

Chemistry 41c

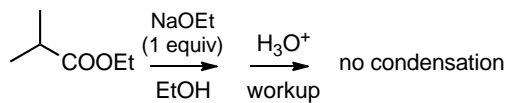
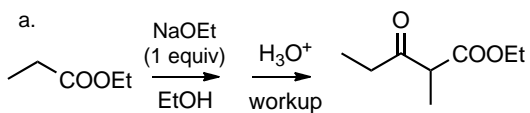
Spring 2013

Final Exam Practice Material

Sample problems & answer key

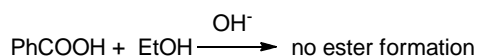
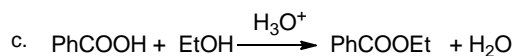
Disclaimer: These sample questions relate most closely to the chapters covered thus far in 41c: 18 (organometallics), 19, 20, 21, 22, 23, 24, and 26. The length of this document does not imply the length of the actual final exam, which is written as a four-hour take-home exercise. The final exam questions will focus primarily on 41c material, but material from earlier quarters is certainly fair game. You will be allowed to only use the following when working your final exam: a calculator, molecular models, Loudon's text & solutions manual, and any class notes associated with 41a-c.

1. (63 points) Shown below are six pairs of reactions in which only the first reaction of each pair is successful. First, using good curved arrow notation, write a complete mechanism for the successful reaction. Then, explain clearly and fully (using drawings where appropriate) why the second reaction does not occur. Simply stating a fact (such as "acid is required") or muttering magic words out of context (such as "resonance" or "inductive") is not a clear and full explanation.

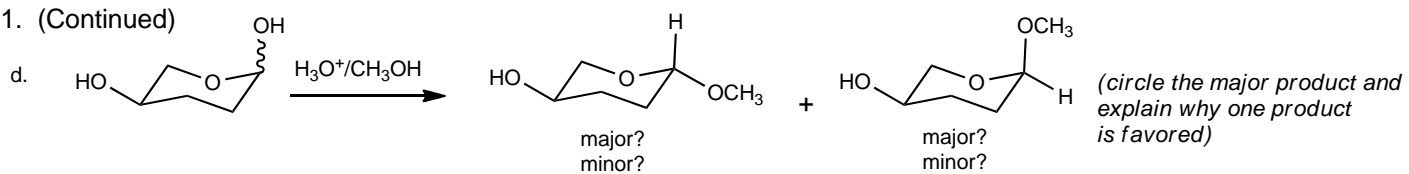


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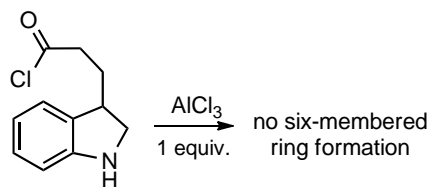
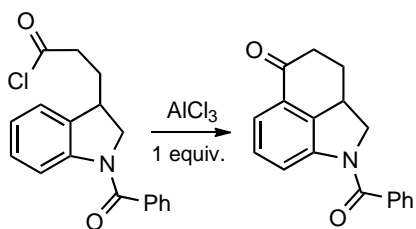
This problem falls outside the scope of 41c.



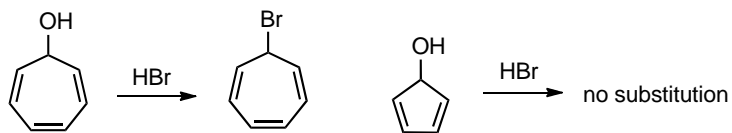
1. (Continued)



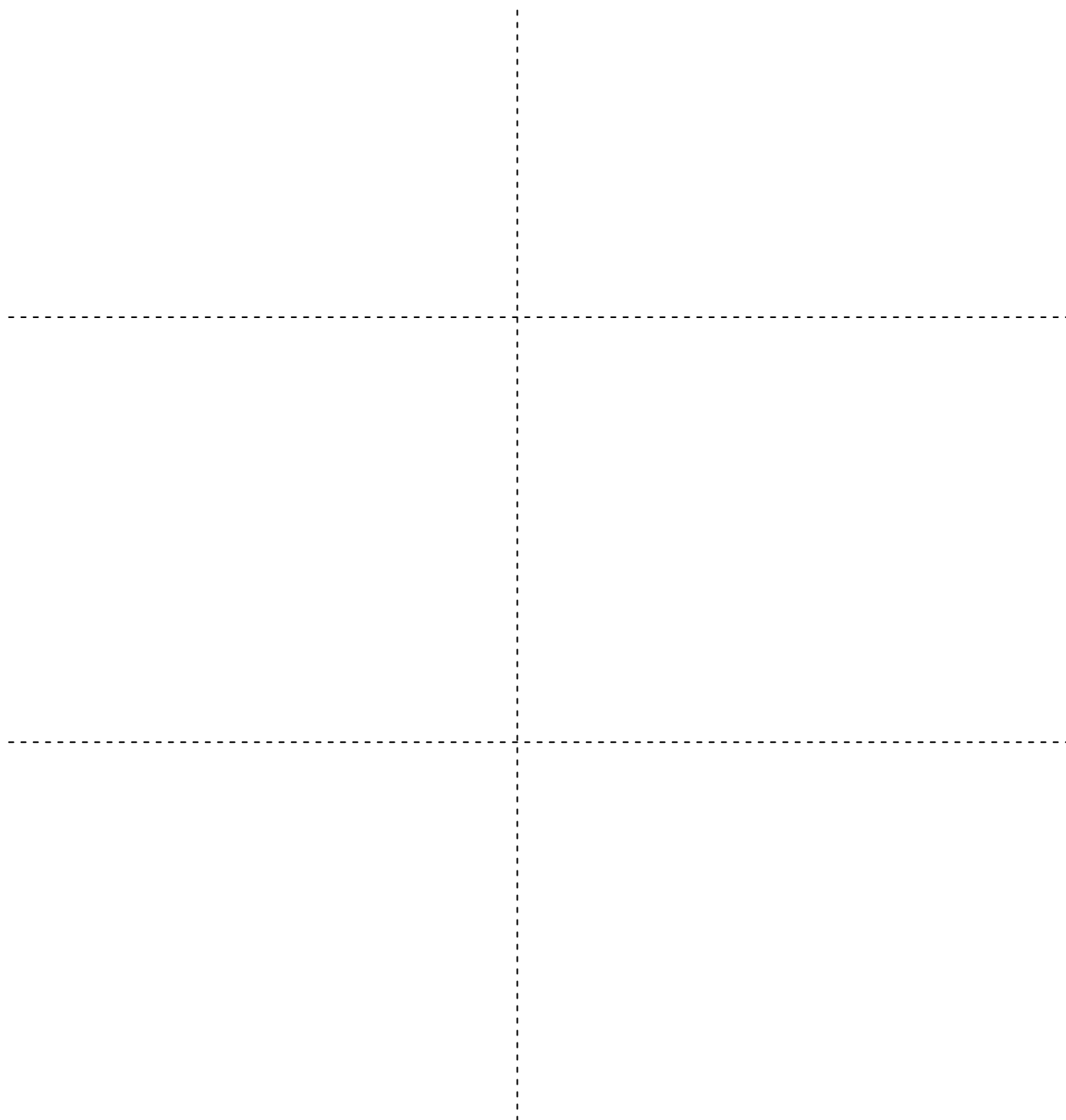
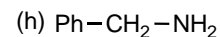
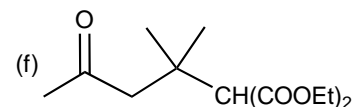
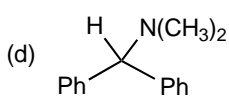
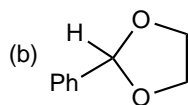
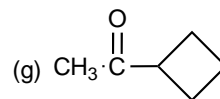
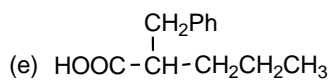
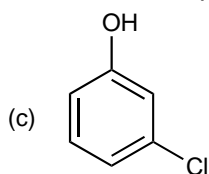
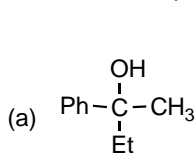
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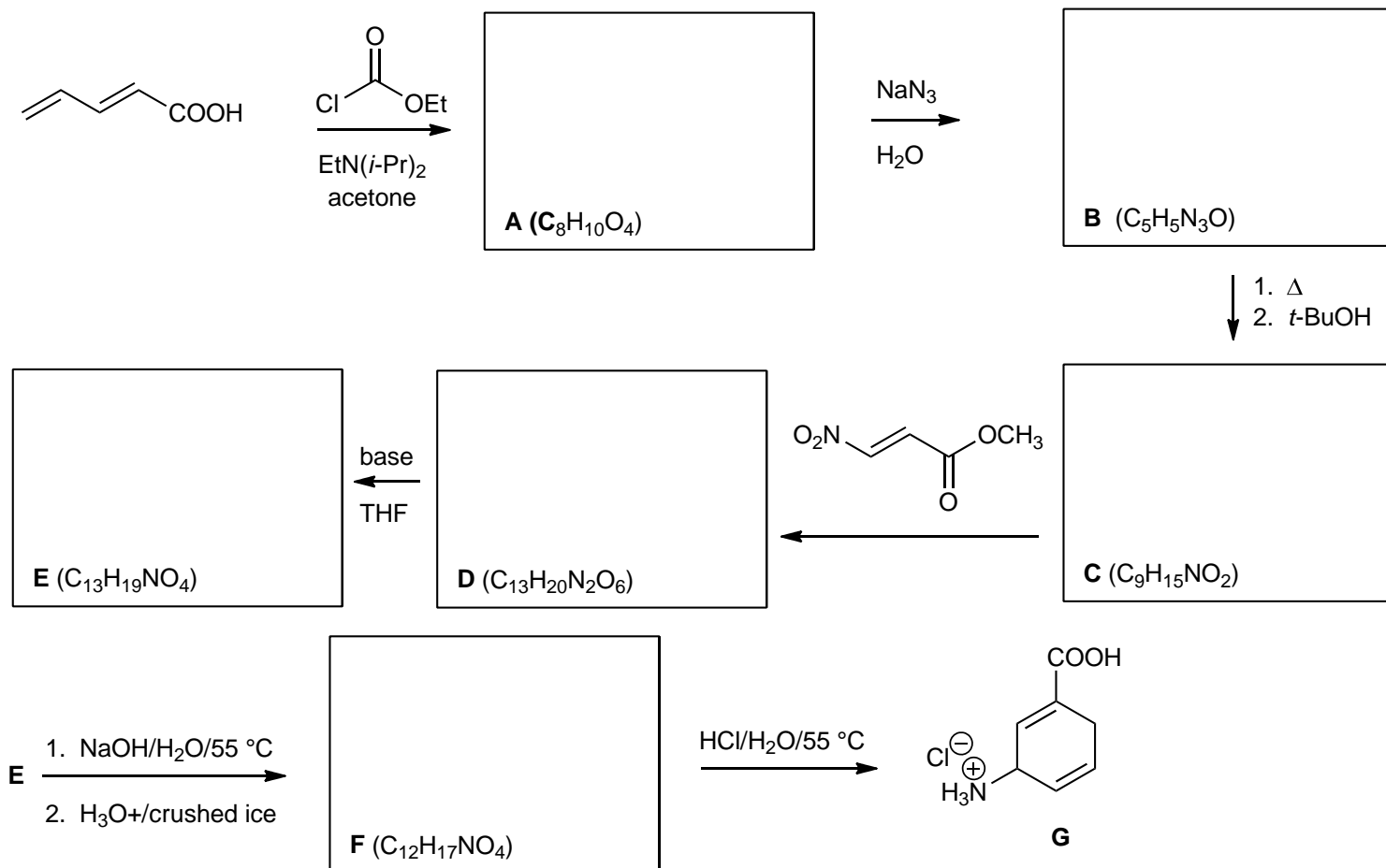
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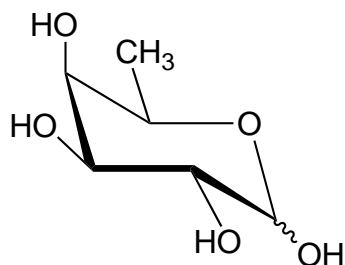
2. (7 pts each) Show how you would synthesize the following molecules. The allowed starting materials are benzene, ethyl acetoacetate, diethyl malonate, other organic materials have three or fewer carbons, and any inorganic materials that you may need. A compound made for one part may be used for another part without your having to make it again. Mechanisms and explanations are not required. Each of these requires at least two steps. Do any six of the eight parts.



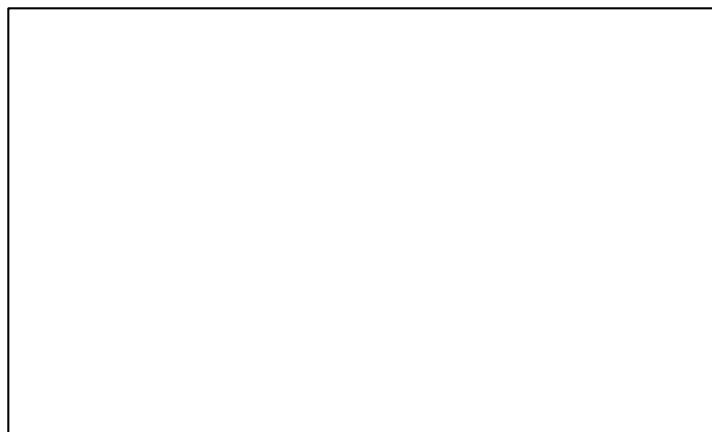
3c. γ -Aminobutyrate transaminase (GABA-T) is the key enzyme controlling the metabolism of γ -aminobutyric acid (GABA), a mammalian inhibitory neurotransmitter. In the following synthesis of the hydrochloride salt of a putative GABA-T inhibitor (**G**), propose structures for intermediates A-F. Indicate relative stereochemistry. (18 points)



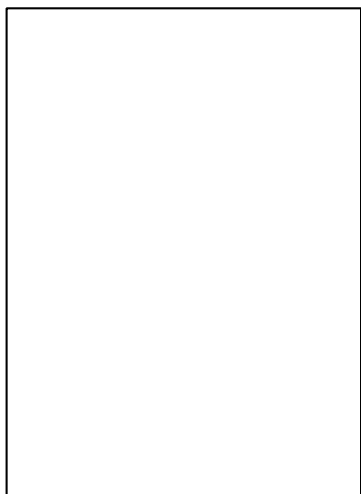
1. Consider (+)-fucopyranose: (a-g, 5 pts each)



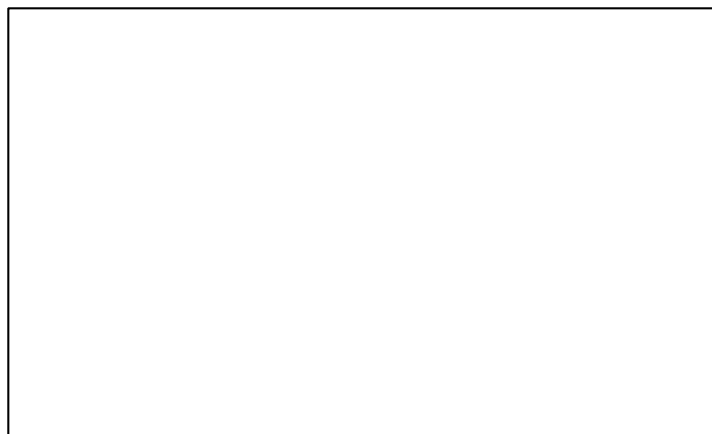
a. Write down the Haworth structure of (+)- α -fucopyranose:



b. Draw the Fischer Projection formula for (+)-fucose:



c. Draw a Haworth structure of β -fucofuranose:

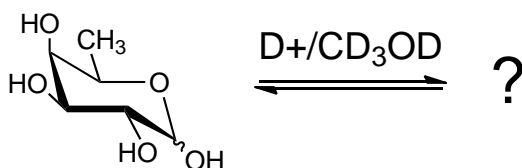


c. Is (+)-fucose a D or L sugar ?

e. (+)-fucose is allowed to equilibrate under the conditions shown below. Unequal amounts of two fucopyranosides are recovered from the reaction mixture. Write the mechanism for this process and, using chair forms, draw and identify the α - and β -fucopyranosides you expect to form.

f. Circle the pyranoside that you expect to be formed as the major component.

g. Justify your answer in part f by presenting a clearly drawn structural analysis (invoke steric and stereoelectronic effects, if relevant to your argument. Use only chair forms and clearly indicate the 3-D relationship of lone pairs and bonds.

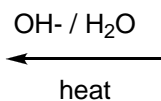
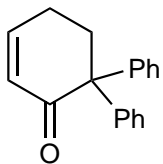


(enter parts e and f here)

7a. What starting materials would you use to make compounds A and B via an intramolecular aldol cyclization? 10 pts

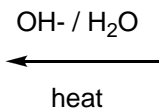
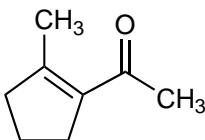
4

A



C

B



D

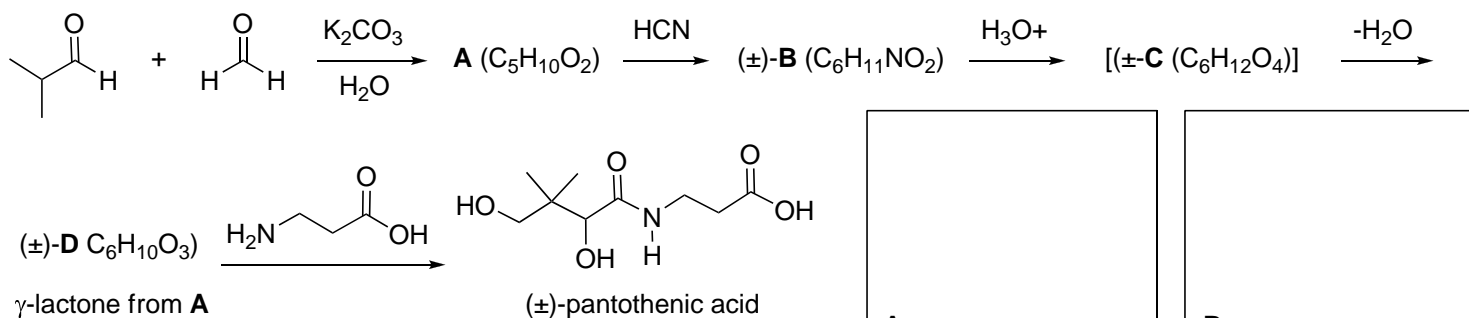
7b. Write a detailed step-by-step mechanism to account for the formation of compound A from C. 10 pts

7c. In your mechanism, **label the retro-aldol step** and push electrons in the appropriate intermediate to show the retro-aldol reaction. 4 pts

7d. Use compound A or B (choose wisely--one would work well and one would not!) and reagents of your own choosing to demonstrate an example of a Michael addition reaction. A detailed mechanism is not necessary--just supply the reagents and the structure of the product. 10 pts

1. Where would you expect to find the labeled oxygen if you carried out an acid-catalyzed hydrolysis of methyl acetate in ^{18}O -labeled water? Write a detailed mechanism to support your answer. (10 pts)

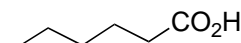
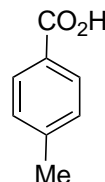
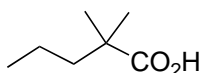
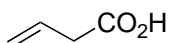
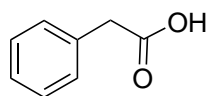
2. (\pm)-Pantethenic acid, an important intermediate in the synthesis of coenzyme A, was prepared by the following route. Give structures for compounds **A-D**: 12 pts



What is the 'name' of the first reaction? (2 pts)

3. The active ingredient of the insect repellent "Off!" is *N,N*-diethyl-*m*-toluamide, $m\text{-CH}_3\text{C}_6\text{H}_4\text{CON}(\text{Et})_2$. Outline a synthesis of this compound starting with *m*-toluic acid. (5 pts)

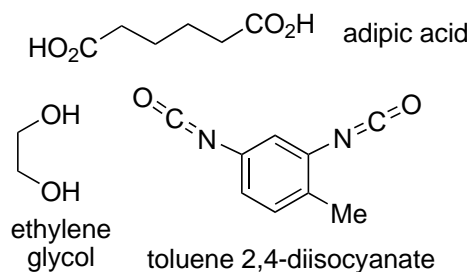
4. Circle the acids that could be prepared by a nitrile synthesis: (5 pts)



5. Using a decarboxylation reaction, outline a synthesis of the following using appropriate starting materials: (6 pts)



6. A typical polyurethane (polycarbamate) can be made by polymerizing adipic acid with an excess of ethylene glycol. The resulting polymer is then treated with toluene 2,4-diisocyanate. (a) Write the structure of the polyurethane. (b) Why is an excess of ethylene glycol used in making the polyester? (8 pts)



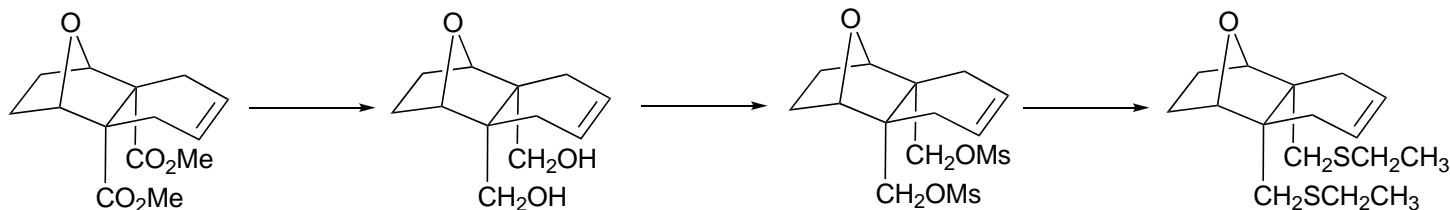
7. When polyurethane foams (perhaps the type you are sitting on at this very moment) are fabricated, a small amount of water is included in the polymerization mixture. The water reacts with one of the monomer molecules to produce a gas, which causes the polymeric material to have trapped bubbles (foam). Use a highly contracted structure (R groups) and explain this chemistry with a mechanism. 8 pts

8. Provided here are the ^1H NMR spectra and IR data for two acyl compounds. Propose a structure for each. (8 pts)

$\text{C}_{10}\text{H}_{12}\text{O}_2$
 ^1H NMR data
 triplet, 1.2 ppm, 3H
 singlet, 3.5 ppm, 2H
 quartet, 4.1 ppm, 2H
 multiplet, 7.3 ppm, 5H
 IR spectrum
 1740 cm^{-1}

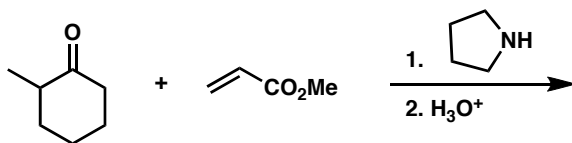
$\text{C}_8\text{H}_{14}\text{O}_4$
 ^1H NMR data
 triplet, 1.2 ppm, 6H
 singlet, 2.5 ppm, 4H
 quartet, 4.1 ppm, 4H
 IR spectrum
 1740 cm^{-1}

9. Suggest reagents (show their structures) for three of the transformations used in Stork's synthesis of Cantheridin: (6 pts)

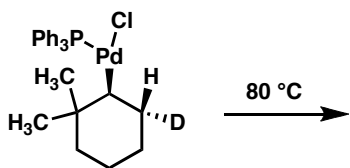


1. Predict the major non-volatile products (if any) of the following reactions or sequences. Clearly mark your answers by placing a **box** around the compound that you believe to be the major product. (5 points each).

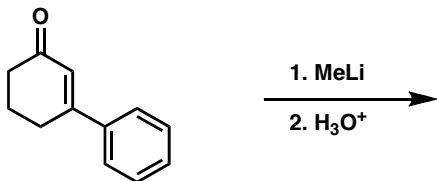
a.



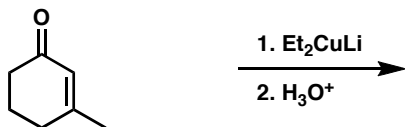
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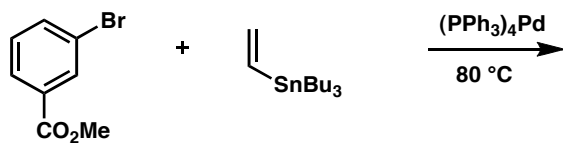
c.



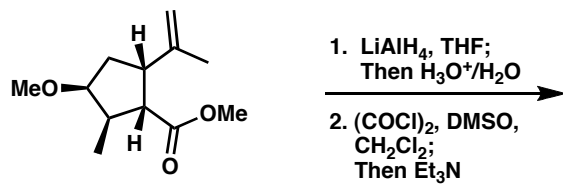
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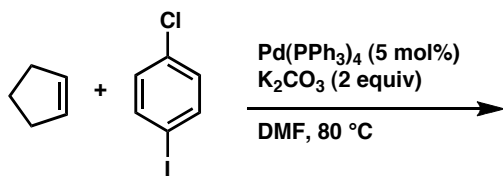
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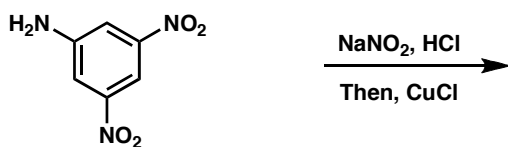
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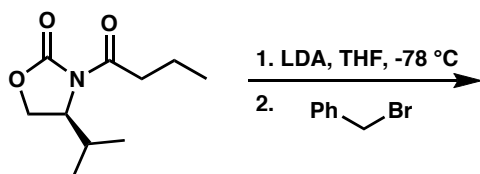
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h.

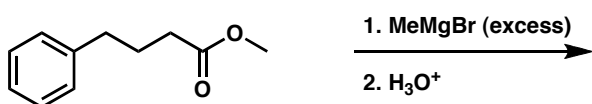


i.



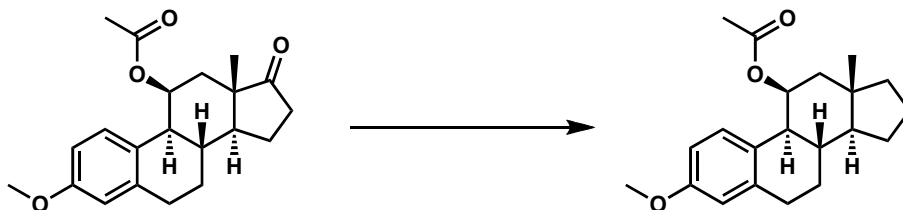
5 point bonus: what is the structure of LDA?

j.

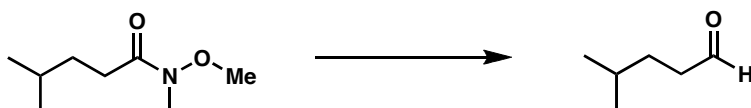


2. Provide reagents for the following transformations. They may be multistep processes, but should not be longer than 5 steps. (5 points each)

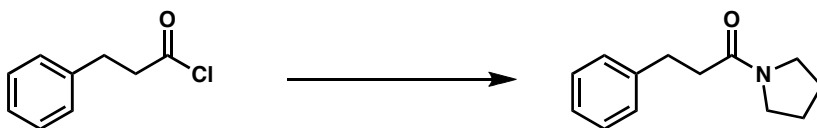
a.



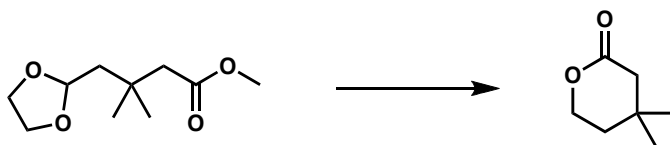
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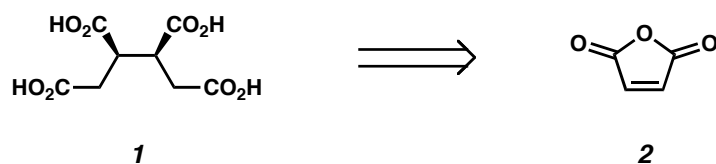
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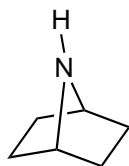


3. Design a synthesis of tetracarboxylic acid **1** starting from maleic anhydride (**2**) and any other materials containing 4 carbons or less. (15 points)



10. A plant biologist friend who studies nitrogen fixation needs access to a supply of pure gaseous nitrogen (N_2) with molecular weight 29. Propose a synthesis of this molecule and specify the chemical source of the ^{15}N isotope (assume that nitrogen is mostly found as the ^{14}N isotope). **Provide a detailed mechanism for your proposed process.** (10 pts)

11. Pomona/Pitzer degree in hand, you happily accept a \$100,000 /yr job with the Oscar Mayer Corporation in the "hot dog development lab." Your first assignment is to work with another new hire and devise a better dog. Your partner hits the additives book while you review the existing ingredient list. Several days pass by. Your partner presents an idea at a group meeting: use Gesundheitamine (an anti-sneeze agent) as an additive: "this way, people who are allergic to hot dogs won't ever even know it", he says. Several minutes pass by as an uncomfortable silence descends upon the room. Out of the corner of your eye you realize the boss is nodding and smiling, somehow impressed with this outlandish proposal. You want no part of it, and can provide sound chemical reasoning as to **why** Gesundheitamine is not an appropriate additive. Start with the ingredient list and provide a detailed **mechanism**, incorporating other chemicals likely to be encountered in the stomach (pH 1.5-2.0), to substantiate your reasoning. This is not an essay question. **It is a mechanism question.** (10 pts)



Gesundheitamine

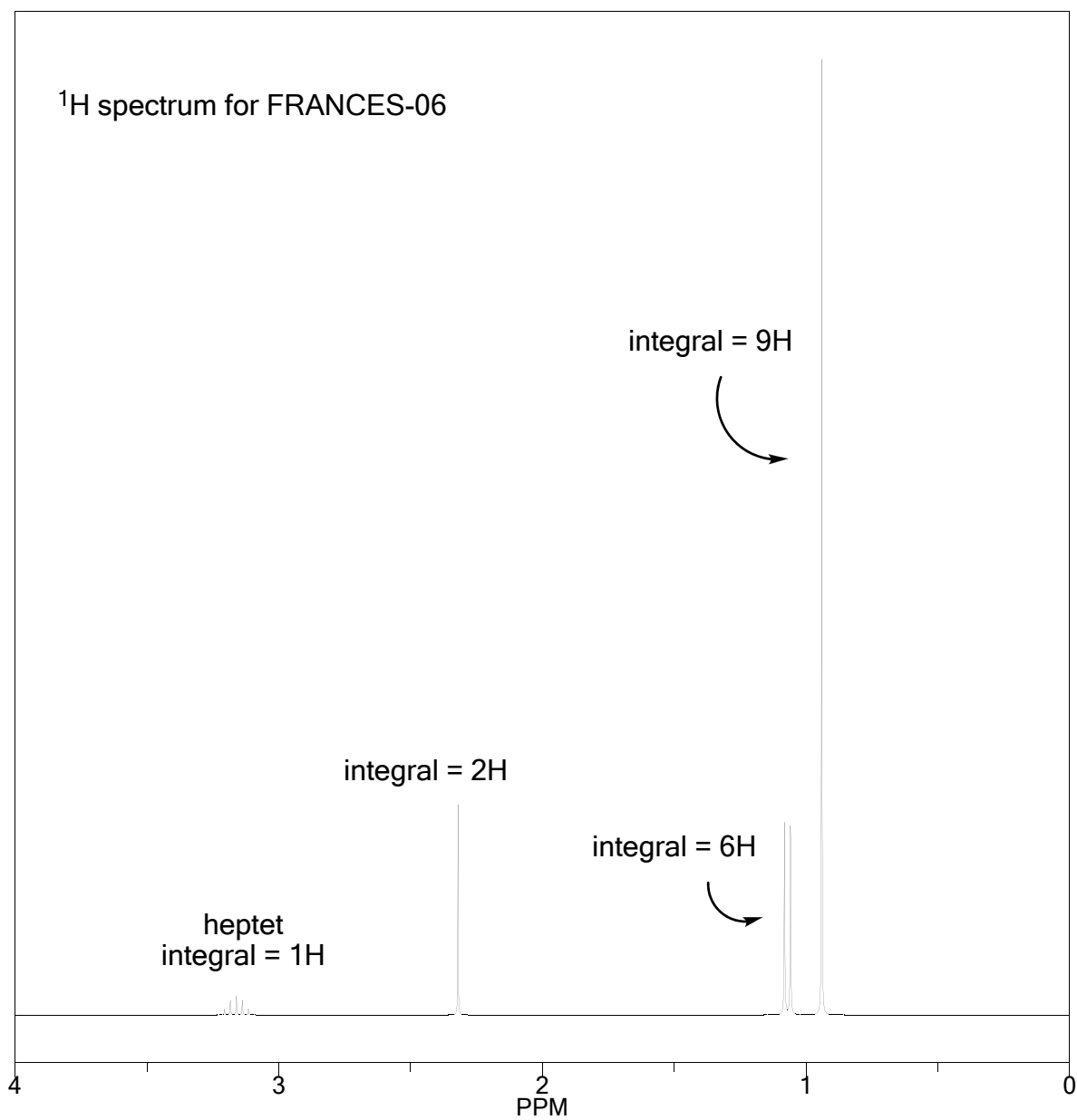
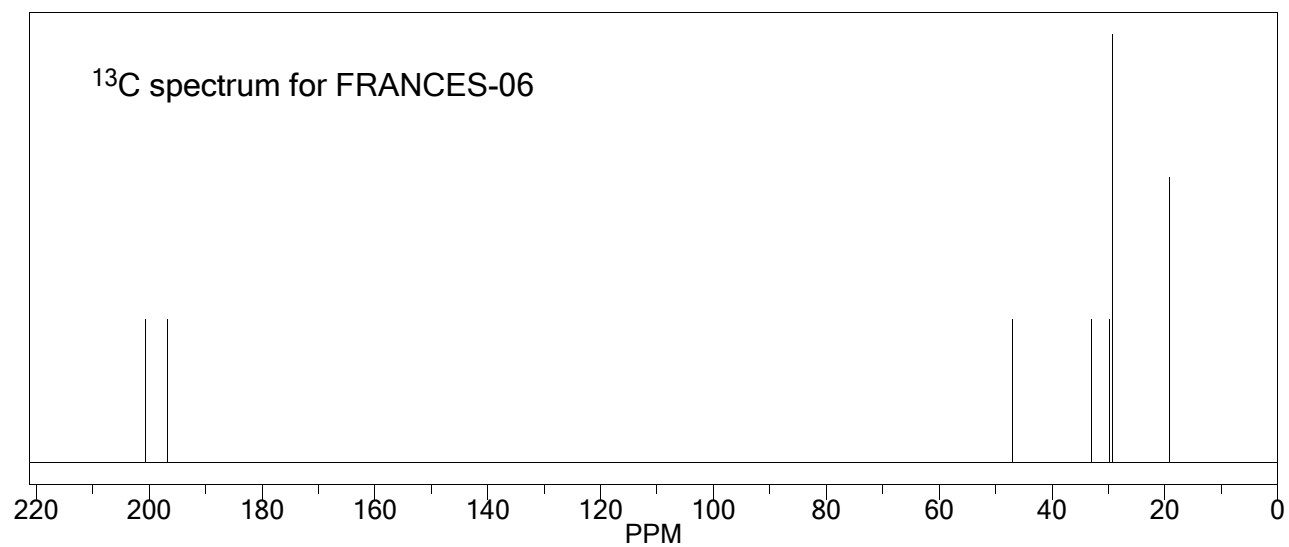
Existing Ingredients: beef, sodium erythrobate, sodium phosphate, sodium nitrite, artificial flavoring.

6. You are presented with a sample exhibiting the following mass-spectral characteristics: $M^+ = 170.13$ (100%), $M+1 = 171.13$ (10.9%). **Sample name = FRANCES-06.** You record proton and carbon NMR spectra (see next page). What is the structure of the compound? This is not an essay question--use the space provided to show me your thought processes as you solve this problem. 14 pts

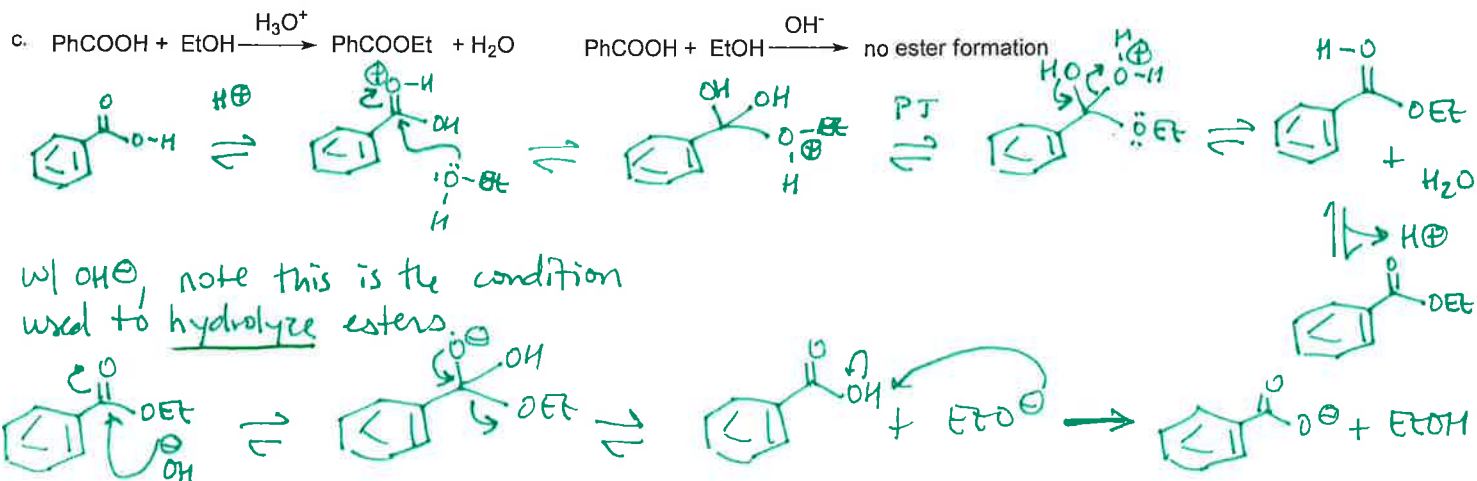
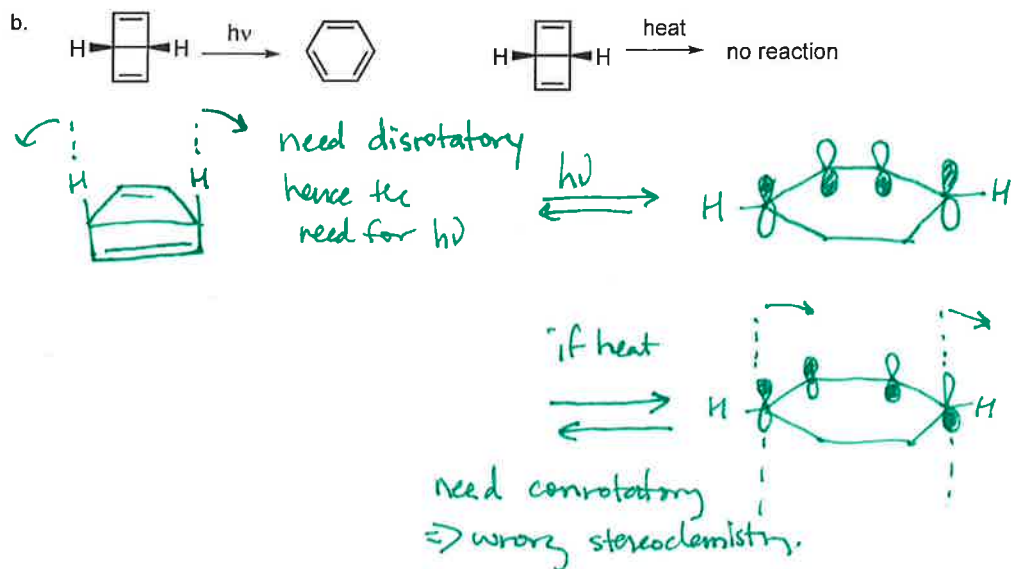
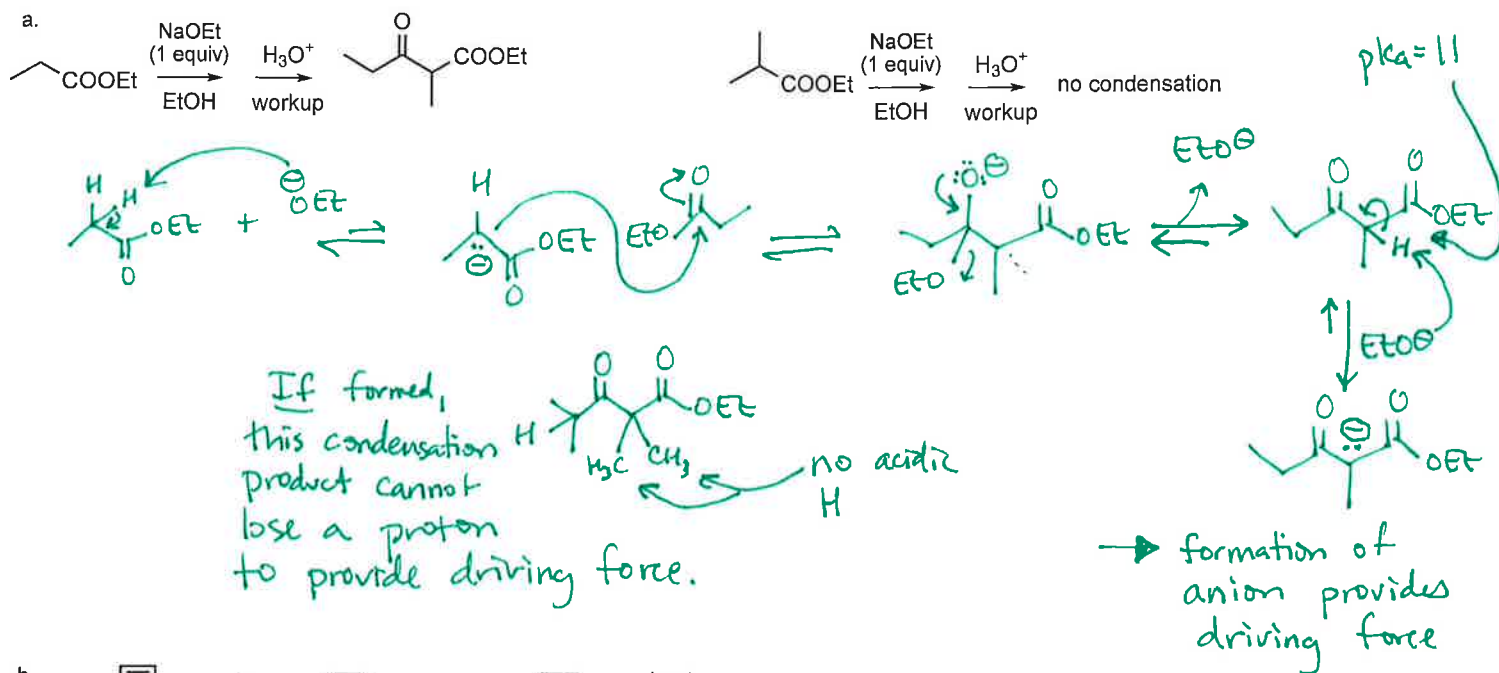
7. Sketch and assign the expected proton NMR spectrum for 2-bromoethanol. 14 pts

5 ppm

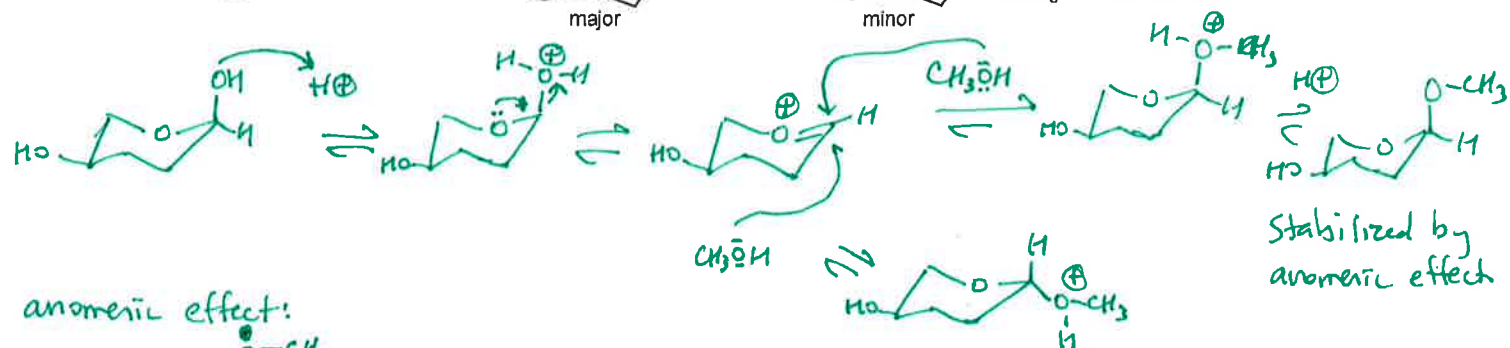
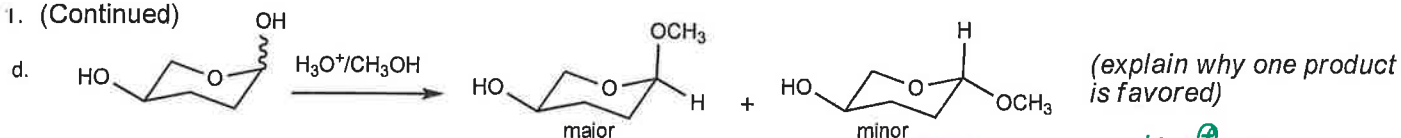
0 ppm



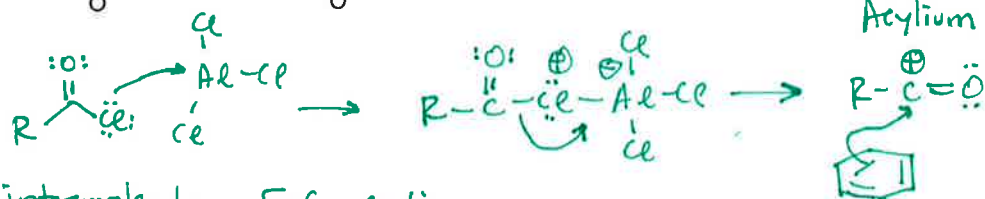
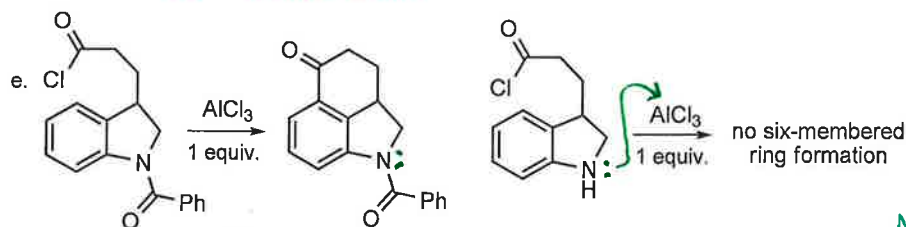
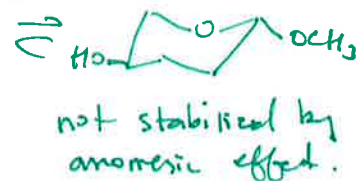
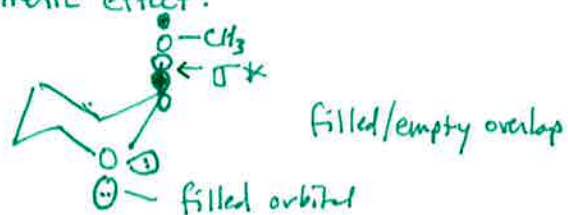
1. (63 points) Shown below are six pairs of reactions in which only the first reaction of each pair is successful. First, using good curved arrow notation, write a complete mechanism for the successful reaction. Then, explain clearly and fully (using drawings where appropriate) why the second reaction does not occur. Simply stating a fact (such as "acid is required") or simply muttering magic words out of context (such as "resonance" or "inductive") is not a clear and full explanation.



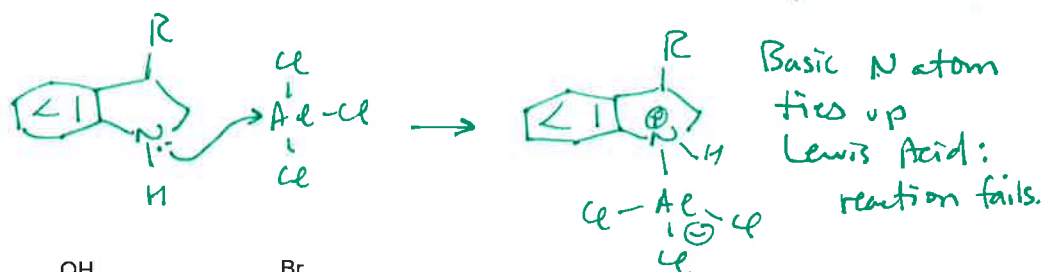
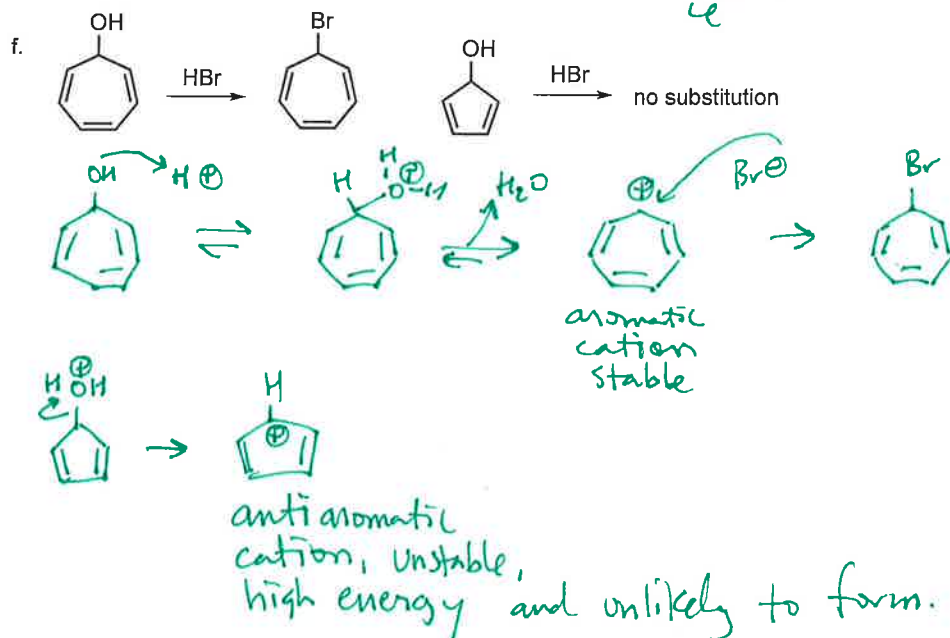
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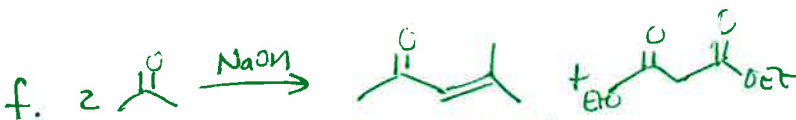
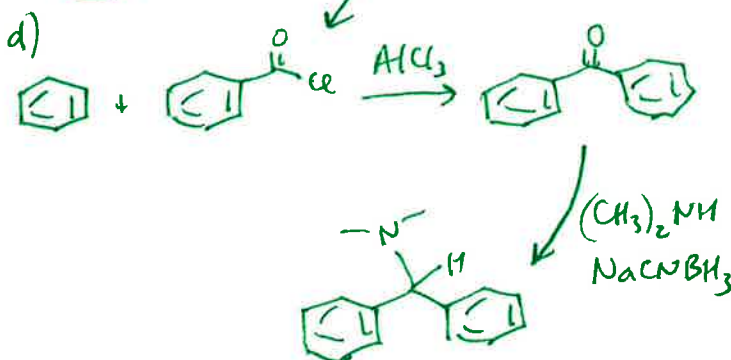
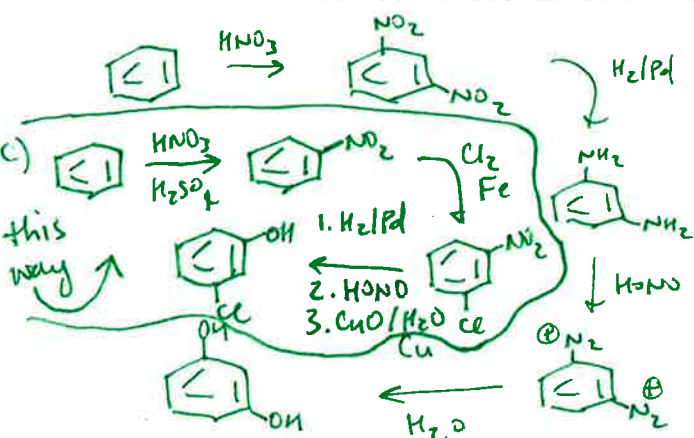
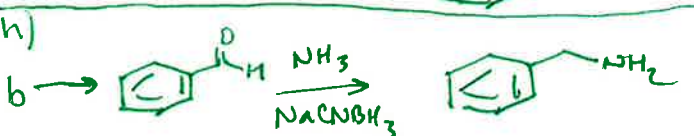
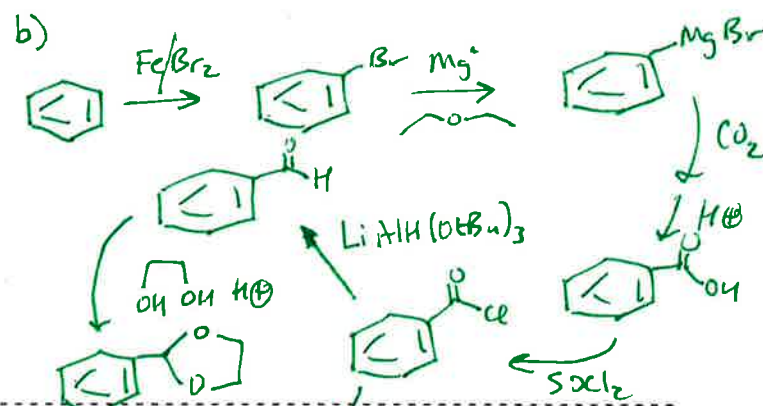
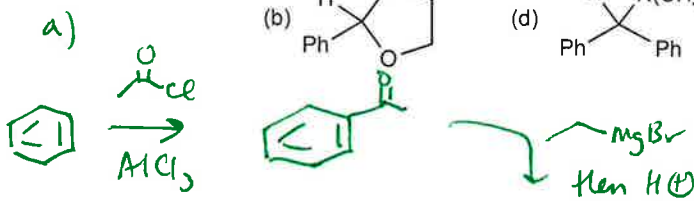
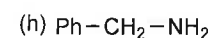
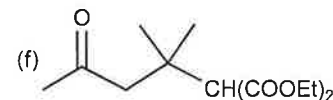
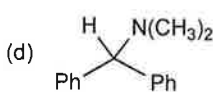
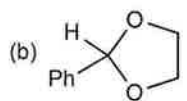
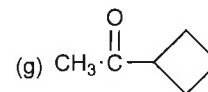
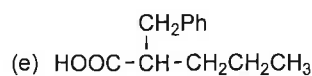
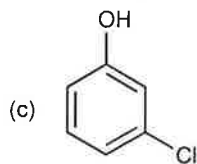
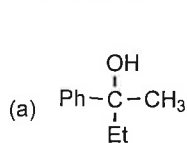
anomeric effect:



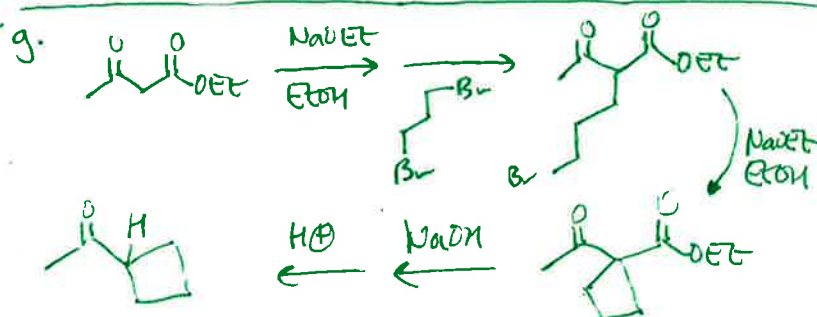
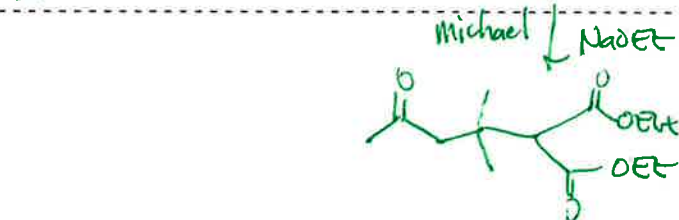
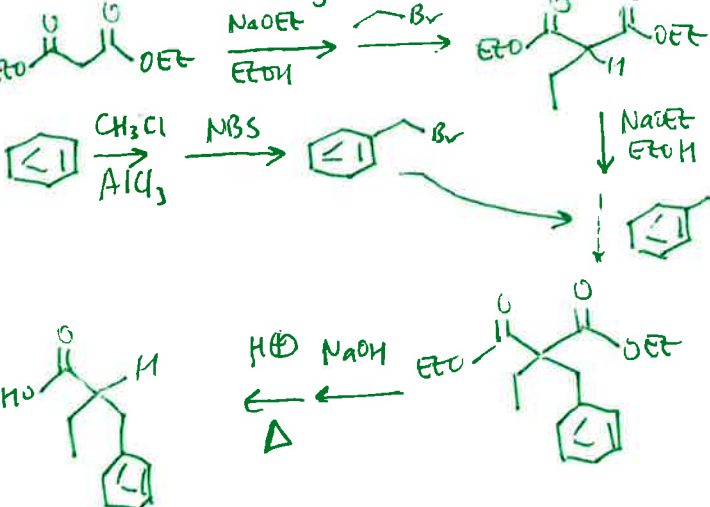
intramolecular F-C reaction

Basic N atom
ties up
Lewis Acid:
reaction fails.

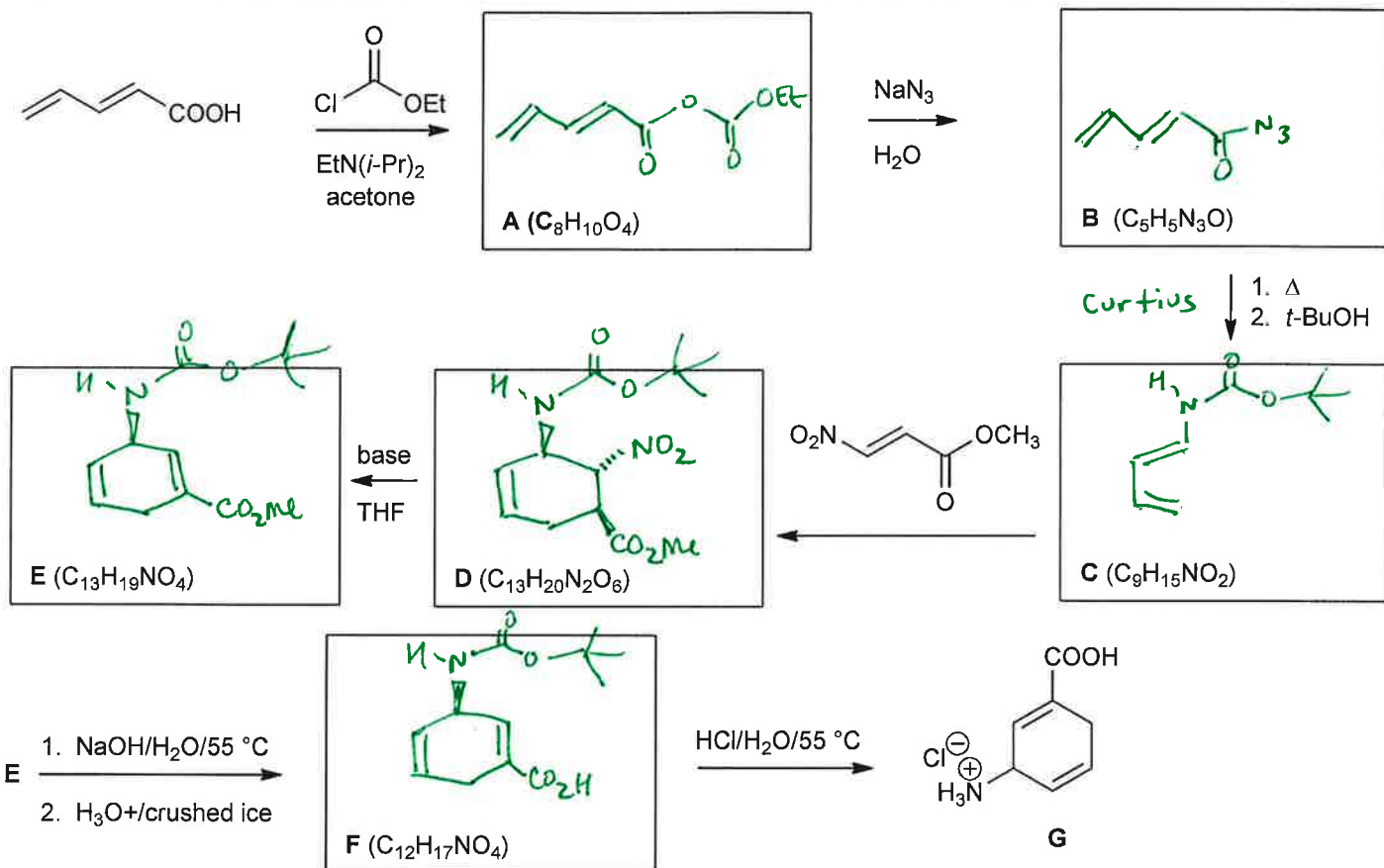
2. (7 pts each) Show how you would synthesize the following molecules. The allowed starting materials are benzene, ethyl acetoacetate, diethyl malonate, other organic materials have three or fewer carbons, and any inorganic materials that you may need. A compound made for one part may be used for another part without your having to make it again. Mechanisms and explanations are not required. Each of these requires at least two steps. Do any six of the eight parts.



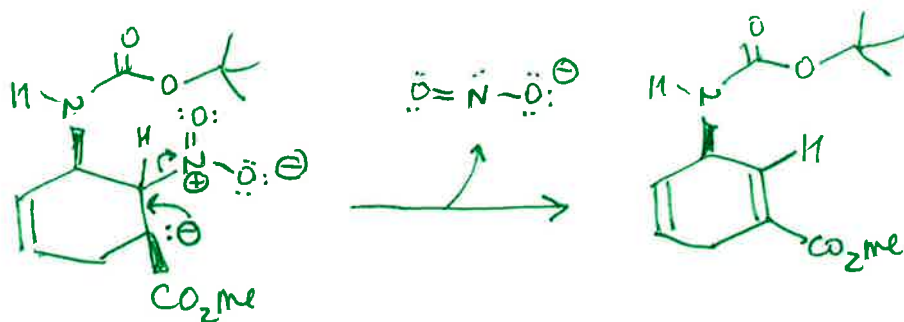
e. Malonic Ester Synthesis



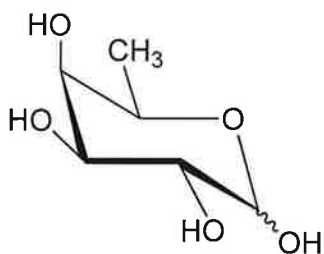
3c. γ -Aminobutyrate transaminase (GABA-T) is the key enzyme controlling the metabolism of γ -aminobutyric acid (GABA), a mammalian inhibitory neurotransmitter. In the following synthesis of the hydrochloride salt of a putative GABA-T inhibitor (**G**), propose structures for intermediates A-F. Indicate relative stereochemistry. (18 points)



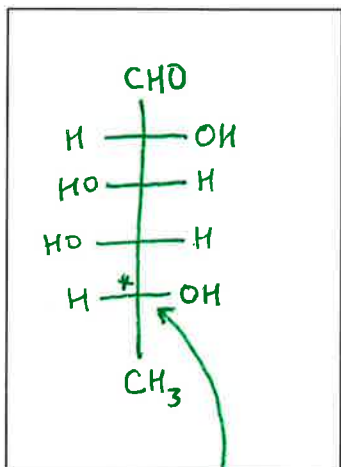
"odd" step in this series: elimination w/ loss of NO_2



1. Consider (+)-fucopyranose: (a-g, 5 pts each)

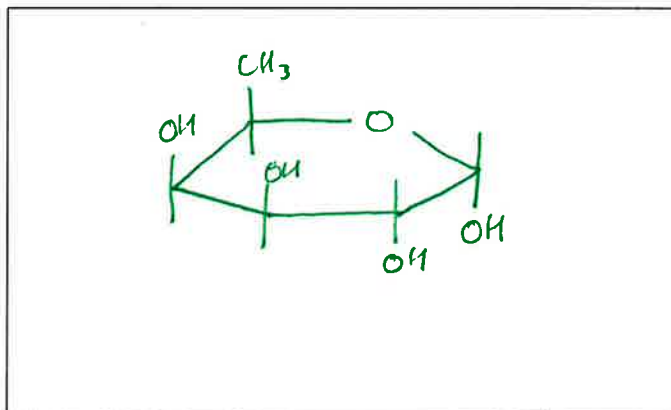


b. Draw the Fischer Projection formula for (+)-fucose:

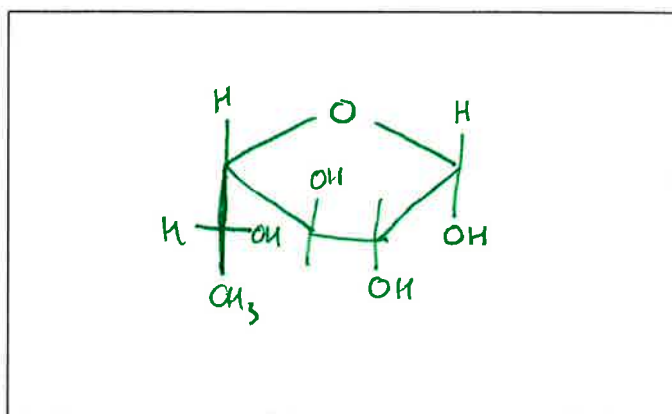


c. Is (+)-fucose a D or L sugar?

a. Write down the Haworth structure of (+)- α -fucopyranose:



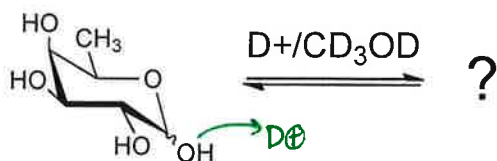
c. Draw a Haworth structure of β -fucofuranose:



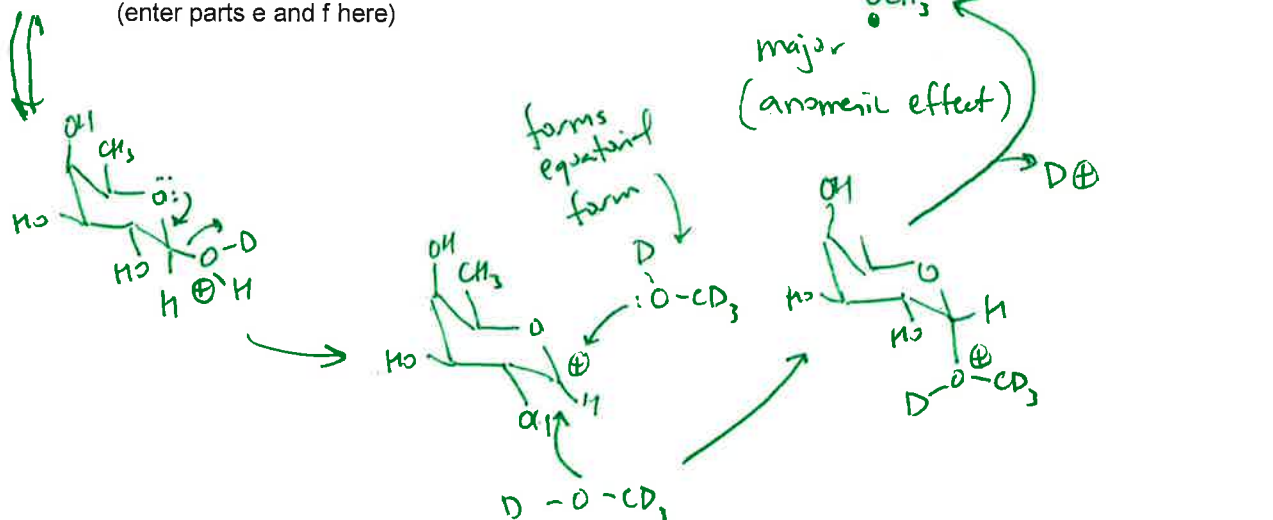
e. (+)-fucose is allowed to equilibrate under the conditions shown below. Unequal amounts of two fucopyranosides are recovered from the reaction mixture. Write the mechanism for this process and, using chair forms, draw and identify the α - and β -fucopyranosides you expect to form.

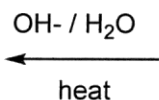
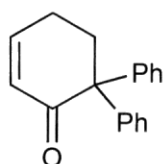
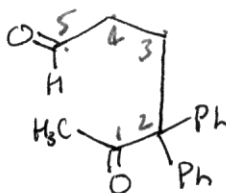
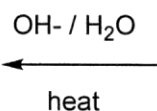
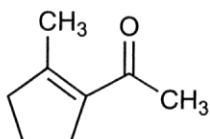
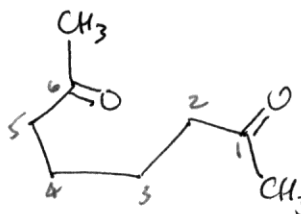
f. Circle the pyranoside that you expect to be formed as the major component.

g. Justify your answer in part f by presenting a clearly drawn structural analysis (invoke steric and stereoelectronic effects, if relevant to your argument. Use only chair forms and clearly indicate the 3-D relationship of lone pairs and bonds.

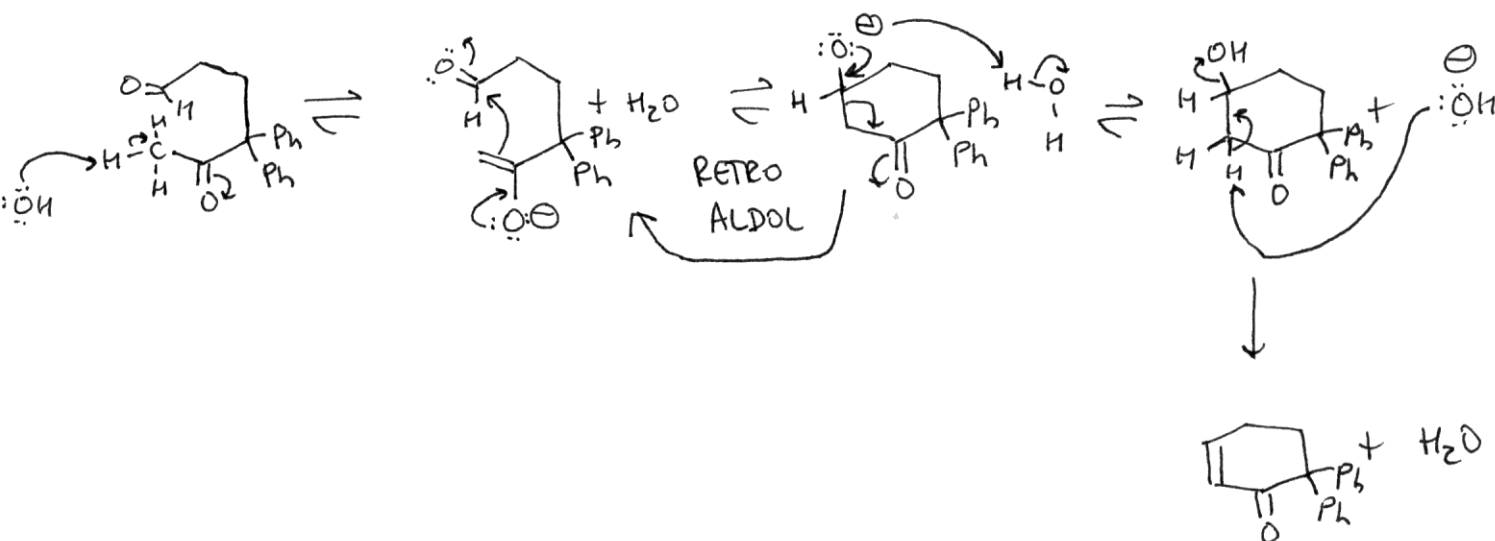


(enter parts e and f here)



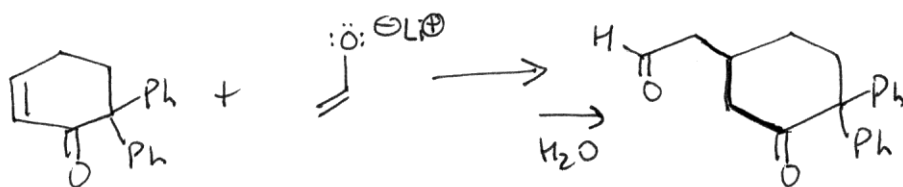
A**C****B****D**

7b. Write a detailed step-by-step mechanism to account for the formation of compound A from C. 10 pts

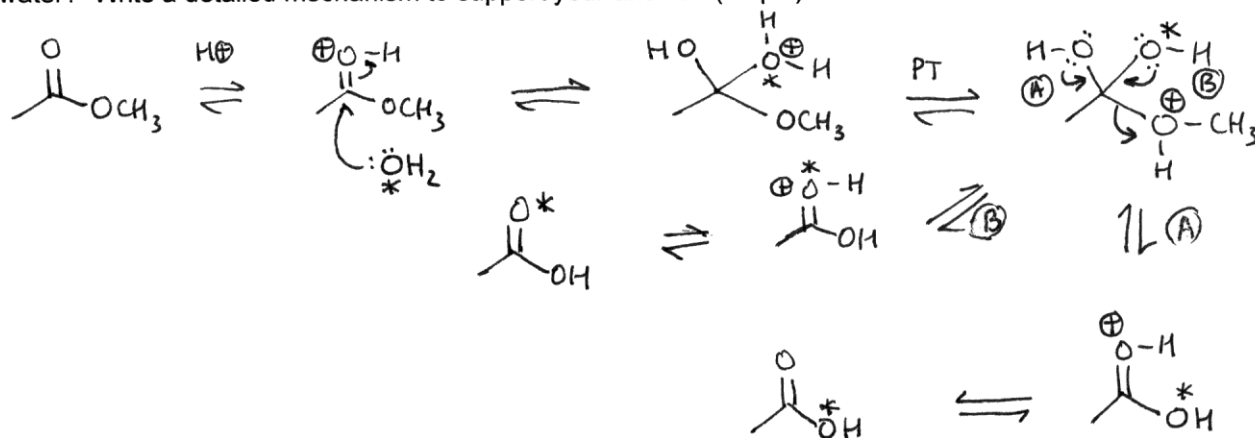
7c. In your mechanism, **label the retro-aldol step** and push electrons in the appropriate intermediate to show the retro-aldol reaction. 4 pts

7d. Use compound A or B (choose wisely—one would work well and one would not!) and reagents of your own choosing to demonstrate an example of a Michael addition reaction. A detailed mechanism is not necessary—just supply the reagents and the structure of the product. 10 pts

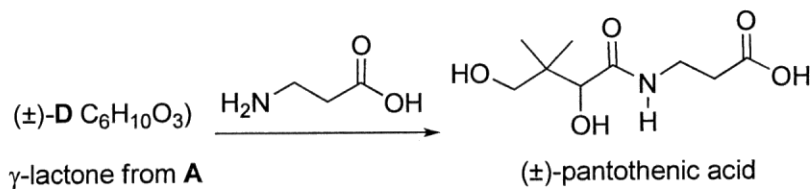
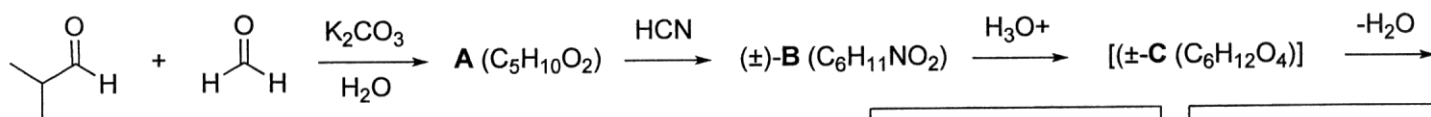
Michael Reaction: Conjugate addition of an enolate



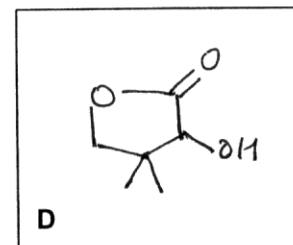
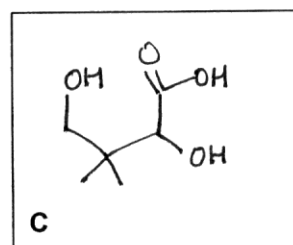
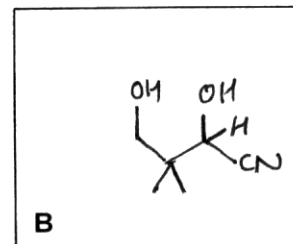
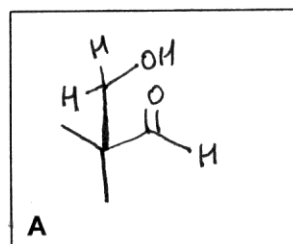
1. Where would you expect to find the labeled oxygen if you carried out an acid-catalyzed hydrolysis of methyl acetate in ^{18}O -labeled water? Write a detailed mechanism to support your answer. (10 pts)



2. (\pm)-Pantethenic acid, an important intermediate in the synthesis of coenzyme A, was prepared by the following route. Give structures for compounds **A-D**: 12 pts



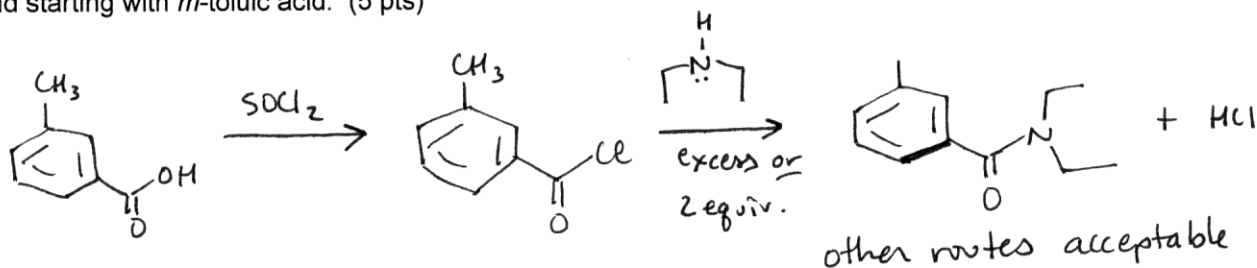
γ -lactone from **A**



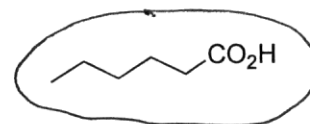
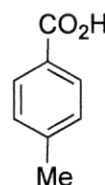
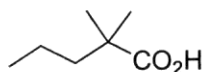
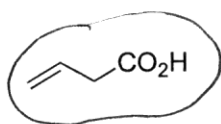
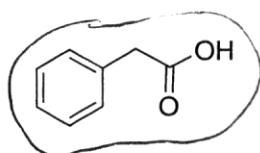
What is the 'name' of the first reaction? (2 pts)

aldol (crossed)

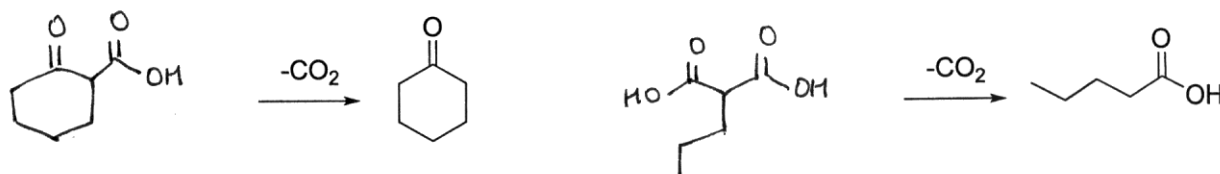
3. The active ingredient of the insect repellent "Off!" is *N,N*-diethyl-*m*-toluamide, $m\text{-CH}_3\text{C}_6\text{H}_4\text{CON}(\text{Et})_2$. Outline a synthesis of this compound starting with *m*-toluic acid. (5 pts)



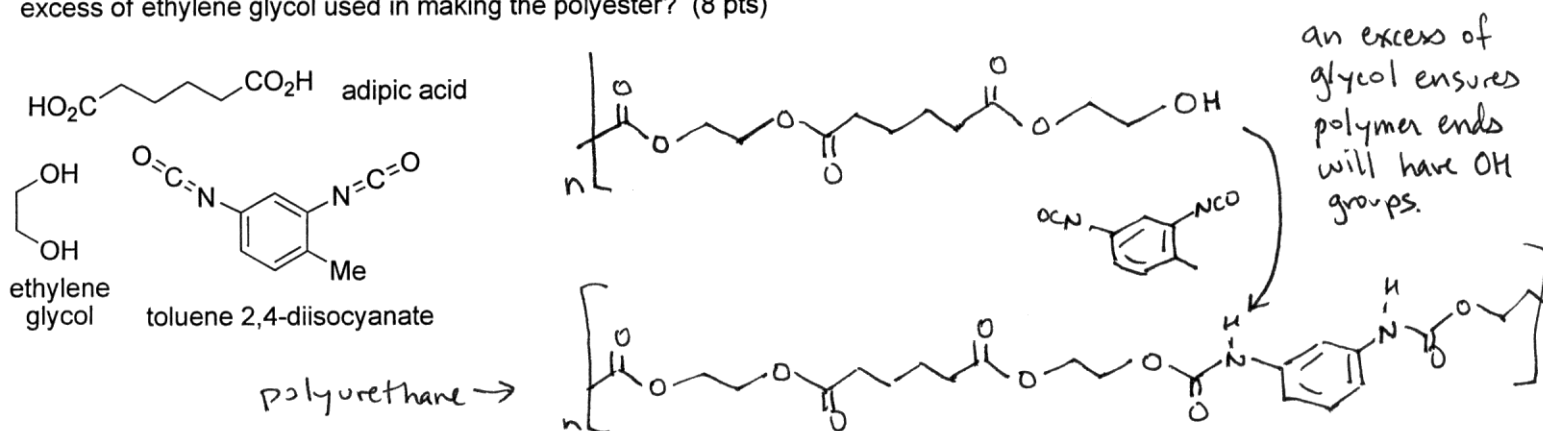
4. Circle the acids that could be prepared by a nitrile synthesis: (5 pts)



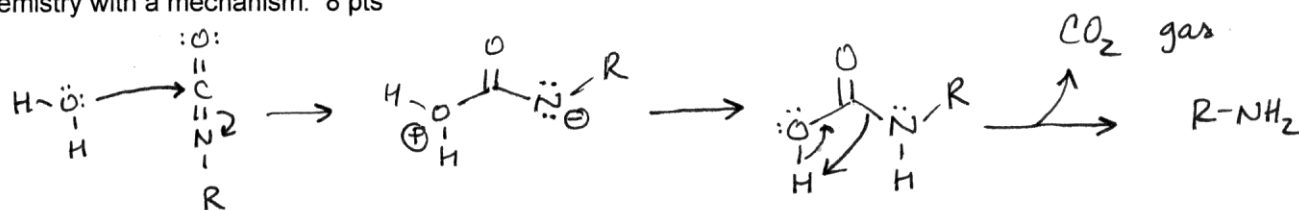
5. Using a decarboxylation reaction, outline a synthesis of the following using appropriate starting materials: (6 pts)



6. A typical polyurethane (polycarbamate) can be made by polymerizing adipic acid with an excess of ethylene glycol. The resulting polymer is then treated with toluene 2,4-diisocyanate. (a) Write the structure of the polyurethane. (b) Why is an excess of ethylene glycol used in making the polyester? (8 pts)



7. When polyurethane foams (perhaps the type you are sitting on at this very moment) are fabricated, a small amount of water is included in the polymerization mixture. The water reacts with one of the monomer molecules to produce a gas, which causes the polymeric material to have trapped bubbles (foam). Use a highly contracted structure (R groups) and explain this chemistry with a mechanism. 8 pts



8. Provided here are the ^1H NMR spectra and IR data for two acyl compounds. Propose a structure for each. (8 pts)

$\text{C}_{10}\text{H}_{12}\text{O}_2$

^1H NMR data

triplet, 1.2 ppm, 3H

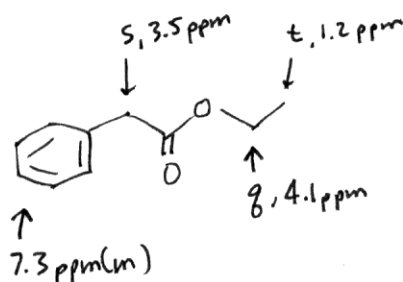
singlet, 3.5 ppm, 2H

quartet, 4.1 ppm, 2H

multiplet, 7.3 ppm, 5H

IR spectrum

1740 cm^{-1}



$\text{C}_8\text{H}_{14}\text{O}_4$

^1H NMR data

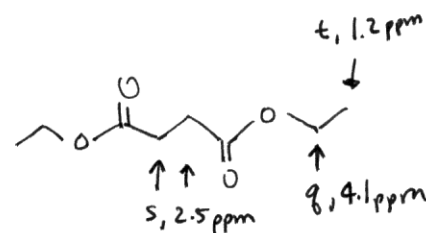
triplet, 1.2 ppm, 6H

singlet, 2.5 ppm, 4H

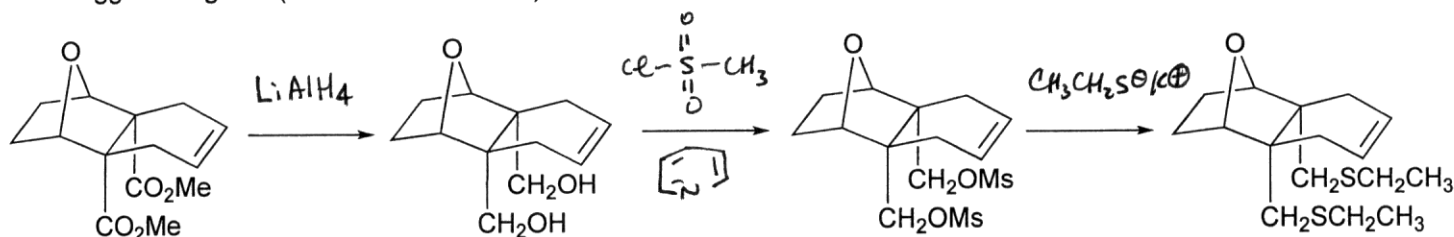
quartet, 4.1 ppm, 4H

IR spectrum

1740 cm^{-1}

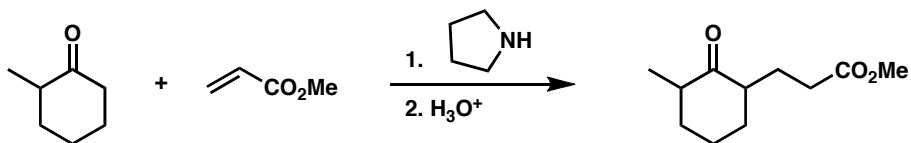


9. Suggest reagents (show their structures) for three of the transformations used in Stork's synthesis of Cantheridin: (6 pts)

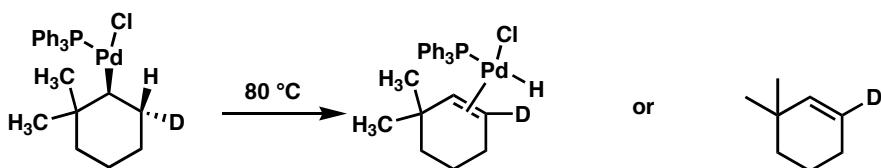


1. Predict the major non-volatile products (if any) of the following reactions or sequences. Clearly mark your answers by placing a **box** around the compound that you believe to be the major product. (5 points each).

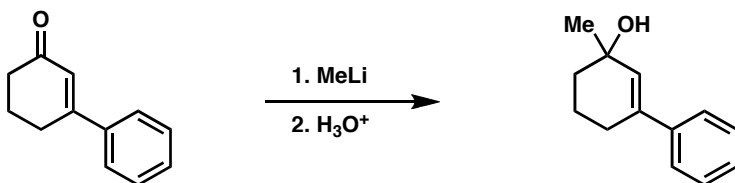
a.



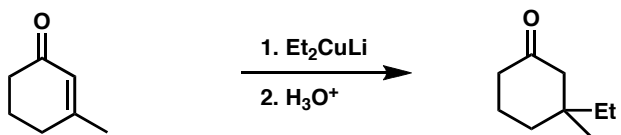
b.



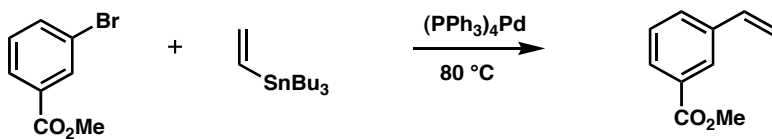
c.



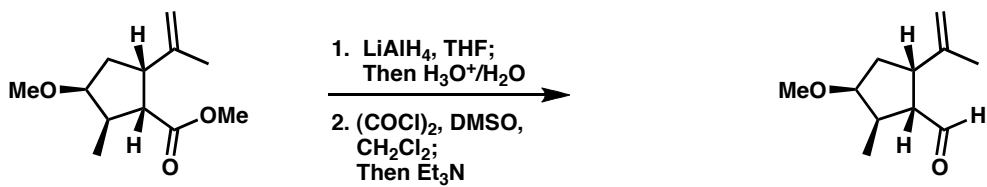
d.



e.

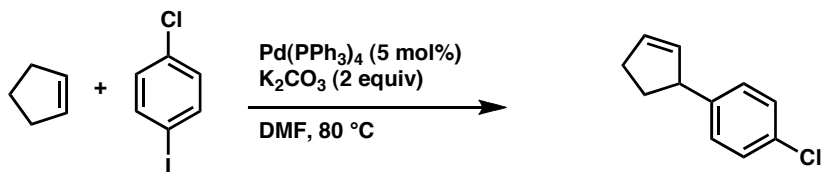


f.

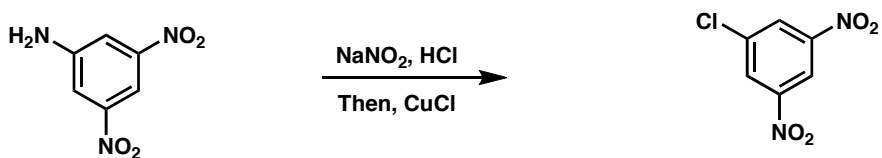


PNAS, 2004, 101, 12073-12078

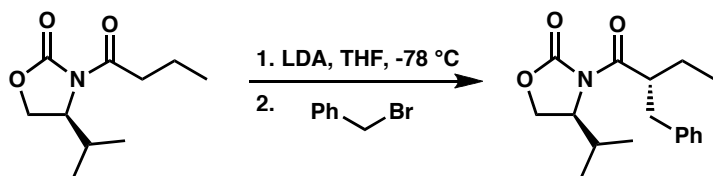
g.



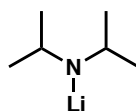
h.

*Can. J. Chem.* **2005**, *83*, 213-219

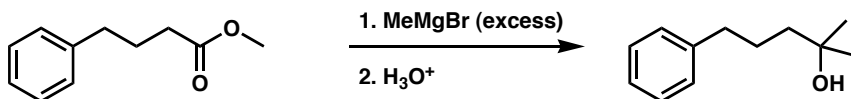
i.



5 point bonus: what is the structure of LDA?

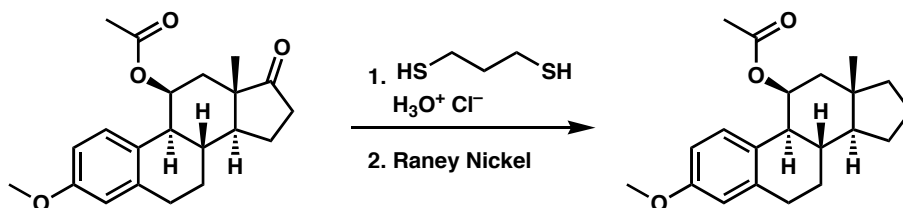


j.



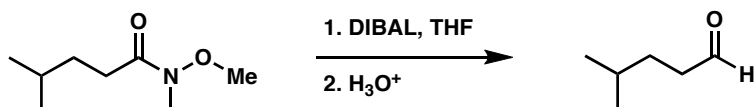
2. Provide reagents for the following transformations. They may be multistep processes, but should not be longer than 5 steps. (5 points each)

a.

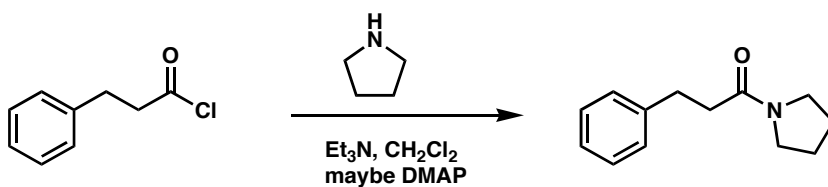


(maybe Clemmenson...not Wolf Kischner)

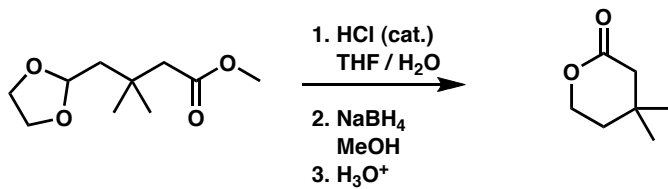
b.



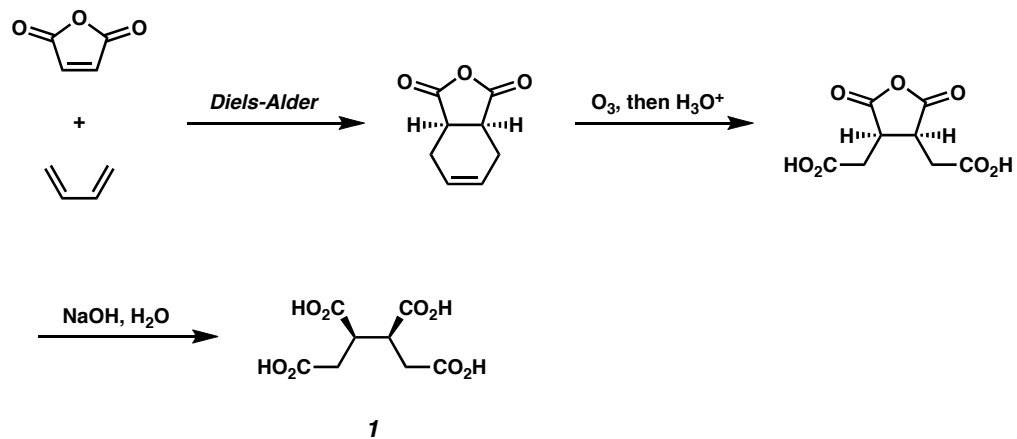
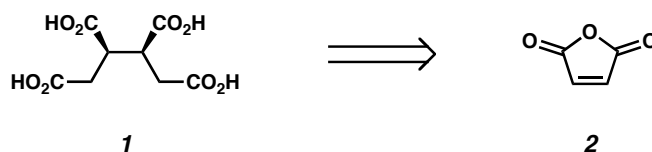
c.



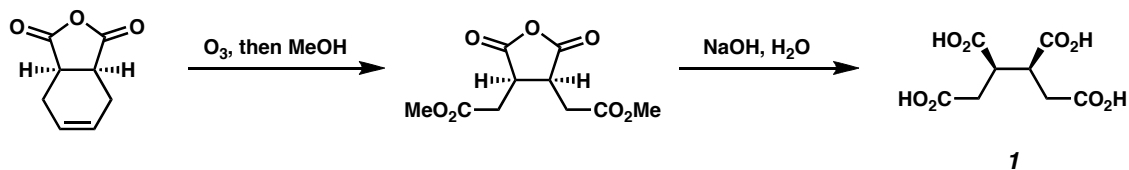
d.



3. Design a synthesis of tetracarboxylic acid **1** starting from maleic anhydride (**2**) and any other materials containing 4 carbons or less. (15 points)



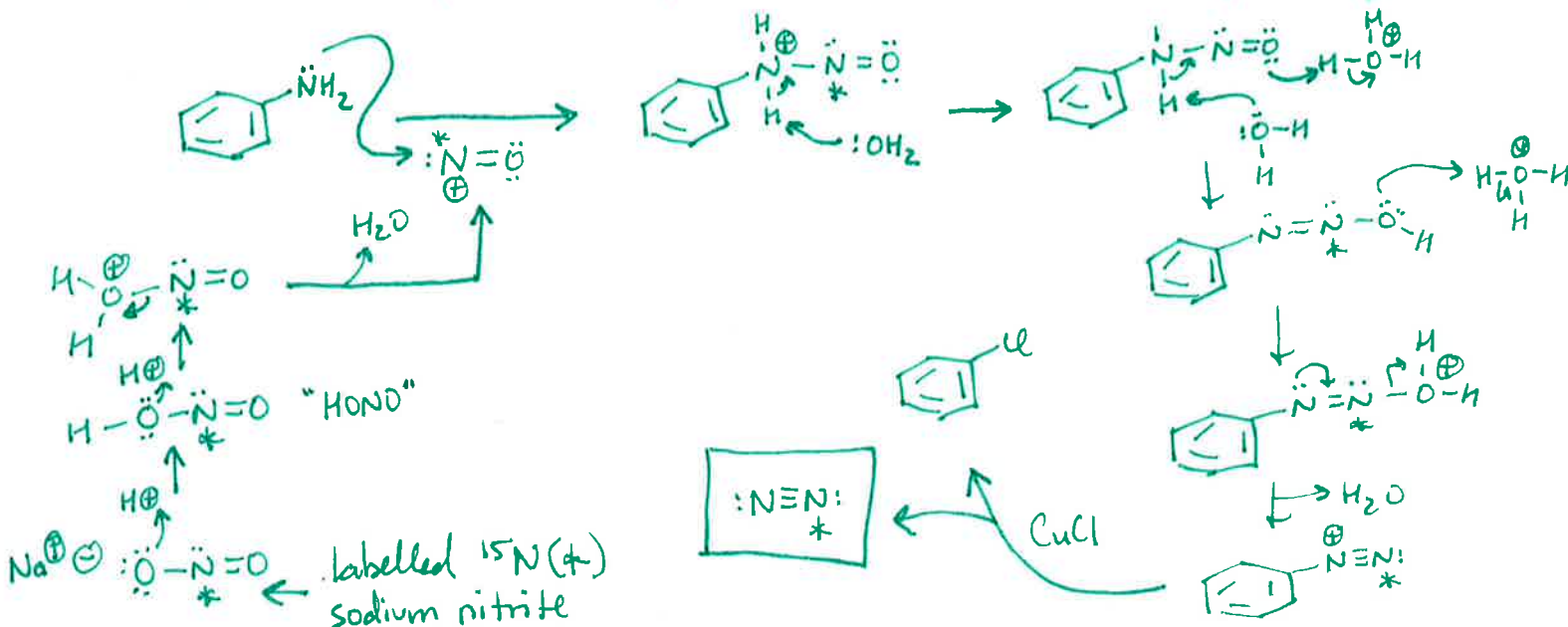
Alternative:



Warren p. 113

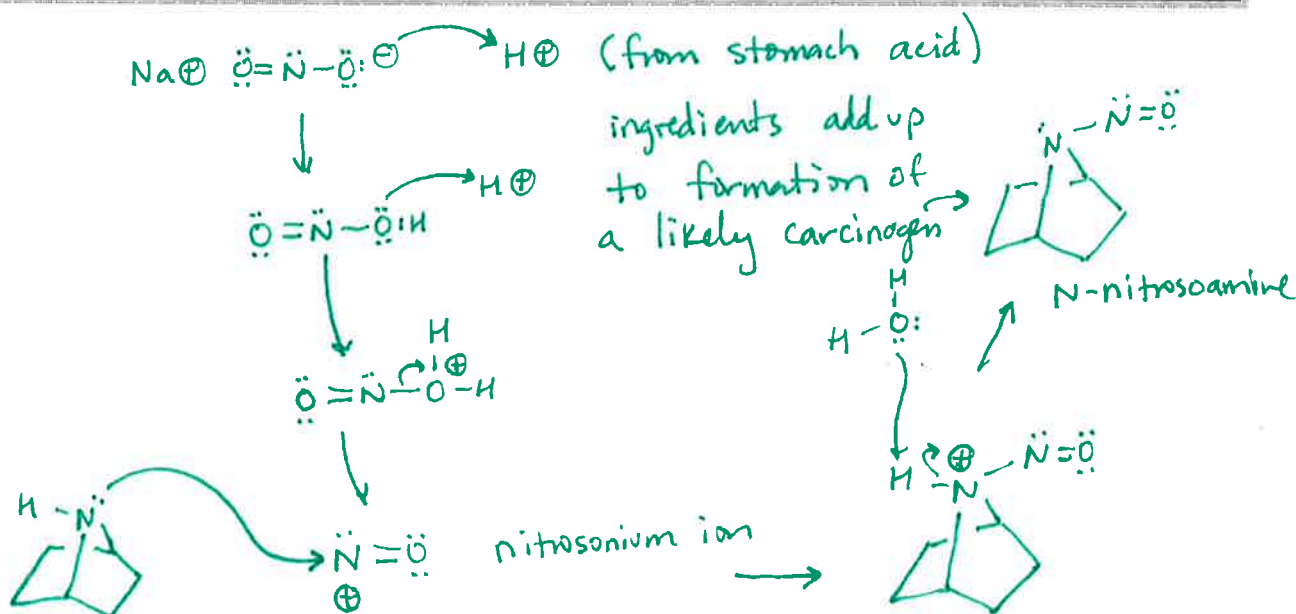
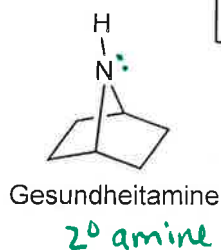
10. A plant biologist friend who studies nitrogen fixation needs access to a supply of pure gaseous nitrogen (N_2) with molecular weight 29. Propose a synthesis of this molecule and specify the chemical source of the ^{15}N isotope (assume that nitrogen is mostly found as the ^{14}N isotope). **Provide a detailed mechanism for your proposed process.** (10 pts)

Nitrogen was seen as a by-product of diazonium salt decomposition in both aryl and alkylamines. We studied the aryl case, so...



11. Pomona/Pitzer degree in hand, you happily accept a \$100,000 /yr job with the Oscar Mayer Corporation in the "hot dog development lab." Your first assignment is to work with another new hire and devise a better dog. Your partner hits the additives book while you review the existing ingredient list. Several days pass by. Your partner presents an idea at a group meeting: use Gesundheitamine (an anti-sneeze agent) as an additive: "this way, people who are allergic to hot dogs won't ever even know it", he says. Several minutes pass by as an uncomfortable silence descends upon the room. Out of the corner of your eye you realize the boss is nodding and smiling, somehow impressed with this outlandish proposal. You want no part of it, and can provide sound chemical reasoning as to **why** Gesundheitamine is not an appropriate additive. Start with the ingredient list and provide a detailed **mechanism**, incorporating other chemicals likely to be encountered in the stomach (pH 1.5-2.0), to substantiate your reasoning. This is not an essay question. **It is a mechanism question.** (10 pts)

Existing Ingredients: beef, sodium erythrobate, sodium phosphate, sodium nitrite, artificial flavoring.




6. You are presented with a sample exhibiting the following mass-spectral characteristics: $M^+ = 170.13$ (100%), $M+1 = 171.13$ (10.9%). **Sample name = FRANCES-06**. You record proton and carbon NMR spectra (see next page). What is the structure of the compound? This is not an essay question--use the space provided to show me your thought processes as you solve this problem. 14 pts

$M+1$ data suggests 10 carbon atoms $10 \times 12 = 120$ mass units

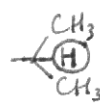
need 50 additional mass units: proton spectrum suggests 18

$120 + 18 = 138$ mass units accounted for 32 required two oxygens?

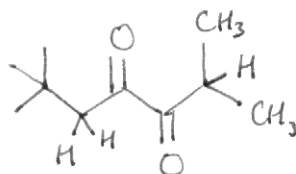
suggest formula: $C_{10}H_{18}O_2$ IHD = 2

^{13}C spectrum suggests two different  groups

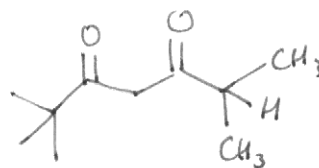
1H spectrum eliminates aldehyde  \therefore Ketones likely

heptet 3.2 ppm 1H  \rightarrow 'isolated' CH_2
 singlet 2.3 ppm 2H
 doublet 1.1 ppm 6H
 singlet 0.9 ppm 9H likely tBu

possible structures:



or



7. Sketch and assign the expected proton NMR spectrum for 2-bromoethanol. 14 pts

