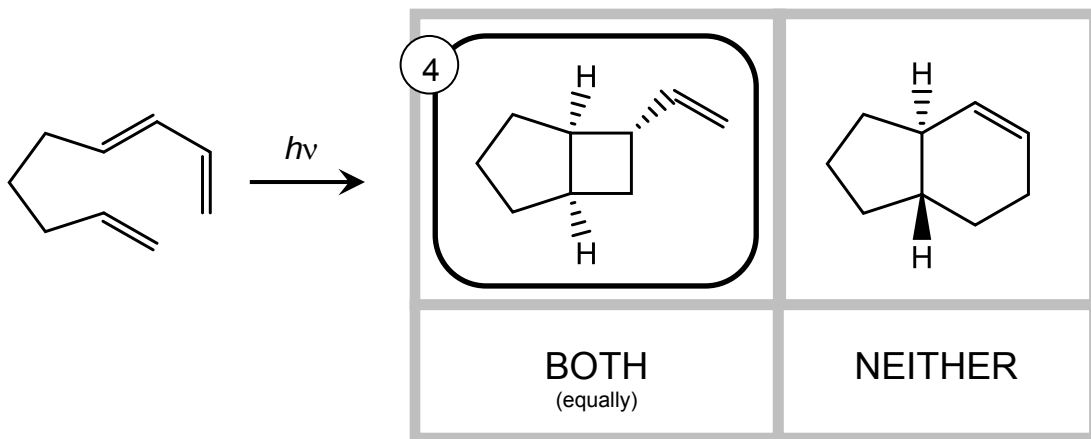
This problem illustrates a Robinson annulation, and essentially asks where the double bond ends up in the product. The reaction works like this:



This illustrates the forward mechanism of the reaction, but the easiest way to solve this problem was probably to think in reverse, by applying the Robinson annulation disconnect to both products, and to see if either one matched the given starting materials. The second one does.

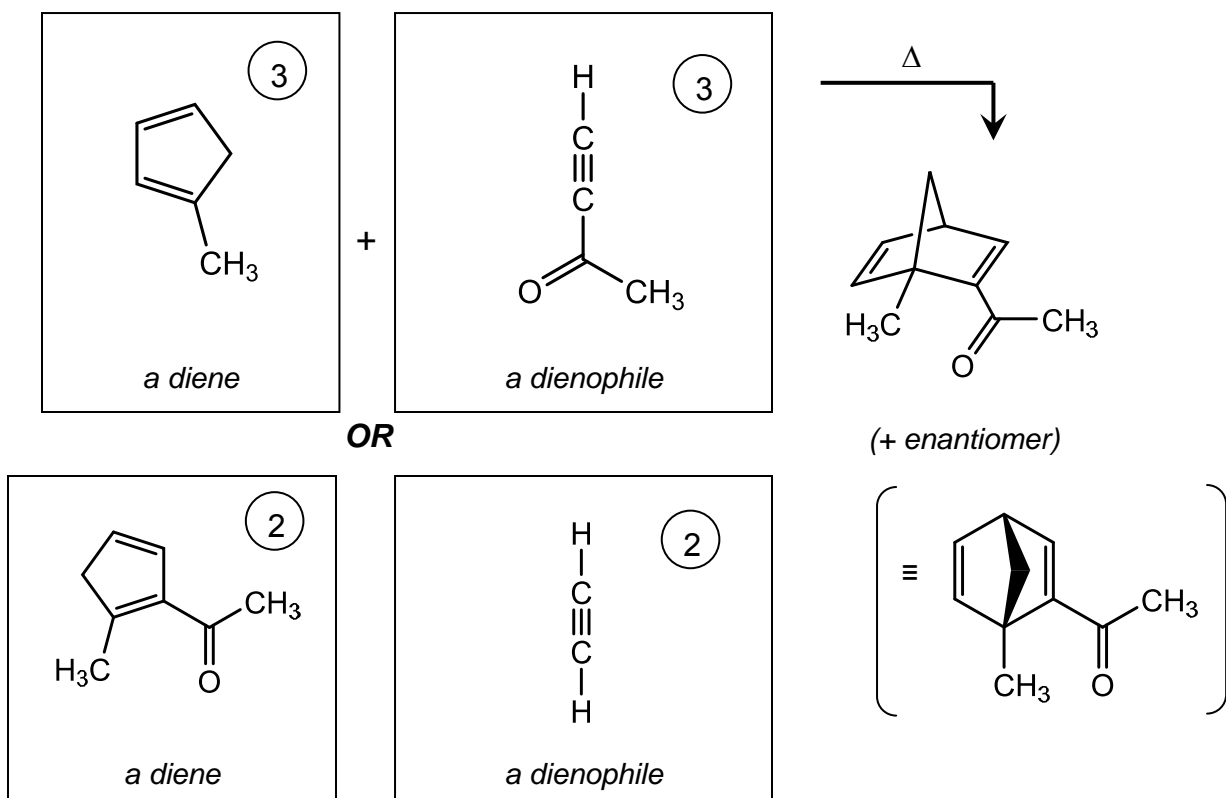


Acyl halides undergo double addition of carbanion nucleophiles like the alkynyl anion here.

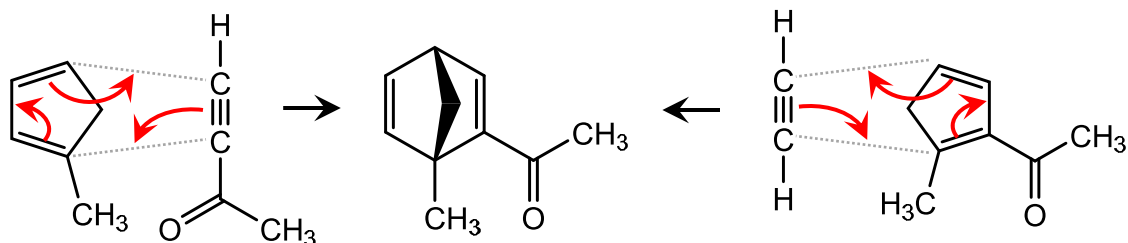


Under photochemical conditions, the [2+2] cycloaddition shown on the left is allowed, while the [4+2] cycloaddition on the right is forbidden under the Woodward-Hoffman rules for cycloadditions.

4. (26 pts) For each of the reactions below, fill in the empty box corresponding to reactants 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 boxes—labeled “diene” and “dienophile”—hint that this is a Diels-Alder reaction. Diels-Alder reactions generate a six membered ring that contains at least one (and usually one) double bond; the product in this reaction has a double-bond-containing six-membered ring, along the base of the molecule. But this ring contains two double bonds, and that suggests that our dienophile will be a triple bond, rather than the usual double bond. Two possible starting material combinations:



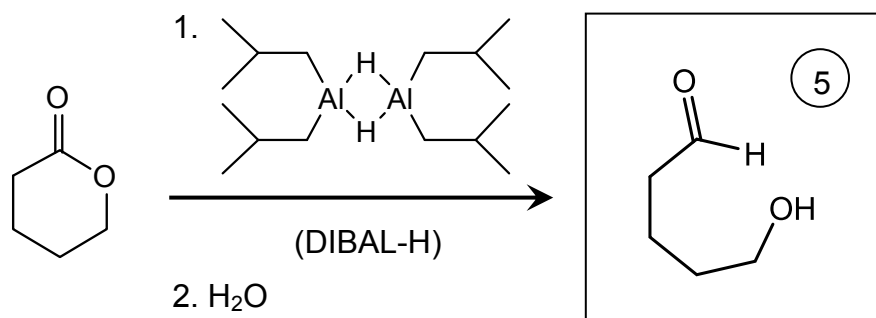
Of these combinations, the one on the left will work much better because it combines an electron-withdrawing dienophile with an electron-donating diene.

Rubric for this part:

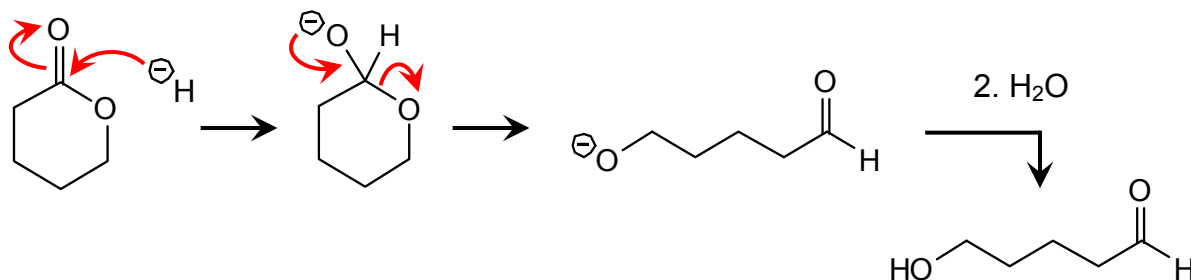
3 points for each correct structure.

2 points for diene/dienophile combination shown with poorer electron demand.

-2 points for each clearly trivial structure mistake. By “trivial”, I mean that it must be clear that you meant to draw the correct answer, but your answer included a trivial error.



DIBAL-H is a sterically hindered hydride source that selectively converts esters to aldehydes, by adding a single hydride (H^-) to the carbonyl group. In this case, the leaving group on the ester is still part of the original molecule:



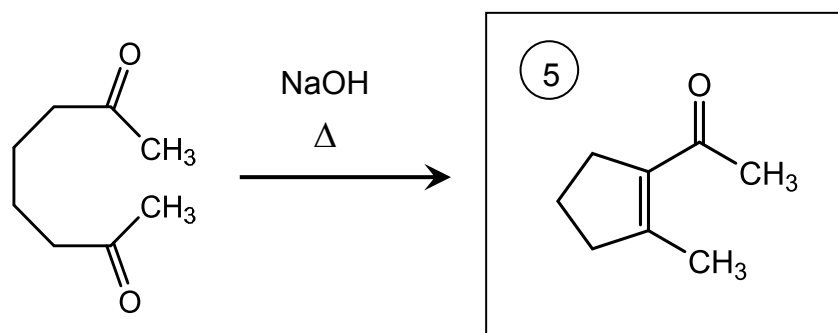
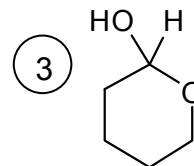
The actual mechanism is a little more complicated than this—the DIBAL-H aluminum atom coordinates the carbonyl oxygen, and then stays coordinated to prevent a second hydride addition—but this is the general idea.

Rubric for this question:

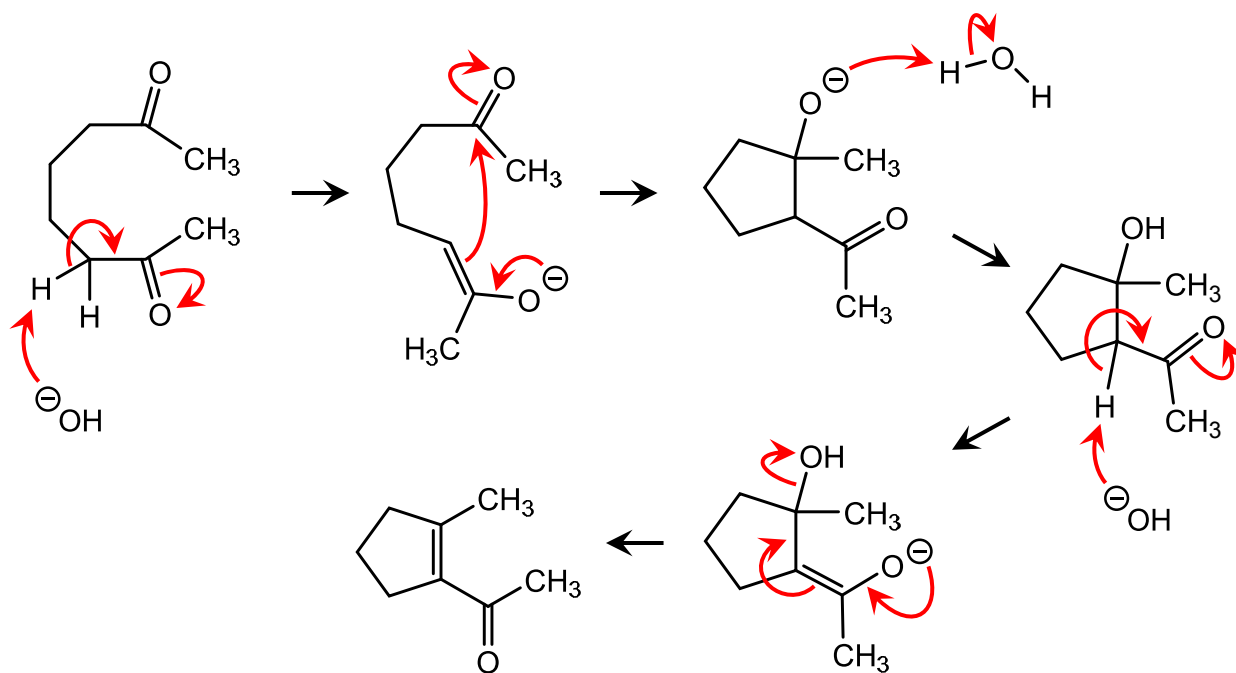
5 points for either correct structure.

3 points partial for stopping at hydride addition, without opening ring.

-2 points for each trivial structure mistake.



Intramolecular aldol reaction:



In this mechanism, I drew the initial deprotonation happening at the more substituted side of the ketone. In class, we talked about one example in which the less substituted side gets deprotonated, because the more substituted enolate can't react.

That's not the case here; the more substituted enolate reacts just fine, to produce a stable 5-membered ring.

Rubric for this question:

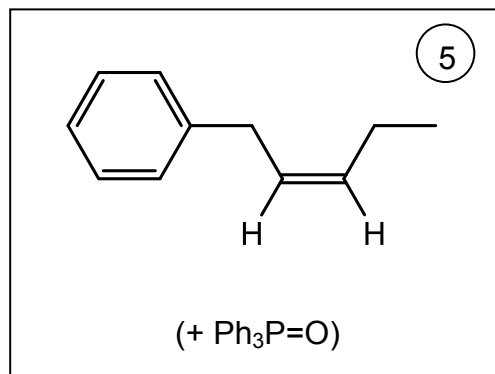
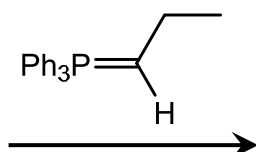
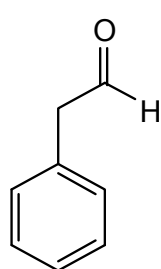
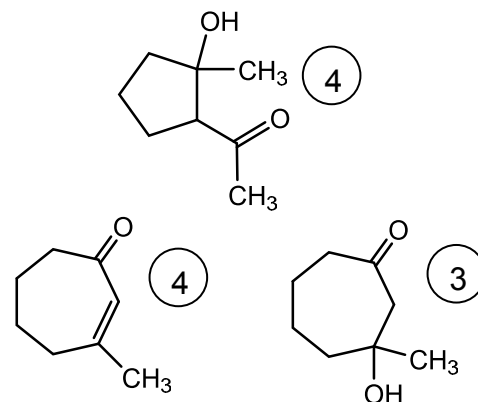
5 points for correct structure.

4 points partial for β -hydroxyketone. Heat will convert this to the α,β -unsaturated ketone.

4 points partial for 7-membered ring α,β -unsaturated ketone. Deprotonation at less-substituted carbon will be disfavored.

3 points partial for 7-membered ring β -hydroxyketone.

-2 points for trivial errors related to these structures.



This is a Wittig reaction, and the preferred alkene product in the Wittig reaction is a *cis*-alkene (even though it is less stable than the *trans*-alkene).

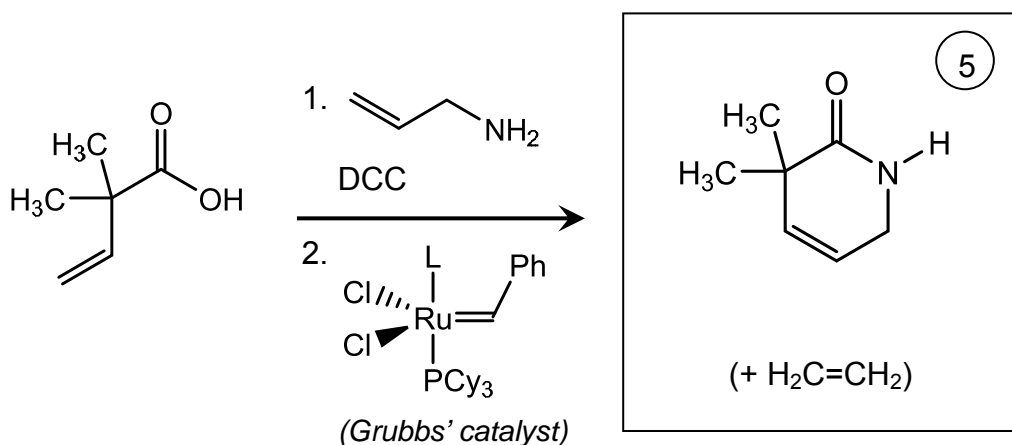
Rubric for this question:

5 points for correct structure.

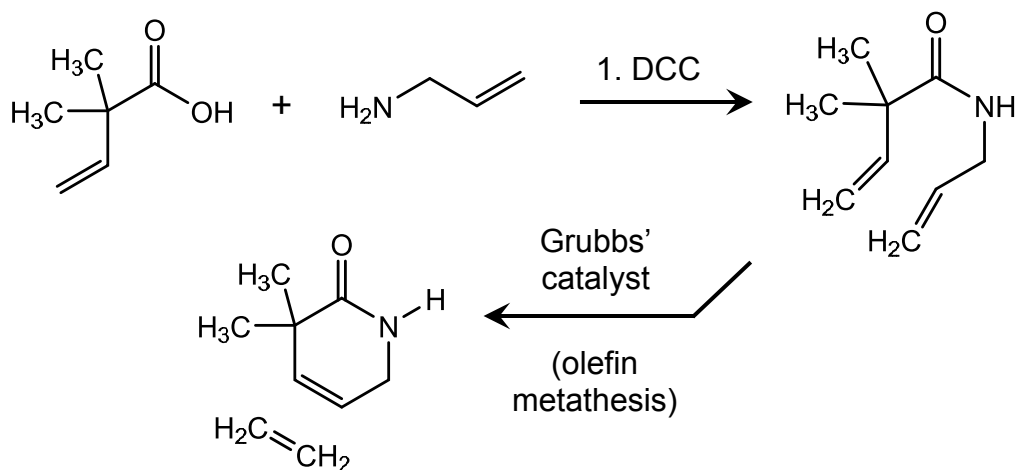
3 points partial for *trans*-alkene.

3 points partial for ethyl group instead of methyl as one of the two alkene substituents.

-2 points for other trivial structure mistakes.



This two-step synthesis combined a DCC coupling reaction with a ring-closing metathesis reaction:

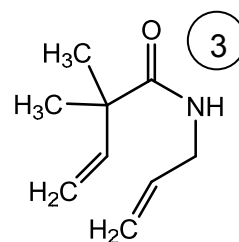


Rubric for this question:

5 points for correct structure.

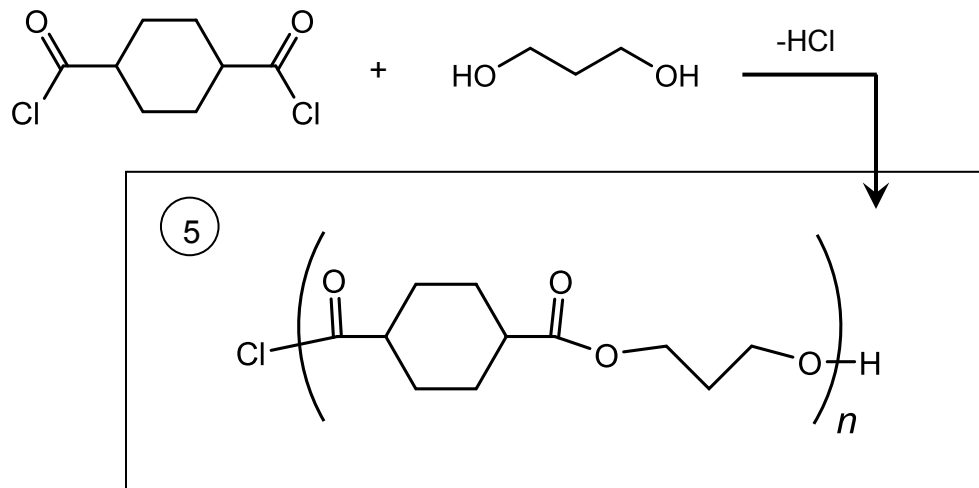
3 points partial for only completing DCC coupling.

-2 points for trivial error. This includes placing the double bond in the wrong position, or creating the wrong ring size.



5. (27 pts)

- a. For each of the polymer syntheses proposed below, draw the polymer product using bracket notation (“[-M-]_n”). 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.



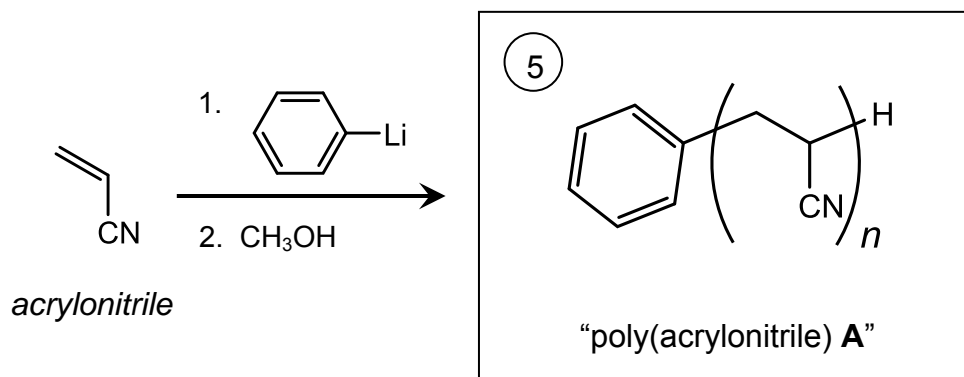
Rubric for this question:

5 points for correct structure.

4 points partial incorrect termini, but otherwise correct.

3 points partial for an answer that is chemically correct except for placement of brackets. Brackets can be placed anywhere that illustrates the alternating repeat unit structure, but they need to be correct--the left side needs to pick up where the right side left off.

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



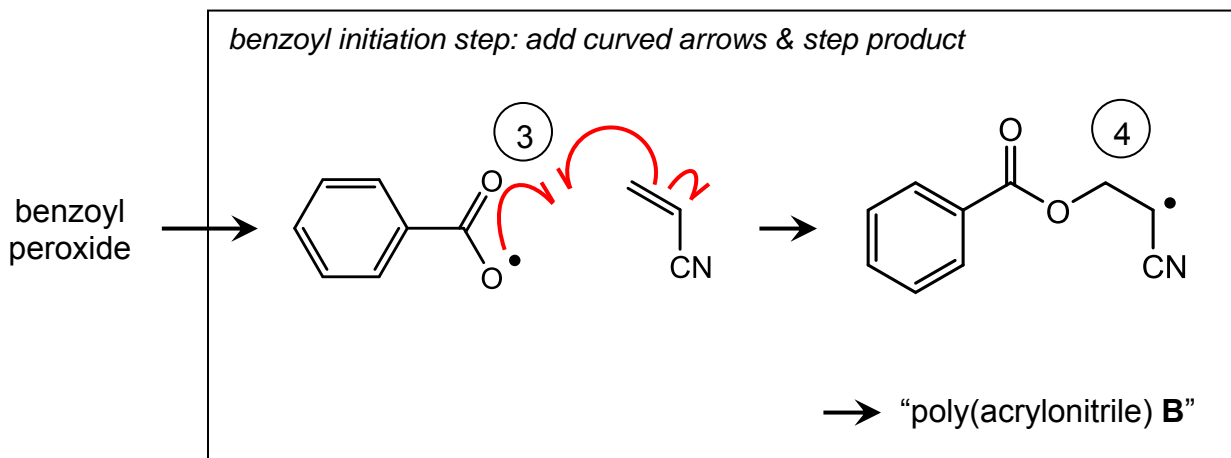
Rubric for this question:

5 points for correct structure.

-2 points for each incorrect terminus.

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

- b. If the second polymerization above were initiated with benzoyl peroxide instead of with an anion, the mechanism of polymerization would be different. In the box below, **add curved arrows** (using “electron pushing”) that show how benzoyl radical would initiate polymerization. Then draw the product of this step.



Rubric for this question (8 points total this box):

Overall notes:

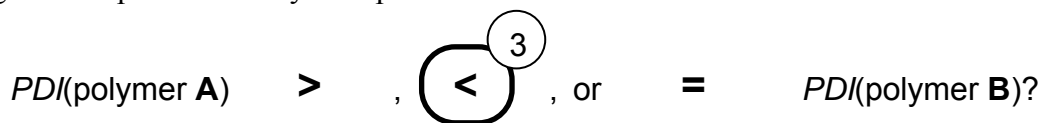
3 points for arrow pushing.

-2 points, for each error (including omission) in drawing arrows. This problem requires single-barbed, unpaired electron arrows.

4 points for intermediate structure.

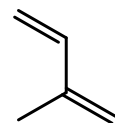
-2 points for trivial structure mistakes.

- c. How would you expect the molecular weight distribution (or “polydispersity”, measured by *PDI*) of the poly(acrylonitrile) polymers **A** and **B** described on this and the previous page to compare? Would you expect

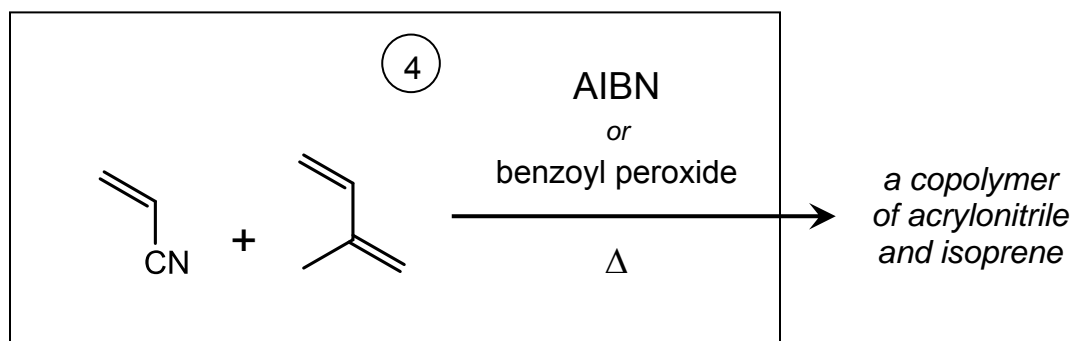


(Circle one answer.)

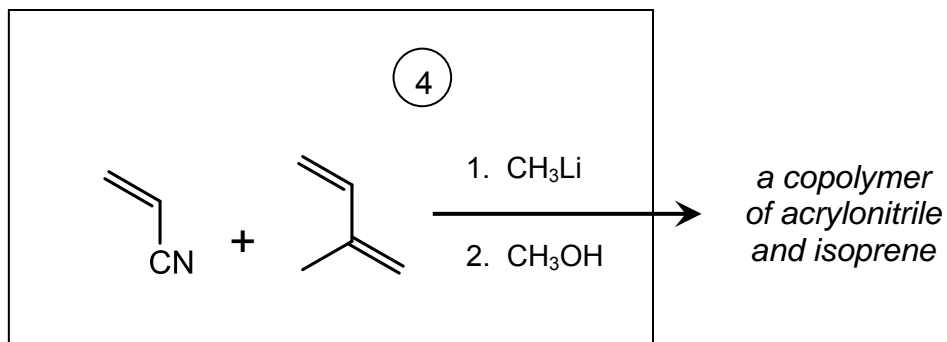
- d. How would you synthesize a **co-polymer** of acrylonitrile and isoprene (the monomer shown at right)? Draw a synthetic recipe for the copolymer in the box below.



isoprene



OR



Rubric for this question:

4 points for any polymerization conditions that combine styrene and isoprene. *No need to draw the structures of the monomer, or the polymer. Any carbanion will work as an initiator (if the recipe is anionic).*

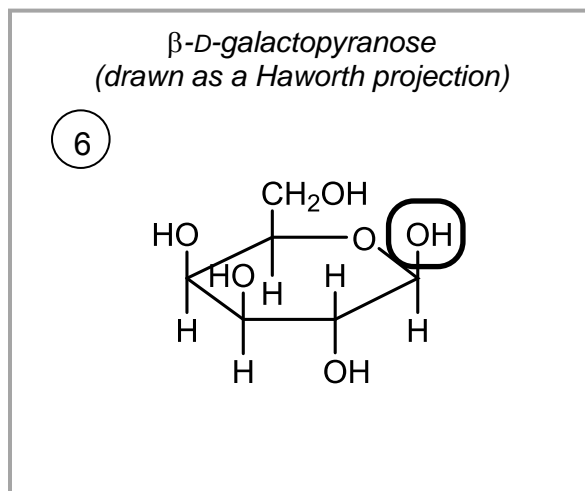
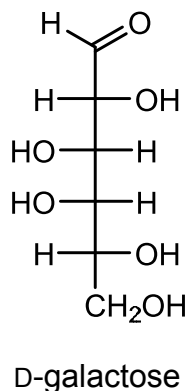
- e. In two words or less, how would you convert your copolymer from a plastic into an elastomer?

Cross-link it. 3

Other answers that we accepted: “vulcanize”, “add sulfur”, or anything that we could equate to cross-linking.

6. (6 pts) D-Galactose, a common aldohexose found in nature, is the C-4 epimer of D-glucose. A Fischer projection of acyclic D-galactose is shown below.

a. Acyclic D-galactose equilibrates with a cyclic, 6-membered-ring (pyranose) form. Draw the structure of the β -anomer of this cyclic galactose as a Haworth projection in the box at right.



b. D-Galactose is combined in nature with D-glucose to form lactose, a disaccharide. Lactose is a glycoside of galactose. Which -OH group in your structure above would be replaced to form a glycoside? **Circle one -OH group.**

Rubric for this question:

4 points for sugar structure.

1 point partial for any Haworth projection of any 6-carbon sugar.

1 point partial for drawing a β -anomer (with the $-\text{CH}_2\text{OH}$ group and C1 -OH group on the same face of the ring).

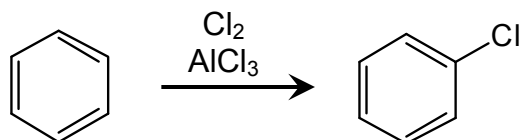
2 points for all stereochemistries other than C1 correct.

(1 point partial for just one incorrect stereochemistry.)

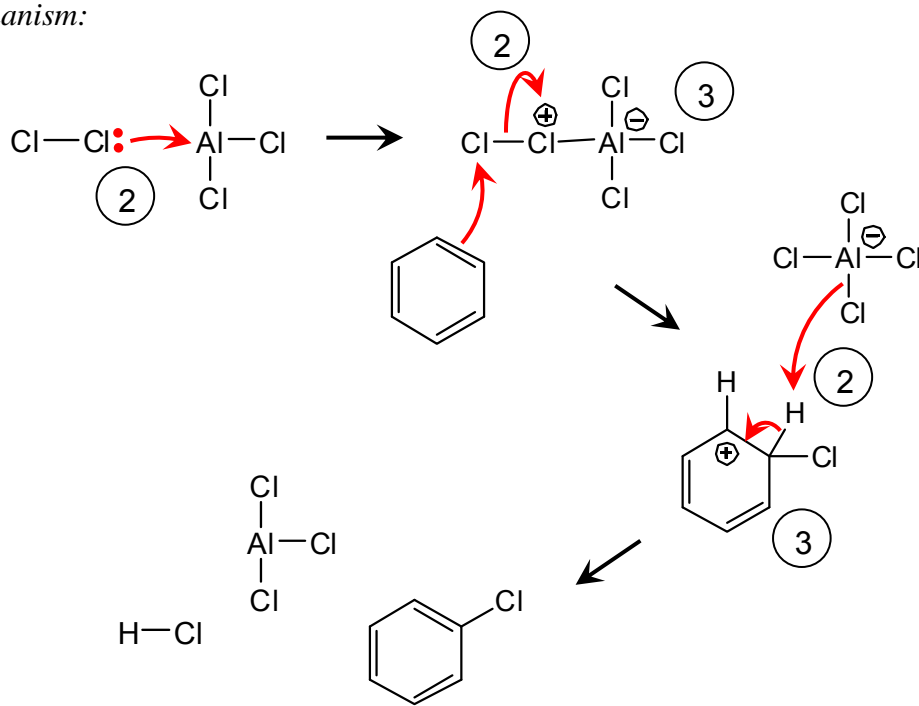
2 points for circling the -OH attached to C1.

A few of you circled an -OH group on the acyclic structure of galactose. There is no -OH group on the acyclic structure that would be replaced to make a glycoside; the -OH group is created by cyclization.

7. (29 pts) **Draw a mechanism** (using “electron pushing”) for each of the reactions shown on the next two pages. 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.



Mechanism:



Rubric for this question (12 points total this part):

2 points for each set of electron-pushing arrows.

3 points for each correct intermediate.

Overall notes:

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

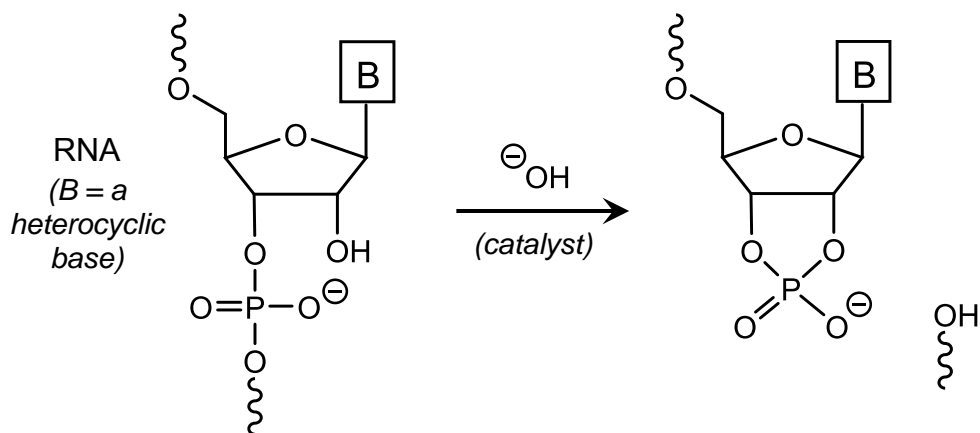
Things that have left (e.g., HCl in last step) and spectators may be omitted.

Each proton transfer must be shown explicitly, with two arrows (one to proton, one from proton-acid bond).

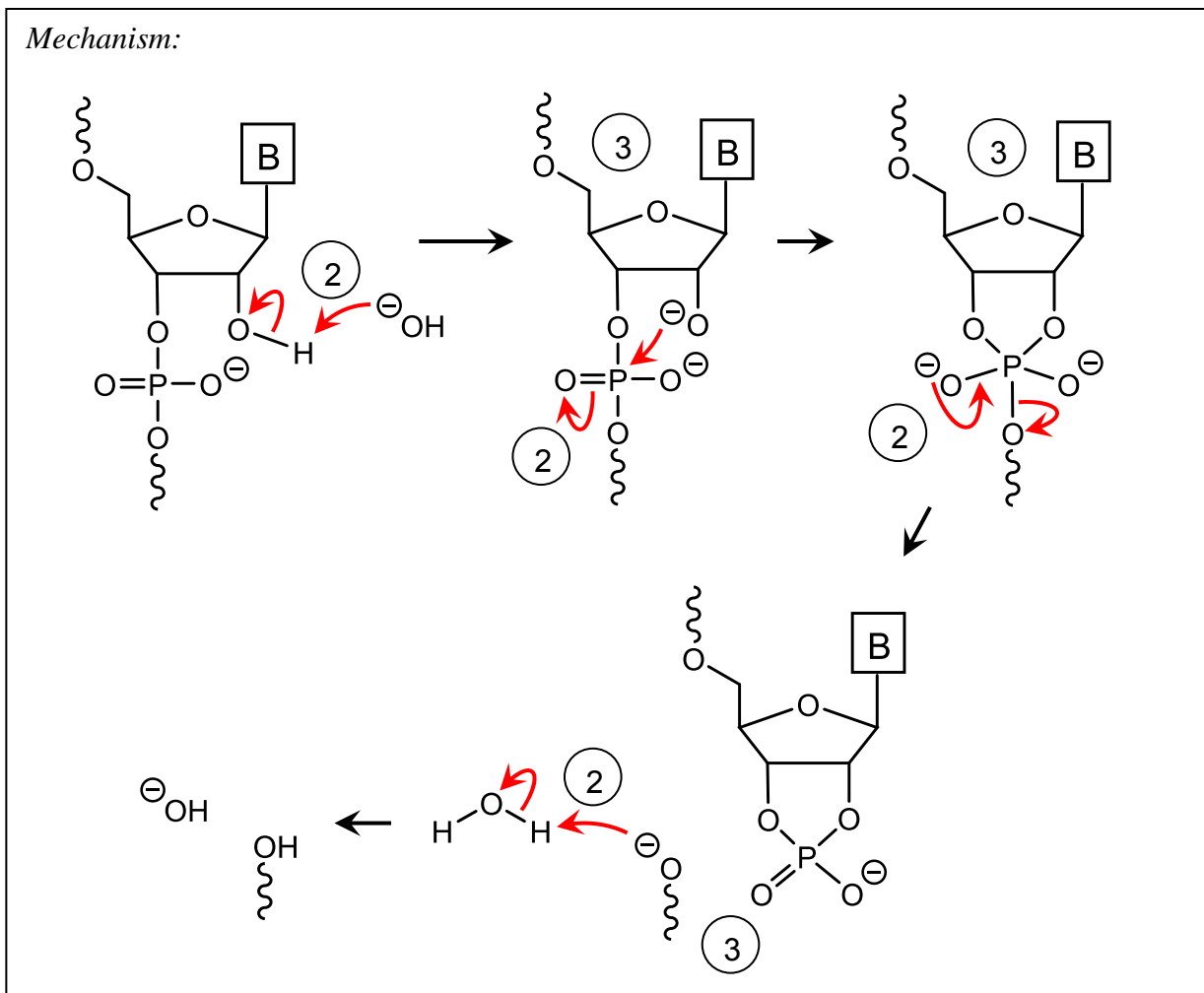
-1 point, for each arrow in each step, for errors (including omission) in drawing arrows. Arrow must start at an electron pair (either a bond or a lone pair), and end at nucleus or bond where electrons will newly interact.

-2 points for each error in charge, valency, structure, base, etc.; if error propagates, points are taken off only for initial error.

-2 points for each use of a generic base instead of AlCl_4^- in the last step.



Mechanism:



Rubric for this question (17 points total this part):

2 points for each set of electron-pushing arrows.

3 points for each correct intermediate.

Overall notes: Same as previous part.

Graders gave partial credit for electron pushing, but not intermediates, in answers that used base catalyst incorrectly.

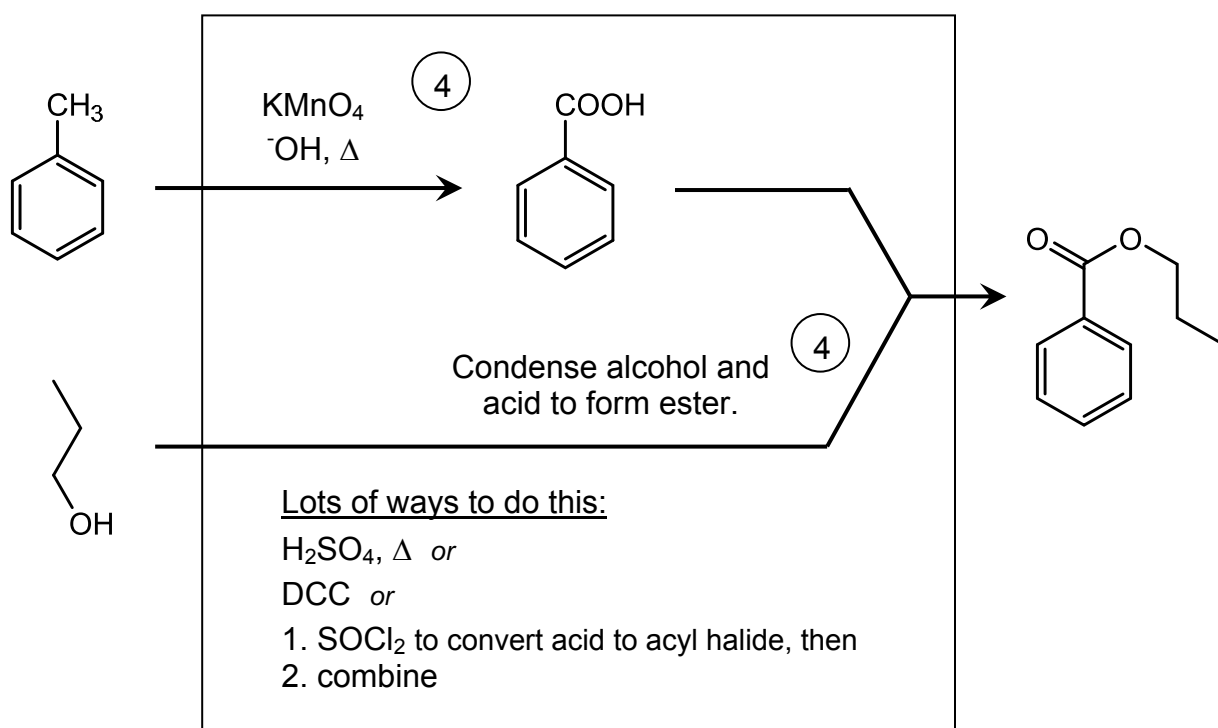
8. (28 pts) Each of the syntheses shown below can be accomplished in just a few steps. For each starting material or set of starting materials, **propose a multistep synthesis** of the product shown. You may use any reagents and reactions we've learned about in class and/or in the text.

General rubric for synthesis problems:

Each synthesis required tasks, listed below. Each task was worth **4 points**. 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.



Rubric for this question:

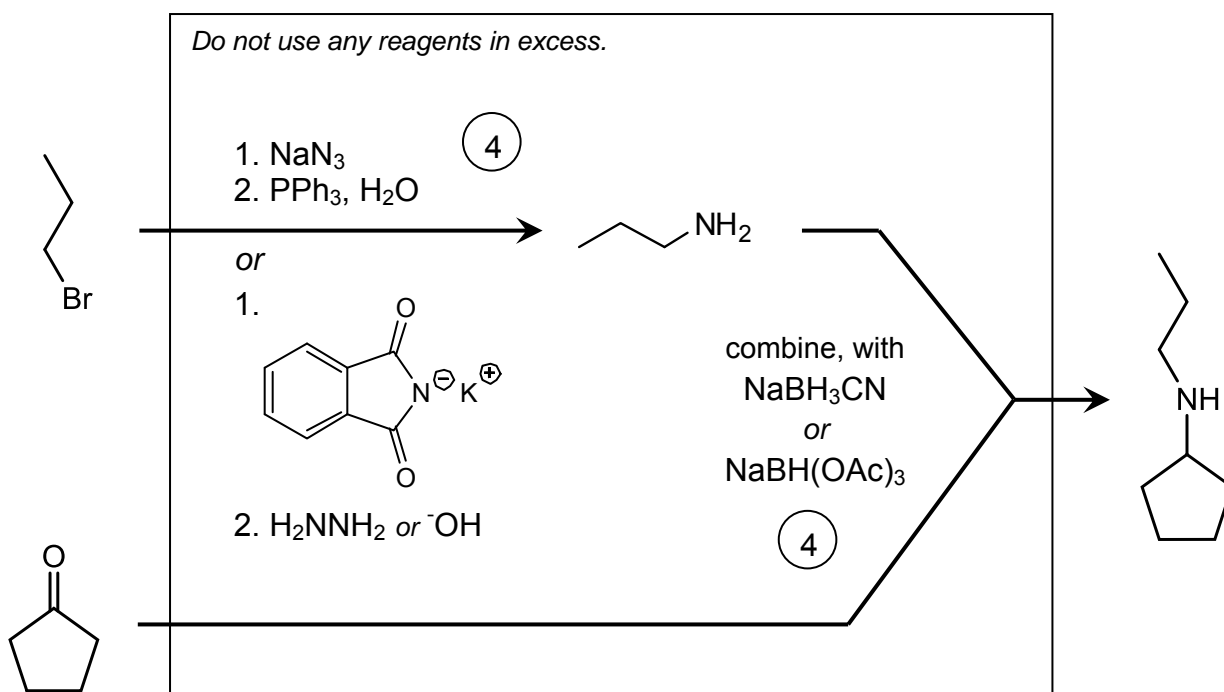
Task 1: Oxidize toluene to carboxylic acid. (4 points.)

Just "KMnO4" was sufficient.

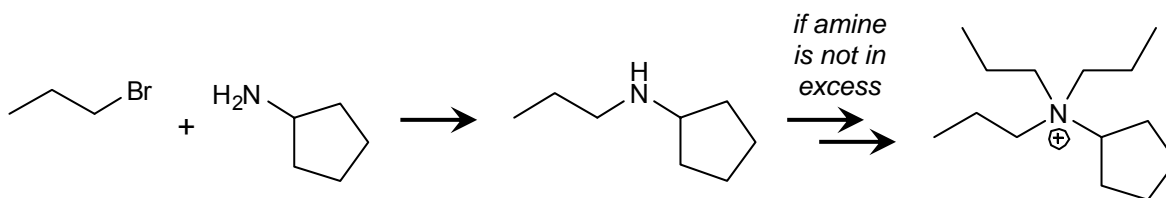
There are longer, more convoluted ways to do this; these could receive less than full credit. Graders had leeway to decide whether length was excessive.

Task 2: Form an ester from the carboxylic acid and amine. (4 points.)

Lots of ways to do this, as shown above.



The limitation that you couldn't use any excess reagents ruled out a couple of approaches here. One method of converting an alkyl halide to a primary amine is to use excess ammonia; the excess is required because once ammonia has been alkylated once, the nitrogen becomes a better nucleophile, and it is difficult to prevent it from being alkylated again. Using a vast excess of ammonia ensures that this will not happen. Similarly, it would be possible to use excess cyclopentyl amine to make the desired product directly:



Again, if the amine is not in excess, it is impossible to stop this process at monoalkylation. Instead, primary amines can be generated either via formation of an intermediate azide, or via the Gabriel synthesis (using potassium phthalimide). The resulting amine can then be added to cyclopentyl ketone in the presence of a very mild hydride source to yield the secondary amine.

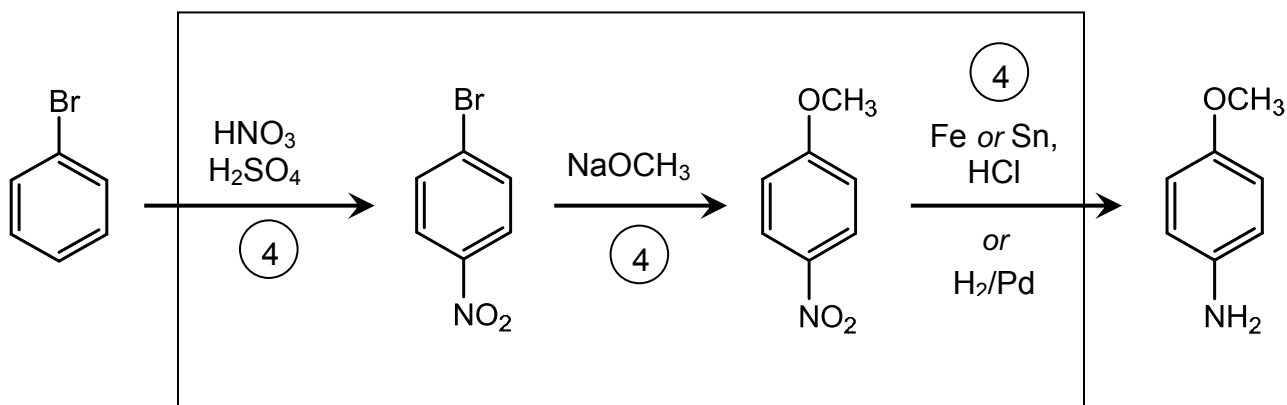
Rubric for this question:

Task 1: Convert alkyl halide to an amine. (4 points.)

2 points partial for making amine with excess ammonia.

Task 2: Combine amine and ketone via reductive amination. (4 points.)

1 point partial for using cyclopentyl halide/tosylate as an $\text{S}_{\text{N}}2$ electrophile. (Won't work; will do $\text{E}2$ instead of $\text{S}_{\text{N}}2$.)



Rubric for this question:

Task 1: Introduce -NO_2 or other π -electron-withdrawing group to enable nucleophilic aromatic substitution. (4 points.)

Groups other than -NO_2 could receive full credit here, but will fail to get credit later because they cannot be converted to an -NH_2 group.

Task 2: Substitute halide for -OCH_3 . (4 points.)

This reaction requires a π -acceptor in the ortho- or para-position to succeed with -OCH_3 . No partial credit without one.

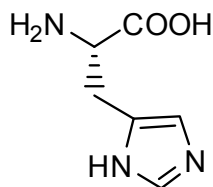
Benzyne mechanism fails with OCH_3 . In addition, even with -OH or -NH_2 , reaction is non-regioselective. No partial credit for using benzyne instead.

Task 3: Introduce NH_2 group. (4 points.)

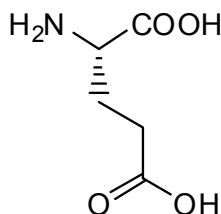
If you didn't do this via reduction of -NO_2 , your proposed method needed to succeed to receive partial credit.

9. (10 pts)

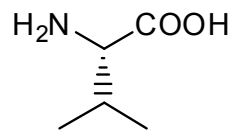
- a. Sort the three amino acids histidine (His), glutamic acid (Glu), and valine (Val) in order of increasing isoelectric point (pI). Write their three-letter abbreviations in the appropriate boxes below.



histidine (His)

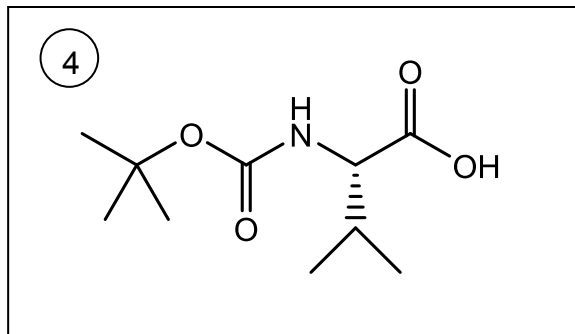


glutamic acid
(Glu)



valine
(Val)

- b. When valine is used in solid-phase peptide synthesis, it typically bears a *tert*-butyloxycarbonyl (*t*Boc) protecting group. In the box at right, draw the structure of *t*Boc-protected valine.



Rubric for part (b):

4 points for correct structure.

Abbreviations weren't permitted—the problem asked for a structure.

2 points partial for any protecting group on nitrogen. (Including an abbreviation.)