NAME (Print): _____

SIGNATURE: _____

Chemistry 310N
Dr. Brent Iverson
Final
May 11, 2012

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

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.

You must have your answers written in PERMANENT ink if you want a regrade!!!! This means no test written in pencil or ERASABLE INK will be regraded.

Please note: We routinely xerox a number of exams following initial grading to guard against receiving altered answers during the regrading process.

FINALLY, DUE TO SOME UNFORTUNATE RECENT INCIDENCTS YOU ARE NOT ALLOWED TO INTERACT WITH YOUR CELL PHONE IN ANY WAY. IF YOU TOUCH YOUR CELL PHONE DURING THE EXAM YOU WILL GET A "0" NO MATTER WHAT YOU ARE DOING WITH THE PHONE. PUT IT AWAY AND LEAVE IT THERE!!!

Page	Points	
1		(26)
2		(19)
3		(16)
4		(11)
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18		(4)
19		(4)
20		(8)
Total		(377)
%		
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HW		
Total Grade		

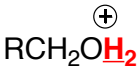
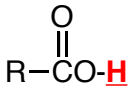
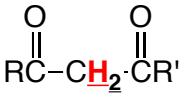
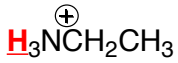
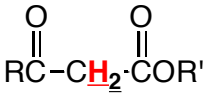
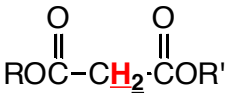
(HW score + Exam Grade) ⟹

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		-7
Protonated alcohol		-2
Hydronium ion		-1.7
Carboxylic acids		3-5
Ammonium ion		9.2
β-Dicarbonyls		10
Primary ammonium		10.5
β-Ketoesters		11
β-Diesters		13
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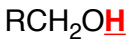
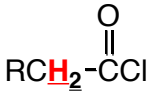
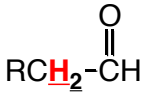
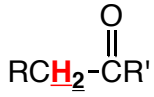
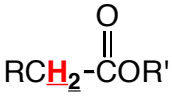
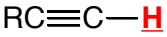
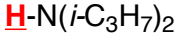
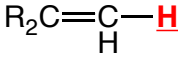
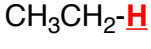
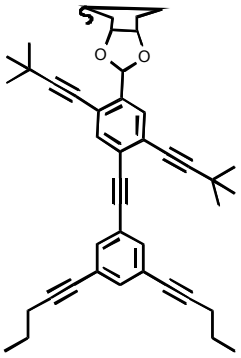
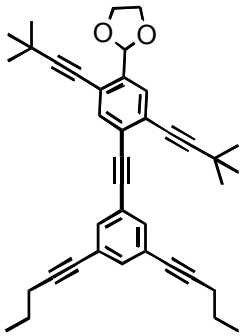
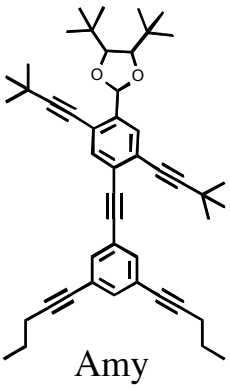
Alcohols		15-19
Acid chlorides		16
Aldehydes		18-20
Ketones		18-20
Esters		23-25
Terminal alkynes		25
LDA		40
Terminal alkenes		44
Alkanes		51



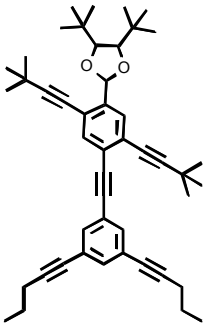
Dr. Iverson



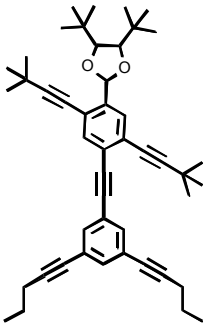
Brian



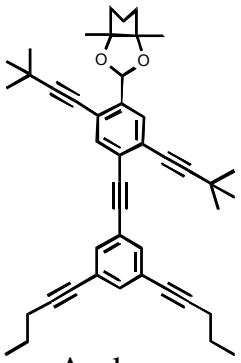
Amy



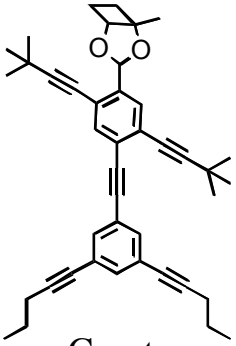
Alex



Katharine



Andrew



Grant

It has been a pleasure getting to know you this semester. I hope that you find this final to be challenging, but fair.

It is the sincere wish of the TA's and myself that you look back on your organic chemistry courses with a sense of pride on how far you have come in two semesters. Wherever your careers take you, we hope you now have the intellectual tools to identify, analyze, and understand molecules.

Have a safe summer and remember to excercise every chance you get. If you stay in shape, you will thank yourself more than you can imagine in a few years!!!

Brent Iverson

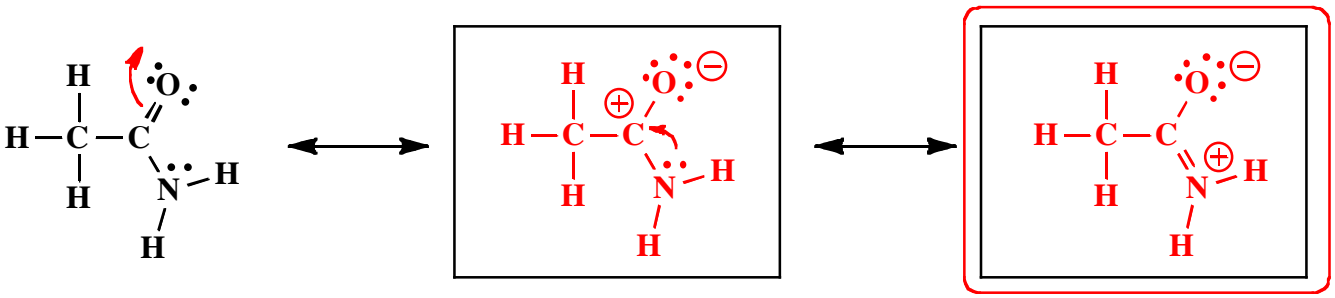
1. (16 points) Suppose a relative of yours is having an MRI. In no more than four sentences, explain to them what is happening when they have the MRI scan. We will be looking for a minumum of 7 key points here.

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**.

What is the most important question in chemistry? ⟸ **Notice This**

Where are the electrons?

2. (8 pts) On the left is drawn the Lewis structure of a simple amide. Draw the two next most important contributing structures in the spaces provided. Be sure to show all lone pairs and formal charges. You do not need to draw arrows on the structures, but you can if it helps you.

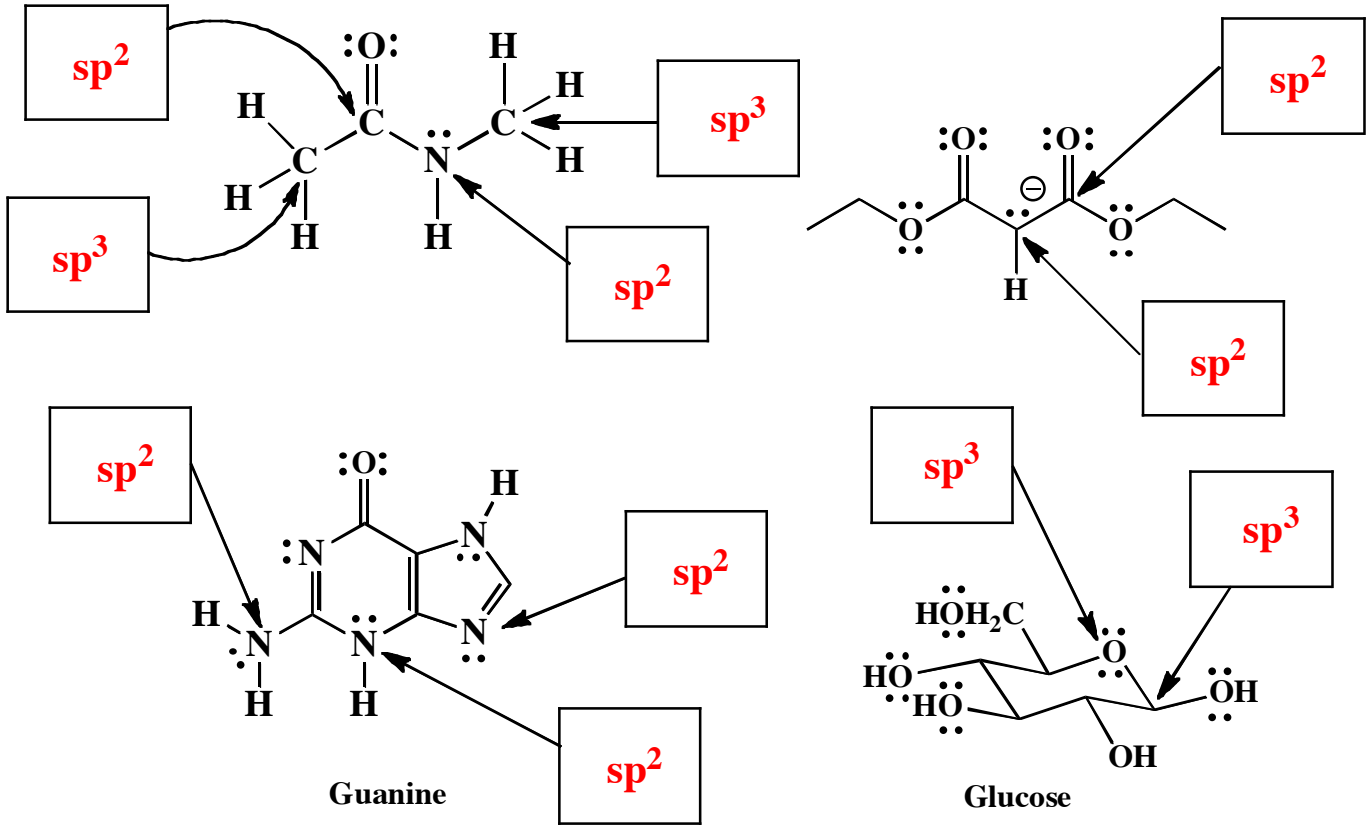


3. (2 pts) An important feature of an amide bond is that there is a partial double bond between the carbonyl carbon and nitrogen. For the contributing structures you drew in Problem **2.**, draw a circle around the one that predicts this partial double bond.

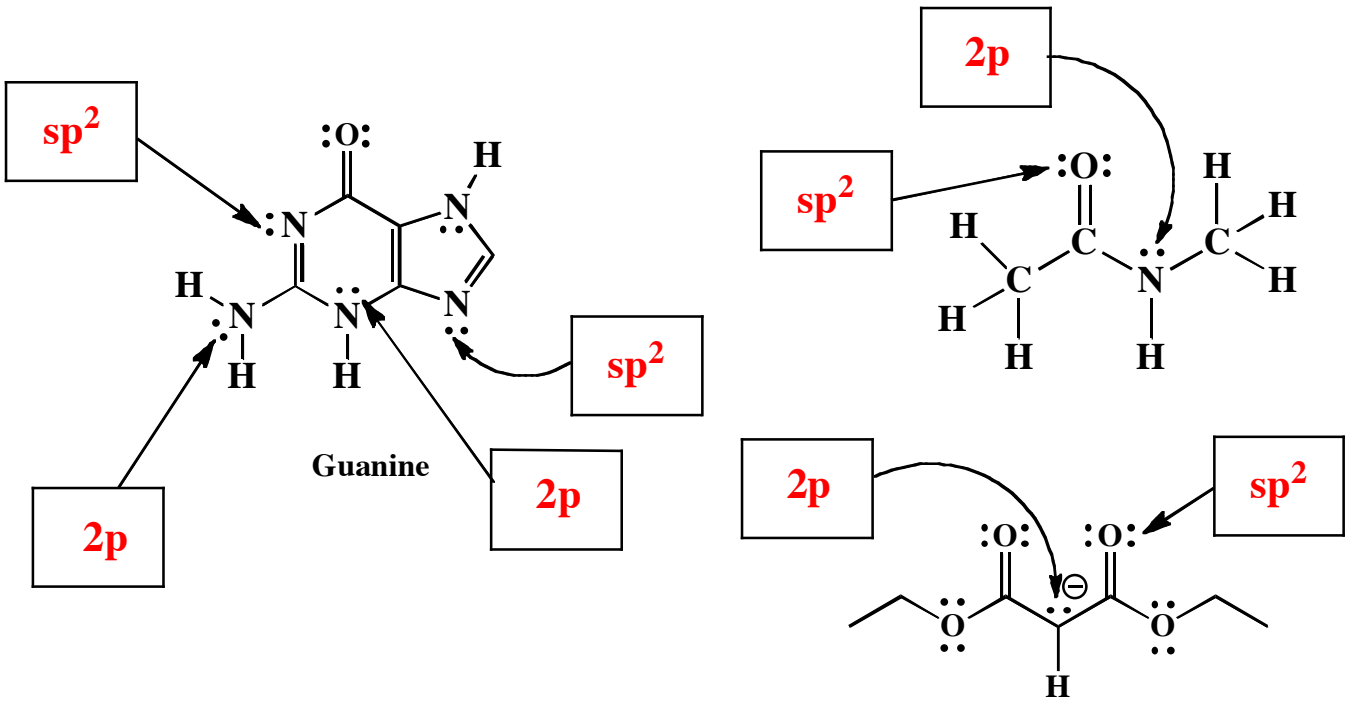
⇑ ⇑ ⇑

Notice This

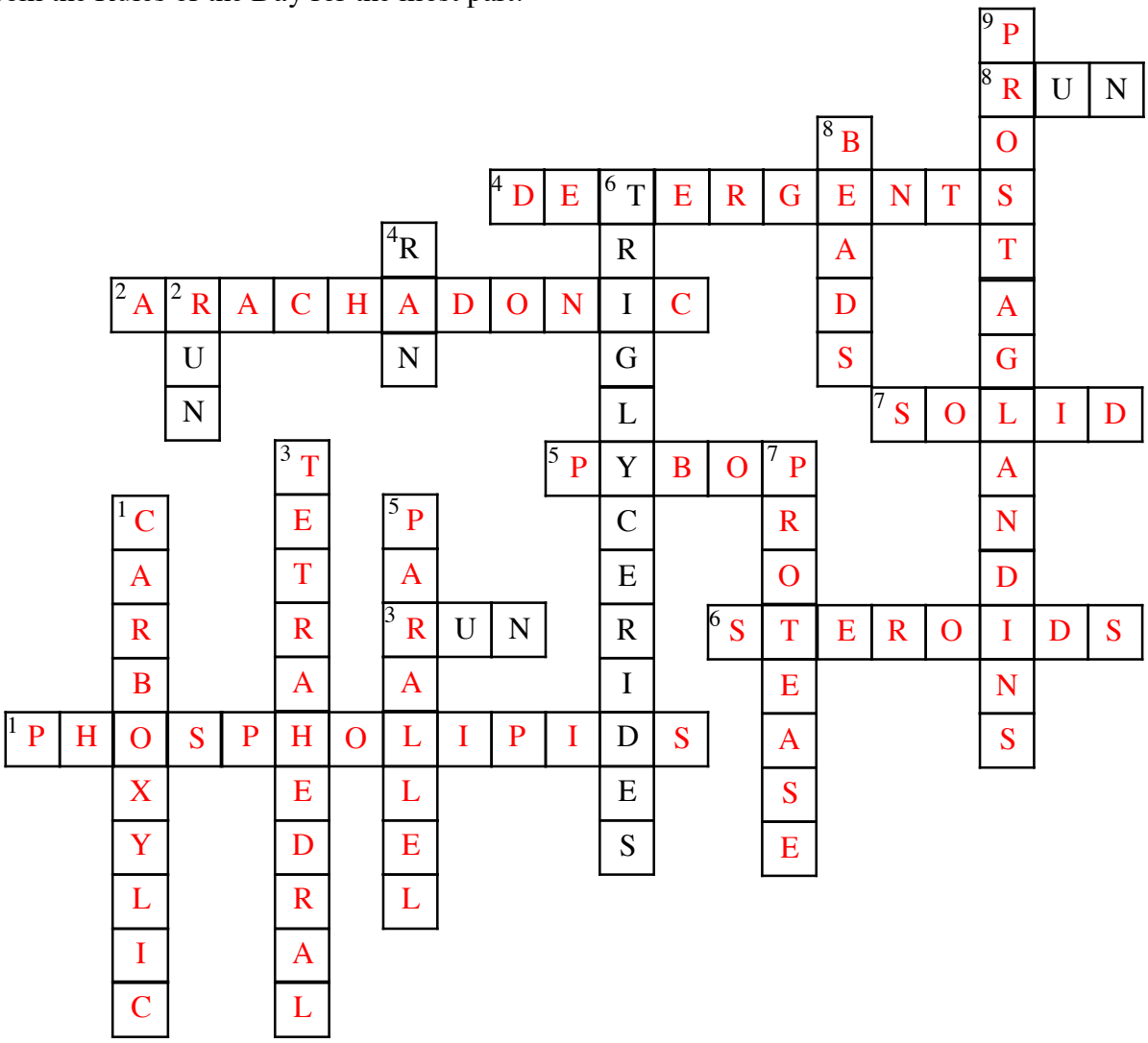
4. (11 pts) In the boxes provided, write the hybridization state of the given atoms.



5. (8 pts) In the boxes provided write the type of atomic orbital that contains the indicated lone pair of electrons.



6. (16 pts) Fill in the crossword puzzle with the word that best fits the sentence. Hint: These were taken from the Rules of the Day for the most part.



ACROSS:

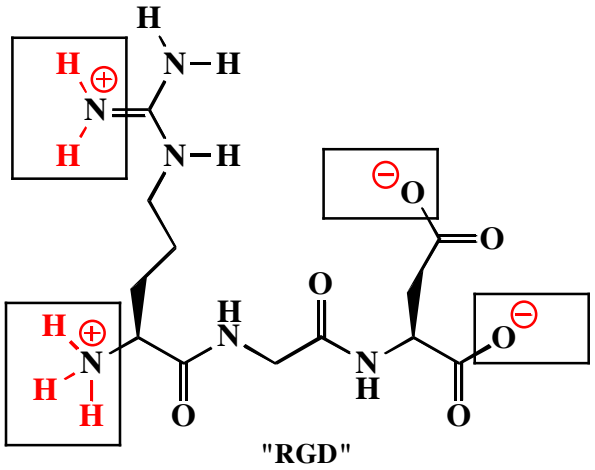
1. **Phospholipids** have two fatty acids and a phosphate group as the third ester on glycerol.
2. **Arachadonic** acid is stored in cells, then converted into an appropriate prostaglandin in response to a stimulus.
3. **Run** every chance you get. Staying healthy for a lifetime is the real secret of success.
4. **Detergents** have a sulfonate group instead of a carboxylate to avoid precipitation in hard water.
5. **PyBOP** is a coupling agent that makes amide bonds in the presence of a carboxylic acid, an amine and a mild base.
6. **Steroids** bind a specific receptor in the cell cytoplasm, then the complex is transported to the cell nucleus to modulate the expression of the genes in entire pathways such as gender differentiation during development.
7. **Solid** phase synthesis has been adapted to most of the reactions we have studied. which allows AUTOMATED syntheses.
8. **Run** every chance you get. Staying healthy for a lifetime is the real secret of success.

6. (cont.)

DOWN:

1. The AIDS protease is an aspartyl protease that uses two **carboxylic** acid groups and a water molecule to hydrolyze an amide bond.
2. **Run** every chance you get. Staying healthy for a lifetime is the real secret of success.
3. The AIDS protease inhibitors are designed to resemble the key **tetrahedral** intermediate of the amide hydrolysis reaction while maximizing complementary contacts within the active site.
4. I just **ran** and I feel great!!
5. Running reactions with molecules attached to beads allows the AUTOMATED synthesis of hundreds of molecules in **parallel**, speeding up the drug discovery process in dramatic fashion.
6. **Triglycerides** are the triester of glycerol bound to three fatty acid chains, usually 12, 14, 16, 18 or 20 carbons long.
7. A polyprotein transcript is produced from the mRNA called GAG-POL that is cleaved into functional proteins by the AIDS **protease**.
8. Many syntheses are carried out with a starting material reversibly attached to **beads**. This has the advantage of allowing exchange of reagents and isolation of products by simple filtration.
9. **Prostaglandins** are 20 carbon molecules involved in mammalian signaling, associated with local response to injury or disease.

7. (11 points) **A)** This semester we have learned a great deal about carboxylic acids, guanidine groups, and amines. Here is an apply what you know problem. The so-called RGD peptides bind to special receptors in the body, including adhesion receptors important for angiogenesis (production of blood vessels). Charge is a major factor that controls binding of RGD peptides to their receptors. Below is the tripeptide Arginine-Glycine-Aspartic acid (RGD). ***In the boxes provided, draw the correct protonation state of the carboxylic acid, amine, or guanidine group at neutral pH, 7.0.*** **You must show all protons and formal charges that are present on the functional groups within the four boxes. For this problem, assume the pK_a values of the carboxylic acids are 4.0, the pK_a value for a protonated amine is 9.2, and the pK_a value for a protonated guanidine group is 13.2.**



"RGD"

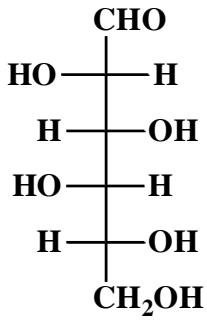
B) What is the total charge on this peptide at pH 7.0? **0**

C) What is the total charge on this peptide at pH 2.0? **+2**

D) What is the total charge on this peptide at pH 11.2? **-1**

8. (2 pts each) I know you were wondering how we were going to test the carbohydrate material. Here is what we came up with. For the following structures, draw a circle around the terms that provide the most accurate description.

A.



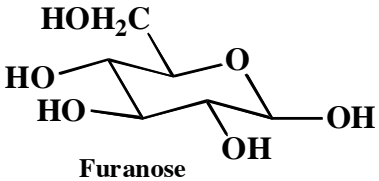
L carbohydrate

D carbohydrate

X-rated carbohydrate

S carbohydrate

B.



Furanose

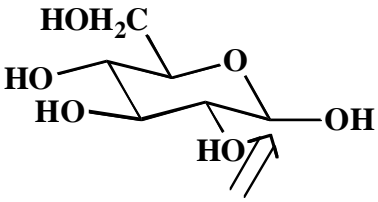
Pyranose

Runny nose

Bloody nose

Bottlenose

C.



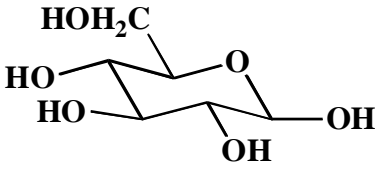
Monomeric carbon

Anomeric carbon

Polymeric carbon

All-American carbon

D.



α-D-Glucose

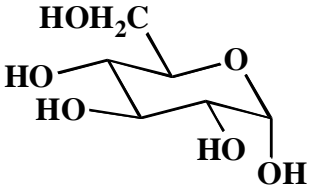
β-D-Glucose

βββ-D-Glucose

ΣAE-D-Glucose

Fiji-D-Glucose

E.



α-D-Glucose

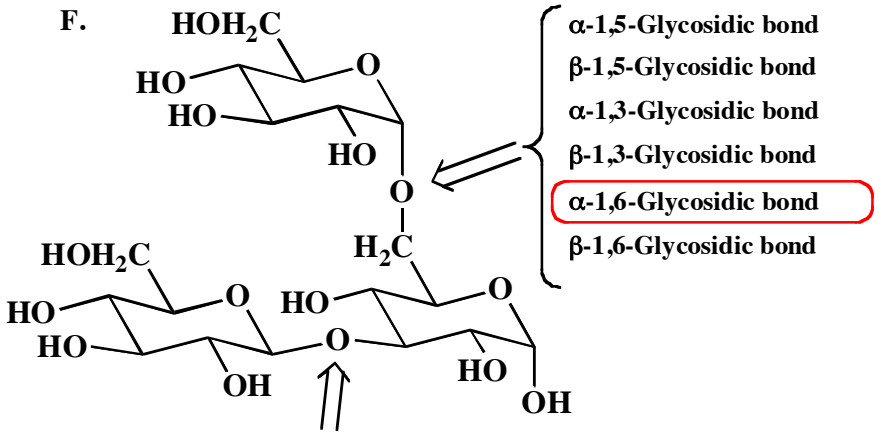
β-D-Glucose

βββ-D-Glucose

ΣAE-D-Glucose

Fiji-D-Glucose

F.



α-1,5-Glycosidic bond

β-1,5-Glycosidic bond

α-1,3-Glycosidic bond

β-1,3-Glycosidic bond

α-1,6-Glycosidic bond

β-1,6-Glycosidic bond

α-1,4-Glycosidic bond

β-1,4-Glycosidic bond

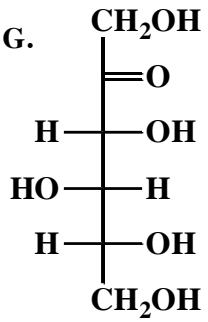
α-1,3-Glycosidic bond

β-1,3-Glycosidic bond

α-1,5-Glycosidic bond

β-1,5-Glycosidic bond

G.



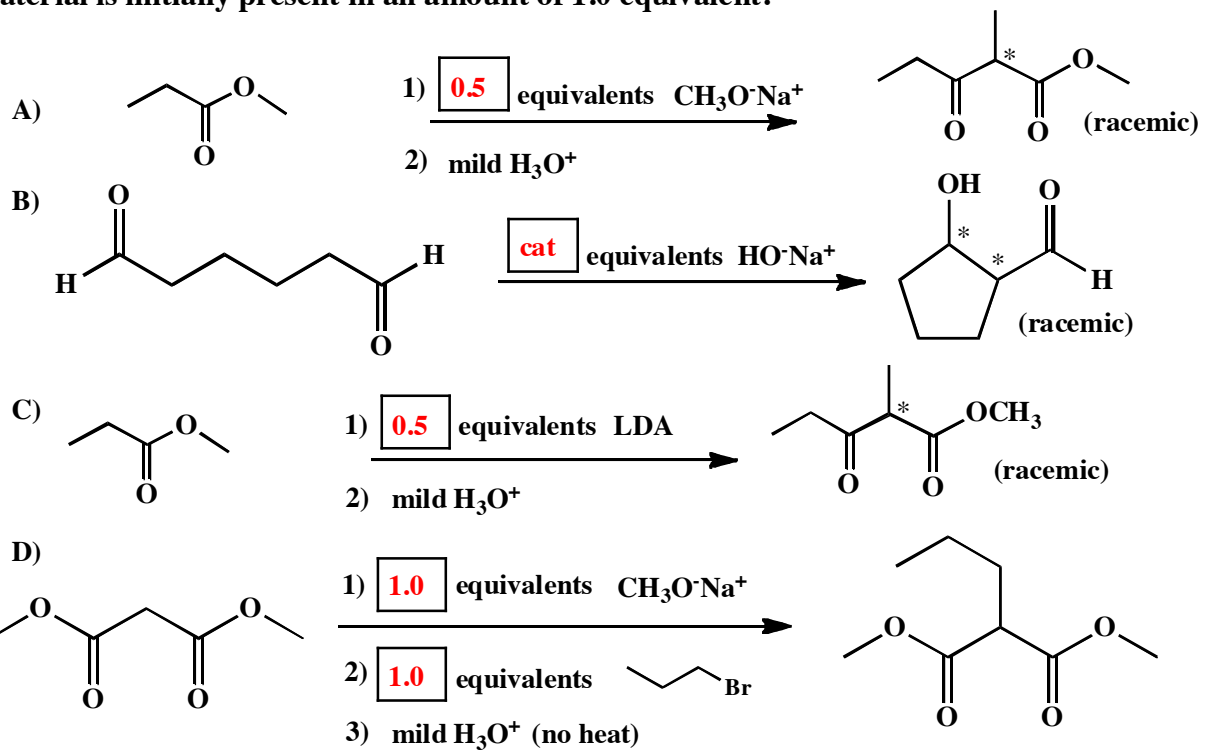
Aldohexose

Ketohexose

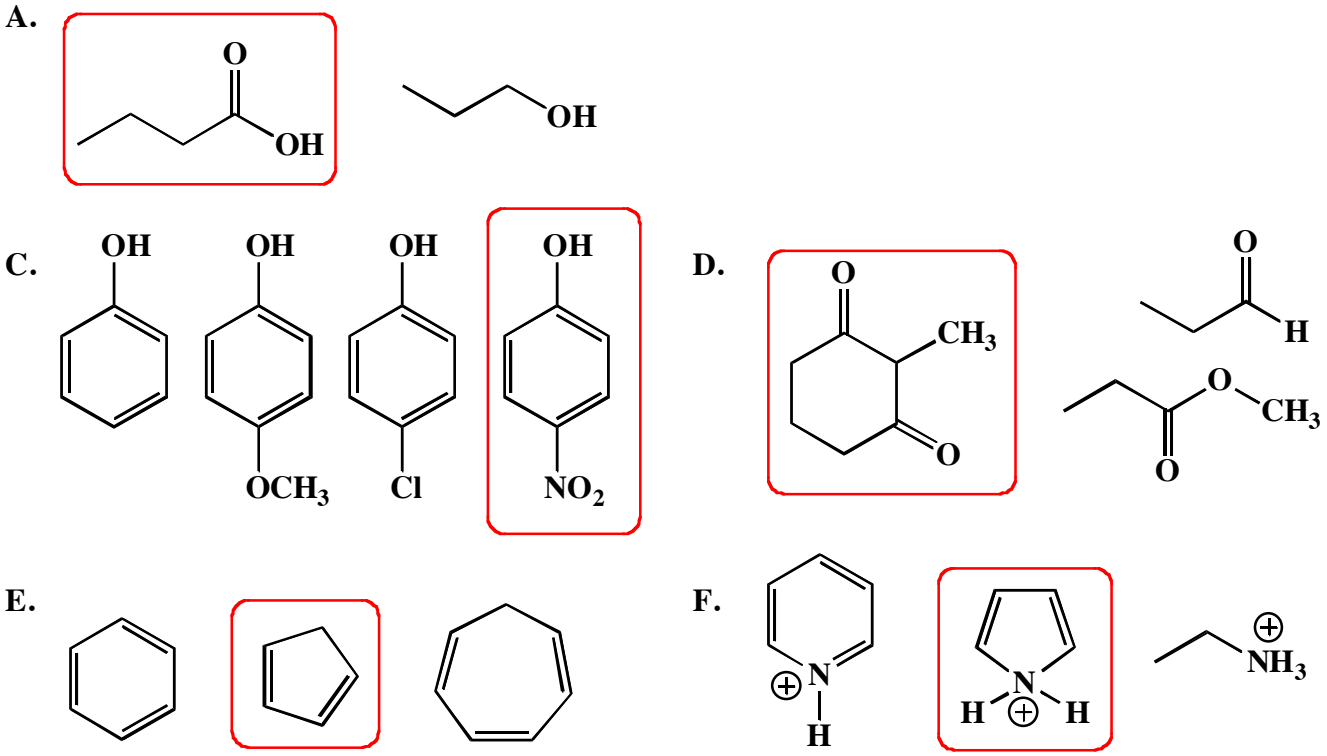
Aldopentose

Pointy toes

9. (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.**

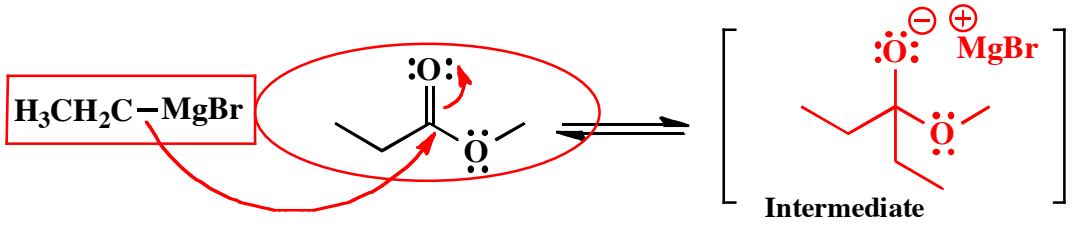


10. (2 points each) For each set, circle the MOST ACIDIC molecule.

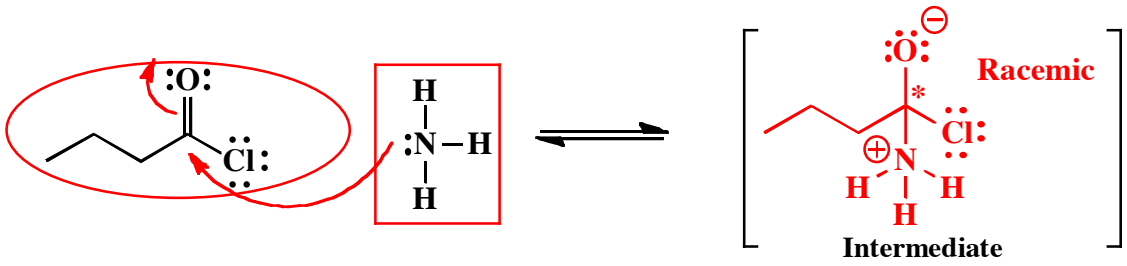


11. (26 points) Many of the reactions we have learned this semester involve steps with nucleophiles reacting with electrophiles. For the following examples of steps in mechanisms we have seen this semester, **1) Draw the intermediate that will be formed when the two molecules react. 2) Draw all formal 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) Label all chiral centers with an asterisk (*) and write "racemic" where appropriate. 5) 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.

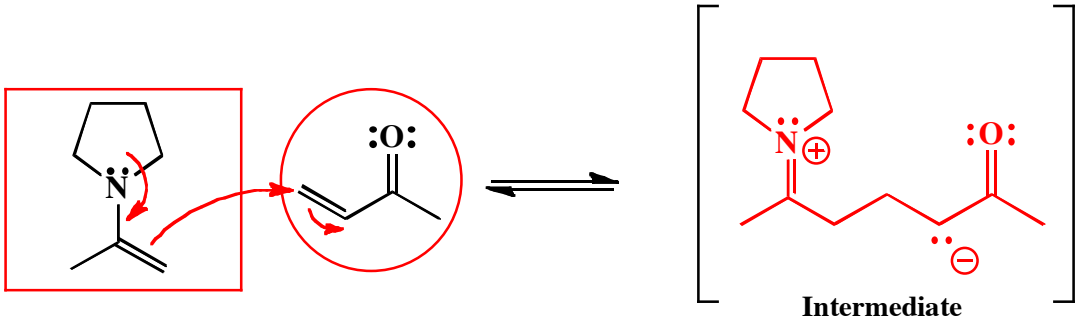
A)



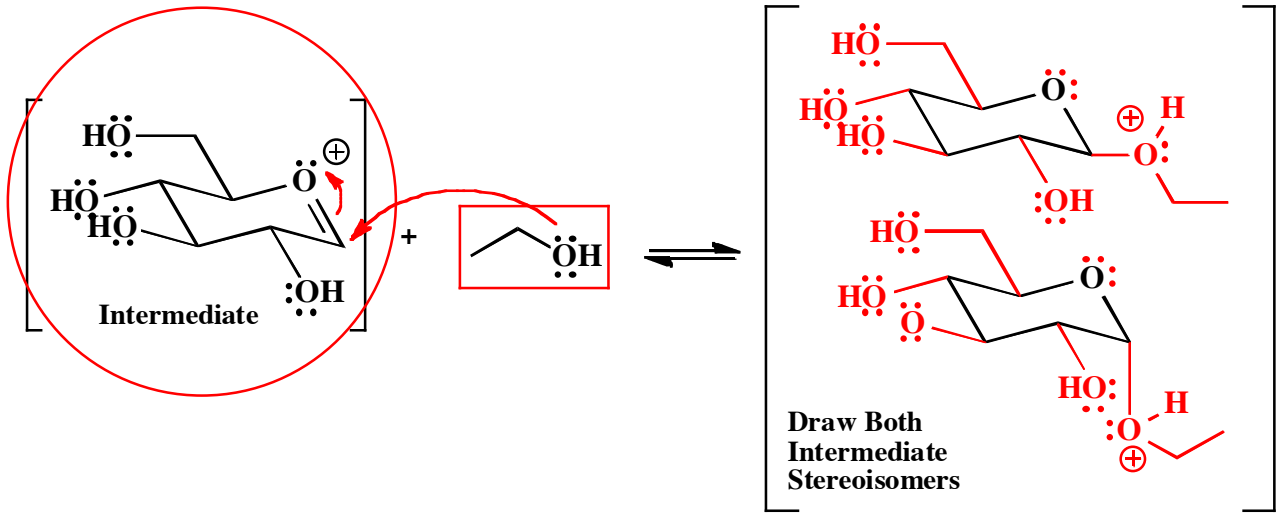
B)



C)

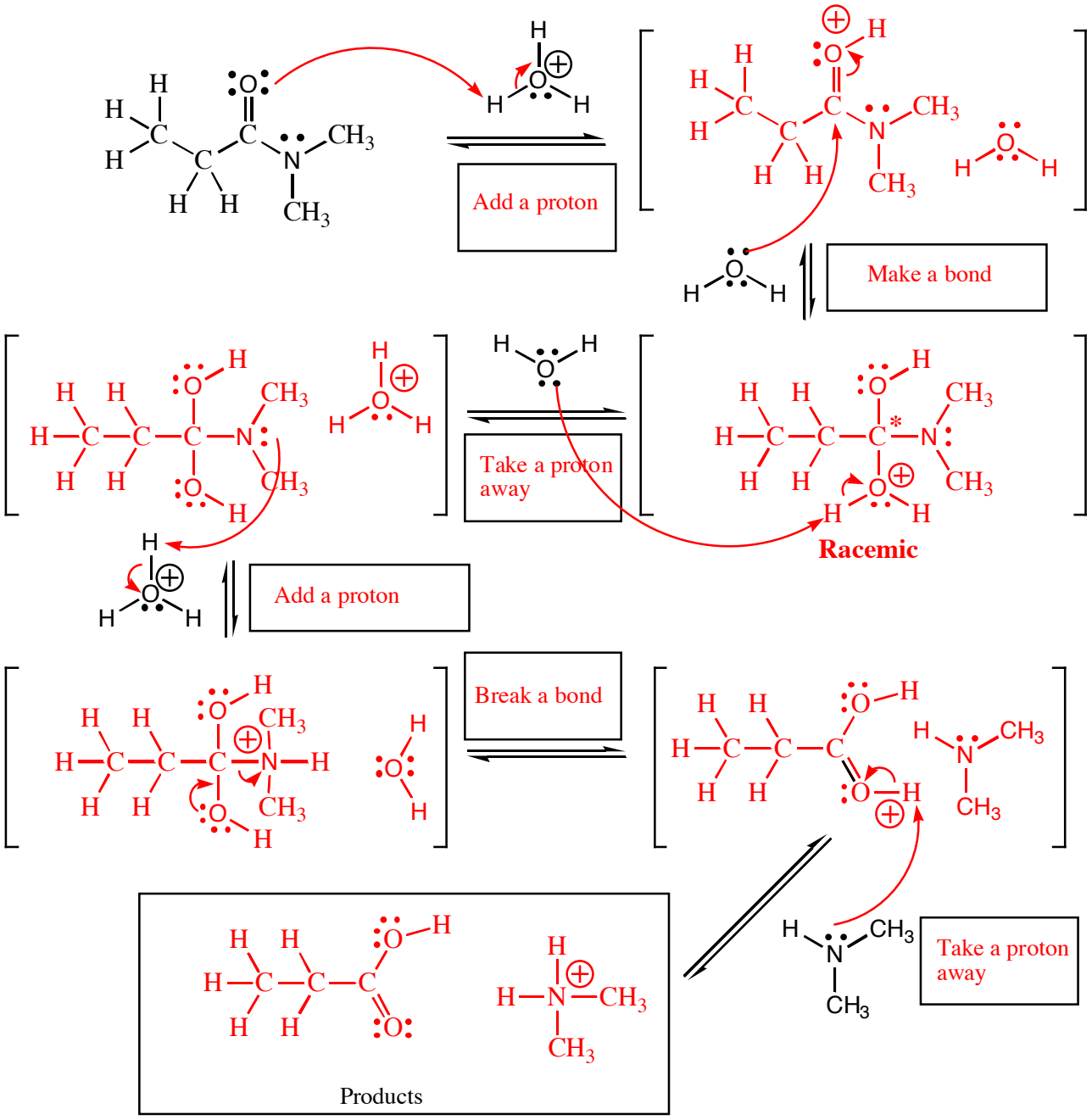


D)



Did you remember to draw boxes and circles?

12. (33 pts. total) Complete the mechanism for the following **acid promoted amide hydrolysis** reaction. **Be sure to show arrows to indicate movement of <u>all</u> electrons, write <u>all</u> lone pairs, <u>all</u> formal charges, and <u>all</u> the products for each step.** Remember, I said <u>all</u> the products for each step. IF A NEW CHIRAL CENTER IS CREATED IN AN INTERMEDIATE OR THE PRODUCTS, MARK IT WITH AN ASTERISK AND LABEL AS "RACEMIC" IF RELEVANT. IN THE BOX BY EACH SET OF ARROWS, WRITE WHICH OF THE 4 MECHANISTIC ELEMENTS IS INDICATED IN EACH STEP OF YOUR MECHANISM (For example, "Add a proton").

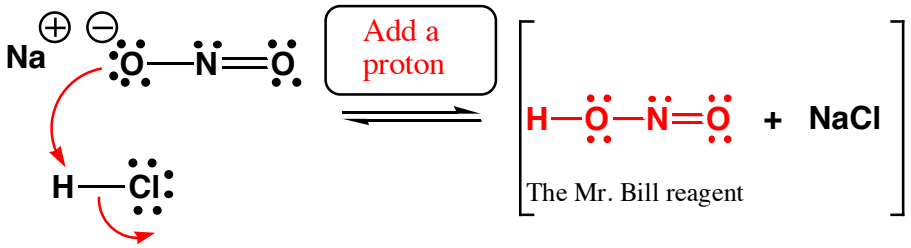


NOTICE THIS

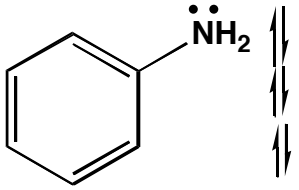
(2 Pts) **In one sentence explain why this reation is reffered to as acid "promoted" rather than acid "catalyzed".**

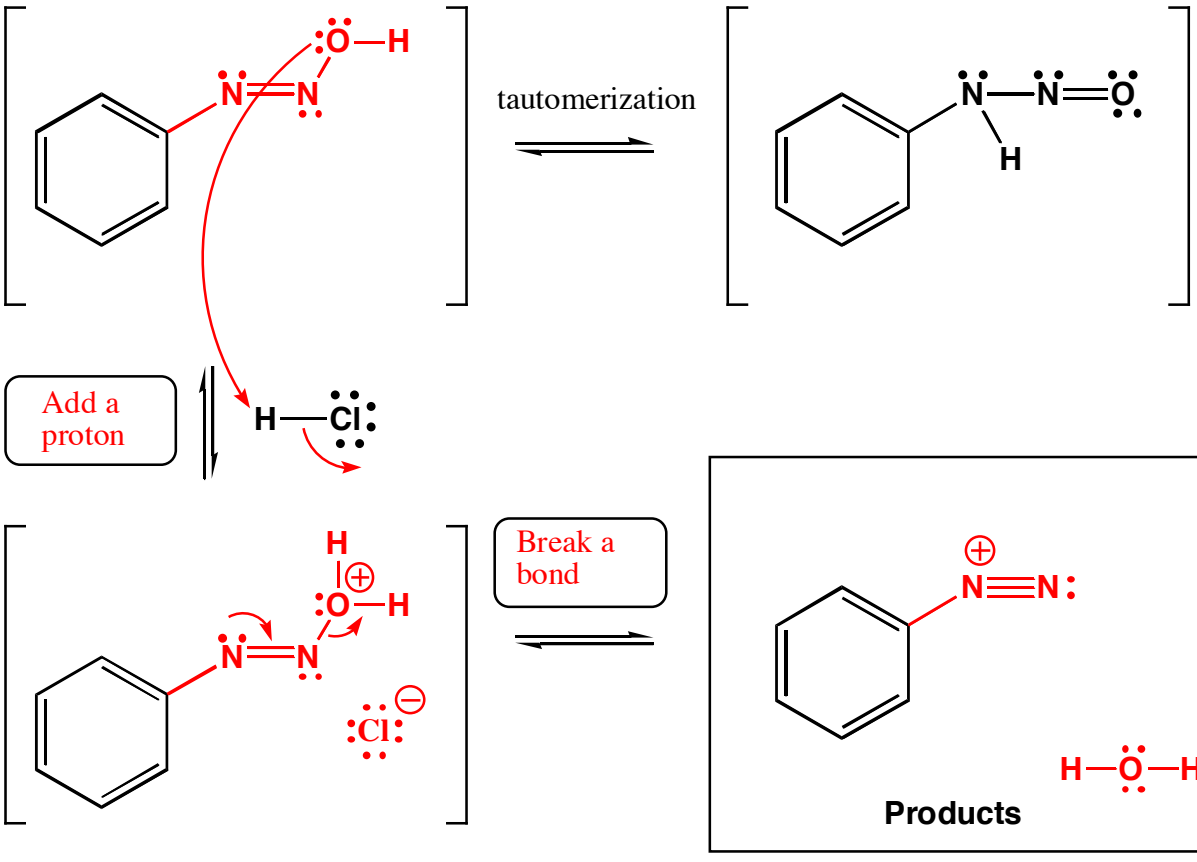
The reaction requires acid in the first step, but the proton is consumed during the reaction leaving an ammonium ion (a much weaker acid) as the protonated product.

12. (17 pts) Complete the mechanism for the Mr. Bill reaction. Be sure to show arrows to indicate movement of all electrons, write all lone pairs, all formal charges, and all the products for each step. Remember, I said all the products for each step. IF A NEW CHIRAL CENTER IS CREATED IN AN INTERMEDIATE OR THE PRODUCTS, MARK IT WITH AN ASTERISK AND LABEL AS "RACEMIC" IF RELEVANT. IN THE BOX BY EACH SET OF ARROWS, WRITE WHICH OF THE 4 MECHANISTIC ELEMENTS IS INDICATED IN EACH STEP OF YOUR MECHANISM (For example, "Add a proton").

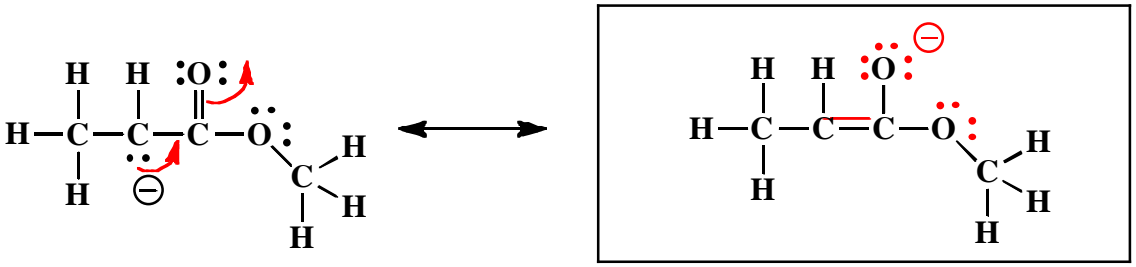


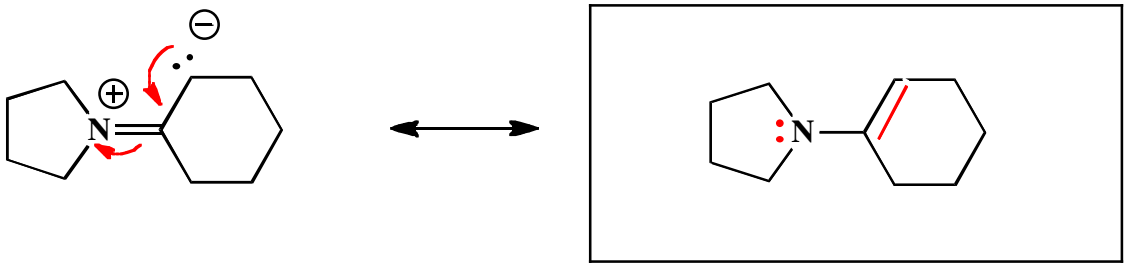
Note we drew a benzene ring in each box to serve as a template and save you a little time

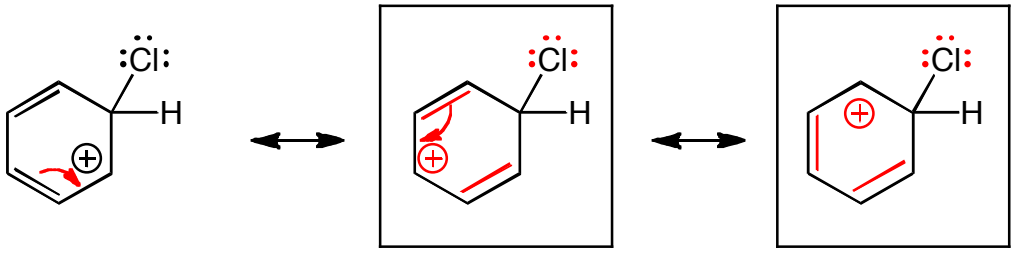


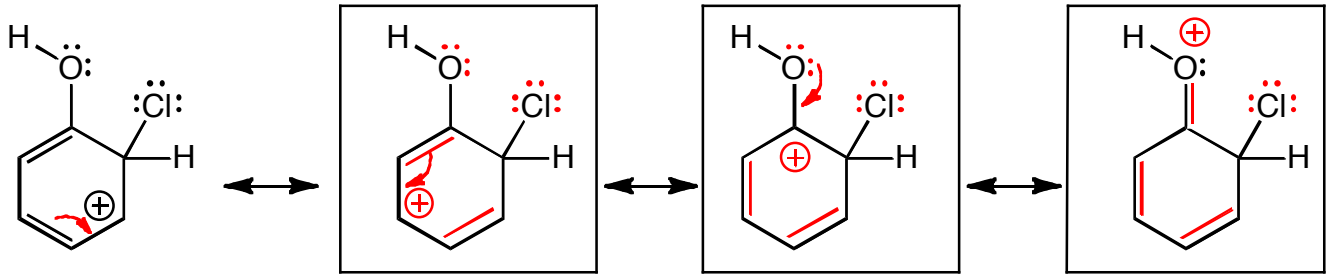


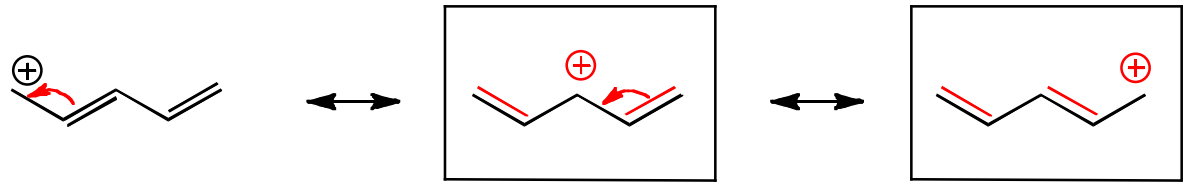
13. (27 pts total) For the following, draw the other important contributing structure or structures (resonance form(s)) we presented in class. You must draw arrows on the structure to the left to indicate the flow of electrons that leads to the contributing structure you draw to the right (All but the rightmost structure on each line has arrows on it). Be sure to show all lone pairs and formal charges on your structures. We have drawn template structures to save you time.



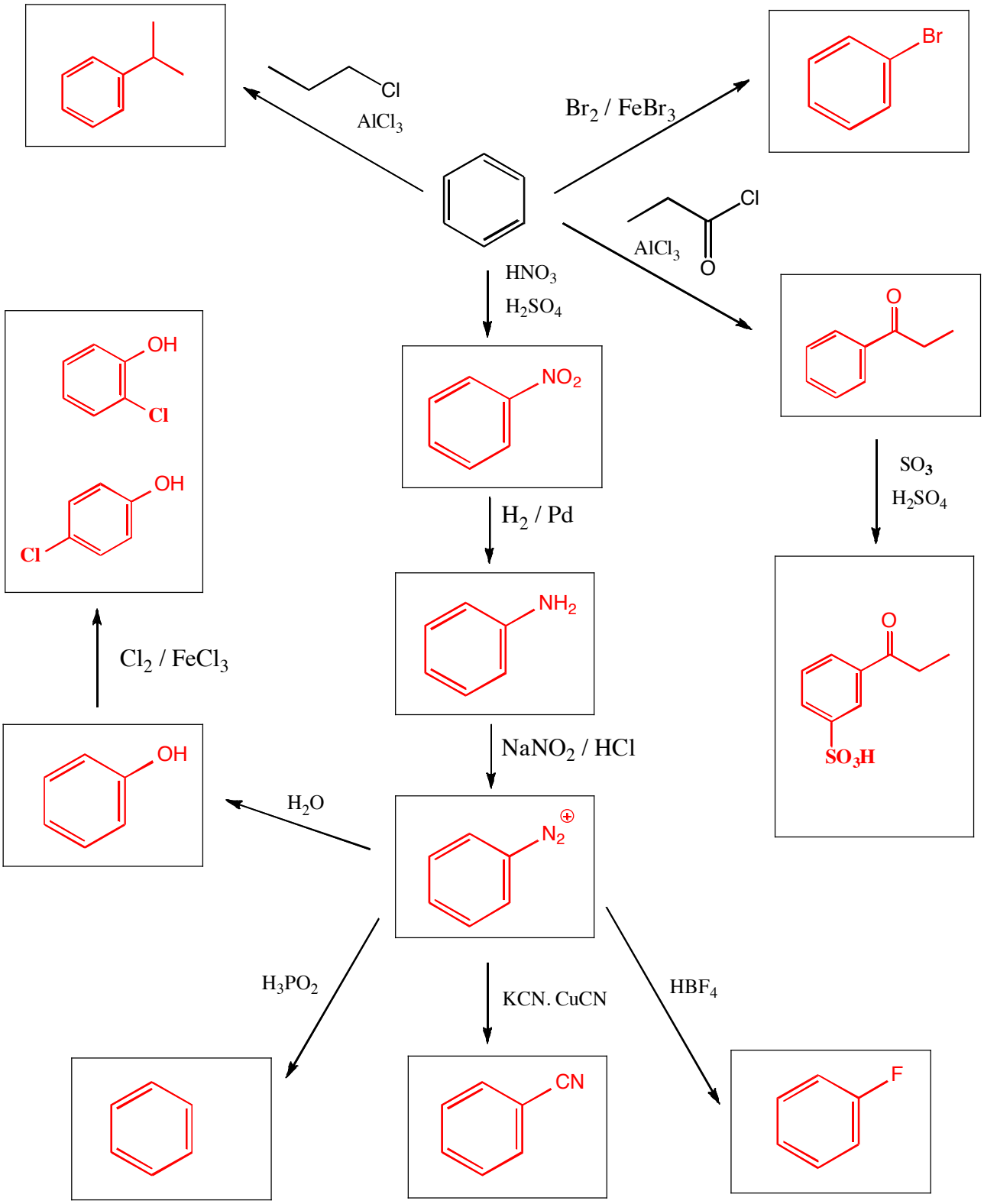




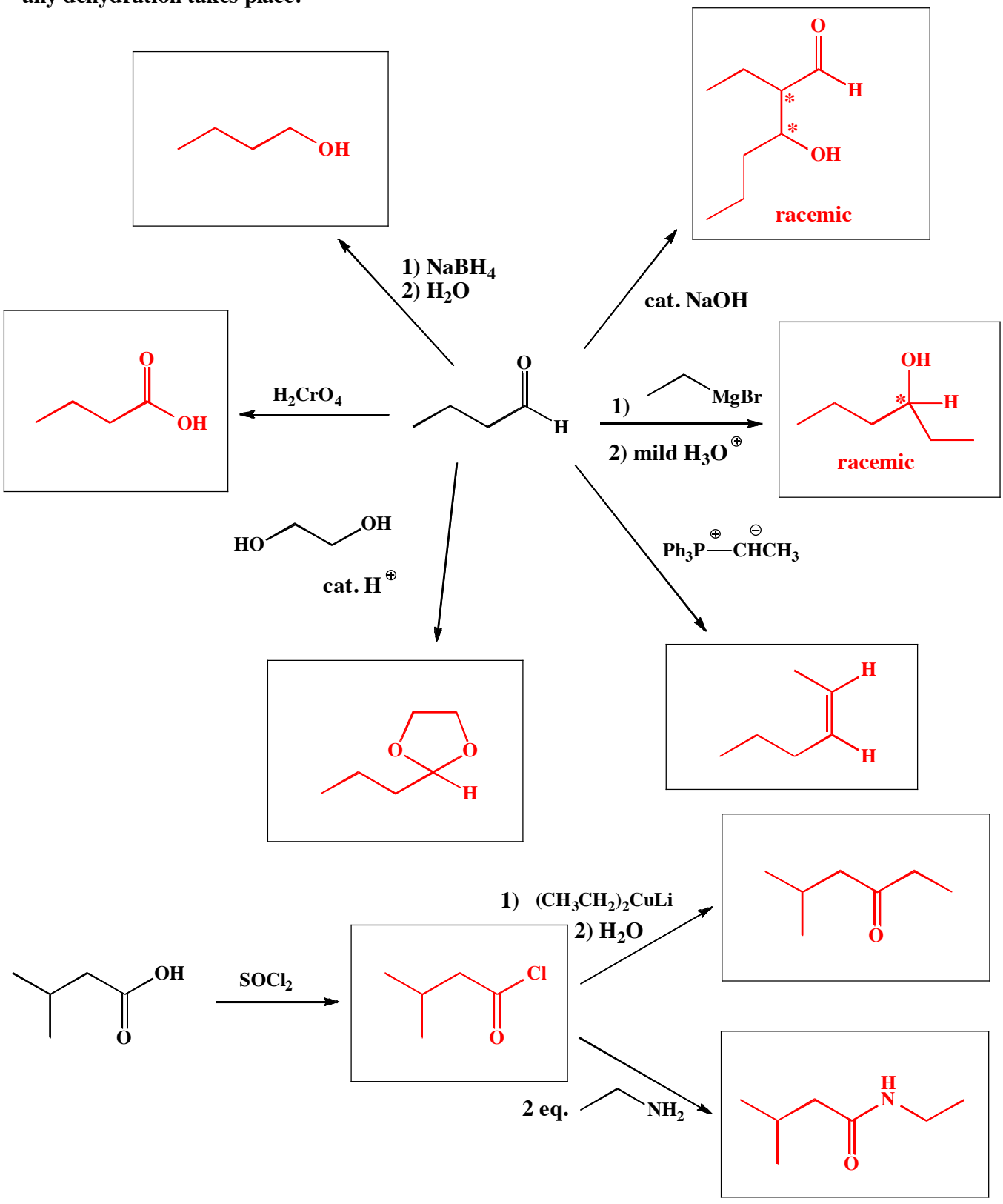




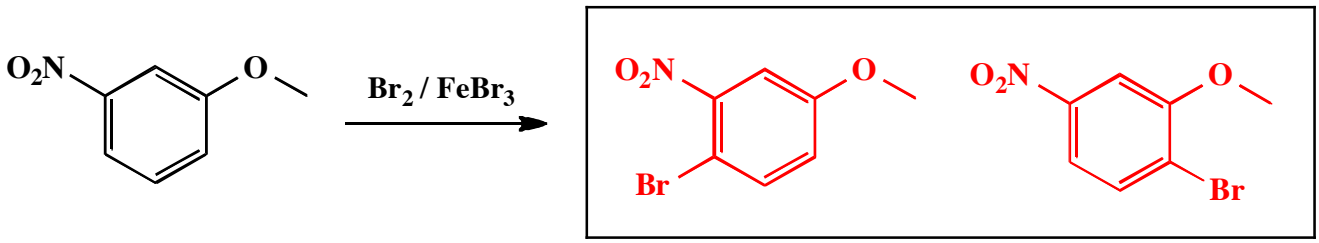
14. (26 pts.) Write the predominant product or products that will occur for each transformation. Assume each reagent only adds once to the ring. If predominantly ortho/para products are predicted, you must draw both.

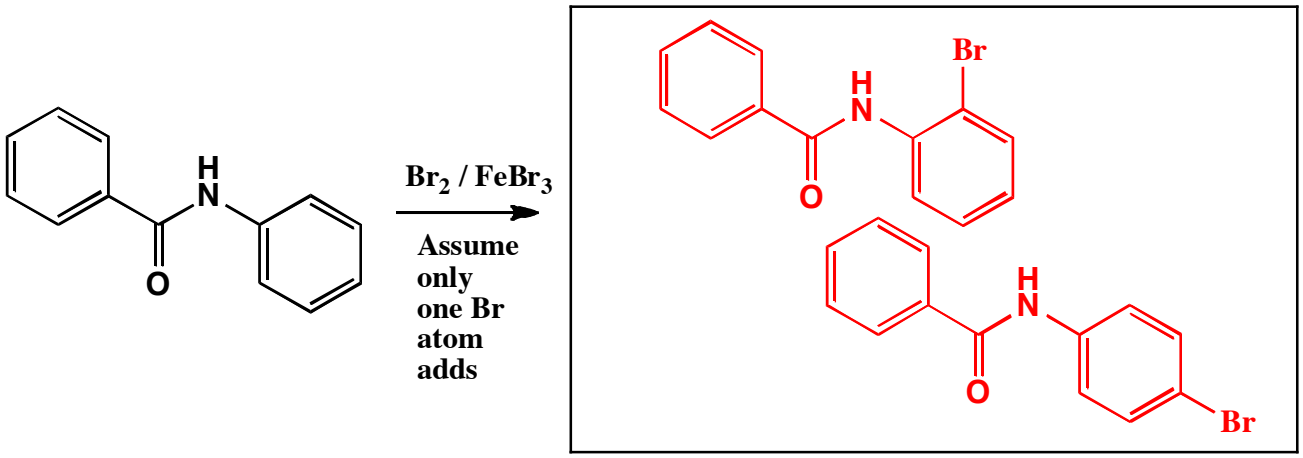


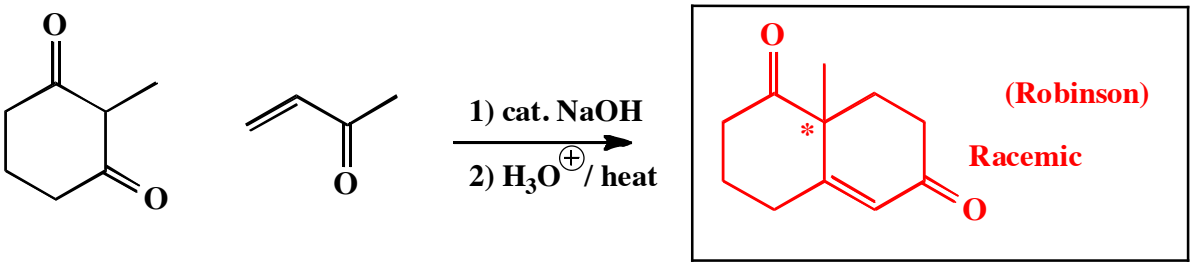
15. (31 pts.) Write the predominant product or products that will occur for each transformation. **If a new chiral center is created and a racemic mixture is formed, mark the chiral center with an asterisk "*" and write "racemic" under the structure. If there is an aldol reaction, draw the product before any dehydration takes place.**

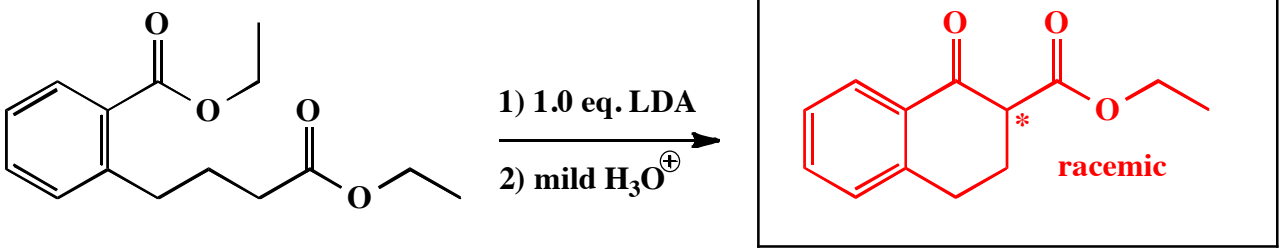


16. (18 pts.) You might find these are harder so take your time. Write the predominant product or products that will occur for each transformation. **If a new chrial center is created and a racemic mixture is formed, mark the chiral center with an asterisk "*" and write "racemic" under the structure. If ortho/para products are made, you must draw both. Note, for this problem, aldols can dehydrate if heated in dilute acid.**

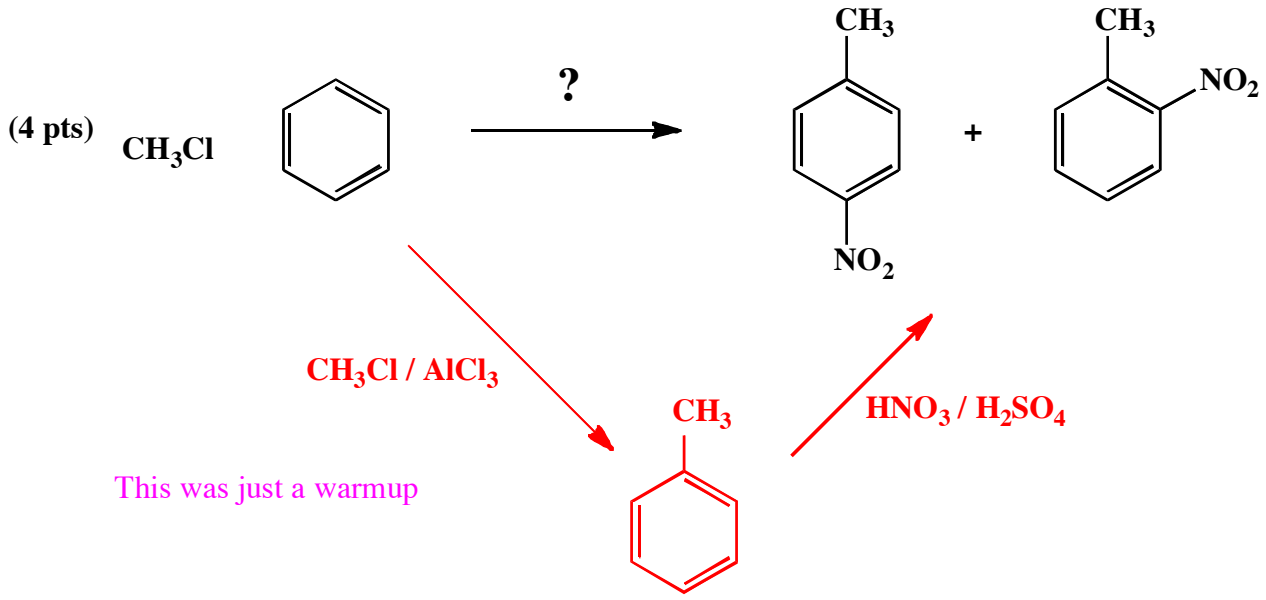




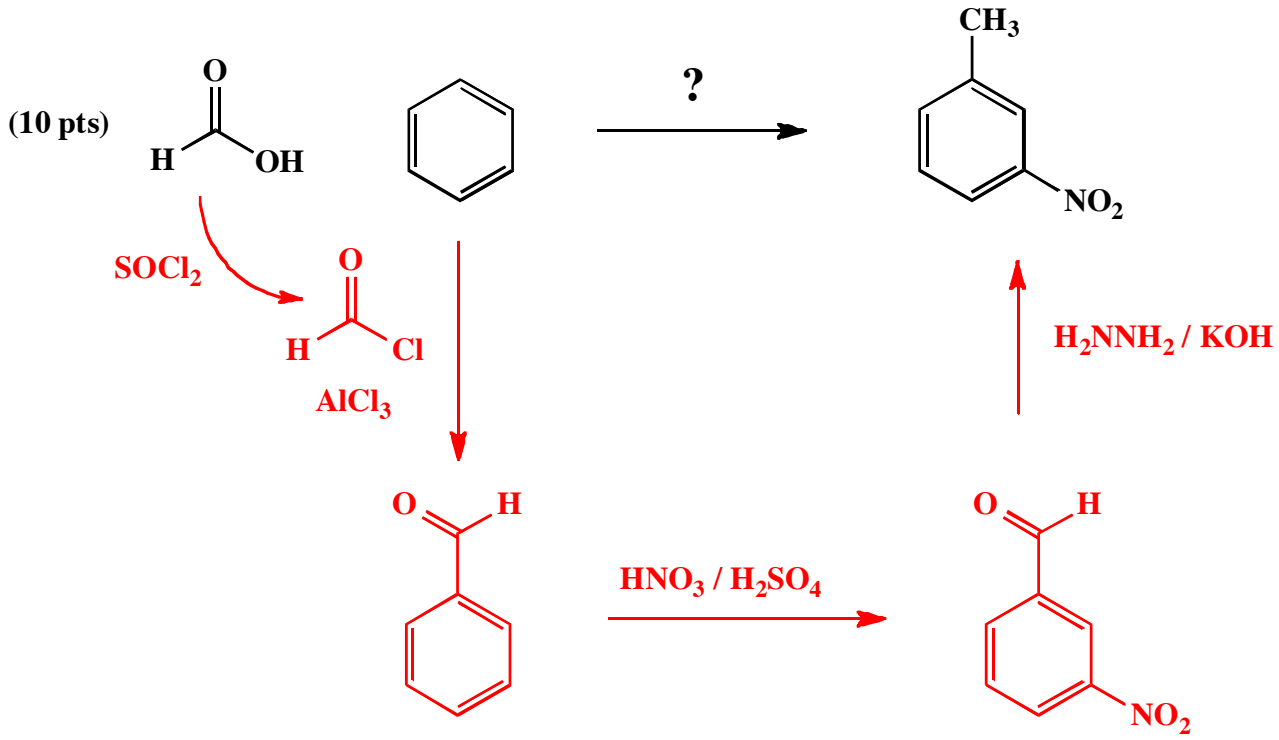




17. Using any reagents turn the starting material into the indicated product. All the carbons in the product must come from the given starting materials. Draw all molecules synthesized along the way. When it doubt, draw the molecule!



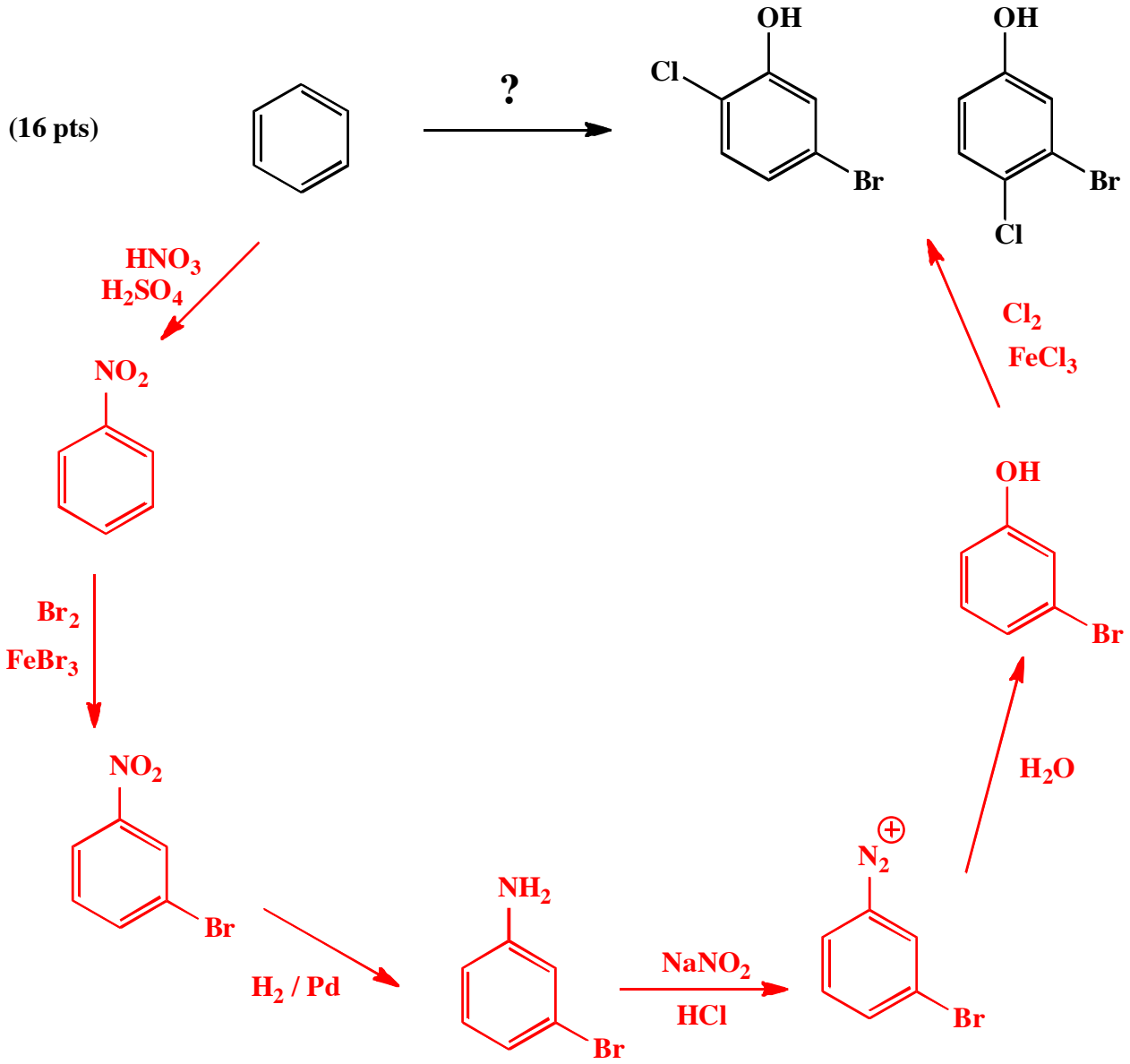
This was just a warmup



Recognize that this one is harder than it looks because the Friedel-Crafts reaction will not work on a ring with a bad group like the nitro group on it. Therefore, the methyl group has to be made using a Wolff-Kishner or Clemmensen reduction following nitration.

17. Using any reagents turn the starting material into the indicated product. All the carbons in the product must come from the given starting materials. Draw all molecules synthesized along the way. When it doubt, draw the molecule! **NOTE: For this one, you are not allowed to separate complex mixtures along the way and pull out just the isomers you want. In other words, the product isomers shown must be the only predominant isomers you make during your synthesis.**

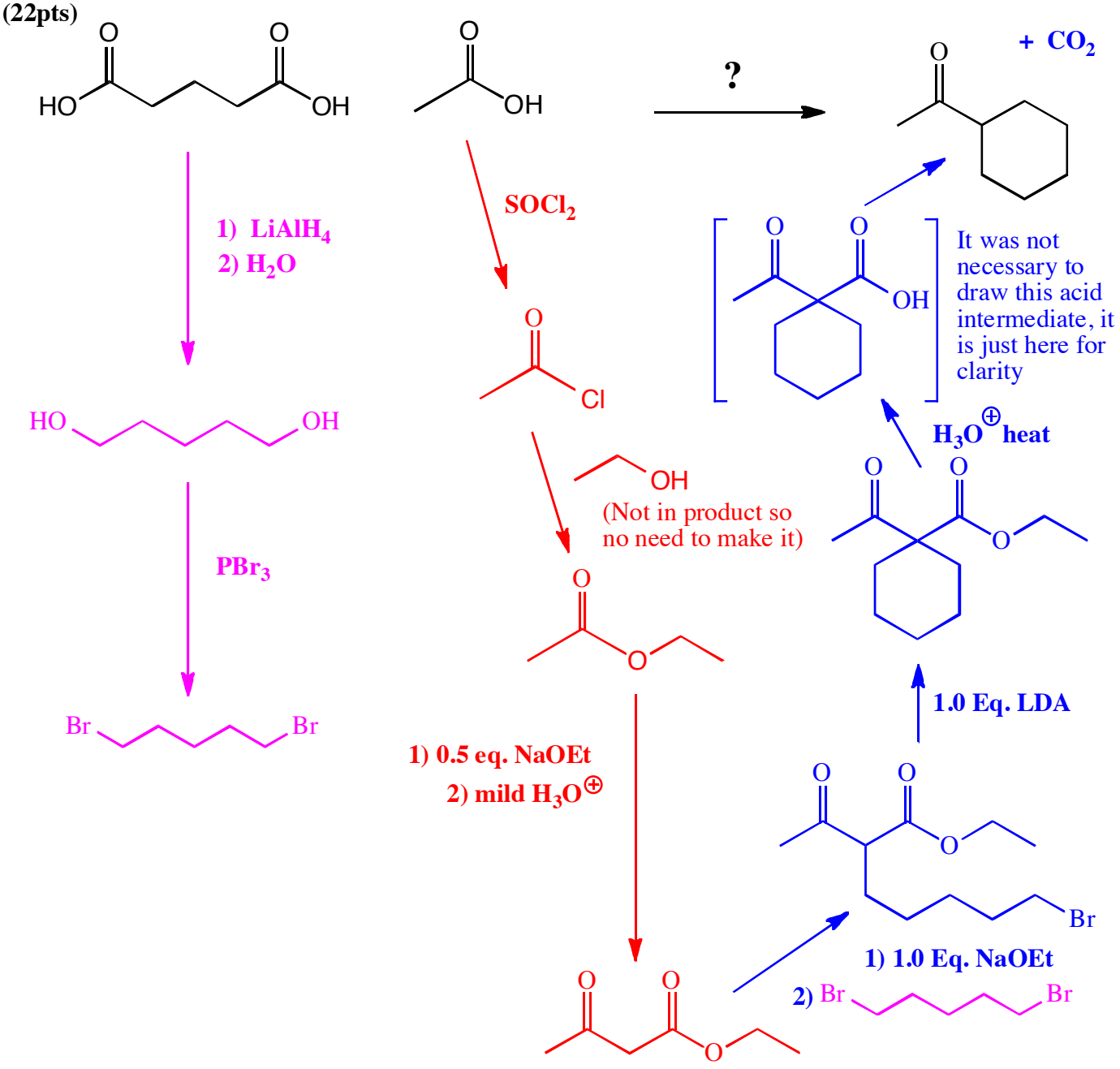
(16 pts)



Recognize that the last reaction had to be the chlorination reaction of the meta bromophenol. This is because we see both the ortho and para chlorination products. **Recognize** that both the OH and Br groups of meta bromophenol are ortho/para directors, so their meta relationship must derive from nitrobenzene, followed by the bromomination reaction, followed by the Mr. Bill reaction and conversion to the phenol with H_2O.

17. Using any reagents turn the starting material into the indicated product. All the carbons in the product must come from the given starting materials, but you may use any carbon containing reagent along the way as long as its carbons do not end up in the product. Draw all molecules synthesized along the way. When it doubt, draw the molecule!

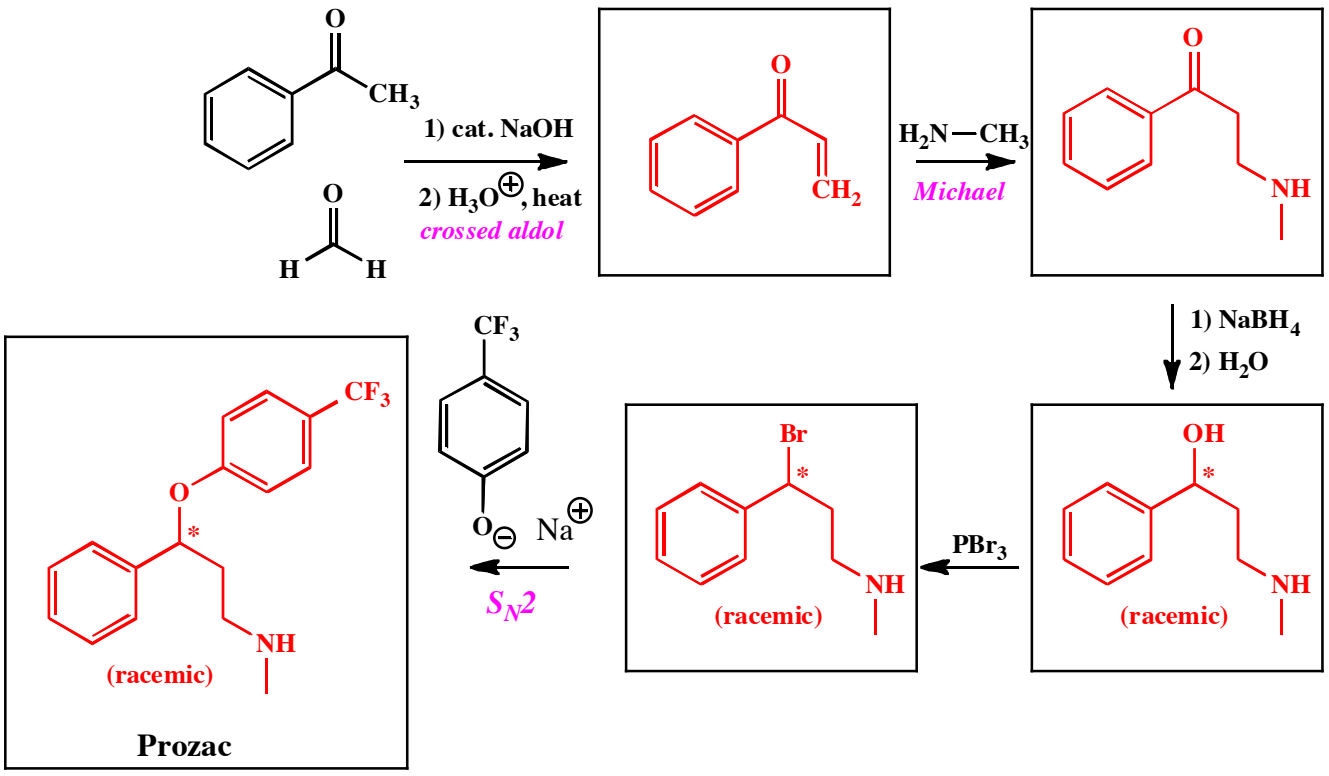
(22pts)



Recognize the product as coming from an acetoester synthesis (methyl ketone is the KRE). The tricky part of this one is **recognizing** that the ring comes from alkylation of ethyl acetoacetate in two sequential steps by 1,5-dibromopentane. **Recognize** that the ethyl acetoacetate comes from the Claisen reaction of ethyl acetate, which in turn comes from ethanol and acetyl chloride, the latter of which comes from reaction of the staring acetic acid with $SOCl_2$. Fischer esterification would have worked to make the ester as well. **Recognize** that the dibromopentane can be derived from the corresponding 1,5 pentanediol, which is the product of reduction of the starting diacid with $LiAlH_4$.

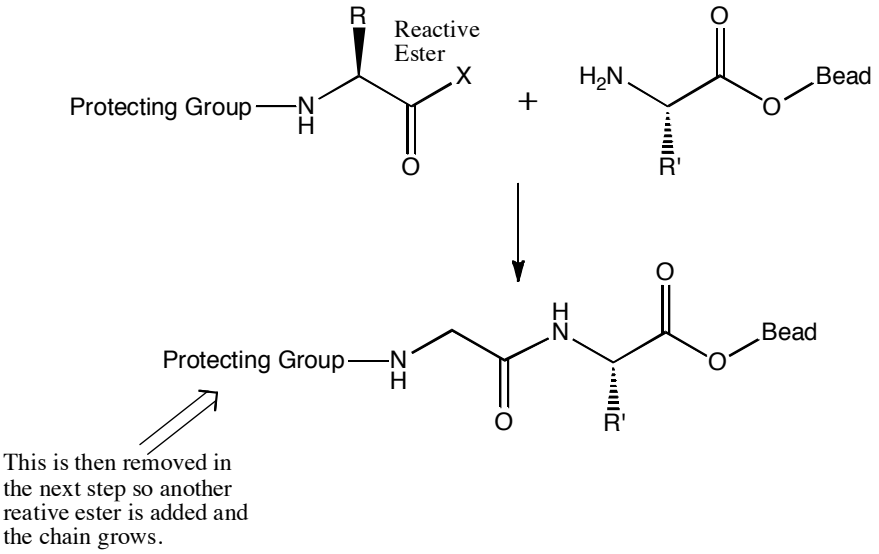
It is time to apply your synthetic knowledge to a real world synthesis problem!

18. (21 pts.) Here is the synthesis of the important pharmaceutical Prozac. You are familiar with all of the chemistry, it just might take you a while to recognize the reactions. **Fill in the boxes with the appropriate structures, and remember to use an asterisk "*" and write "racemic" to indicate any new chiral centers created along the way. Hint: not listed in order, this set of transformations includes a Michael reaction, an S_N2 reaction, a reduction reaction, conversion of a OH group to a halide and an aldol reaction WITH dehydration.**

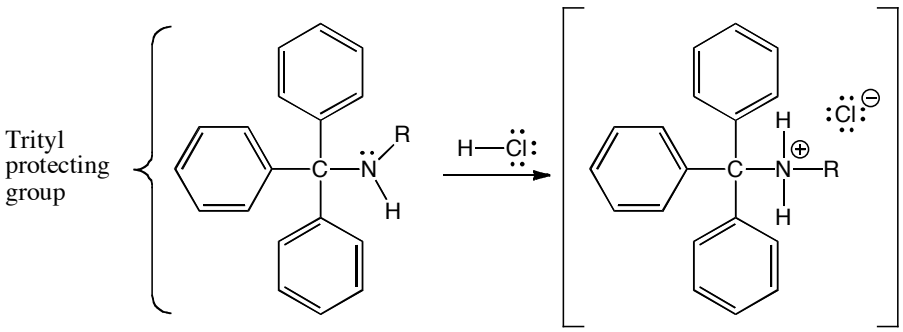


Here is an MCAT style passage question.

One of the key technical challenges associated with synthesizing peptides or small proteins from amino acids concerns the protecting groups required for the amine groups. In each coupling step, whether carried out on a bead or in solution, one amino group is used as a nucleophile, reacting with a reactive ester of some sort. For this to work, the amine group on the reactive ester molecule must be blocked with a protecting group as shown. The ideal amine protecting group will be easy to put on, then stable to the conditions required to make the amide bond. Then after the amide bond is made, it must be easy to take off again so the next reactive ester can be added and the chain continued.



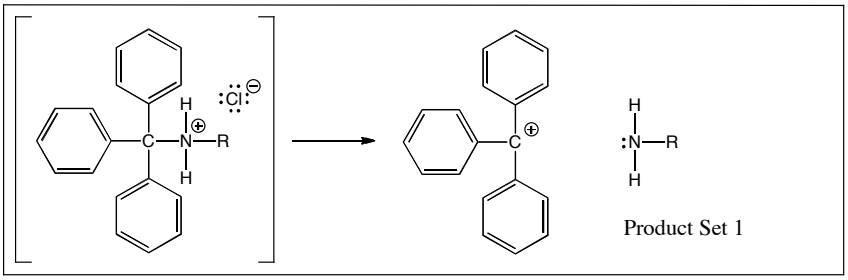
One of the earliest amine protecting groups developed was the triphenylmethyl group, most often referred to by its nickname, the "trityl" group. The trityl group is stable to base and is removed in acid such as HCl. Following is the first step in the reaction to remove a trityl group in acid.

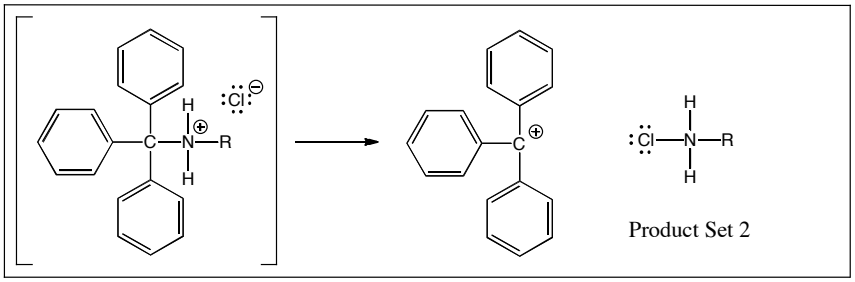


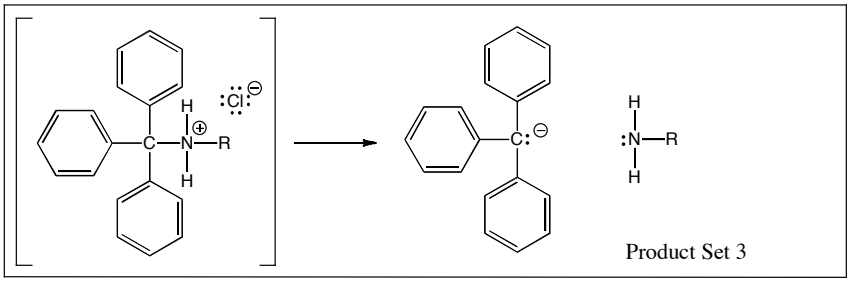
The above step is a classic example of which fundamental mechanistic element:

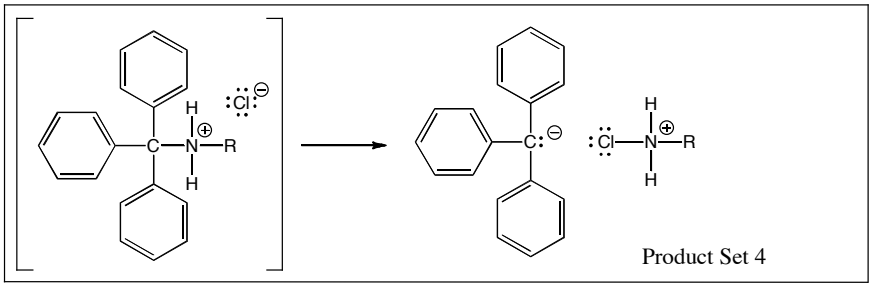
A. Make a bond
B. Break a bond
C. Add a proton
D. Take a proton away

The intermediate formed in the first step is unstable and will immediately react to give two products.





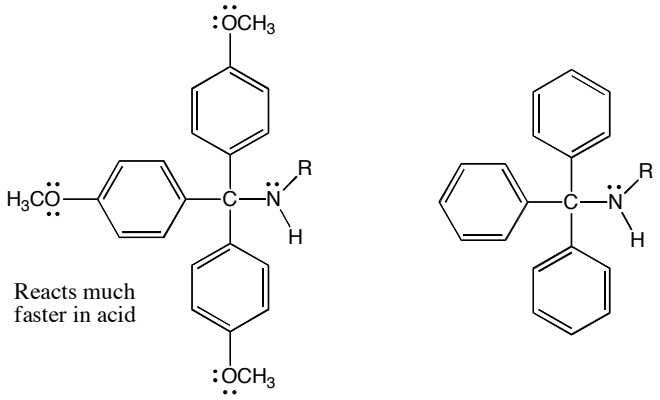




Which is the correct product set for this reaction.

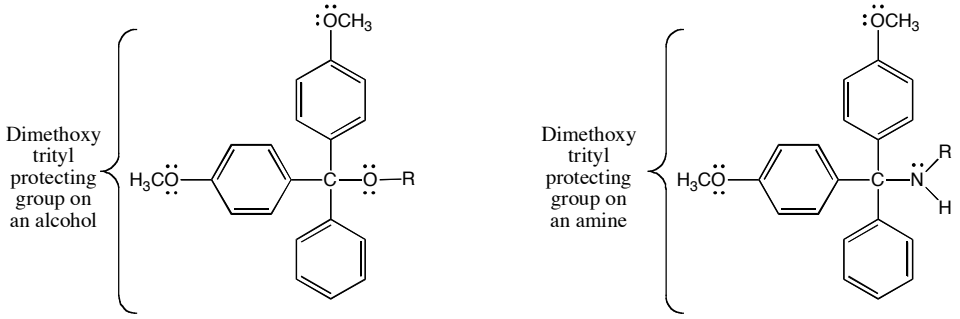
A. Product Set 1
B. Product Set 2
C. Product Set 3
D. Product Set 4

Your answer to the last problem should explain the following observation: A trityl group with one, two, or especially three methoxy groups on it is MUCH more reactive in acid than the parent trityl group .



A. The methoxy groups withdraw electron density from the aromatic rings and stabilize a negative charge on the central C atom of the trityl group.
B. The methoxy groups donate electron density into the aromatic rings and stabilize a negative charge on the central C atom of the trityl group.
C. The methoxy groups withdraw electron density from the aromatic rings and stabilize a positive charge on the central C atom of the trityl group.
D. The methoxy groups donate electron density into the aromatic rings and stabilize a positive charge on the central C atom of the trityl group.

Alcohol groups are commonly masked with the trityl protecting group as well in the form of a trityl ether. The dimethoxytrityl group is particularly popular as a protecting group for primary alcohols.



Which of these reacts faster?

In fact, the dimethoxyltrityl group is used to protect the primary alcohol group in the commercial solid phase synthesis of DNA and RNA. Would you expect a dimethoxy trityl protecting group to fall off of the alcohol or amine the fastest and why?

A. The dimethoxytrityl group will fall off of the amine faster because the amine is more basic and therefore easier to protonate in the first step of the mechanism.
B. The dimethoxytrityl group will fall off of the alcohol faster because the ether is more basic and therefore easier to protonate in the first step of the mechanism.
C. I could not come up with any other explanations, it really is A. or B.
D. Do not pick C. or D.