NAME (Print): ______________________________

Chemistry 320N
2nd Midterm Exam
March 9, 2023

EID _______________

SIGNATURE: ______________________________

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

Please Note: Please take your time. You have three hours to take this exam. Please do not rush, we want you to show us everything you have learned this semester so far! Making careless mistakes is not good for anyone! If you find yourself getting anxious because of a problem, skip it and come back. Please do not second guess yourself! Keep track of the questions worth a lot of points. (This does not mean they are hard, it just means we think they cover important material.)

One last thing: I recommend you close your eyes for a moment, then take some nice deep breaths before you begin. YOU GOT THIS!

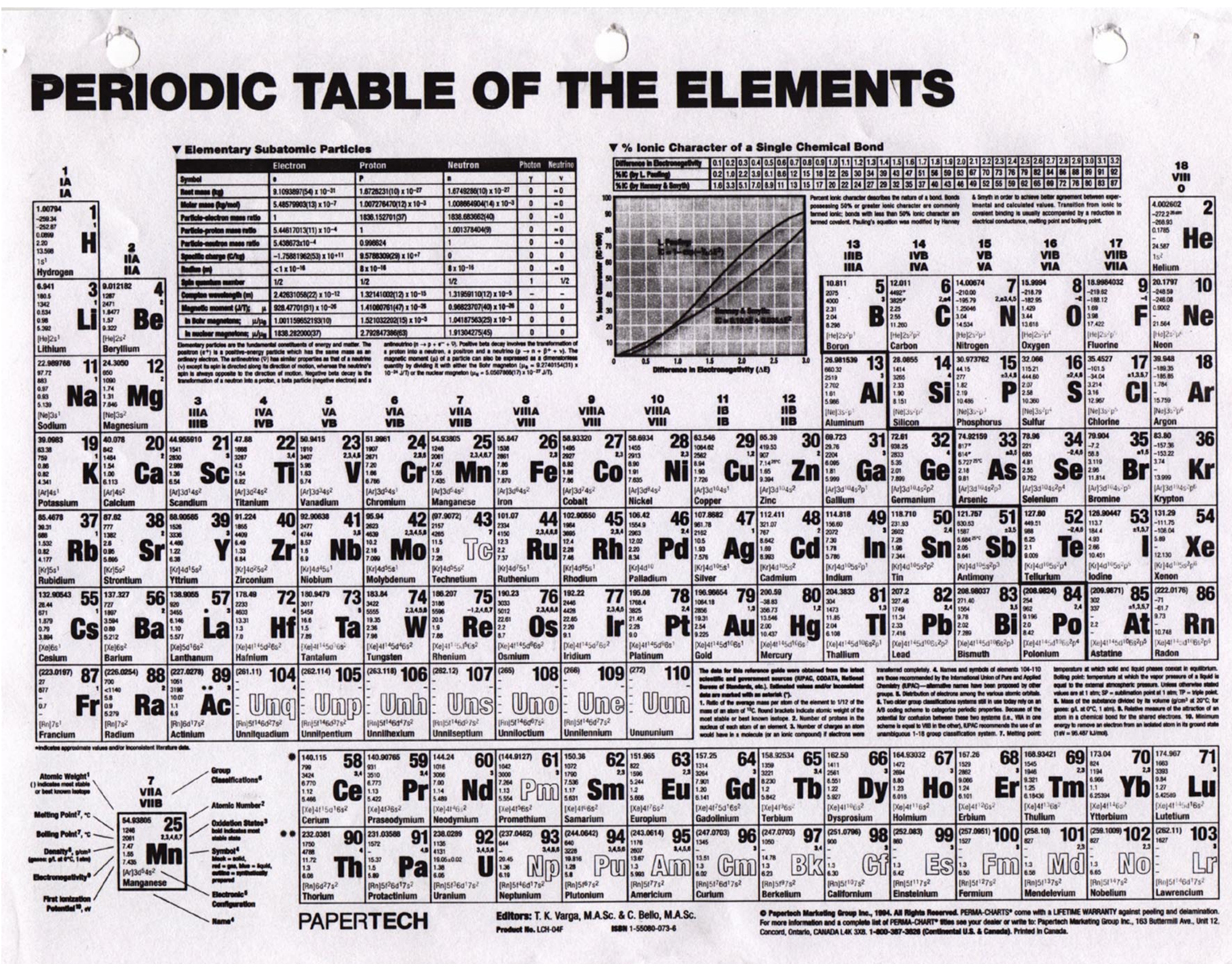
FINALLY, DUE TO SOME UNFORTUNATE RECENT INCIDENTS YOU ARE NOT ALLOWED TO INTERACT WITH YOUR CELL PHONE IN ANY WAY. IF YOU TOUCH YOUR CELL PHONE DURING THE EXAM YOU WILL GET A "0" NO MATTER WHAT YOU ARE DOING WITH THE PHONE. PUT IT AWAY AND LEAVE IT THERE!!!

Student Honor Code

"As a student of The University of Texas at Austin, I shall abide by the core values of the University and uphold academic integrity."

____

(Your signature)



Compound		pK_a
Hydrochloric acid	$\underline{H}$-Cl	-7
Protonated alcohol	$RCH_2O\underline{H_2}^{+}$	-2
Hydronium ion	$\underline{H}_3O^{+}$	-1.7
Carboxylic acids	$R-C(=O)O-\underline{H}$	3-5
Thiols	$RCH_2S\underline{H}$	8-9
Ammonium ion	$\underline{H}_4N^{+}$	9.2
β-Dicarbonyls	$RC(=O)-C\underline{H_2}-C(=O)R'$	10
Primary ammonium	$\underline{H}_3N^{+}CH_2CH_3$	10.5
β-Ketoesters	$RC(=O)-C\underline{H_2}-C(=O)OR'$	11
β-Diesters	$ROC(=O)-C\underline{H_2}-C(=O)OR'$	13
Water	$HO\underline{H}$	15.7
Alcohols	$RCH_2O\underline{H}$	15-19
Acid chlorides	$RC\underline{H_2}-C(=O)Cl$	16
Aldehydes	$RC\underline{H_2}-C(=O)H$	18-20
Ketones	$RC\underline{H_2}-C(=O)R'$	18-20
Esters	$RC\underline{H_2}-C(=O)OR'$	23-25
Terminal alkynes	$RC\equiv C-\underline{H}$	25
LDA	$\underline{H}$-$N(i\text{-}C_3H_7)_2$	40
Terminal alkenes	$R_2C=C(H)-\underline{H}$	44
Alkanes	$CH_3CH_2-\underline{H}$	51

Signature______________________________ Pg 1 ____________(32)

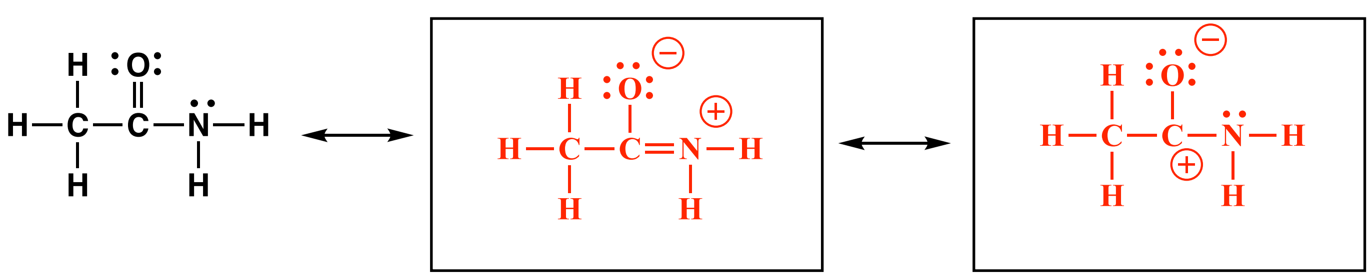
1. (5 pts) What is the most important question in organic chemistry?

Where are the electrons?

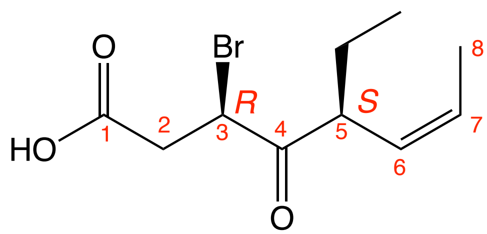
2. (1 pt each) Fill in each blank with the word that best completes the sentences. Yep, this is the MRI paragraph!

The popular medical 1. ___diagnostic___ technique of 2. ___magnetic___ 3. ___resonance___ imaging (MRI) is based on the same principles as 4. ___NMR___ , namely the 5. ___flipping___ (i.e. 6. ___resonance___) of nuclear 7. ___spins___ of H atoms by radio 8. ___frequency___ irradiation when a patient is placed in a strong 9. ___magnetic___ field. Magnetic field 10. ___gradients___ are used to gain imaging information, and rotation of the 11. ___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 12. ___slices___ that when stacked make up the three-dimensional image of 13. ___relative___ amounts of 14. ___H___ atoms, especially the 15. ___H___ atoms from 16. ___water___ and 17. ___fat___ , in the different tissues.

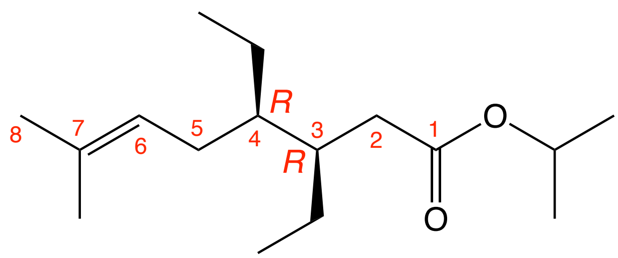
3. (10 pts) Amides are best represented as the hybrid of three contributing structures. Draw the second and third important contributing structures in the spaces provided.



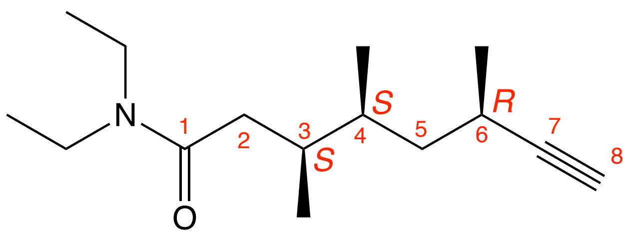
4. (6 pts each) From the list below, select the letter associated with the IUPAC name that is correct for each structure.



The letter corresponding to the IUPAC name of this molecule is **F.**



The letter corresponding to the IUPAC name of this molecule is **A.**



The letter corresponding to the IUPAC name of this molecule is **H.**

A. isopropyl (3*R*,4*R*)-3,4-diethyl-7-methyl-6-octenoate

B. isopropyl (3*S*,4*R*)-3,4-diethyl-7-methyl-6-octenoate

C. isopropyl (3*S*,4*S*)-3,4-diethyl-7-methyl-6-octenoate

D. (*R*,*E*)-3-bromo-5-ethyl-4-oxo-5-octenoic acid

E. (2*R*,5*S*,*Z*)-2-bromo-5-ethyl-4-oxo-6-octenoic acid

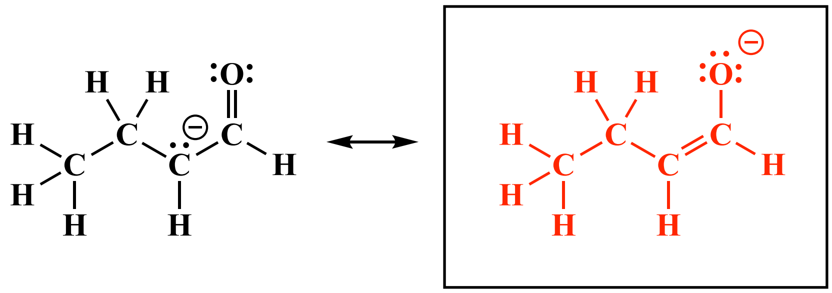
F. (3*R*,5*S*,*Z*)-3-bromo-5-ethyl-4-oxo-6-octenoic acid

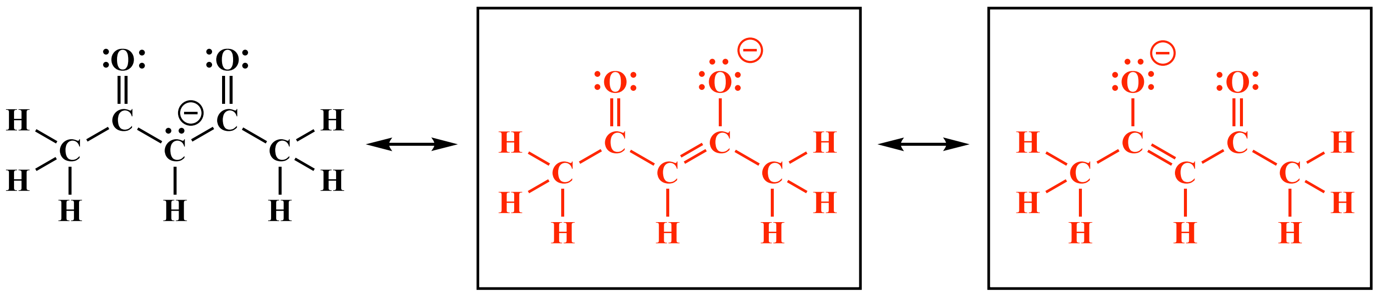
G. (3*S*,4*S*,6*R*)-3-butyl-*N*-ethyl-4,6-dimethyl-*N*-propyl-7-octynamide

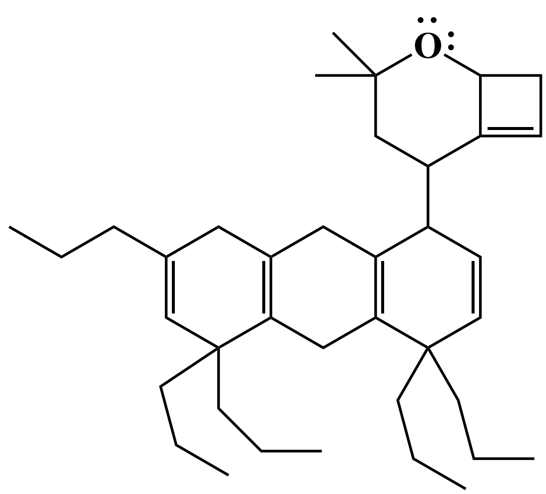
H. (3*S*,4*S*,6*R*)-*N*,*N*-diethyl-3,4,6-trimethyl-7-octynamide

I. (3*S*,4*R*,*E*)-3-butyl-*N*-ethyl-4,6-dimethyl-*N*-propyl-5-octenamide

5. (9 pts each) For the two different enolates shown below, draw the other important contributing structures. Make sure to show all electrons and formal charges.





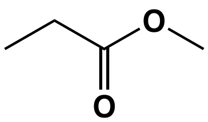


3,3-dimethyl-5-(4,4,5,5,7-pentapropyl-1,4,5,8,9,10-hexahydroanthracen-1-yl)-2-oxabicyclo[4.2.0]oct-6-ene

Also known as Fifi, a miniature, and I mean miniature, Chihuahua

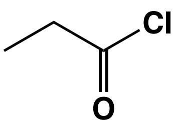
6. (17 pts) Being able to recognize the chemical personality of different species is one of the most important skills you can develop in Organic Chemistry. Fill in the appropriate circle to indicate whether each structure is a nucleophile or electrophile in bond-making ("Make a Bond") steps of mechanisms you have seen. Note that these species might be acids or bases in certain situations, but we will ignore that for this problem.

6.1



● Electrophile
○ Nucleophile

6.2

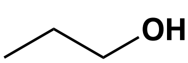


● Electrophile
○ Nucleophile

6.3 $H_3C-C\equiv \overset{\oplus}{N}-H$

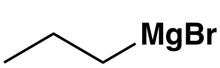
● Electrophile
○ Nucleophile

6.4



○ Electrophile
● Nucleophile

6.5

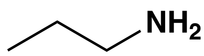


○ Electrophile
● Nucleophile

6.6 $LiAlH_4$

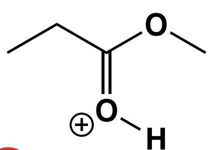
○ Electrophile
● Nucleophile

6.7



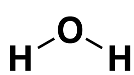
○ Electrophile
● Nucleophile

6.8



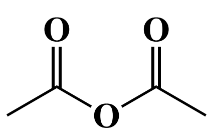
● Electrophile
○ Nucleophile

6.9



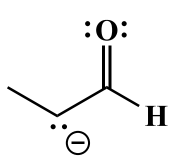
○ Electrophile
● Nucleophile

6.10



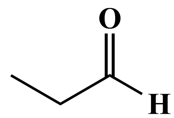
● Electrophile
○ Nucleophile

6.11



○ Electrophile
● Nucleophile

6.12

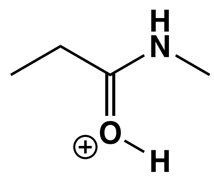


● Electrophile
○ Nucleophile

6.13 $^{\ominus}O-H$

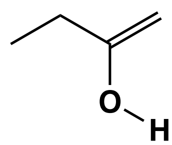
○ Electrophile
● Nucleophile

6.14



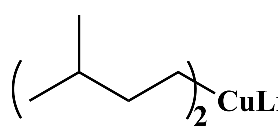
● Electrophile
○ Nucleophile

6.15



○ Electrophile
● Nucleophile

6.16



○ Electrophile
● Nucleophile

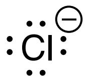
6.17 $NaBH_4$

○ Electrophile
● Nucleophile

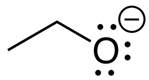
Signature____________________________ Pg 5 _______ (16)

7. (12 pts) These are the ranking questions.

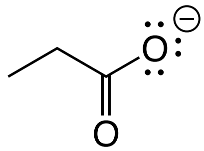
A) Rank the following with respect to anion stability, WITH A "1" UNDER THE MOST STABLE ANION AND "4" UNDER THE LEAST STABLE ANION, AND THEN "2" AND "3" AS APPROPRIATE.



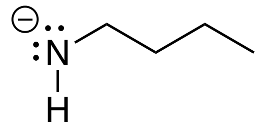
1



3

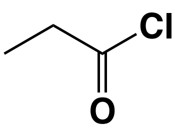


2

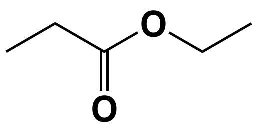


4

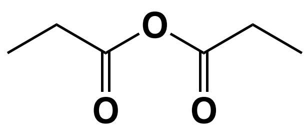
B) Rank the following with respect to reactivity with nuucleophiles, WITH A "1" UNDER THE MOST REACTIVE AND "4" UNDER THE LEAST REACTIVE, AND THEN "2" AND "3" AS APPROPRIATE.



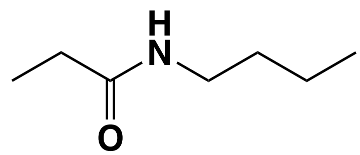
1



3



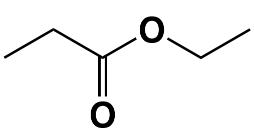
2



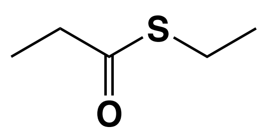
4

C) Thioesters (S in place of O in an ester) are important in biochemistry, being present in molecules such as Acetyl-CoA. Recall that anions increase in stability down a row of the periodic table as a function of increasing atomic radius (larger atoms have the negative charge spread over a larger area). Which of these two will be more reactive with nucleophiles?

The S atom is larger, so RS⊖ is more stable and a better leaving group, so thioesters are more reactive than normal esters.

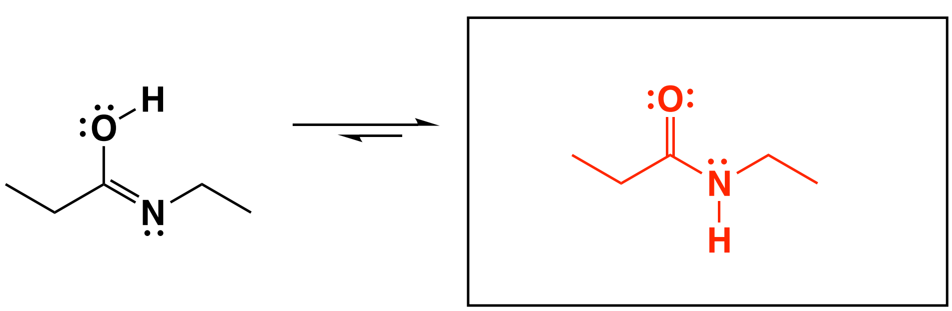


○ More reactive with nucleophiles
● Less reactive with nucleophiles



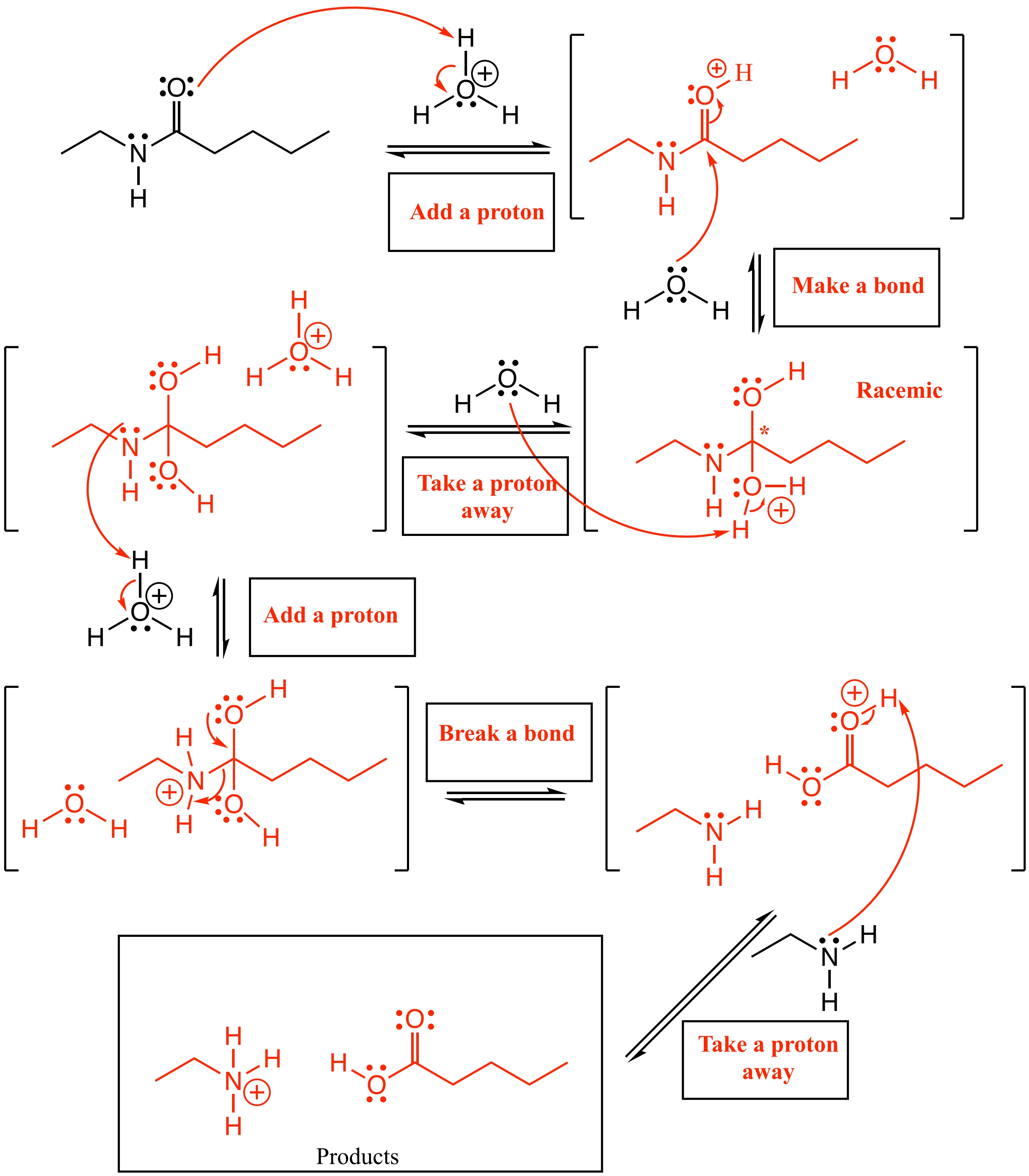
● More reactive with nucleophiles
○ Less reactive with nucleophiles

8. (4 pts) The following molecule spontaneously tautomerizes to a more stable species. **Draw the more stable species in the box provided.** There is no need to draw arrows here, but you do need to add all lone pairs and formal charges that are appropriate.

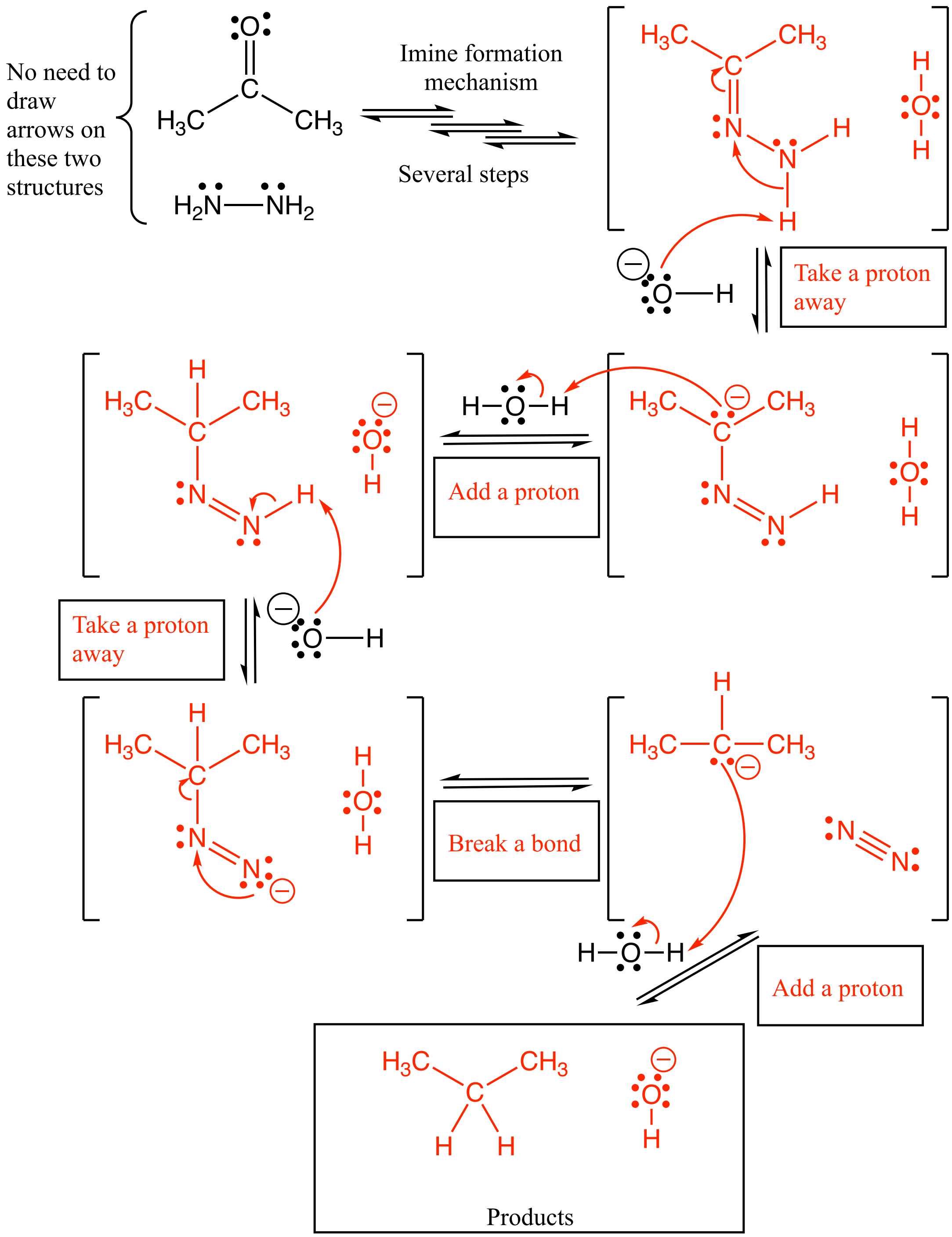


Signature___________________________ __________(35)

7. (35 pts) For this acid promoted amide hydrolysis reaction, use **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. IF A NEW CHIRAL CENTER IS CREATED IN AN INTERMEDIATE, MARK IT WITH AN ASTERISK AND LABEL THE MOLECULE AS "RACEMIC" IF APPROPRIATE. <u>FOR ALL CHIRAL PRODUCTS YOU MUST DRAW ALL ENANTIOMERS WITH WEDGES AND DASHES AND WRITE "RACEMIC' IF APPROPRIATE</u>. In the boxes provided by the arrows, write which of the 4 most common mechanistic elements describes each step (make a bond, break a bond, etc.).**

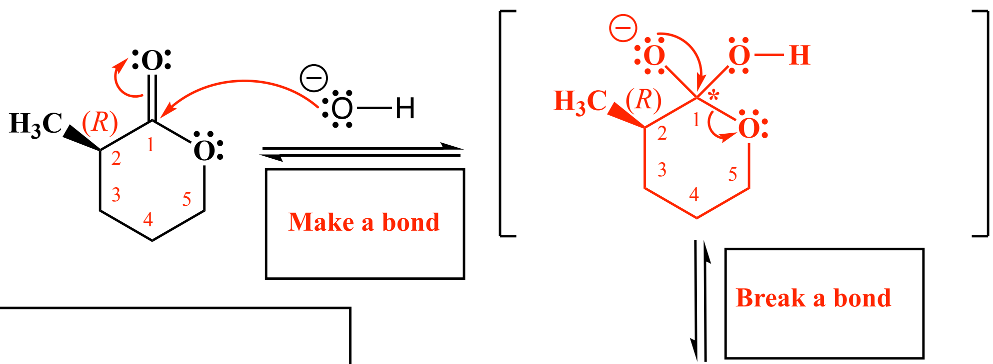


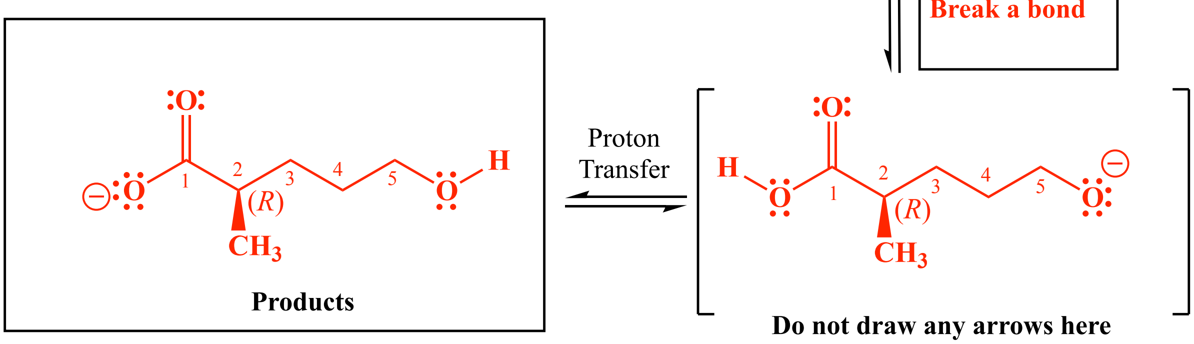
8. (34 pts) For this Wolff-Kishner reaction, use **arrows to indicate movement of <u>all</u> electrons, write <u>all</u> lone pairs, <u>all</u> formal charges, and <u>all</u> the products for each step. IF A NEW CHIRAL CENTER IS CREATED IN AN INTERMEDIATE, MARK IT WITH AN ASTERISK AND LABEL THE MOLECULE AS "RACEMIC" IF APPROPRIATE. <u>FOR ALL CHIRAL PRODUCTS YOU MUST DRAW ALL ENANTIOMERS WITH WEDGES AND DASHES AND WRITE "RACEMIC' IF APPROPRIATE</u>. In the boxes provided by the arrows, write which of the 4 most common mechanistic elements describes each step (make a bond, break a bond, etc.).**

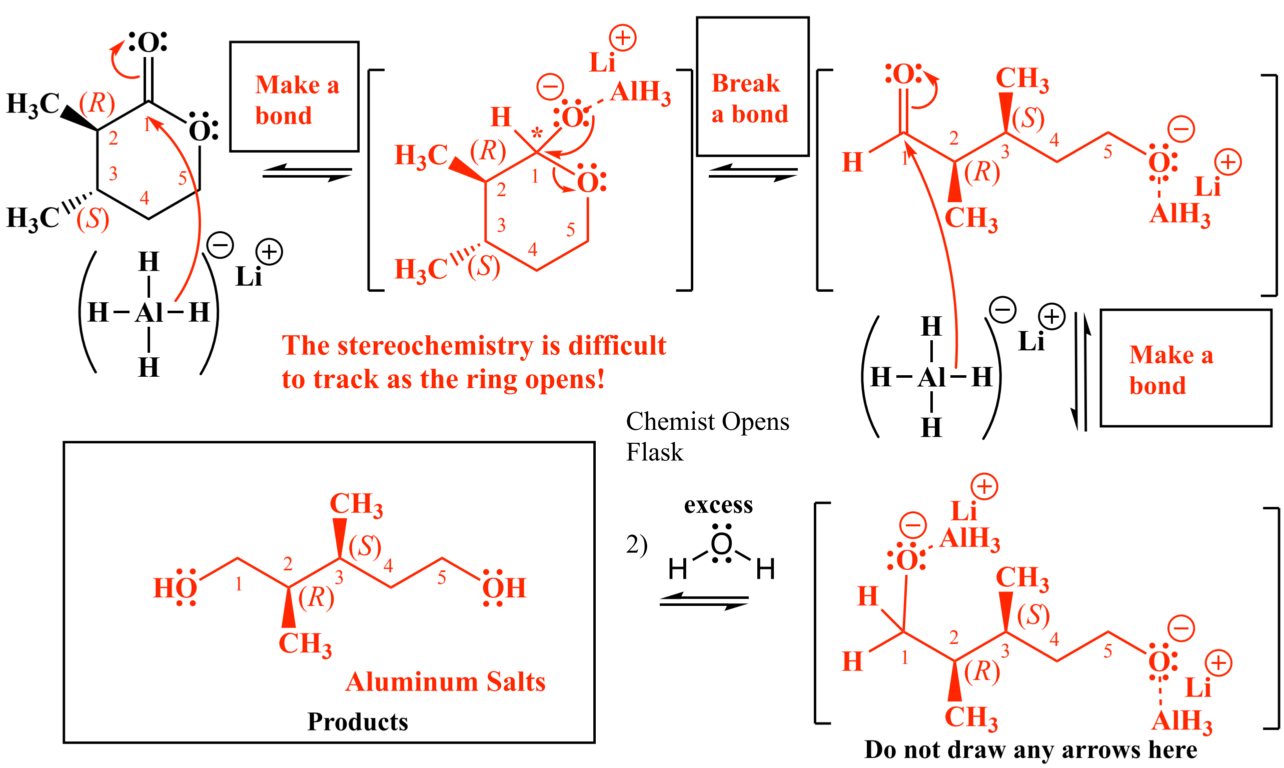


9. (30 pts) For these two reactions, use **arrows to indicate movement of all electrons, write all lone pairs, all formal charges, and all the products for each step. IF A NEW CHIRAL CENTER IS CREATED IN AN INTERMEDIATE, MARK IT WITH AN ASTERISK AND LABEL THE MOLECULE AS "RACEMIC" IF APPROPRIATE. FOR ALL CHIRAL PRODUCTS YOU MUST DRAW ALL ENANTIOMERS WITH WEDGES AND DASHES AND WRITE "RACEMIC' IF APPROPRIATE. In the boxes provided by the arrows, write which of the 4 most common mechanistic elements describes each step (make a bond, break a bond, etc.).**

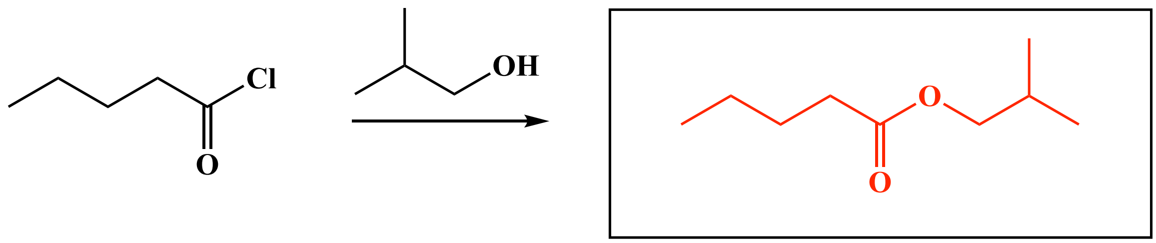
Note: Due to the special nature of this starting material, you are not supposed to draw arrows on the last intermediate in each case.

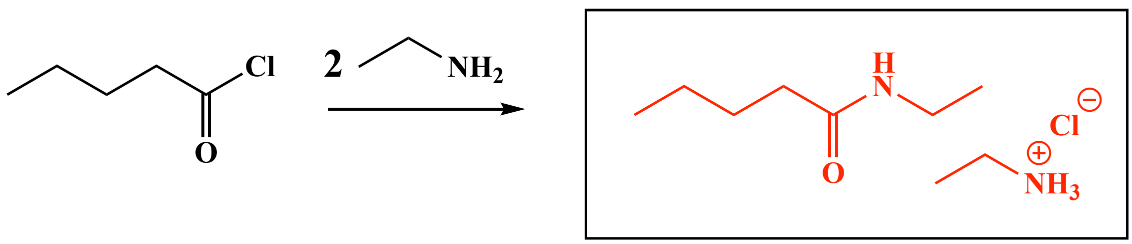


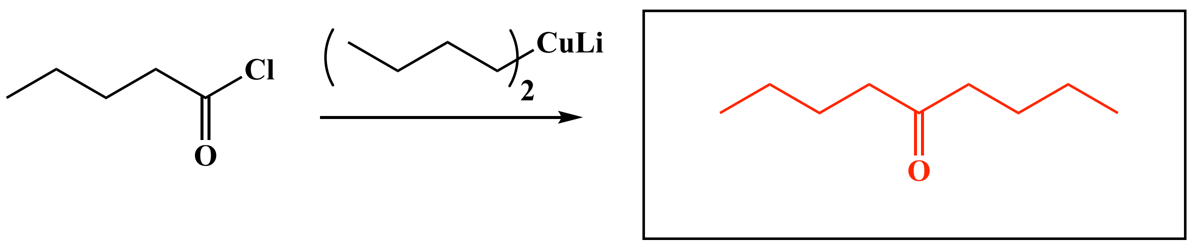


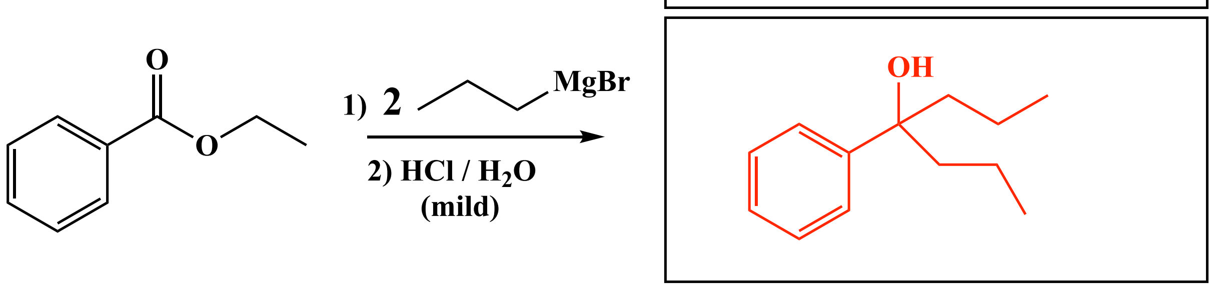


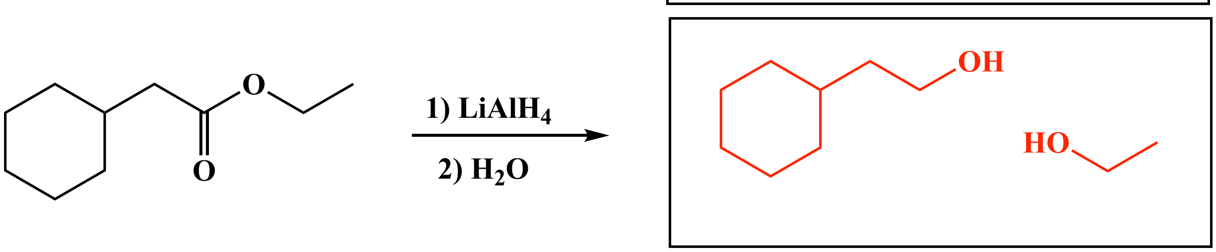
10. (3 or 5 pts.) Write the predominant product that will occur for each transformation. If a new chiral center is created and a racemic mixture is formed, you must draw both enantiomers and write "racemic" under the structure. Use wedges (▬) and dashes (⋯) to indicate stereochemistry. For these, you do not have to worry about metal salts in the products.

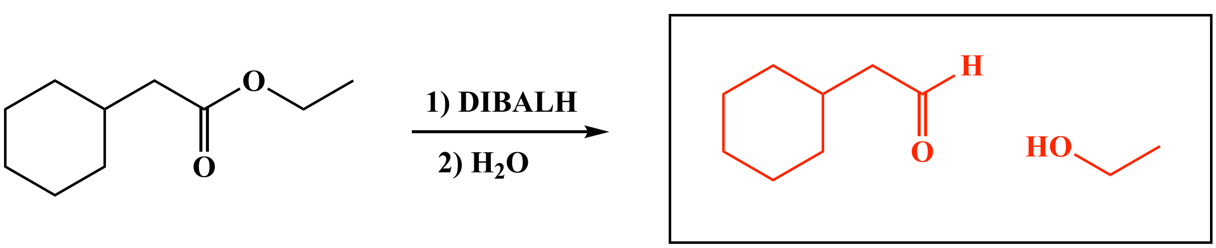












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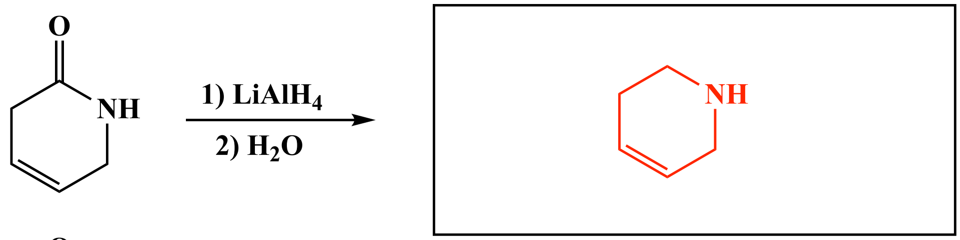
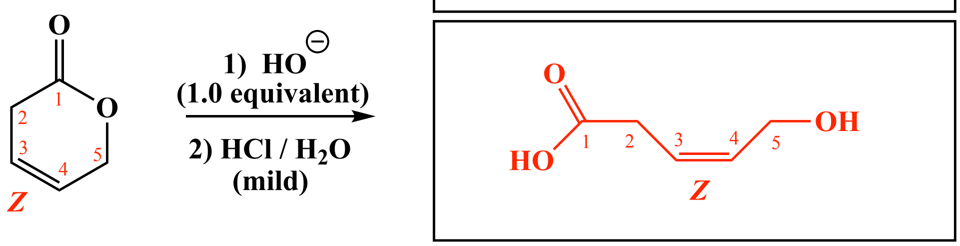
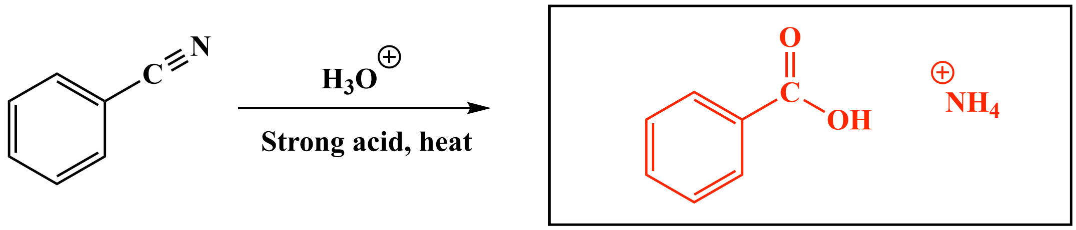
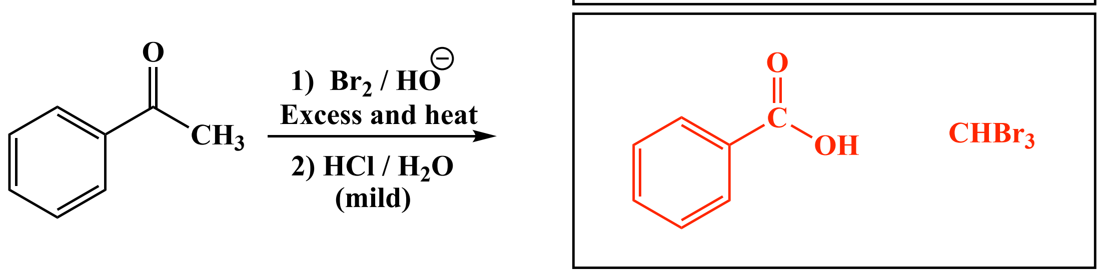
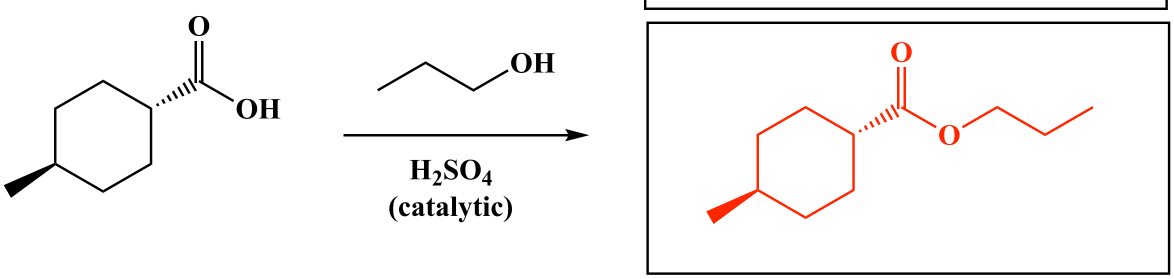
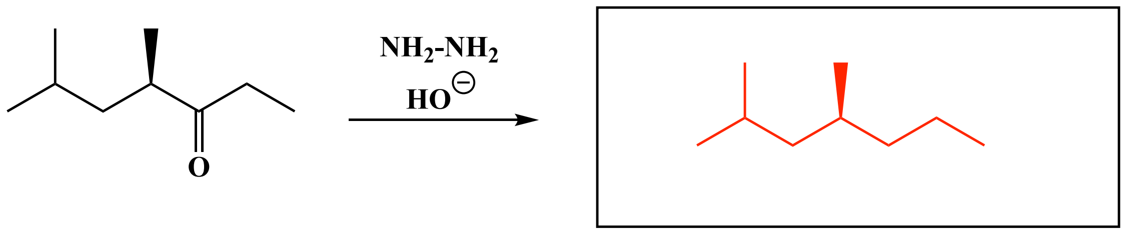




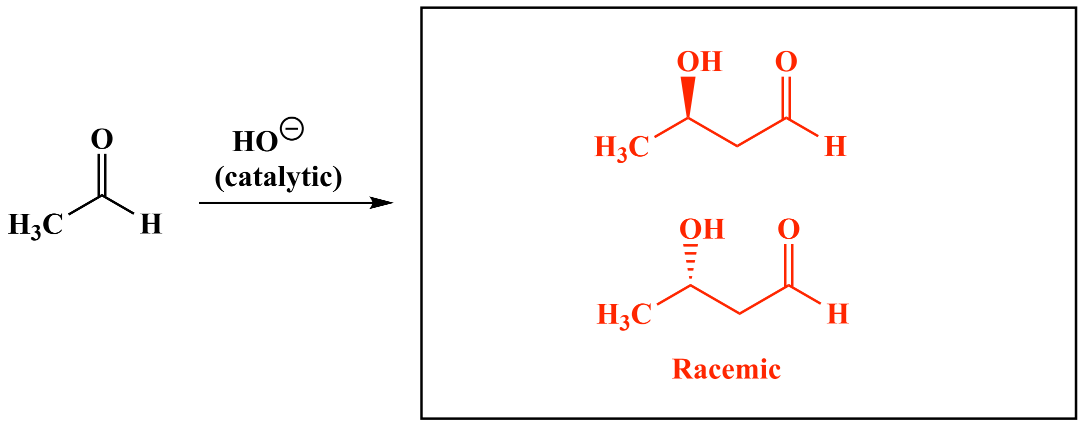


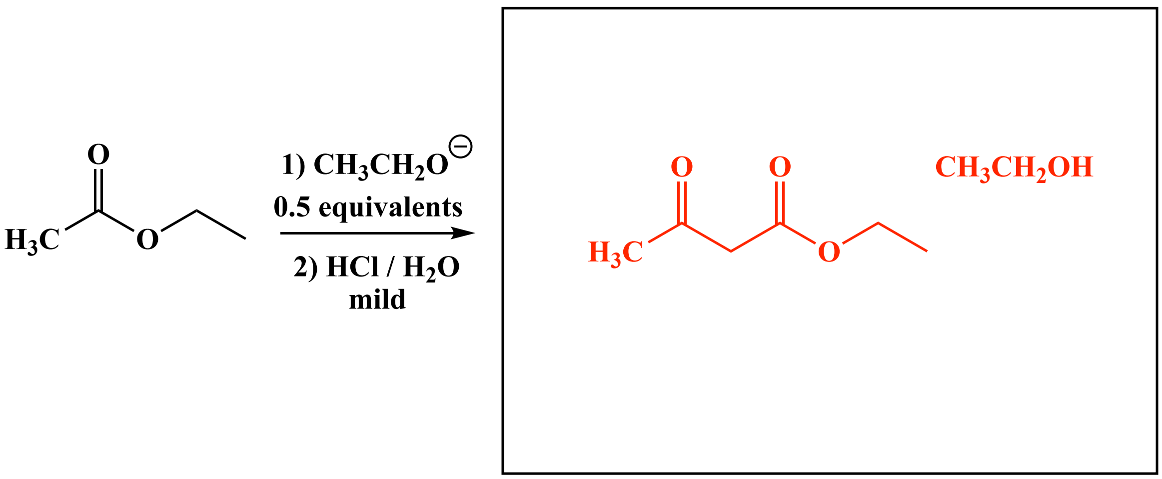


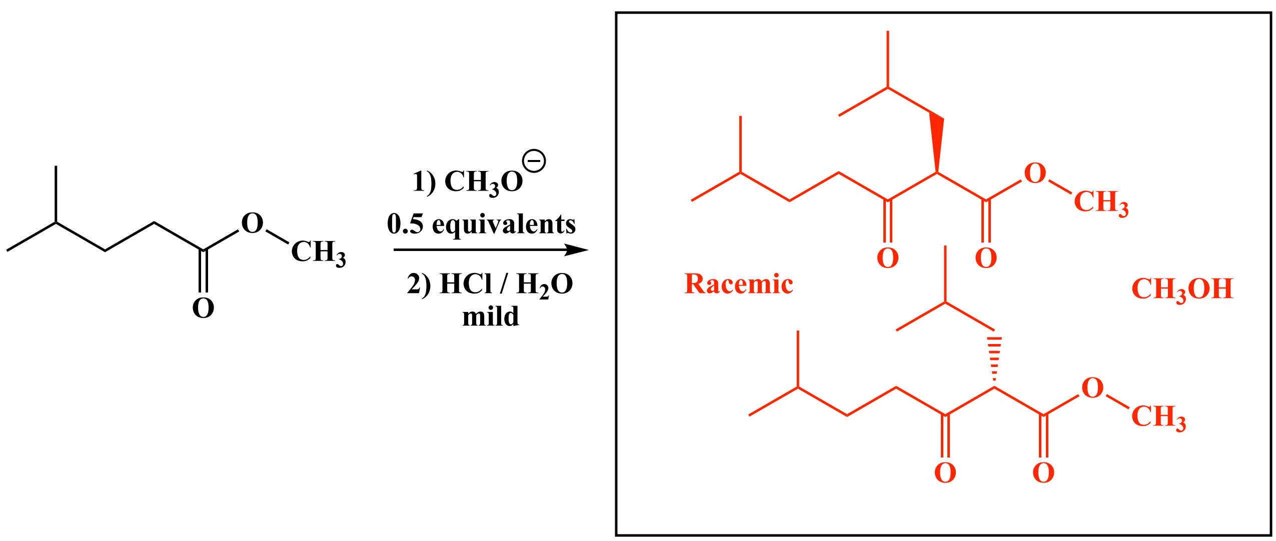




10. (3 or 5 pts.) Write the predominant product that will occur for each transformation. If a new chiral center is created and a racemic mixture is formed, you must draw both enantiomers and write "racemic" under the structure. Use wedges (▬) and dashes (········) to indicate stereochemistry. For these, you do not have to worry about metal salts in the products.

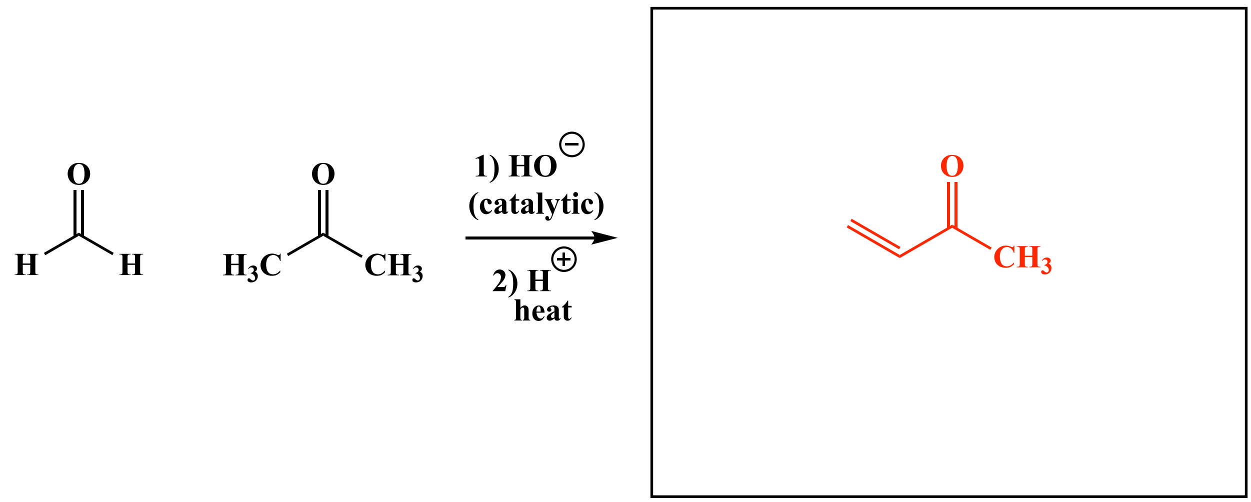


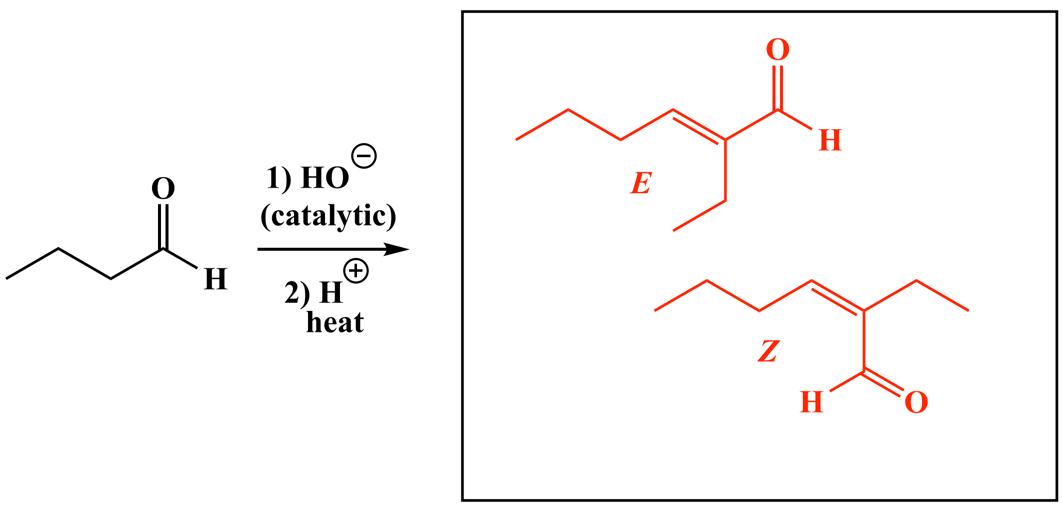




10. (4 or 6 pts.) Write the predominant product that will occur for each transformation. If a new chiral center is created and a racemic mixture is formed, you must draw both enantiomers and write "racemic" under the structure. Use wedges (▬) and dashes (······) to indicate stereochemistry. For these, you do not have to worry about metal salts in the products.

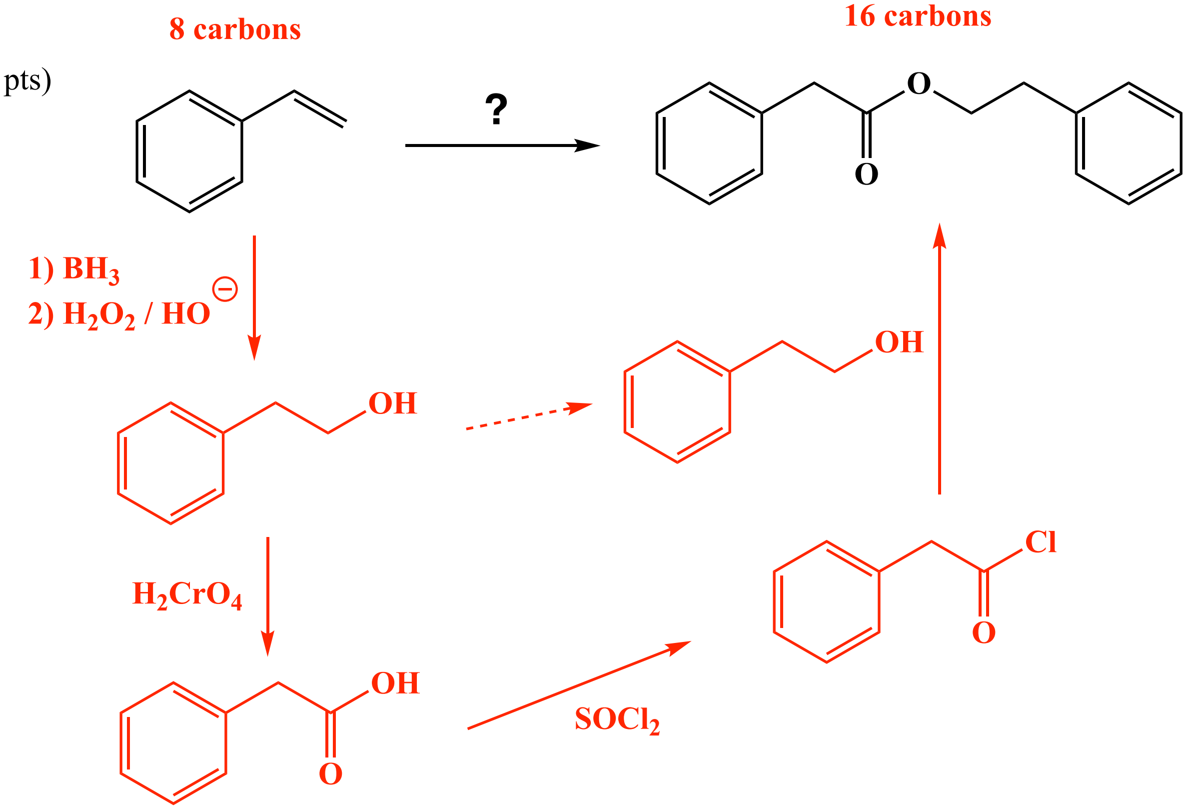
There is a lot to think about here. Please take your time. ASSUME THESE DEHYDRATE.





11. These are synthesis questions. You need to show how the starting material can be converted into the product(s) shown. You may use any reactions we have learned provided that the product(s) you draw for each step is/are the predominant one(s). Show all the reagents you need. Show each molecule synthesized along the way and be sure to pay attention to the regiochemistry and stereochemistry preferences for each reaction. You must draw all stereoisomers formed, and use wedges and dashes to indicate chirality at each chiral center. Write racemic when appropriate. **All the carbons of the product must come from carbons of the starting material.**

A) (10 pts)



Recognize that the product is an ester with 16 carbon atoms, and the starting material has 8 carbon ator Therefore, two starting material molecules will be combined in the product. **Recognize** also that the C- single bond next to the carbonyl of an ester is the one that can be made. Therefore, the last reaction is between an acid chloride and an alcohol as shown (also could be Fischer esterification using a carboxyl acid and an alcohol with catatlytic H_2SO_4). The alcohol can be made from the starting alkene using hydroboration/oxidation (BH_3 / H_2O_2 and $HO^{\ominus}$), and the acid can be made from oxidizing that alcohol with H_2CrO_4. The acid chloride is made from the acid using $SOCl_2$.

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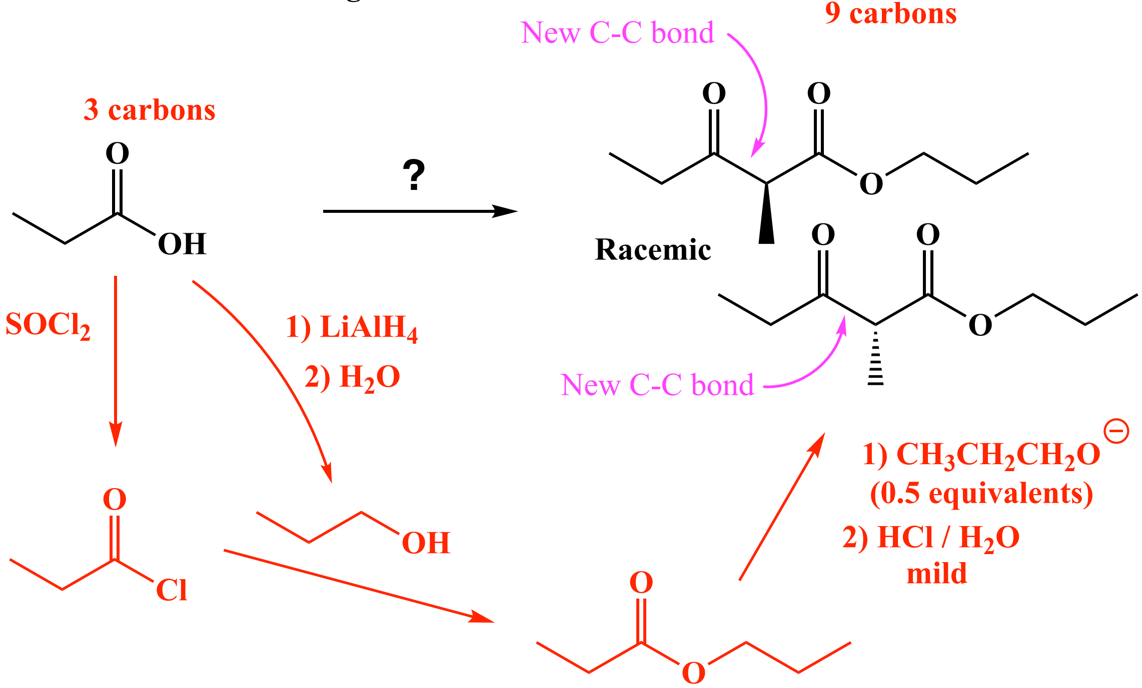
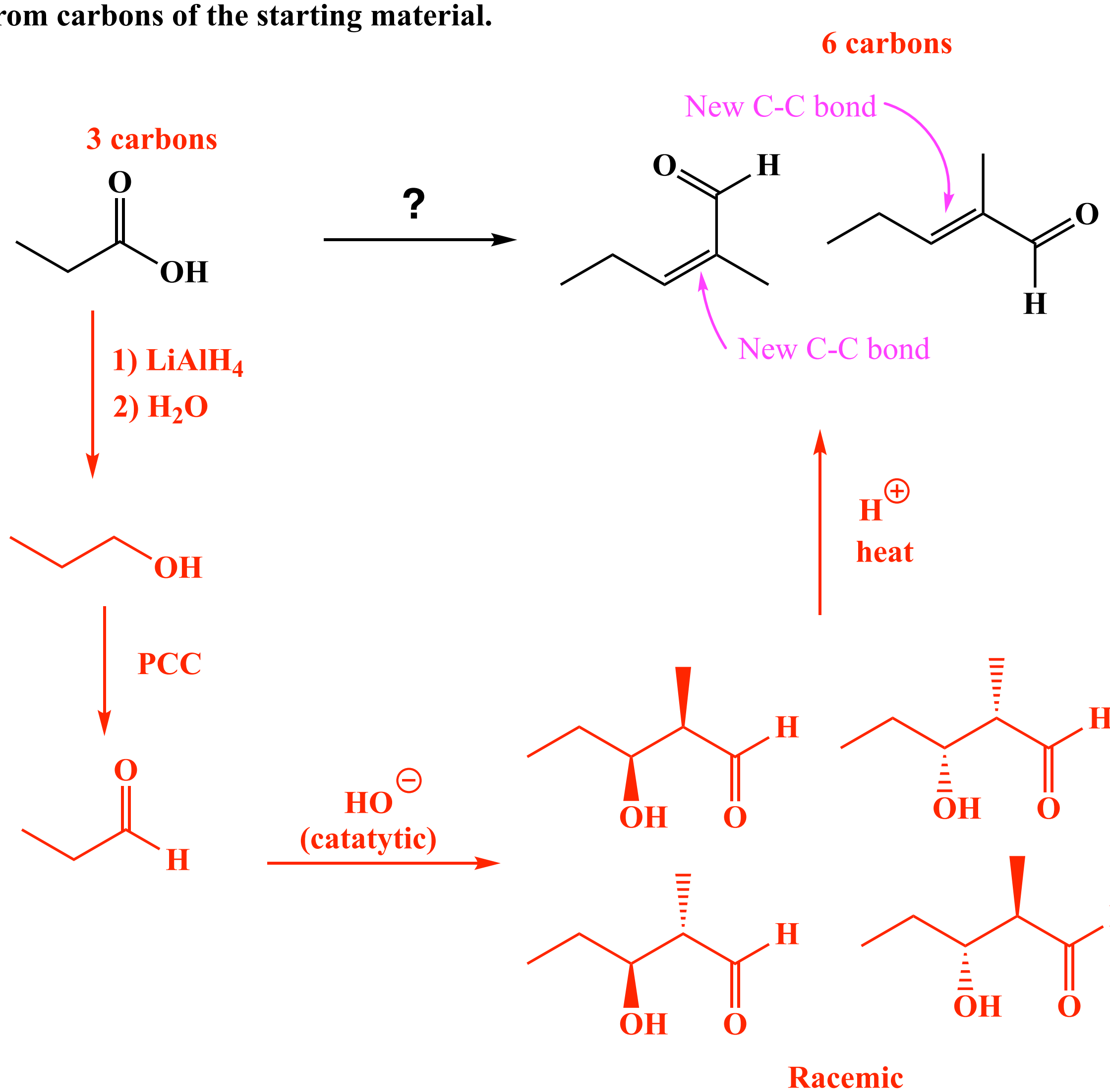
B) (10 pts)



Recognize the product as a β-keto ester, with a new C-C bond between the α and β carbons, the KRE of Claisen condensation reaction. Given that, the last reaction must be a Claisen condensation reaction usin propyl propanoate as shown. That ester can be made from the corresponding acid chloride and 1-propano or alternatively, a Fischer esterification using 1-propanol and propionic acid (the starting material). The acid chloride can be made using SOCl$_2$ and proprionic acid. The 1-propanol can be made by reducing th proprionic acid starting material with LiAlH$_4$ followed by H$_2$O.

11. These are synthesis questions. You need to show how the starting material can be converted into the product(s) shown. You may use any reactions we have learned provided that the product(s) you draw for each step is/are the predominant one(s). Show all the reagents you need. Show each molecule synthesized along the way and be sure to pay attention to the regiochemistry and stereochemistry preferences for each reaction. You must draw all stereoisomers formed, and use wedges and dashes to indicate chirality at each chiral center. Write racemic when appropriate. **All the carbons of the product must come from carbons of the starting material.**

C) (10 pts)

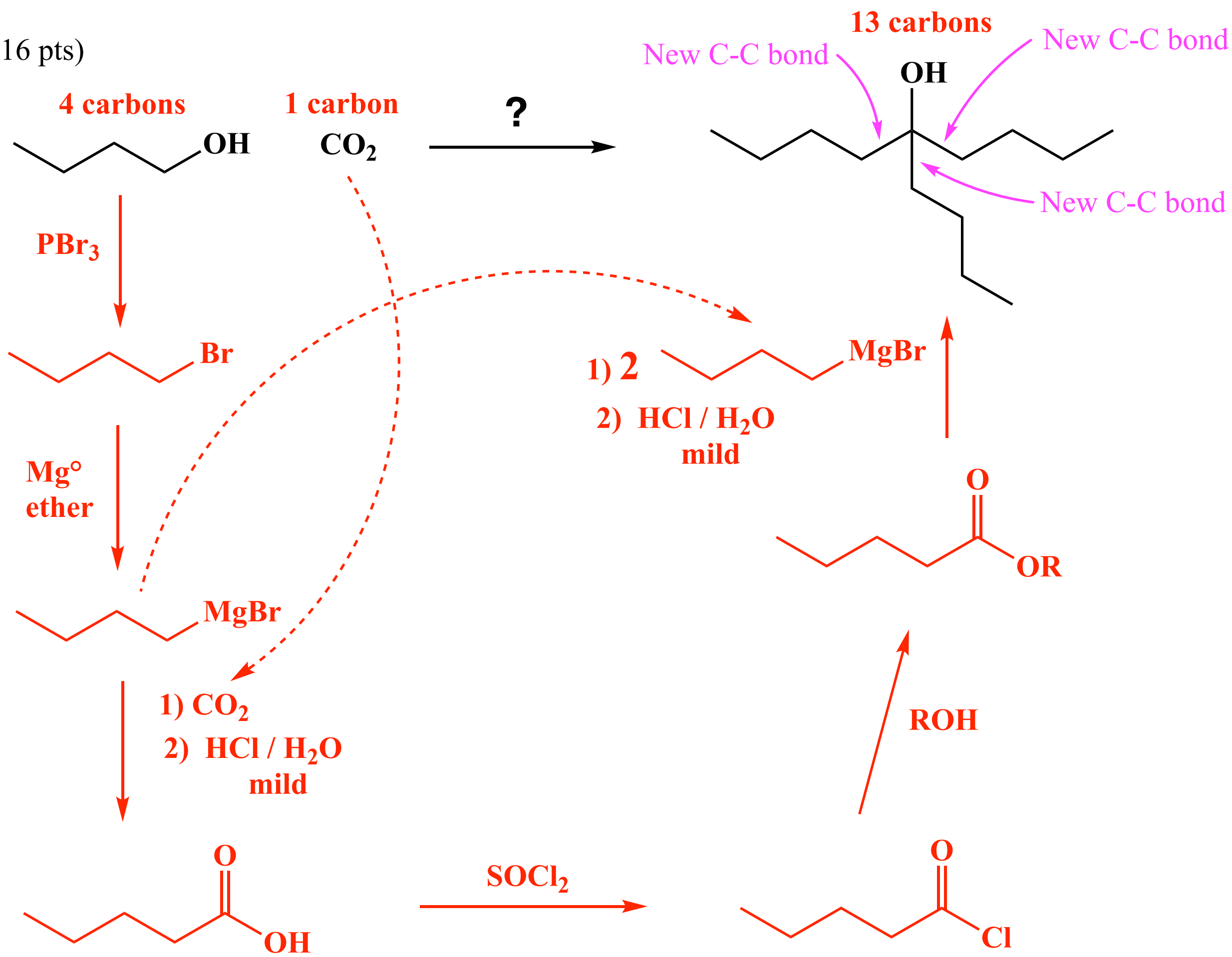


Recognize the *E* and *Z* alkene mixture of products as α,β-unsaturated aldehydes, the KRE of an aldol reaction followed by dehydration. **Recognize** further that there are 6 carbons in the product and 3 carbons in the starting material, so the new C=C bond must be as indicated, exactly as expected for an aldol dehydration. Therefore the last step is a dehydration of the aldol products indicated. The most difficult part of this synthesis is keeping track of all four β-hydroxy aldehyde aldol stereoisomer products! The aldol reaction uses catalytic $HO^{\ominus}$ with propanal, and the propanal can be made from the proprionic acid starting material using reduction to 1-propanol with $LiAlH_4$ then H_2O followed by reaction of PCC with the 1-propanol.

Signature_____________________________ Pg 15 _____________(16)

11. These are synthesis questions. You need to show how the starting material can be converted into the product(s) shown. You may use any reactions we have learned provided that the product(s) you draw for each step is/are the predominant one(s). Show all the reagents you need. Show each molecule synthesized along the way and be sure to pay attention to the regiochemistry and stereochemistry preferences for each reaction. You must draw all stereoisomers formed, and use wedges and dashes to indicate chirality at each chiral center. Write racemic when appropriate. **All the carbons of the product must come from carbons of the starting material.**

D) (16 pts)

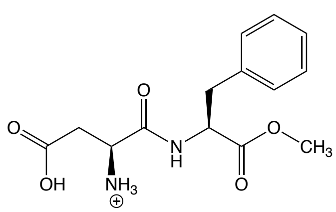


Recognize the product as a tertiary alchohol with two identical four-carbon alkyl groups attached to the C atom of the alcohol, the KRE of an ester reacting with 2 equivalents of a butyl Grignard reagent. **Recognize** further that the product has 13 carbons, and the starting alcohol has 4 carbons. Also, the starting ester must have 5 carbons on the carbonyl side, not 4. Therefore, the ester must be derived from a 5-carbon acid chloride, that, in turn, must come from pentanoic acid. The pentanoic acid can be made from the butyl Grignard reagent reacting with the CO_2 starting material. That makes sense because the butyl Grignard reagent is the same one needed in the last step of the process to react with the corresponding ester. The butyl Grignard reagent can be made from the starting 1-butanol following reaction with PBr_3 and then Mg° in ether. Finally, the ester needed for the last step can be made from the five-carbon acid chloride and an alcohol (ROH) such as ethanol, or from pentanoic acid reacting with an alcohol (ROH) such as ethanol using Fischer esterification. Note the ROH such as ethanol does not have to come from the starting materials because those carbons do NOT end up in the product. Of course, you could always use the starting 1-butanol if you want!

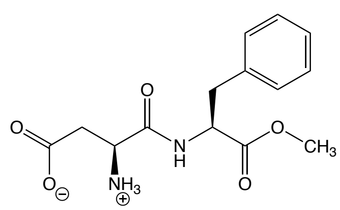
16. (16 pts) Here is an "Apply What you Know" Problem. You have not seen this directly, but based on what you know you CAN figure out the answers to the following questions. Aspartame, aka Nutrasweet® or Equal®, is one of the most popular artificial sweeteners used today. It is about 200 times sweeter than table sugar (sucrose), so very little goes a long way. According to the FDA "the use of aspartame as a general purpose sweetener… is safe." That safety makes sense in light of the structure. Instead of being an entire synthetic framework, or even a carbohydrate derivative as one might have expected, Aspartame is composed of the common and naturally occurring *amino acids* aspartic acid and phenylalanine, connected through an ordinary amide bond. There is a methyl ester on the carboxylic acid end of the phenylalanine. Because so little needs to be used in food or drinks to provide the desired sweetness, and because the structure is composed of amino acids, the number of calories associated with aspartame in a food or drink is negligible.

Phosphoric acid is added to soda to provide tartness and prevent bacteria from growing. The phosphoric acid lowers the pH of soda to between 2.5 to 3.2. For example, Diet Coke, a product that contains aspartame in place of sugar or high fructose corn syrup, has a pH that has been measure as 3.1 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4808596/).

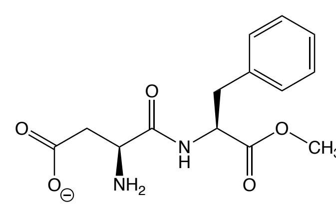
A) Aspartame has two pKa values, the first is 3.19 and the second is 7.87. At a pH of exactly 3.19, almost exactly the pH of Diet Coke, what is the protonation state of aspartame?



A



B



C

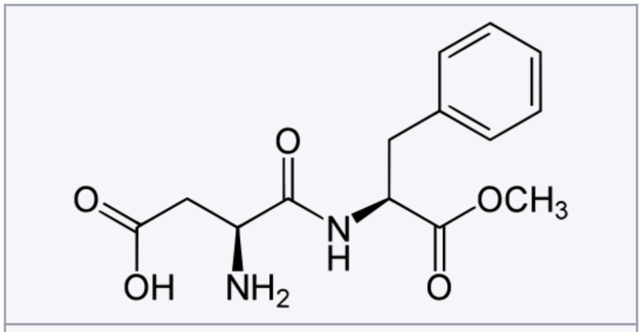
- ○ Structure A
- ○ Structure B
- ○ Structure C
- ● A 1:1 Mixture of Structure A and Structure B

B) At pH 6.0, what is the protonation state of aspartame?

- ○ Structure A
- ● Structure B
- ○ Structure C
- ○ A 1:1 Mixture of Structure B and Structure C

Below, I have attached a screen shot of the Wikipedia page for Aspartame (March 5, 2023).

Aspartame[1]

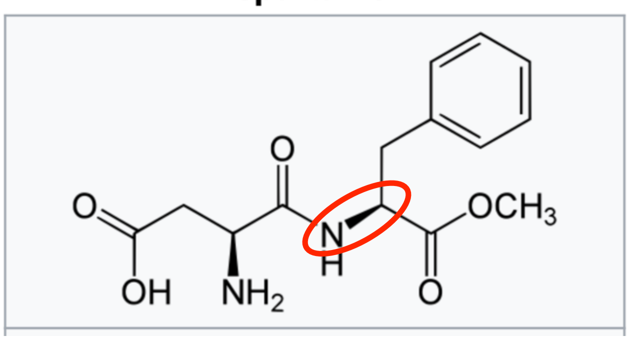


C) At what pH is the structure shown the correct protonation state of Aspartame?

- ○ pH = 3.19
- ○ pH = 7.0
- ○ pH = 10
- ● There is no pH at which this could be the corret protonation state

Look at the C-N bond that is circled below.

Aspartame[1]



Recall that in organic chemistry, a bond that is drawn as a normal line is intended to be in the plane of the paper, a bond that is drawn as a wedge indicates that the atom at the wider end of the wedge is above the plane of the paper, and for a dashed bond, the atom at the wider end of the dash is below the plane of the paper.

D) Given what you know about the geometry of amide bonds, is this an appropriate way to represent the stereochemistry in aspartame?

- ○ Yes, all of the bonds in this Wikipedia structure are drawn appropriately
- ● No, the circled bond would have to be in the same plane as the paper, and therefore a normal line, because the N atom is sp^2 hybridized and planar.

E) Drinks containing aspartame need to be stored in cold temperatures to avoid losing their sweet taste. For example, if Diet Coke is stored in the Texas heat for several weeks it will rapidly lose sweetness. **Examine the Aspartame structure carefully. Inside the box provided, in no more than two sentences, explain why aspartame loses sweetness when exposed to heat.**

In the acidic pH of soft drinks (pH 3 or so), the heating causes the methyl ester to hydrolyze to a carboxlyic acid and methanol according to the mechanism we learned. The hydrolyzed acid of aspartame is not sweet.

I hope you all have a wonderful spring break. Please make a promise to yourself to take some time to do things you really enjoy. YOU DESERVE IT, after all, you are in OChem II! And, of course, all of next week make sure to EXERCISE EVERY CHANCE YOU GET. Our 3.1 mile challenge is coming up the first week of April!