

NAME (Print): _____

Chemistry 310N
Dr. Brent Iverson
Final
May 8, 2008

SIGNATURE: _____

Please print the
first three letters
of your last name
in the three boxes

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Please Note: This test may be a bit long, but there is a reason. I would like to give you a lot of little questions, so you can find ones you can answer and show me what you know, rather than just a few questions that may be testing the one thing you forgot. **I recommend you look the exam over and answer the questions you are sure of first**, then go back and try to figure out the rest. Also make sure to **look at the point totals** on the questions as a guide to help budget your time.

For synthesis problems GO FOR PARTIAL CREDIT EVEN IF YOU DO NOT KNOW THE ENTIRE ANSWER!!!WRITE DOWN WHAT YOU DO KNOW IN THE REACTION SEQUENCE SOMEWHERE. YOU WILL GET PARTIAL CREDIT IF IT IS CORRECT

Note: You must have your answers written in pen if you want a regrade!!!!

Honor Code

The core values of the University of Texas at Austin are learning, discovery, freedom, leadership, individual opportunity, and responsibility. Each member of the University is expected to uphold these values through integrity, honesty, trust, fairness, and respect toward peers and community.

(Your signature)

Compound		pK _a
Hydrochloric acid	H-Cl	-7
Protonated alcohol	$\text{RCH}_2\text{O}^+\text{H}_2$	-2
Hydronium ion	H_3O^+	-1.7
Protonated Amide	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{N}^+\text{H}_3$	-0.5
Carboxylic acids	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\text{H}$	3-5
Ammonium ion	H_4N^+	9.2
β-Dicarbonyls	$\text{RC}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}'$	10
β-Ketoesters	$\text{RC}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{OR}'$	11
β-Diesters	$\text{ROC}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{OR}'$	13
Water	HOH	15.7
Alcohols	RCH_2OH	15-19
Acid chlorides	$\text{RCH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{Cl}$	16
Aldehydes	$\text{RCH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{H}$	18-20
Ketones	$\text{RCH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}'$	18-20
Esters	$\text{RCH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{OR}'$	23-25
Terminal alkynes	$\text{RC}\equiv\text{C}-\text{H}$	25
LDA	$\text{H}-\text{N}(\text{i-C}_3\text{H}_7)_2$	40
Terminal alkenes	$\text{R}_2\text{C}=\underset{\text{H}}{\text{C}}-\text{H}$	44
Alkanes	$\text{CH}_3\text{CH}_2-\text{H}$	51

1. (14 points) Suppose a relative of yours is having an MRI. In no more than four sentences, explain to them what is happening when they have the MRI scan. We will be looking for a minimum of 7 key points here.

The popular medical diagnostic technique of **magnetic resonance imaging (MRI)** is based on the **same principles as NMR**, namely the **flipping (i.e. resonance) of nuclear spins of protons** by **radio frequency irradiation** when a patient is placed in a **strong magnetic field**. **Magnetic field gradients** are used to gain imaging information, and **rotation of the gradient around the center of the object** gives imaging in an entire plane (**i.e. slice inside patient**). In an MRI image, you are looking at **individual slices that when stacked make up the three-dimensional image of relative amounts of protons, especially the protons from water and fat, in the different tissues.**

2. (1 pt each) Fill in each blank with the word that best completes the following sentences about NMR.

For organic chemistry, NMR is primarily concerned with atoms having a spin quantum number of 1/2. The two most important isotopes for organic chemistry structure determination by NMR are ^1H and ^{13}C . Of these two, ^1H is a common isotope and the predominant isotope found in molecules, while ^{13}C is very rare.

The key to the NMR experiment is that in a strong external magnetic field, the difference in energy between nuclear spin states is proportional to that field. For ^1H atoms, the two nuclear spin states are referred to as + 1/2 and - 1/2.

When irradiated with electromagnetic radiation of a wavelength that corresponds to the exact energy difference between nuclear spin states, the energy is absorbed, a process referred to as resonance. The wavelength used for irradiation is in the radio frequency range of the electromagnetic spectrum.

Electron density is induced to move in a strong external magnetic field, and this movement induces a magnetic field that is opposed to the external magnetic field. This has the effect of shielding the underlying nuclei from the external magnetic field. The signal for an H atom with greater electron density around it will come at lower ppm in an NMR spectrum compared to a similar H atom with less electron density.

3. (21 pts) Fill in each blank with the word that best completes the following sentences.

Think of electron density as _____ **waves** _____, in which you can get extra stability when they add constructively, and you lose stability when they cancel each other (add destructively).

You generate as many new molecular orbitals as _____ **atomic** _____ orbitals used to create them. Approximately half are _____ **bonding** _____ molecular orbitals (waves add constructively) and are filled with electron density, and half are _____ **antibonding** _____ molecular orbitals (waves add destructively) and are not filled with electron density.

Adjacent 2p orbitals overlap, allowing the _____ **pi** _____ electron density to delocalize into all the adjacent 2p orbitals, their wave functions adding constructively to provide stability.

Absorbance of a photon by a molecule corresponds to promotion of a(n) _____ **electron** _____ from a filled _____ **molecular** _____ **orbital** _____ to an unfilled

_____ **molecular** _____ **orbital** _____. In the visible region, this usually involves _____ **pi** _____ bonding and antibonding molecular orbitals, and conjugation _____ **increases** _____ (increases/decreases) the wavelength of absorption.

Molecules appear to our eye to be a combination of the wavelengths

_____ **reflected** _____ (not _____ **absorbed** _____).

According to the Huckel definition of aromaticity, molecules will be aromatic if they are 1)

_____ **monocyclic** _____, 2) _____ **flat** _____, 3) all the ring atoms are _____ **sp²** _____ hybridized (sp in rare cases) and 4) there are $4n + 2$ _____ **pi** _____

electrons, where $n = 0, 1, 2, 3, 4, 5, 6, \dots$. The 36 kcal/mol extra stability (unreactivity) of aromatic

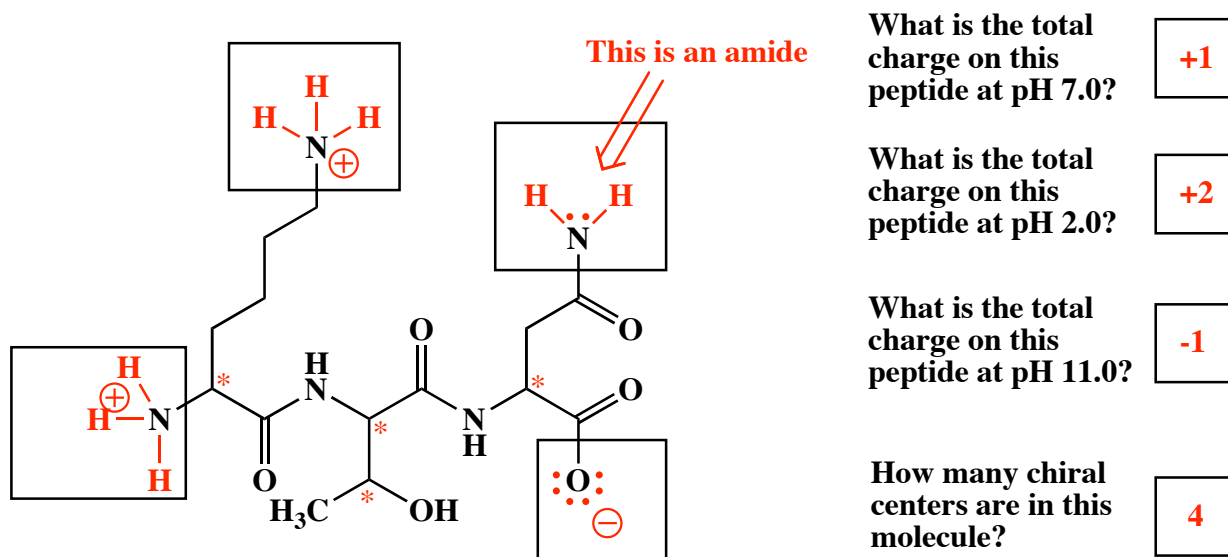
species derives from putting all the _____ **pi** _____ electrons in low energy

molecular orbitals that extend over the _____ **sp²** _____ hybridized ring atoms. These

molecular orbitals involve overlap (in phase and out of phase) of the _____ **2p** _____

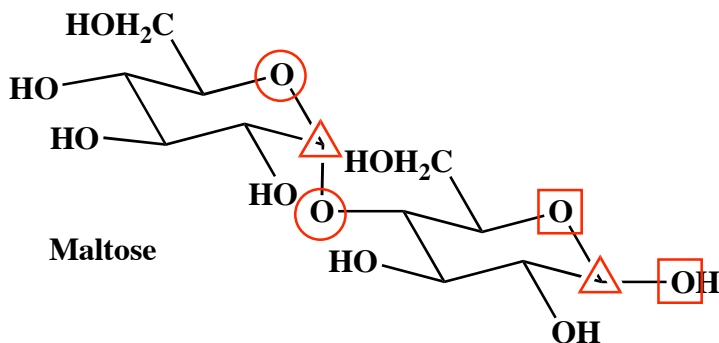
atomic orbitals on each atom of the ring.

4. (16 points) **A)** This semester we have learned a great deal about both carboxylic acids and amines. Here is an apply what you know problem. The following three amino acid sequence (Lysine-Threonine-Asparagine) is found in a prion protein, an infectious species that does not contain nucleic acid. Its structure is shown below. **Complete the following peptide structure by adding all appropriate hydrogen atoms, lone pairs, and formal charges that will be present when this peptide is in buffered water at pH 7.0.** Assume the pKa value for a protonated amine (RNH_3^+) is 9.2, pKa value for a carboxylic acid is 4.0, and the pKa for a protonated amide (RC(O)NH_3^+) is -0.5.



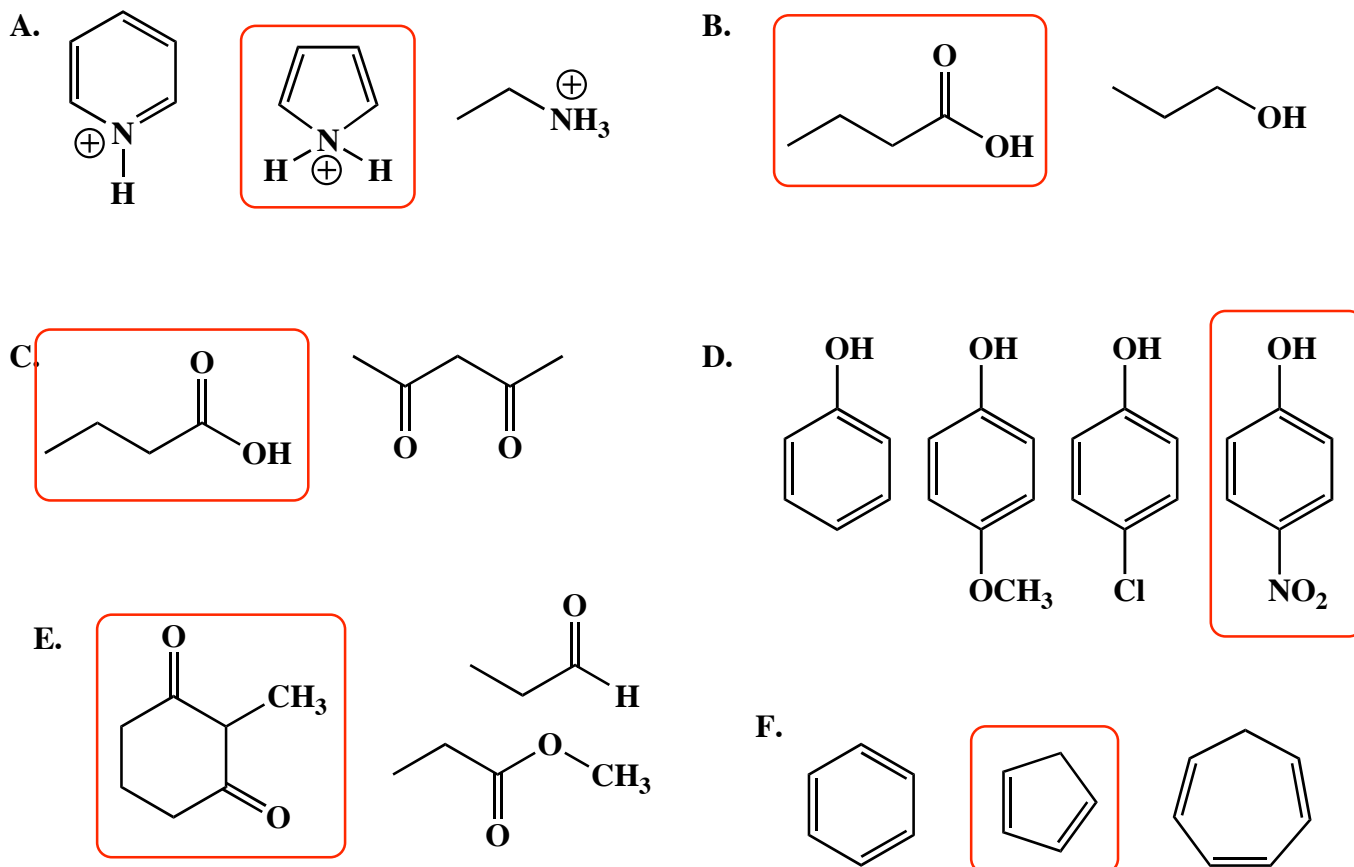
5. (16 points) **A)** On the following disaccharide called maltose, **circle** the O atoms of all acetal functional groups, and **draw a box** around the O atoms of all hemiacetal functional groups.

B) Next **draw a triangle** around each anomeric carbon atom.

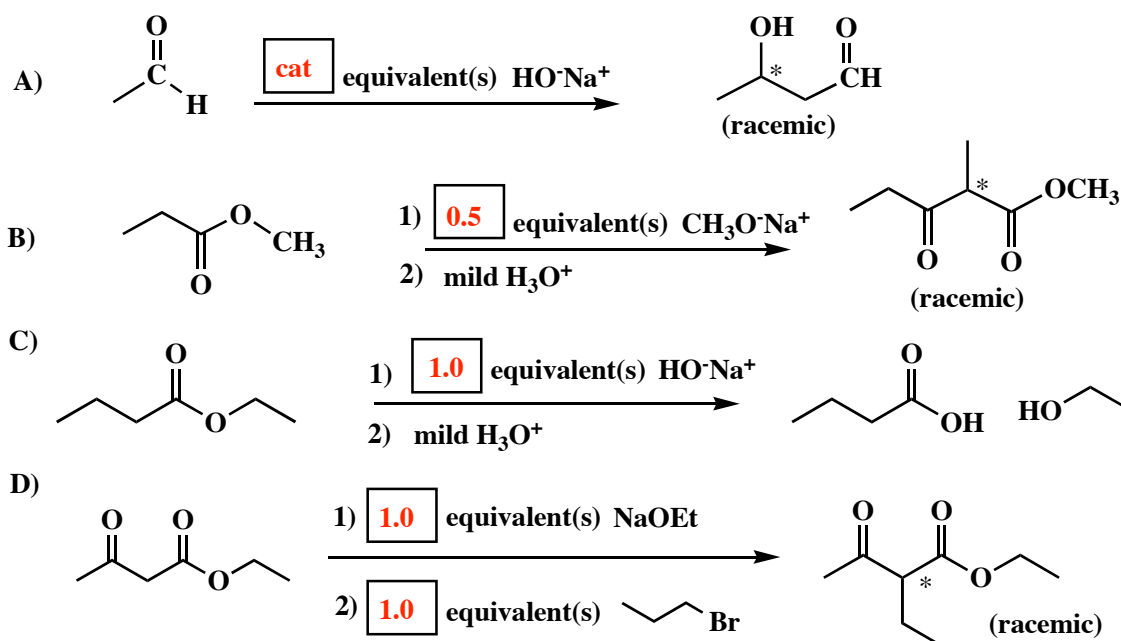


- C) Are the two carbohydrates pentoses or hexoses? hexoses
- D) Is the carbohydrate on the left in the α or β form? α
- E) Is the glycosidic bond best described as $\alpha 1,4$; $\alpha 1,6$; $\beta 1,4$; or $\beta 1,6$? $\alpha 1,4$
- F) How many chiral centers does the molecule have? 10
- G) Are the two carbohydrates aldoses or ketoses? aldoses

6. (2-4 points each) For each set, circle the MOST ACIDIC molecule.

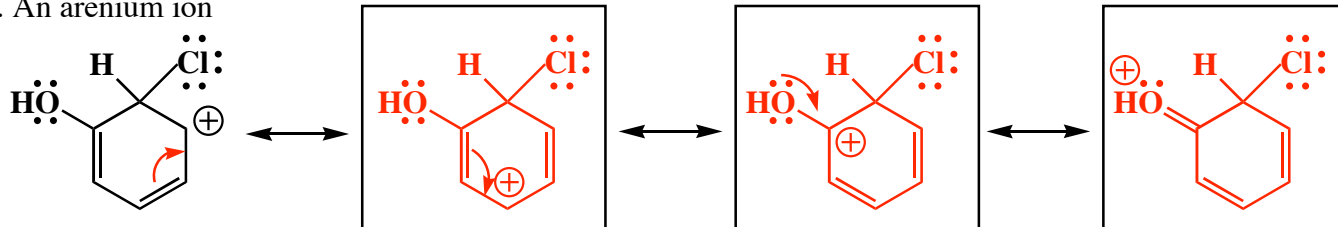


7. (2 pts each) In each of the boxes over an arrow, write the minimum number of equivalents of the specified reagent required to carry out the reaction shown to completion. If only a catalytic amount is needed, write "CAT". Note: You must assume the carbonyl compound starting material is initially present in an amount of 1.0 equivalent.

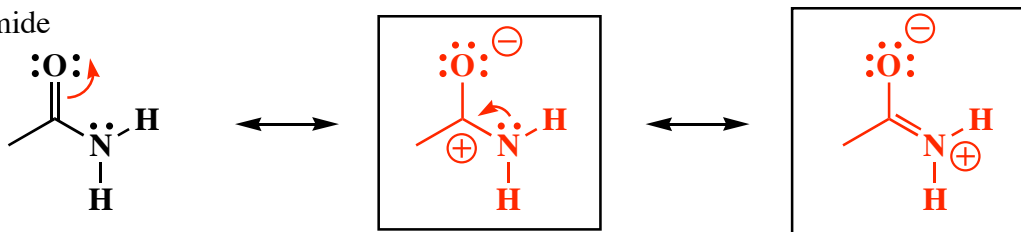


8. (20 pts) Resonance contributing structures are important for both units covered by this exam, namely enolates and aromatic molecules. On the following, **draw the indicated number of most important resonance contributing structures**. Show all lone pairs, pi bonds and formal charges. Use arrows to indicate the redistribution of electrons on each molecule to the left, that leads to the contributing structure you draw immediately to its right. (Only the structure on the farthest right on each line has no arrows on it). We drew template structures for you to save time.

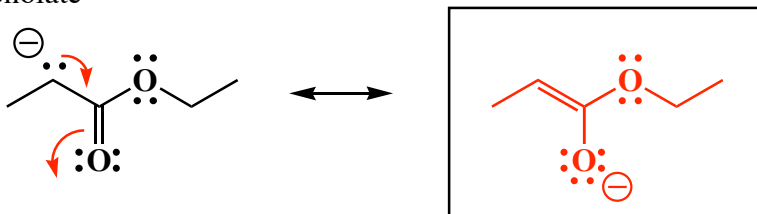
A. An arenium ion



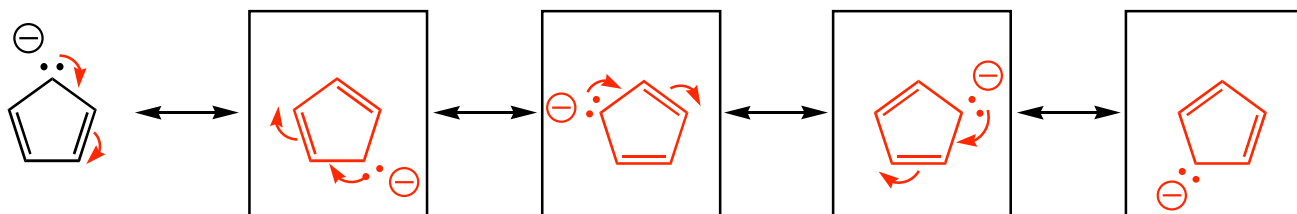
B. An amide



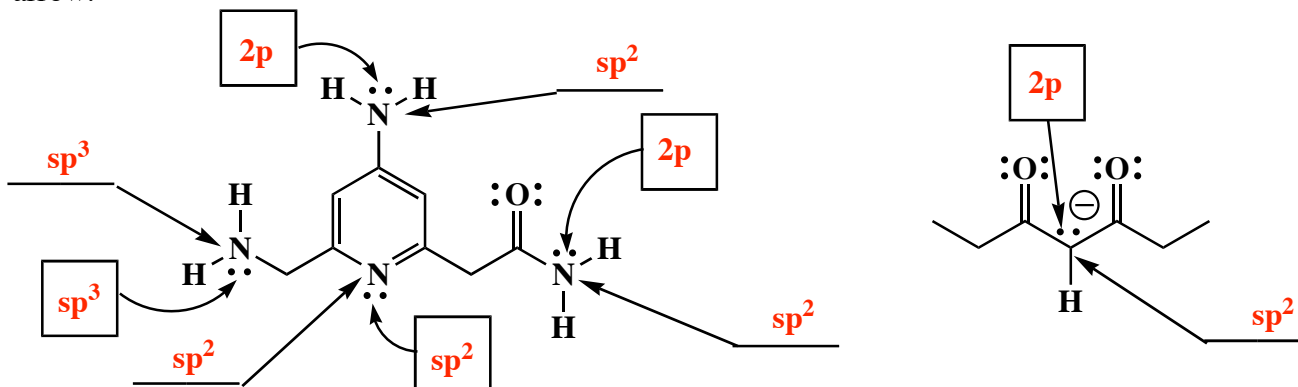
C. An enolate



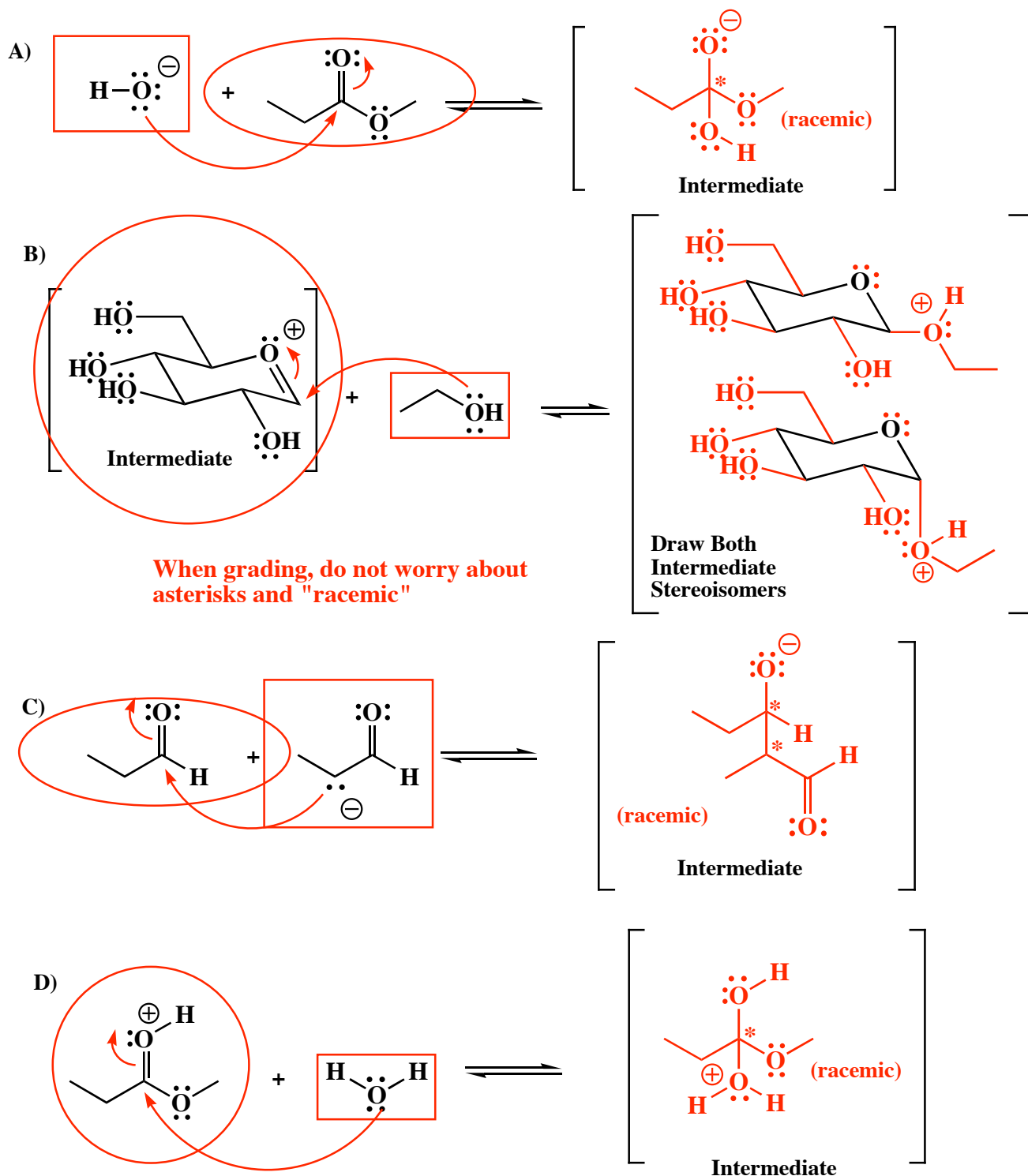
D. An aromatic anion



9. (2 pts each) **On the lines provided**, state the hybridization state of each atom indicated in the following molecule. **In the box provided**, state what type of atomic orbital contains the lone pair indicated by the arrow.

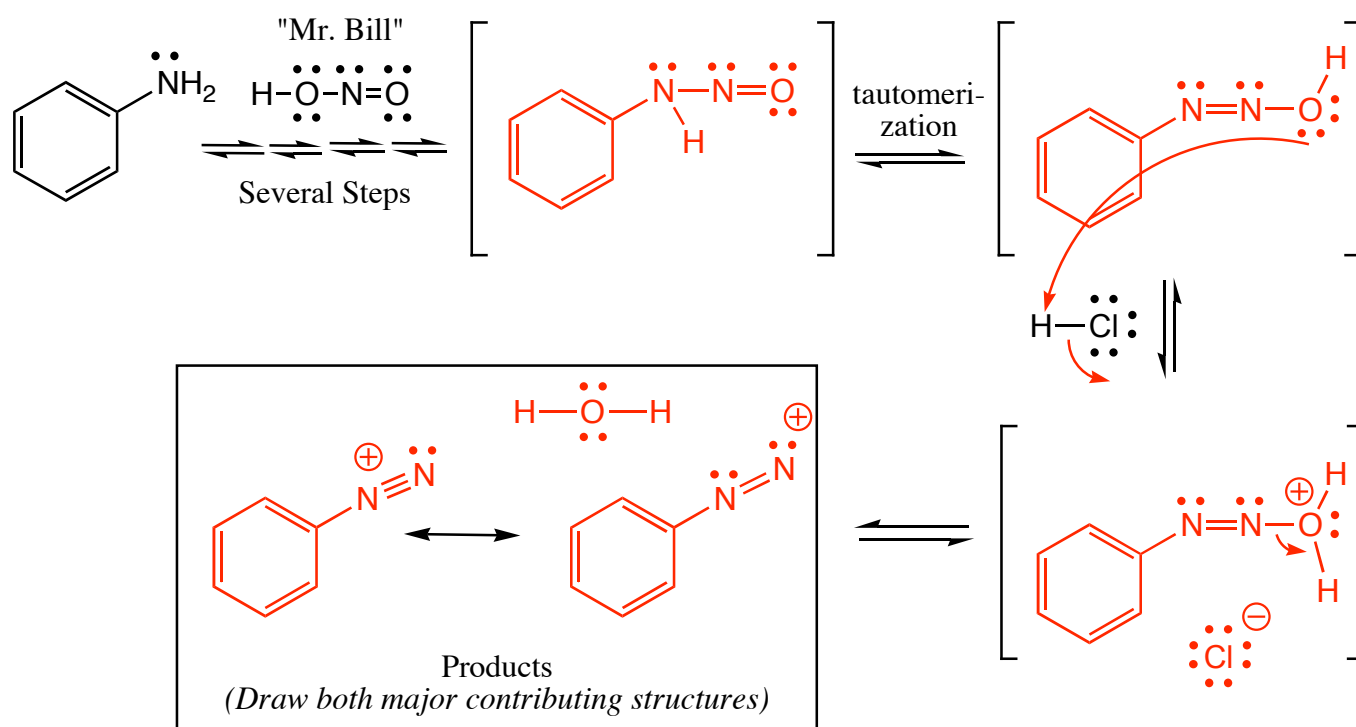
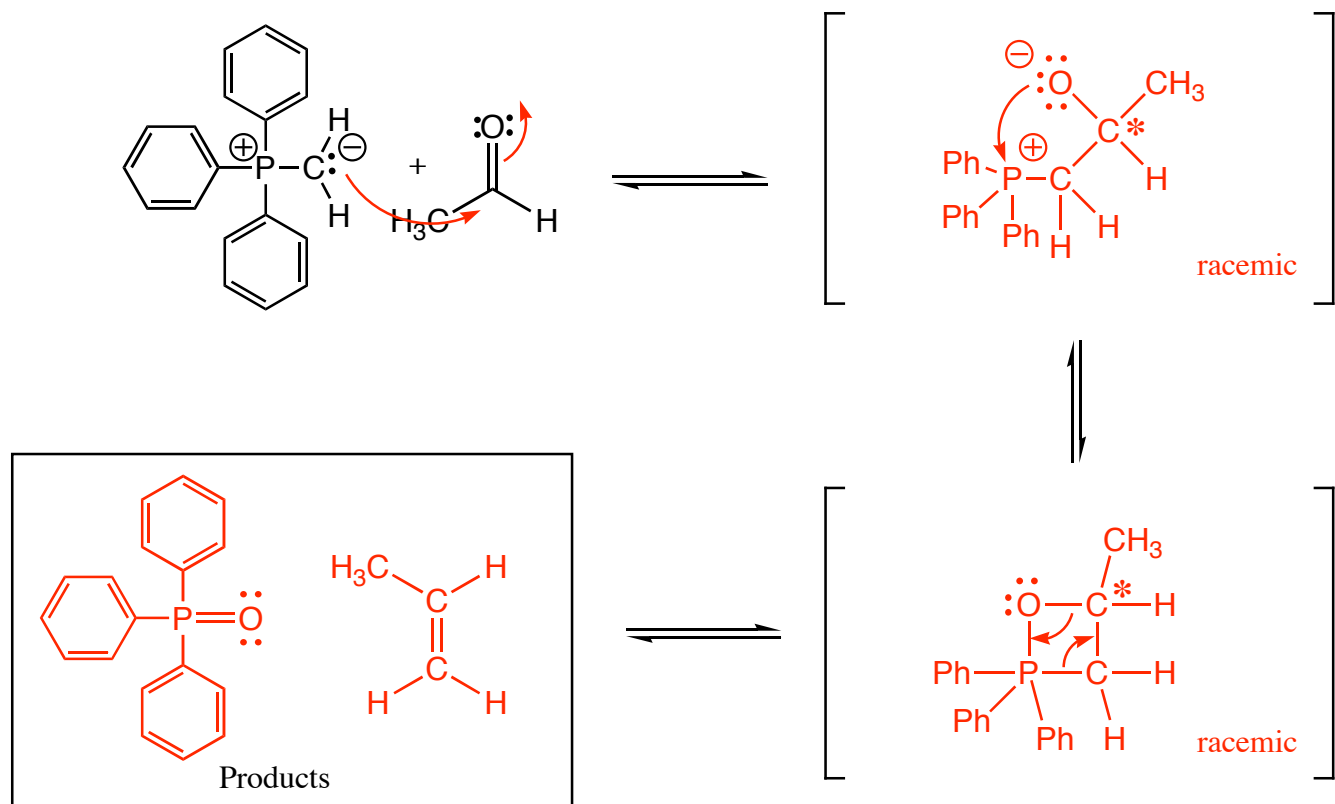


10. (26 points) Many of the reactions we have learned this semester involve steps with nucleophiles reacting with electrophiles. For the following examples of steps in mechanisms we have seen this semester, 1) **Draw the intermediate that will be formed when the two molecules react.** 2) **Draw all formal charges and lone pairs on the intermediates.** 3) **Draw arrows on the starting materials to indicate the flow of electrons that leads to the intermediate.** 4) **Finally, draw a box around the nucleophile and a circle around the electrophile in each case.** There is no need to draw products or any further steps of the mechanisms. You might want to read these directions again so you know what we want.

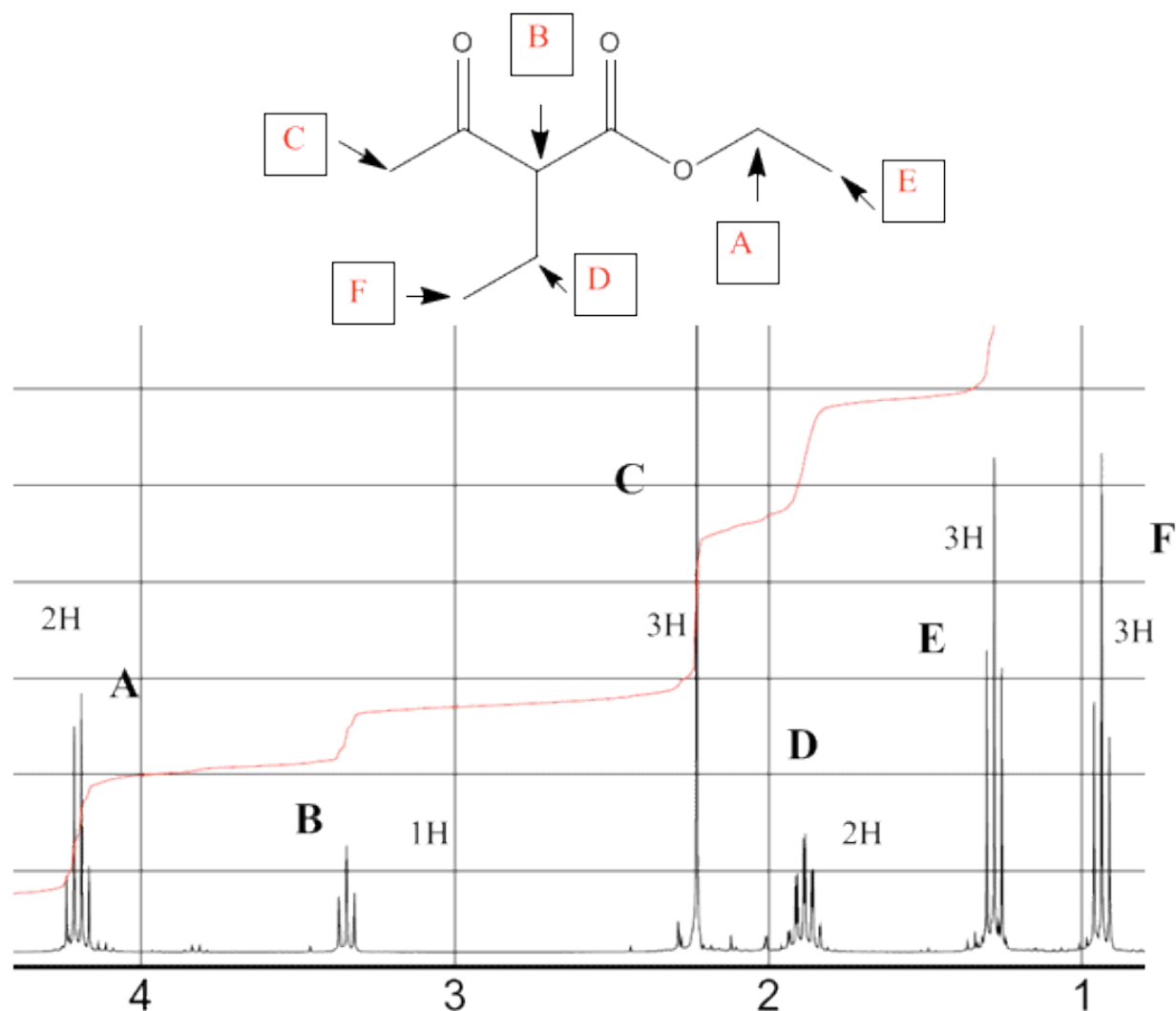


Did you remember to draw boxes and circles?

11. (28 pts) Complete the mechanisms below for a Wittig reaction and the Mr. Bill reaction. Use arrows to show the movement of all electrons, and be sure to draw all lone pairs of electrons and all formal charges. If a racemic product is formed, just put an asterisk (*) next to the chiral center and write "racemic" under it.



12. A) (12 points) Each signal in the NMR spectrum below is assigned a letter. In the boxes below, write the letter of the signal that corresponds to the **protons attached to** the carbon indicated.



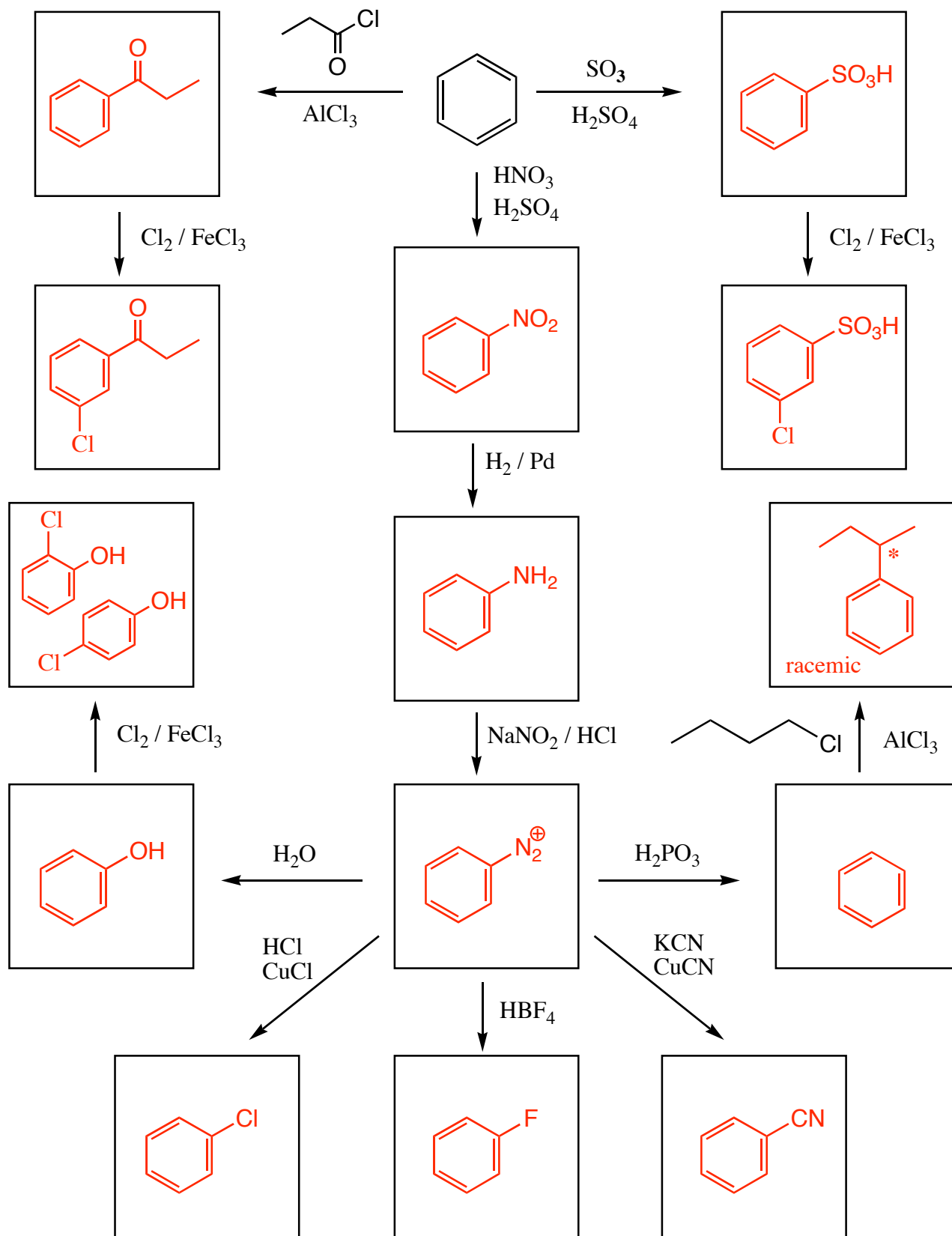
In 1 to 3 words, give an example of a reaction you have learned that will produce a product with the following characteristic feature (3 points each):

B) a new C=C bond to a former carbonyl carbon _____ Wittig _____

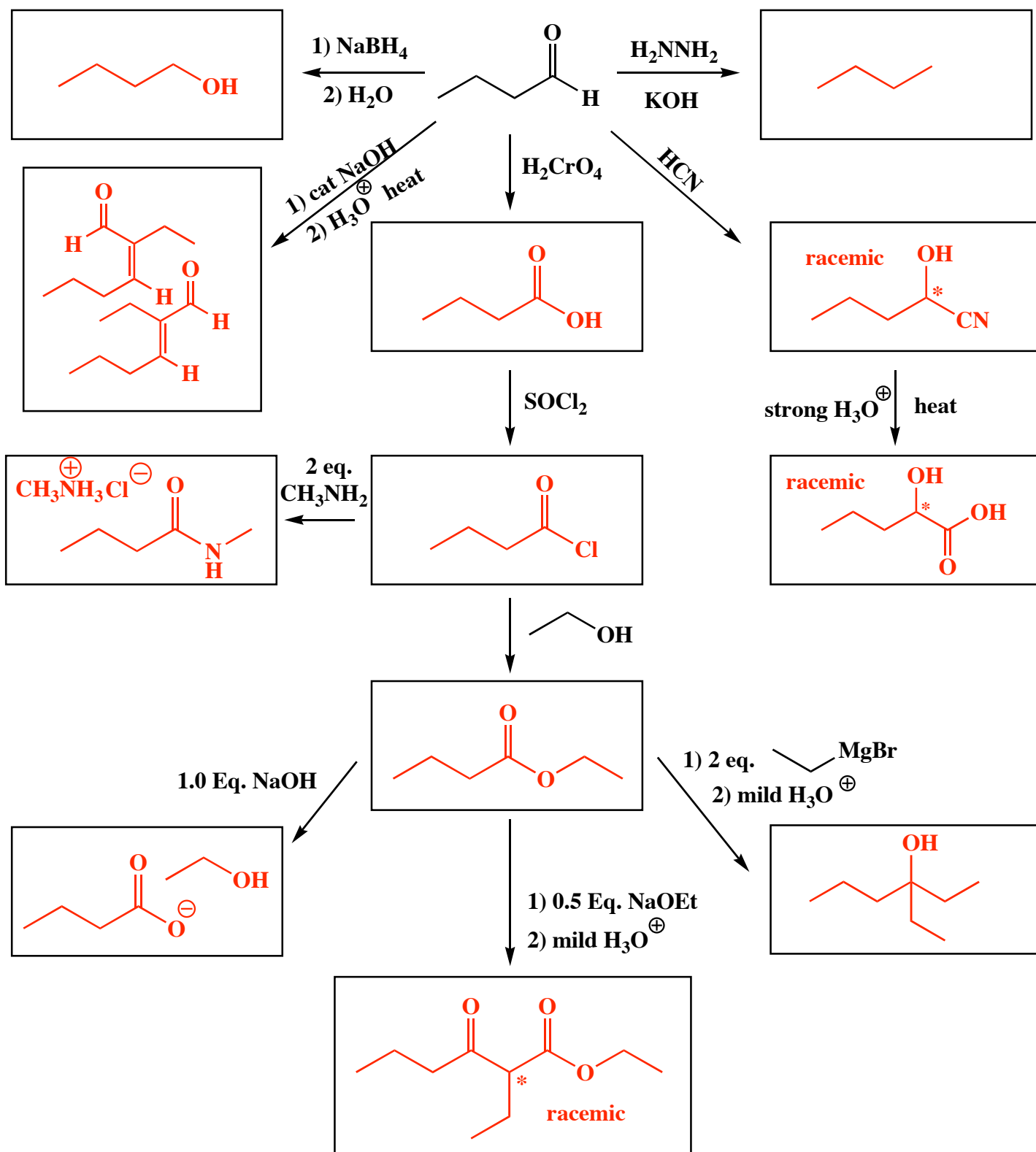
C) a new C-C bond to a carbon alpha to a carbonyl carbon _____ Claisen or Aldol _____

D) a new C-C bond to a carbon beta to a carbonyl carbon _____ Michael _____

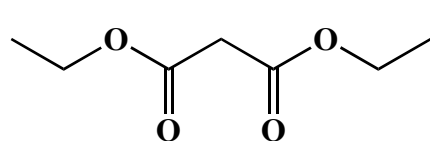
13. (46 pts.) Write the predominant product or products that will occur for each transformation. Assume each reagent only adds once to the ring. **If predominantly ortho/para products are predicted, you must draw both.** If a chiral center is created, use an asterisk and write "racemic" as appropriate.



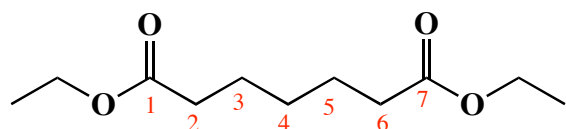
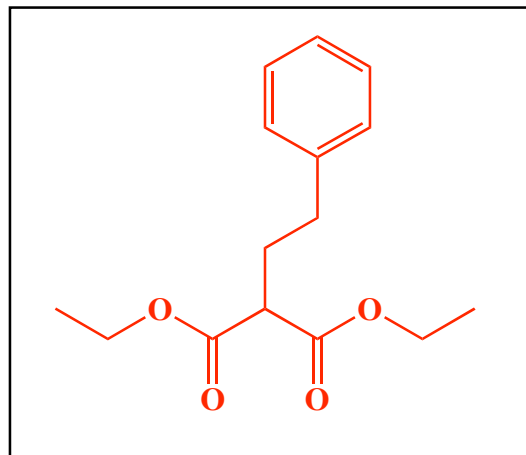
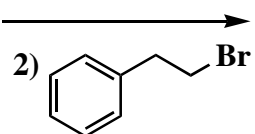
14. (44 pts.) Write the predominant product or products that will occur for each transformation. For aldol reactions, assume dehydration takes place and you must draw both E and Z products unless one predominates by a substantial margin. Label any new chiral centers with an asterisk and write "racemic" if appropriate.



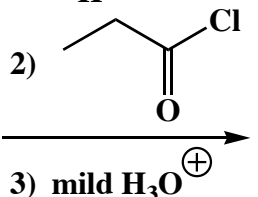
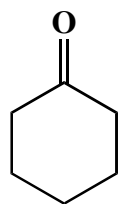
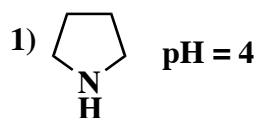
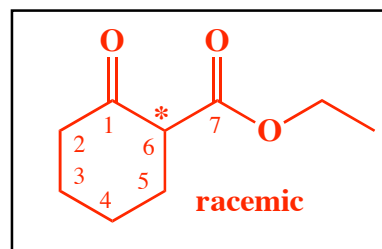
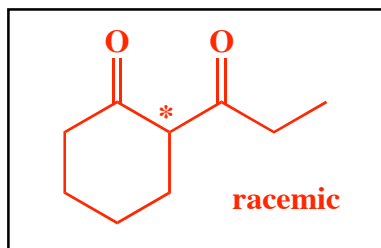
15 (5 pts. each) These are a little harder, so take your time. Write the predominant product or products that will occur for each sequence of transformations. For aldol reactions, assume dehydration takes place and you must draw both E and Z products unless one predominates by a substantial margin. Label any new chiral centers with an asterisk and write "racemic" if appropriate.



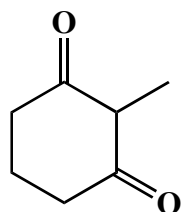
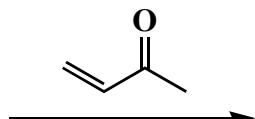
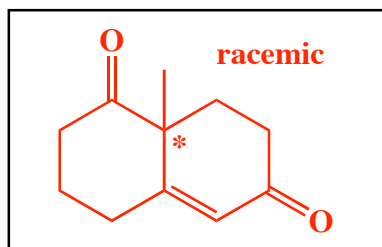
1) 1.0 Eq. NaOEt



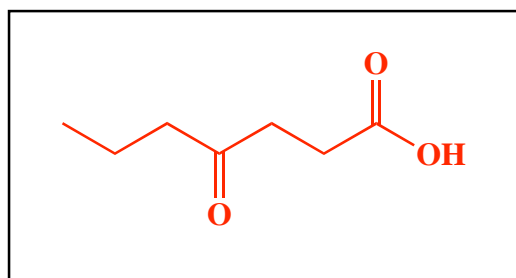
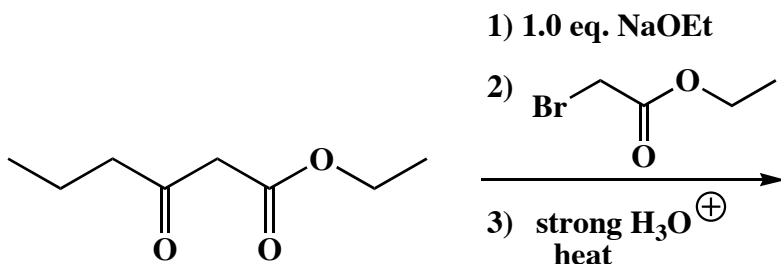
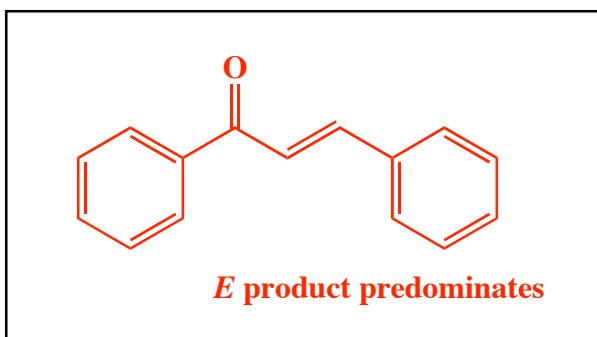
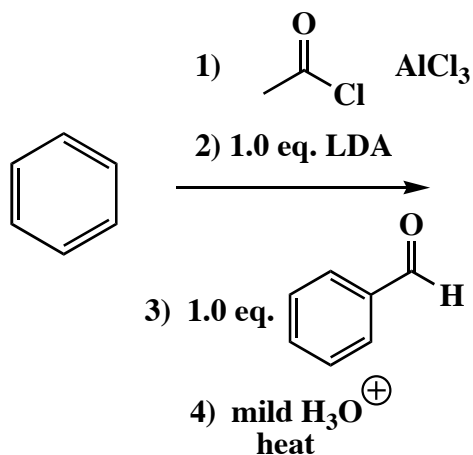
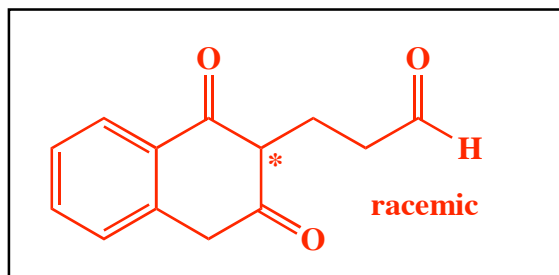
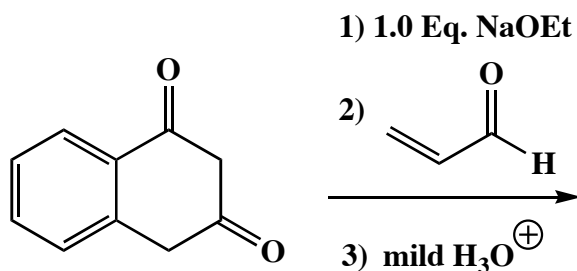
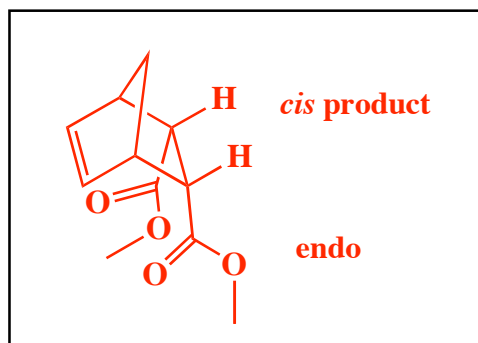
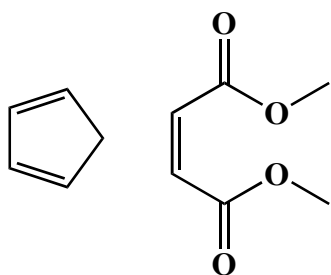
1) 1.0 Eq. NaOEt

3) mild H_3O^+ 

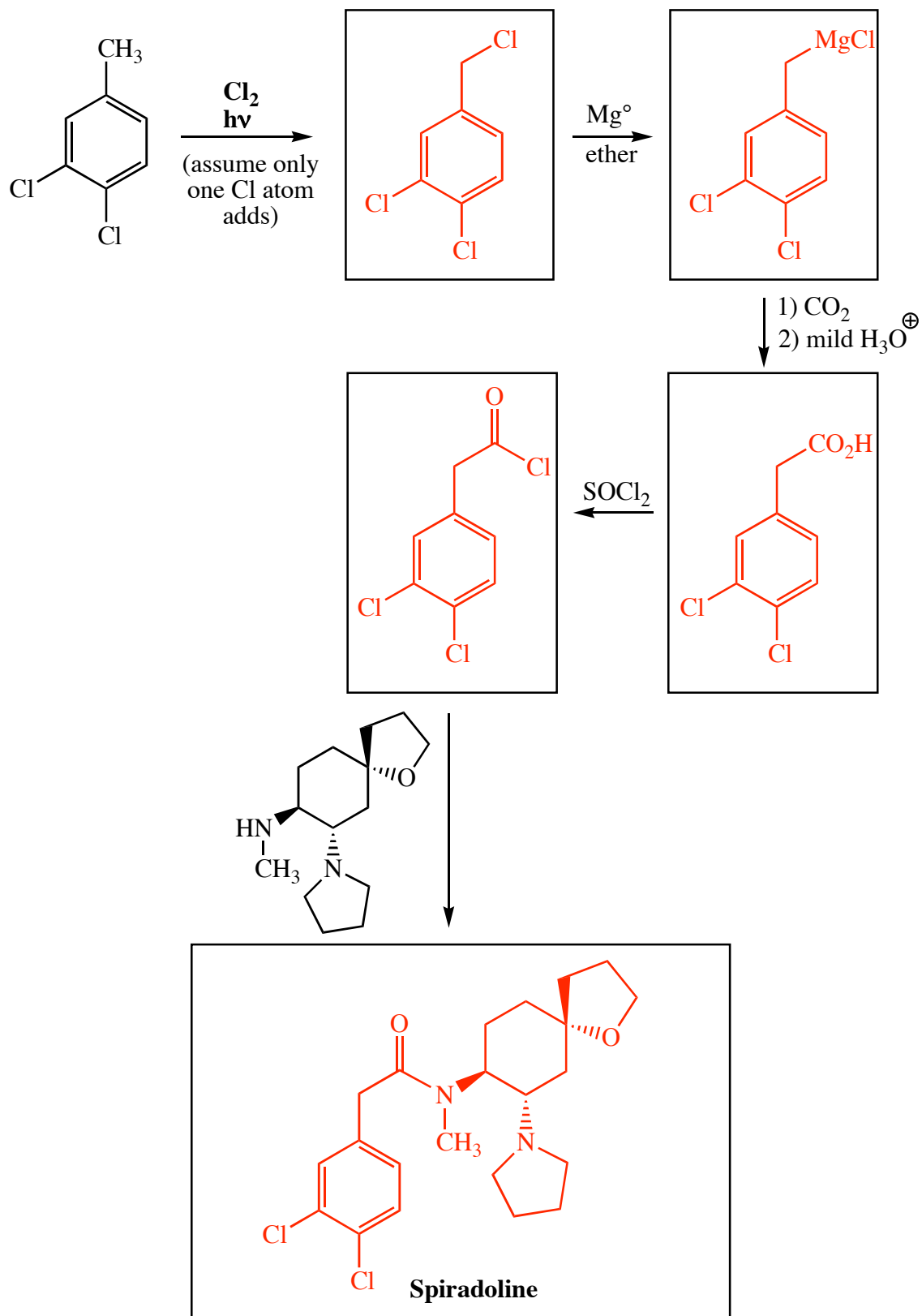
1) cat. NaOH

2) mild H_3O^+ 

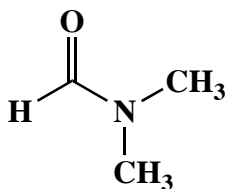
15 cont. (5 pts. each) These are a little harder, so take your time. Write the predominant product or products that will occur for each sequence of transformations. For aldol reactions, assume dehydration takes place and you must draw both *E* and *Z* products unless one predominates by a substantial margin. Label any new chiral centers with an asterisk and write "racemic" if appropriate.



16. (17 pts) Here is the end of an actual synthesis of a powerful opioid analgesic called spiradoline. Fill in the boxes with the appropriate molecules. Use wedges and dashes to indicate the appropriate stereochemistry.



17. (10 points) *N,N*-Dimethylformamide (DMF) is a very popular solvent.



(*N,N*-Dimethylformamide (DMF))

A) How many different signals would you expect in the $^1\text{H-NMR}$ spectrum of DMF taken at room temperature? In no more than two sentences, explain your answer.

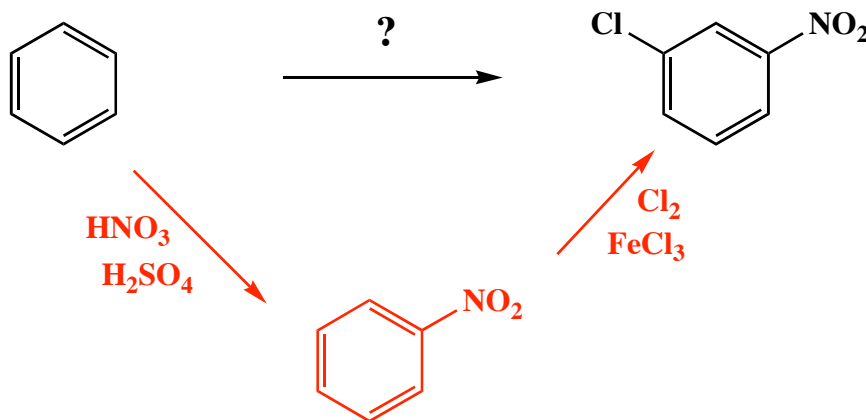
There will be three signals, one from the H atom and one from each of the two methyl groups. The methyl groups are not equivalent because amide bonds do not rotate at room temperature.

B) Would you expect DMF to be good at dissolving polar molecules? In no more than two sentences explain your answer.

Yes, DMF is good at dissolving polar molecules because the strong dipole moment of the C=O bond allows for strong solvation of other molecules that are polar (have bonds with large dipole moments). The carbonyl oxygen can also take part in H bonding with molecules that have hydrogen bond donor groups (O-H, N-H, etc.).

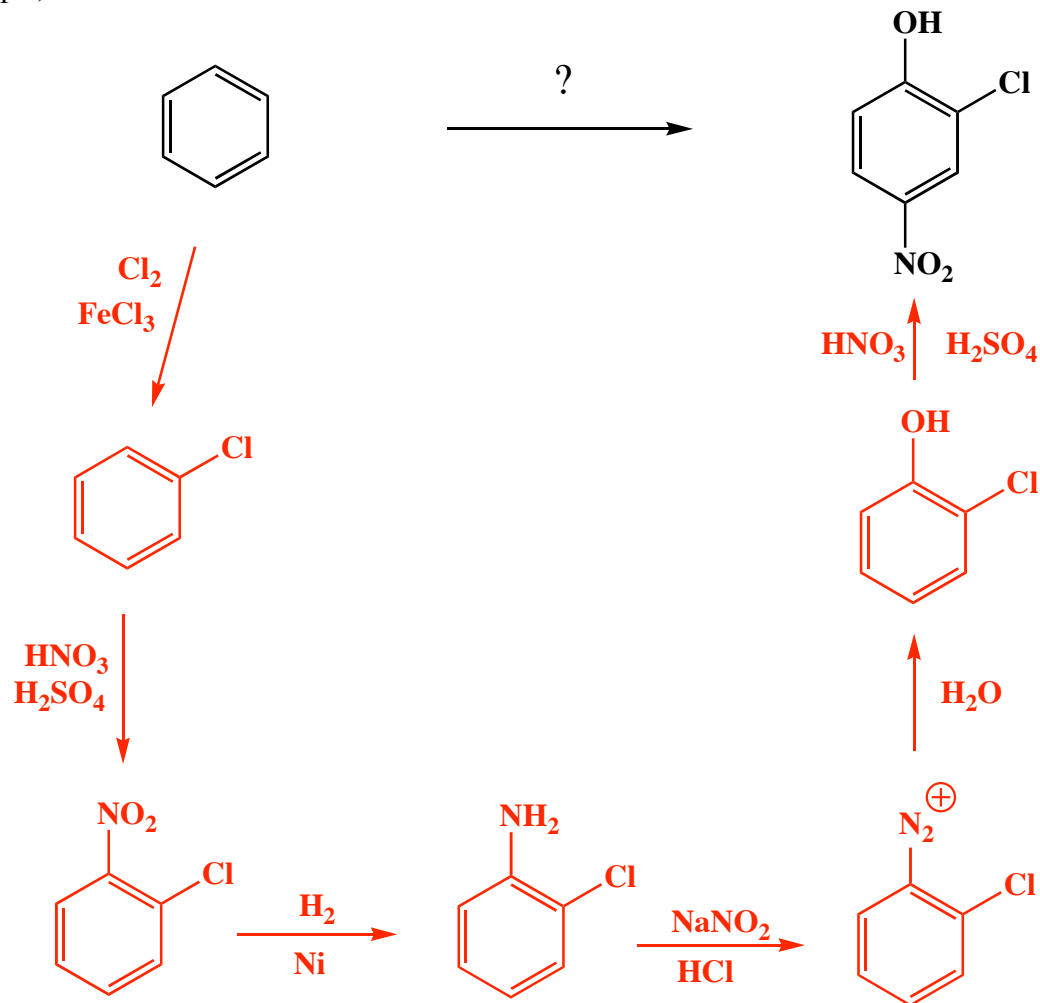
18. Using any reagents turn the starting material into the indicated product. All the carbons in the product must come from the given starting material or starting materials. Draw all molecules synthesized along the way. When in doubt, draw the molecule! If an ortho/para mixture will be the major products of a reaction, you can choose whether you would like to isolate the ortho or para product for your synthesis.

A) (4 pts)



18. Using any reagents turn the starting material into the indicated product. All the carbons in the product must come from the given starting material or starting materials. Draw all molecules synthesized along the way. When in doubt, draw the molecule! If an ortho/para mixture will be the major products of a reaction, you can choose whether you would like to isolate the ortho or para product for your synthesis.

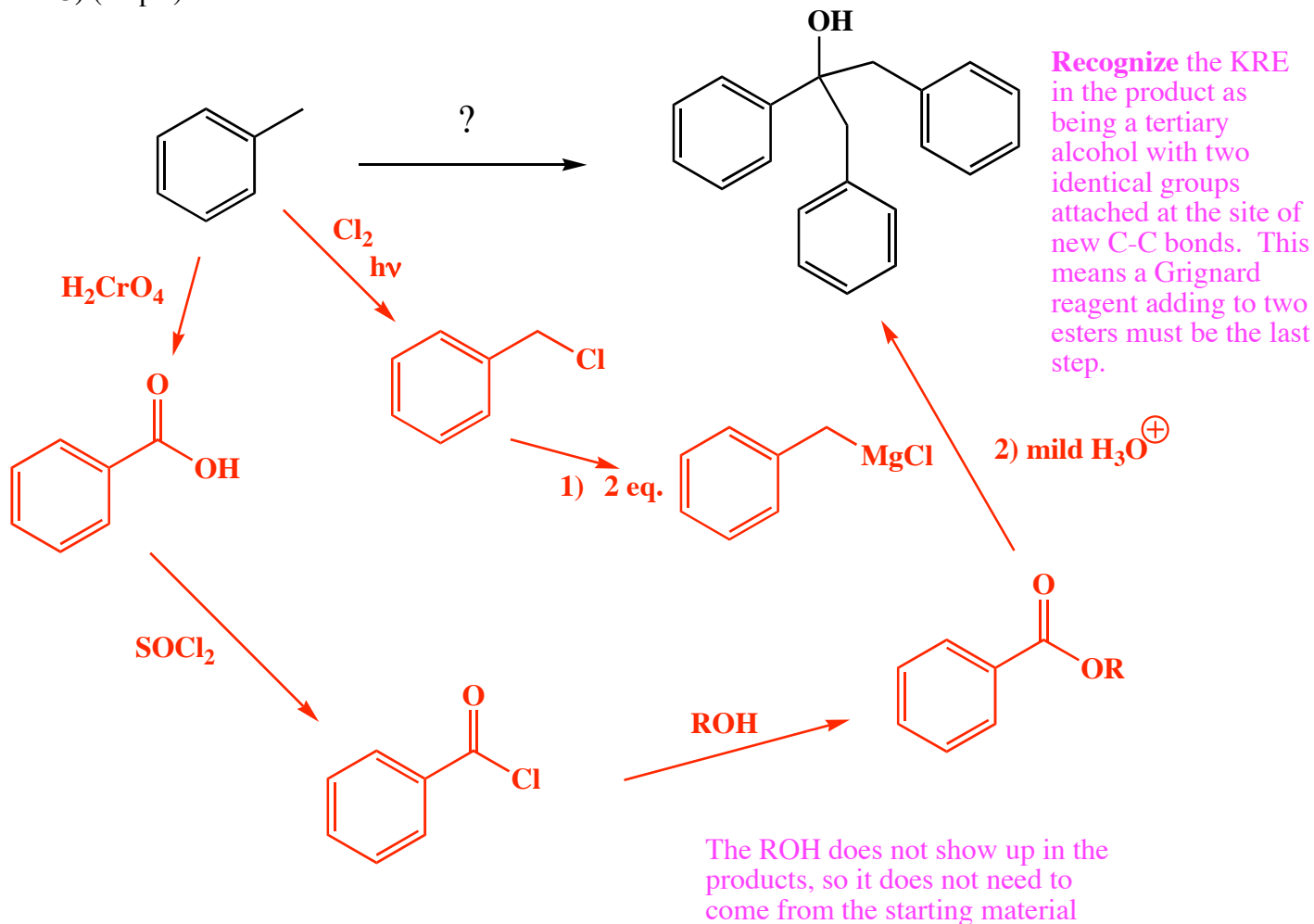
B) (16 pts)



There are more than one correct answer to this one. For example, it is also correct to create the diazonium ion first, followed by conversion to phenol, then addition of the Cl atom and nitro group in any order.

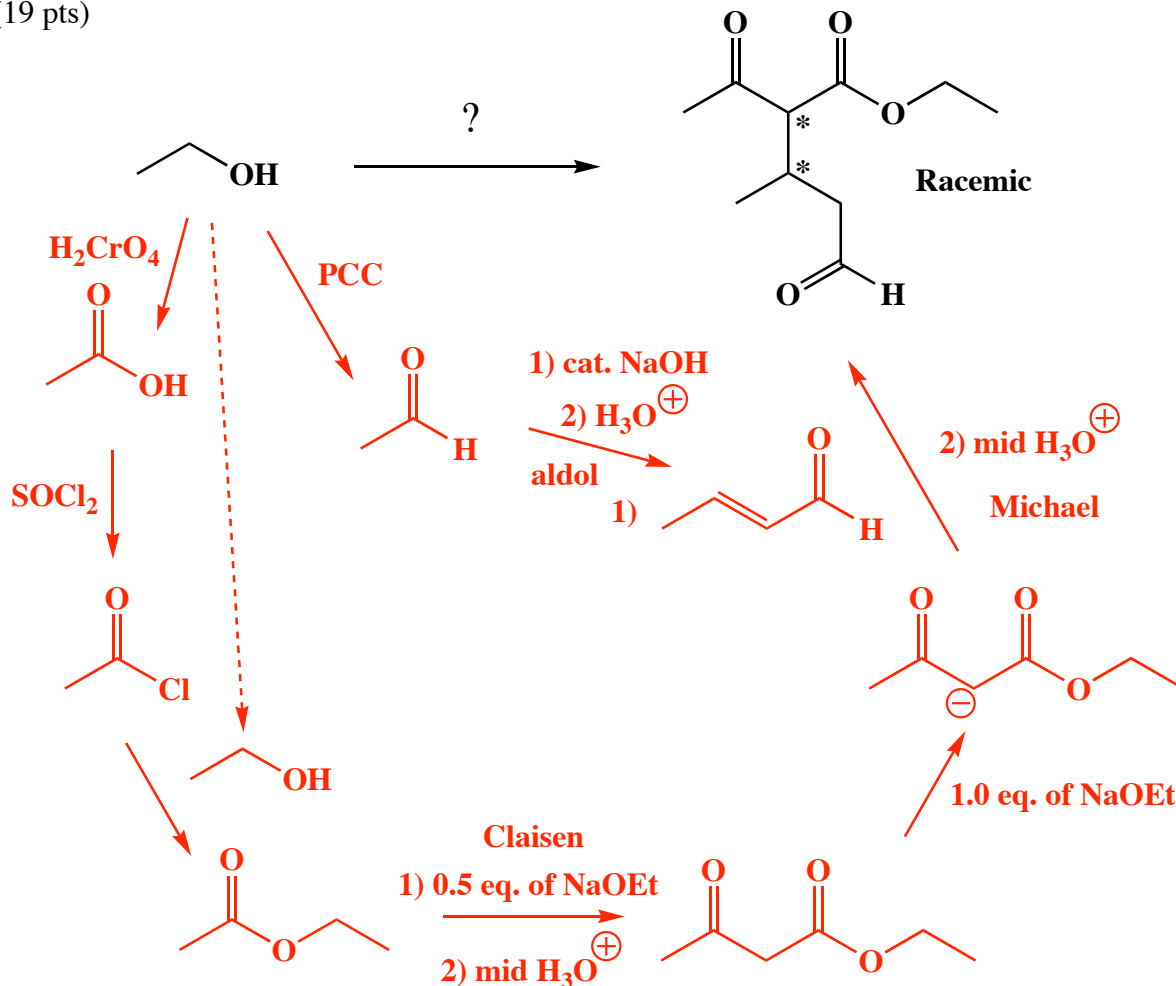
18. Using any reagents turn the starting material into the indicated product. All the carbons in the product must come from the given starting material or starting materials. Draw all molecules synthesized along the way. When it doubt, draw the molecule! If an ortho/para mixture will be the major products of a reaction, you can choose whether you would like to isolate the ortho or para product for your synthesis.

C) (16 pts)



18. Using any reagents turn the starting material into the indicated product. All the carbons in the product must come from the given starting material or starting materials. Draw all molecules synthesized along the way. When in doubt, draw the molecule! If an ortho/para mixture will be the major products of a reaction, you can choose whether you would like to isolate the ortho or para product for your synthesis.

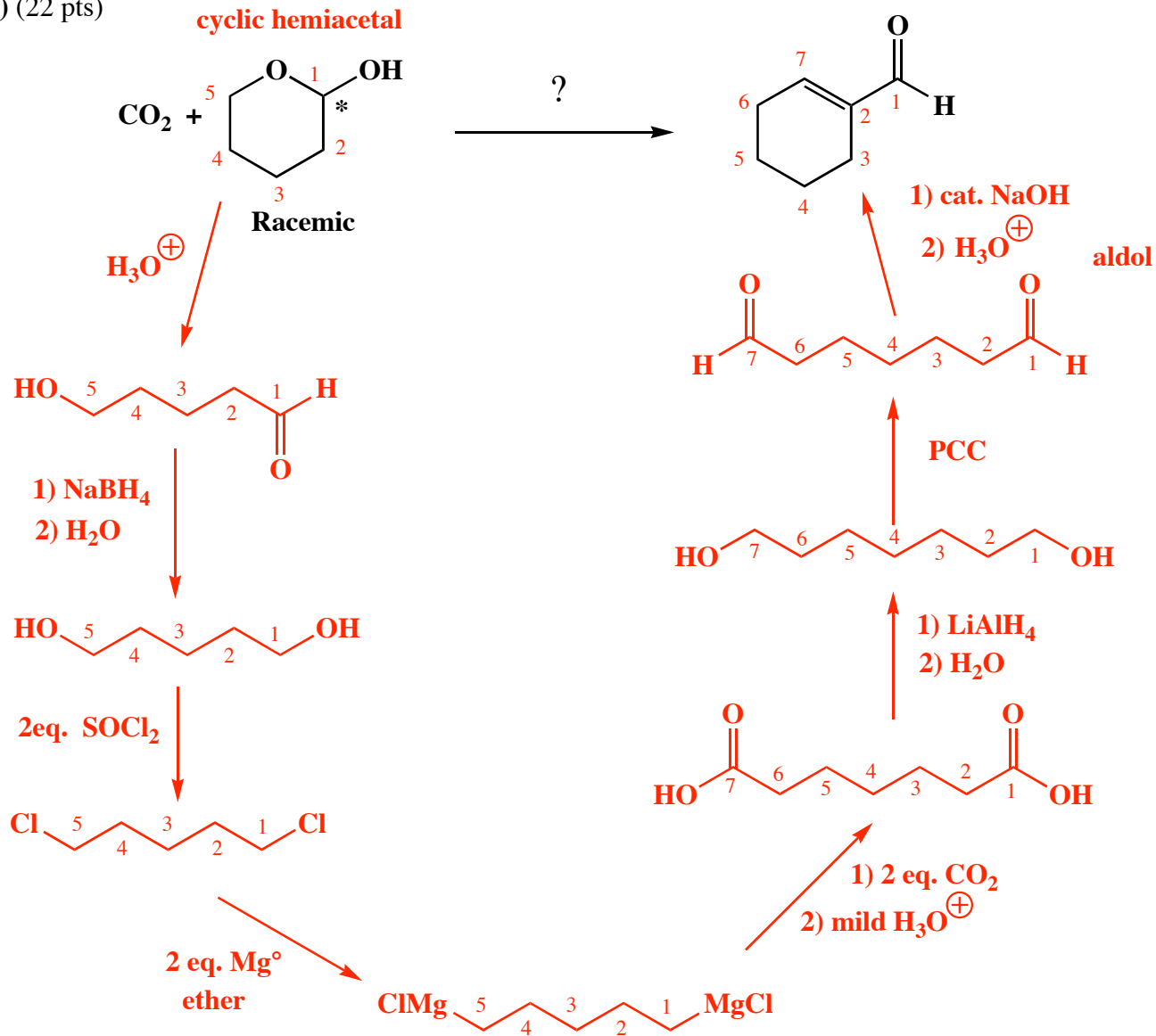
D) (19 pts)



Recognize the KRE of the product as a nucleophile added β to the carbonyl (aldehyde), meaning a Michael reaction was used. The two pieces of the Michael reaction are an α,β unsaturated aldehyde and the anion of a β -ketoester, which are themselves KREs of an aldol reaction and Claisen condensation, respectively. Analyzing the structures of the α,β unsaturated aldehyde and β -ketoester reveals that they can each be derived from two carbon starting materials, available from ethanol as shown. This problem illustrates the power of enolate reactions to construct large, complex molecules from relatively simple starting materials,

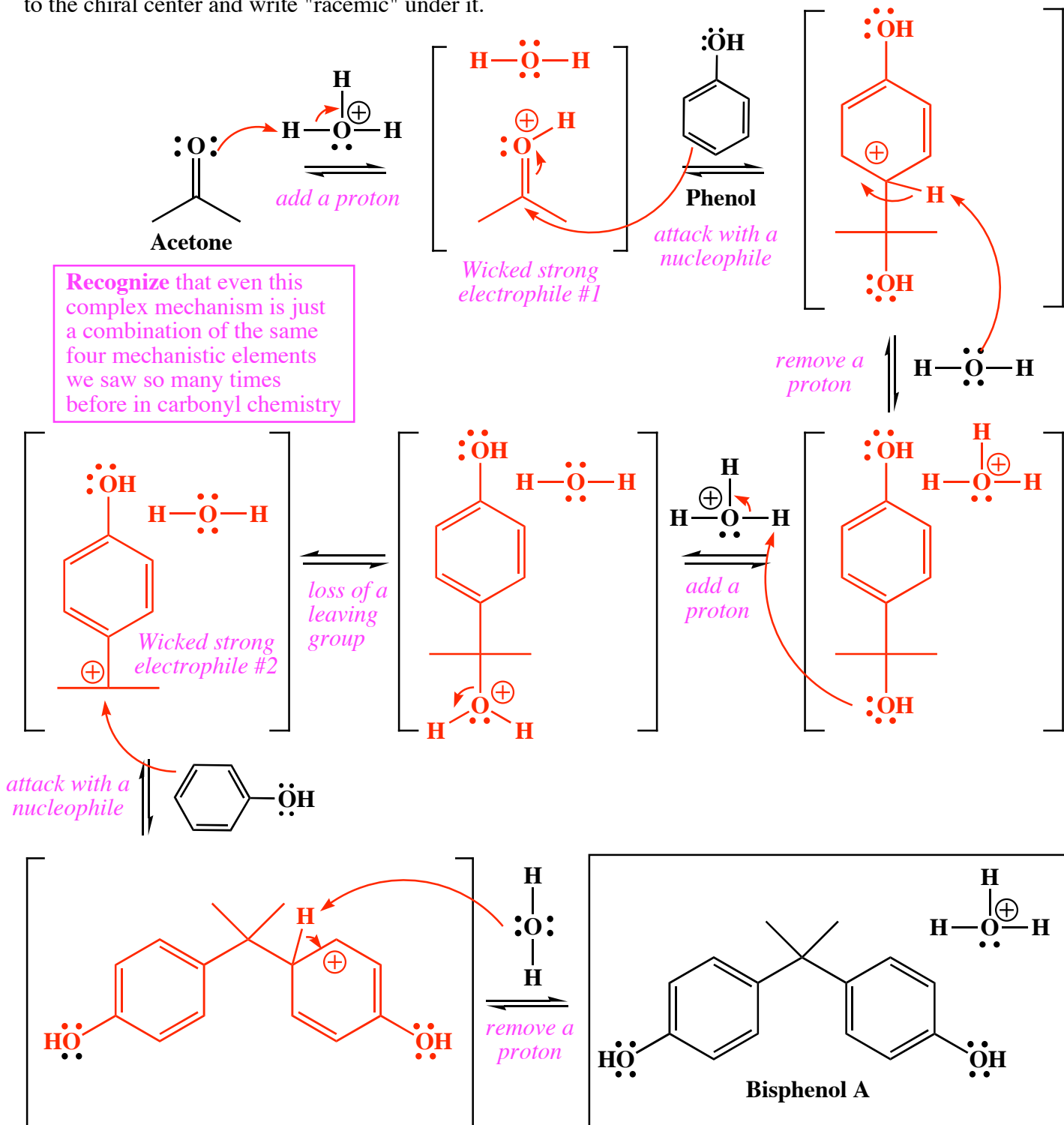
18. Using any reagents turn the starting material into the indicated product. All the carbons in the product must come from the given starting material or starting materials. Draw all molecules synthesized along the way. When it doubt, draw the molecule! If an ortho/para mixture will be the major products of a reaction, you can choose whether you would like to isolate the ortho or para product for your synthesis.

E) (22 pts)



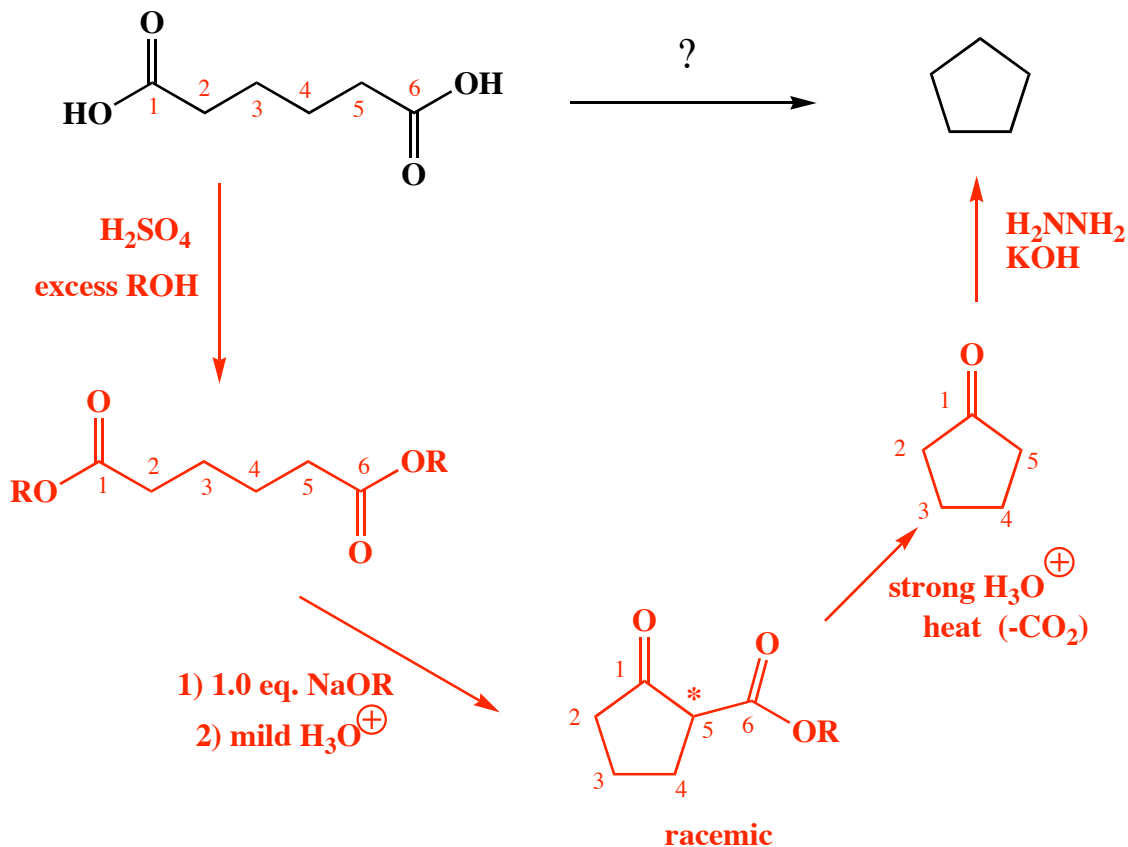
Recognize the product as a cyclic α,β unsaturated aldehyde, the KRE of an intramolecular aldol reaction taking place on a dialdehyde. Counting carbons in the product reveals 7 carbons in the dialdehyde. The starting material has only five carbons, so two carbons must be added using CO_2 . **Recognize** the starting material as a cyclic hemiacetal. Therefore, propose that the cyclic hemiacetal is opened in acid followed by the sequence of reduction to the 1,5-diol, conversion to the dihalide then the di-Grignard reagent. Reaction with CO_2 gives a diacid of seven carbons, that can be reduced to the 1,7 diol then oxidized to the desired seven carbon dialdehyde using PCC.

19. (24 pts) Here is an all-time first for my class. This is an "apply what you know" mechanism question. Even though you have not seen this before, **all of the steps are related to ones you have seen.** **Bisphenol A** has been in the news lately for concerns about health as it leeches out of plastic Nalgene water bottles. Complete the mechanisms below that shows how bisphenol A is synthesized from phenol and acetone in strong acid. Use arrows to show the movement of all electrons, and be sure to draw all lone pairs of electrons and all formal charges. If a racemic product is formed, just put an asterisk (*) next to the chiral center and write "racemic" under it.



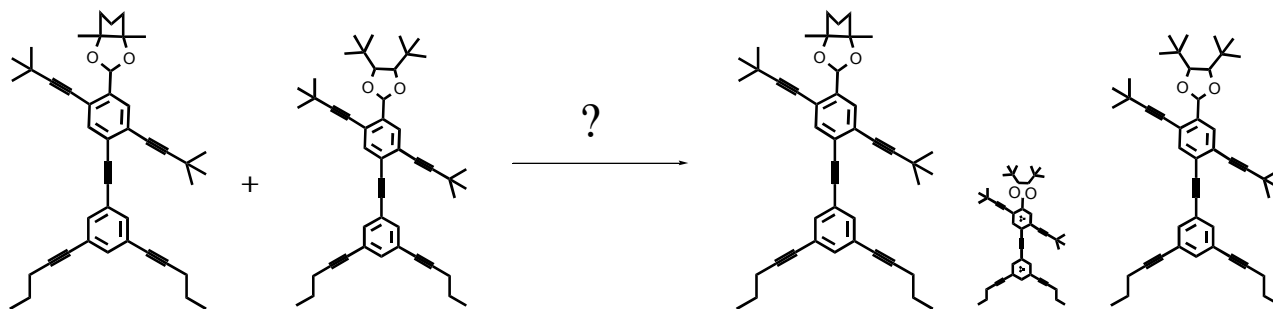
20. I think this one is a real challenge and it is not worth a lot of points so I wanted you to save it until last. Using any reagents turn the starting material into the indicated product. All the carbons in the product must come from the given starting material or starting materials. Draw all molecules synthesized along the way. When it doubt, draw the molecule!

(10 pts)



In many ways this is the hardest synthesis problem because the KRE (a β keto ester) for the Claisen reaction was removed by the last reduction step. Nevertheless, we wanted you to **recognize** that the product is a simple five membered ring meaning that one carbon atom must be lost from the starting material (that contains six carbons in a chain). The best way you know to lose one carbon atom is to heat a β keto acid or β diacid to remove CO_2 . Because a cyclic β keto acid is the KRE for a Dieckmann condensation, propose to convert the diacid to a diester followed by a Dieckmann condensation. Hydrolysis of the ester groups with heating in aqueous acid leads to loss of CO_2 and formation of cyclopentanone, that is reduced with a Wolff-Kishner reaction (or Clemmensen) to give the cyclopentane product.

Synthesis Question for Chemistry Nerds



We hoped this would send you home with a smile. I realize it is a pretty nerdy form of humor, but what the heck, we are chemists.

Page	Points
1	(30)
2	(21)
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6	(26)
7	(28)
8	(21)
9	(46)
10	(44)
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(HW score + Exam Grade) \implies