**NAME (Print):** _____

**SIGNATURE:** _____

**Chemistry 320N**
**Dr. Brent Iverson**
**2nd Midterm**
**March 23, 2017**

**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. PLEASE PUT IT AWAY AND LEAVE IT THERE!!!**

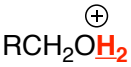
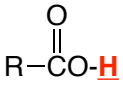
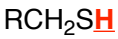
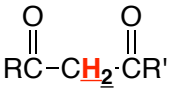
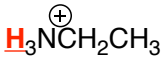
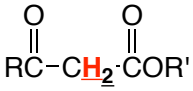
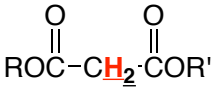
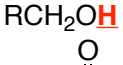
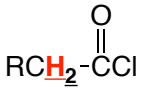
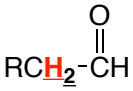
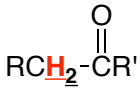
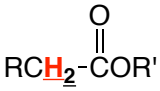
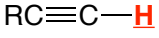
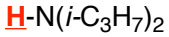
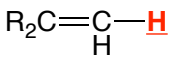
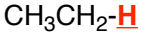
| Page | Points | |
|---|---|---|
| 1 | | (34) |
| 5 | | (18) |
| 6 | | (22) |
| 7 | | (12) |
| 8 | | (24) |
| 9 | | (35) |
| 10 | | (34) |
| 11 | | (14) |
| 12 | | (22) |
| 13 | | (19) |
| 14 | | (13) |
| 15 | | (22) |
| 16 | | (13) |
| 17 | | (10) |
| Total | | (292) |

## 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 |  | -7 |
| Protonated alcohol |  | -2 |
| Hydronium ion |  | -1.7 |
| Carboxylic acids |  | 3-5 |
| Thiols |  | 8-9 |
| Ammonium ion |  | 9.2 |
| β-Dicarbonyls |  | 10 |
| Primary ammonium |  | 10.5 |
| β-Ketoesters |  | 11 |
| β-Diesters |  | 13 |
| Water |  | 15.7 |
| 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 |

**Signature**_____ Pg 1 _____(34)

# DO NOT TEAR OUT THIS PAGE!!

You must write the answers for the questions on the next four pages on this single sheet.

Question 1, page 2 (5 pts) Write the correct letter, A), B), C), D) or E) corresponding to the order of reactivity of the molecules, listed from most to least reactive.

C)

Question 2, page 2 (5 pts) Write the correct letter, A), B), C), D) or E) corresponding to the order of reactivity, listed from most to least reactive.

E)

Question 3, page 3 (5 pts) Write the correct letter, A), B), C), D) or E) corresponding to the order of acidity, listed from most to least acidic.

D)

Question 4, page 3 (5 pts) Write the correct letter, A), B), C), D) or E) corresponding to the order of acidity, listed from most to least acidic.

D)

Question 5, page 3 (5 pts) Write the hybridization state of the atoms indicated by the arrows.

5.1 $sp^2$ 5.2 $sp^2$ 5.3 $sp^2$ 5.4 $sp^3$ 5.5 $sp^2$

Question 6, page 4 (6 pts) Write "can rotate" or "cannot rotate" corresponding to whether the bond indicated by the arrows can rotate or cannot rotate freely at room temperature.

6.1 **can rotate** 6.2 **cannot rotate** 6.3 **cannot rotate**

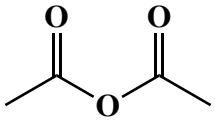
6.4 **can rotate** 6.5 **can rotate** 6.6 **cannot rotate**

Question 7, page 4 (3 pts) Is the fragment of cobra toxin shown as it would be at very high pH or very low pH?

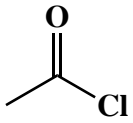
**very high pH**

## *Write the answers to these questions on the answer sheet on page 1*

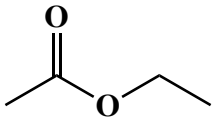
**1.** (5 pts) Rank order all of the following with respect to reactivity with a nucleophile such as water at neutral pH. **On the answer sheet on page 1 write the letter corresponding to the correct order of reactivity,** ranked from most to least reactive for the molecules labeled as (a) - (d).



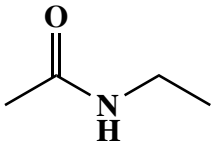
**(a)**



**(b)**



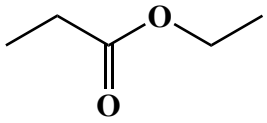
**(c)**



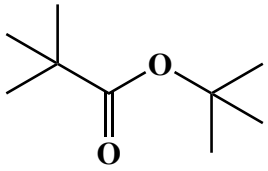
**(d)**

| | most reactive | | | least reactive |
|---|---|---|---|---|
| **A)** | **(a)** | **(b)** | **(c)** | **(d)** |
| **B)** | **(b)** | **(a)** | **(d)** | **(c)** |
| **C)** | **(b)** | **(a)** | **(c)** | **(d)** |
| **D)** | **(c)** | **(b)** | **(a)** | **(d)** |
| **E)** | **(c)** | **(d)** | **(b)** | **(a)** |

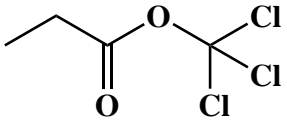
**2.** (5 pts.) Rank order all of the following with respect to reactivity with a nucleophile such as water at neutral pH. **On the answer sheet on page 1 write the letter corresponding to the correct order of reactivity,** ranked from most to least reactive for the molecules labeled as (a) - (c).



**(a)**



**(b)**

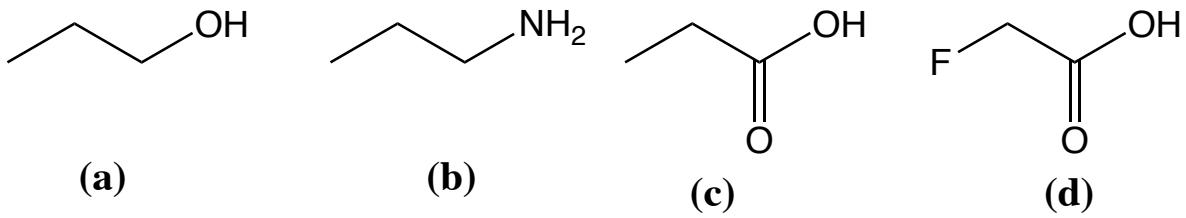


**(c)**

| | most reactive | | least reactive |
|---|---|---|---|
| **A)** | **(a)** | **(b)** | **(c)** |
| **B)** | **(a)** | **(c)** | **(b)** |
| **C)** | **(b)** | **(c)** | **(a)** |
| **D)** | **(c)** | **(b)** | **(a)** |
| **E)** | **(c)** | **(a)** | **(b)** |

## *Write the answers to these questions on the answer sheet on page 1*

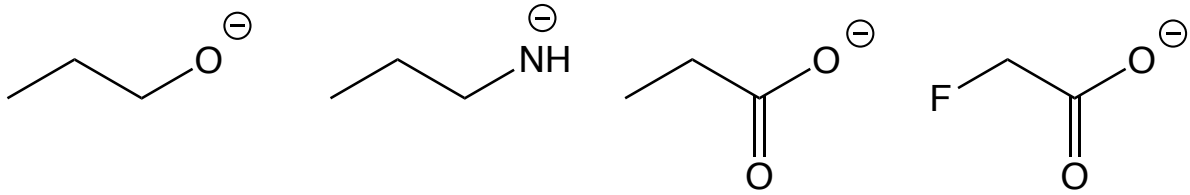
**3.** (5 pts) Rank the following molecules with respect to overall acidity. **On the answer sheet on page 1, write the letter corresponding to the correct order of acidity,** ranked from most to least acidic for the molecules labeled as (a) - (d).




**(a)** **(b)** **(c)** **(d)**

| | most acidic | | | least acidic |
|---|---|---|---|---|
| **A)** | **(a)** | **(c)** | **(b)** | **(d)** |
| **B)** | **(a)** | **(b)** | **(d)** | **(c)** |
| **C)** | **(c)** | **(a)** | **(b)** | **(d)** |
| **D)** | **(d)** | **(c)** | **(a)** | **(b)** |
| **E)** | **(d)** | **(b)** | **(c)** | **(a)** |

**4.** (5 pts) Rank the following molecules with respect to overall anion stability. **On the answer sheet on page 1, write the letter corresponding to the correct order of anion stability,** ranked from most to least stable for the anions labeled as (a) - (d).

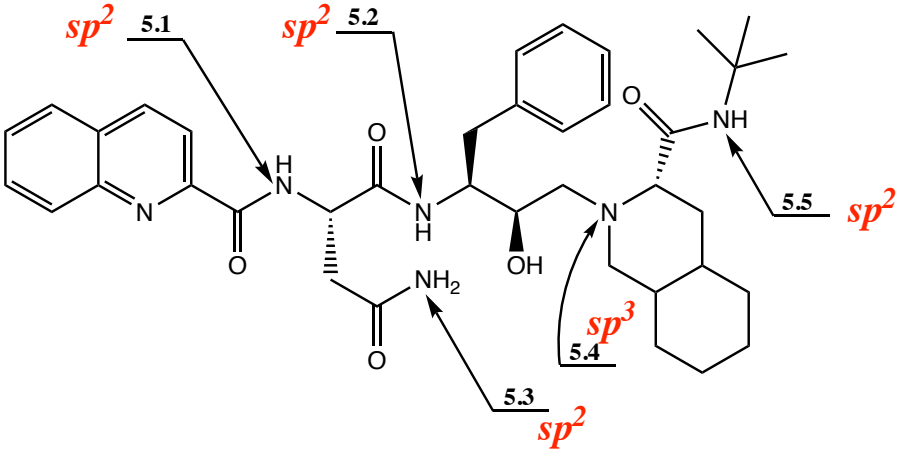



**(a)** **(b)** **(c)** **(d)**

| | most stable | | | least stable |
|---|---|---|---|---|
| **A)** | **(a)** | **(c)** | **(b)** | **(d)** |
| **B)** | **(a)** | **(b)** | **(d)** | **(c)** |
| **C)** | **(c)** | **(a)** | **(b)** | **(d)** |
| **D)** | **(d)** | **(c)** | **(a)** | **(b)** |
| **E)** | **(d)** | **(b)** | **(c)** | **(a)** |

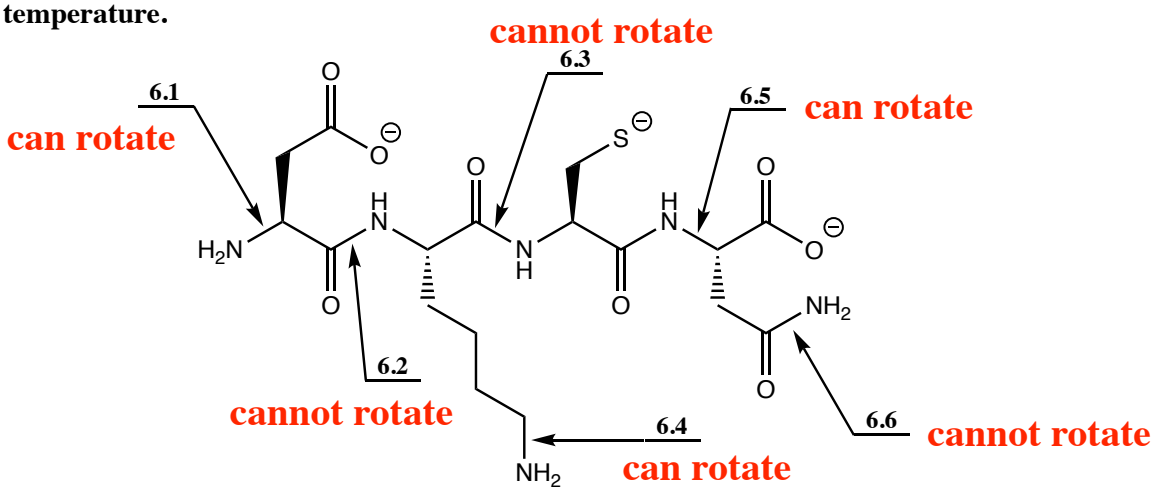
## *Write the answers to these questions on the answer sheet on page 1*

**5** (5 points) On the answer sheet on page 1, indicate the **hybridization state of each atom identified** by the arrows.




**Saquinavir** - An effective treatment for AIDS (AIDS protease inhibitor)

**6.** (6 points) On the answer sheet on page 1, indicate whether the indicated **C-N bond can or cannot rotate at room temperature.**



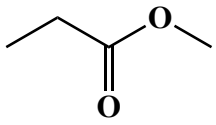

**These are the last four amino acids of one of the most potent Egyptian cobra toxins**

**7.** (3 points) On the answer sheet on page 1, indicate whether the above cobra toxin fragment is shown in very high (greater than 12) or very low (less than 2) pH?

**NOTICE THIS**

**Very high pH as the carboxylic acids and even the amine groups are deprotonated**

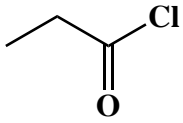
**8.** (18 pts) In a bond-making step of a reaction, a nucleophile donates the electron pair that will make the new bond, and an electrophile accepts the electron pair in the process. The following species are either nucleophiles or electrophiles in reaction mechanisms we have learned. Note for this problem we are ignoring any proton transfer steps, we are just interested in whether the following can best be considered a nucleophile or an electrophile. **ON THIS PAGE CIRCLE "nucleophile" or "elctrophile" to indicate the reactivity of each structure.**

8.1 

Nucleophile
Electrophile

8.2 $LiAlH_4$

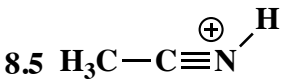
Nucleophile
Electrophile

8.3 

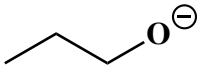
Nucleophile
Electrophile

8.4 $Br_2$

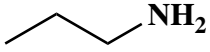
Nucleophile
Electrophile

8.5 

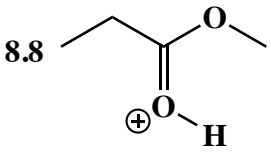
Nucleophile
Electrophile

8.6 

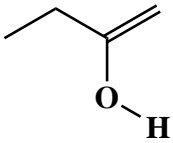
Nucleophile
Electrophile

8.7 

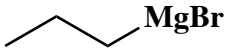
Nucleophile
Electrophile

8.8 

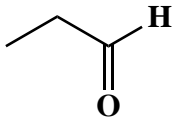
Nucleophile
Electrophile

8.9 

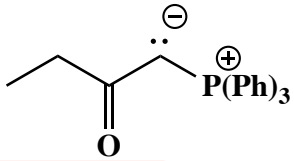
Nucleophile
Electrophile

8.10 

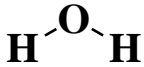
Nucleophile
Electrophile

8.11 

Nucleophile
Electrophile

8.12 

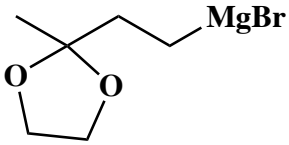
Nucleophile
Electrophile

8.13 

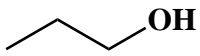
Nucleophile
Electrophile

8.14 

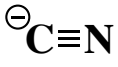
Nucleophile
Electrophile

8.15 

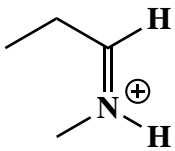
Nucleophile
Electrophile

8.16 

Nucleophile
Electrophile

8.17 

Nucleophile
Electrophile

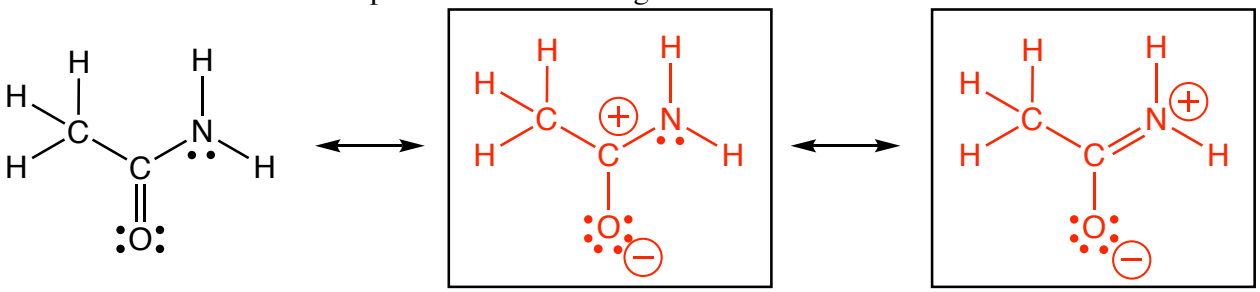
8.18 

Nucleophile
Electrophile

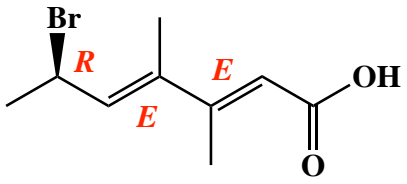
**9.** (14 points) Suppose a relative of yours is having an MRI. In no more than four sentences, explain to them what is happening when they have the MRI scan. We wil be looking for a minimum of 7 key points here.

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

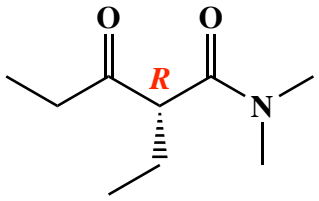
**10.** (8 points) Draw the two most important resonance contributing structures of the amide shown below. Be sure to show all lone pairs and formal charges. You do not have to draw arrows on this one.



**11. (4 pts each) In the space provided, write the IUPAC name (including stereochemistry where appropriate) for the following two molecules:**



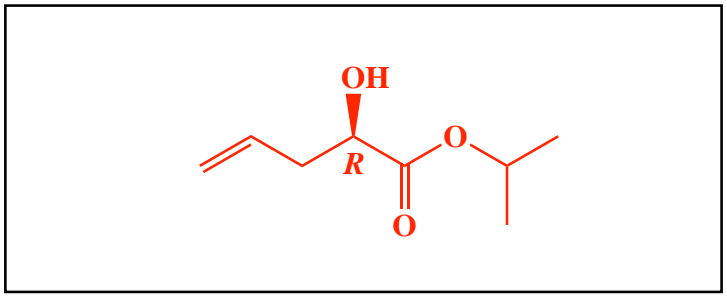

**(*R*,2*E*,4*E*)-6-bromo-3,4-dimethyl-2,4-heptadienoic acid or**
**(*R*,2*E*,4*E*)-6-bromo-3,4-dimethylhepta-2,4-dienoic acid**

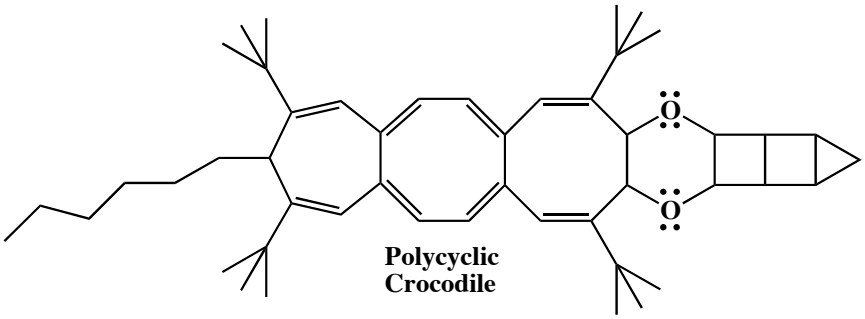



**(*R*)-2-ethyl-*N*,*N*-dimethyl-3-oxopentanamide**

**12. (4 pts) In the space provided, draw the following molecule:**

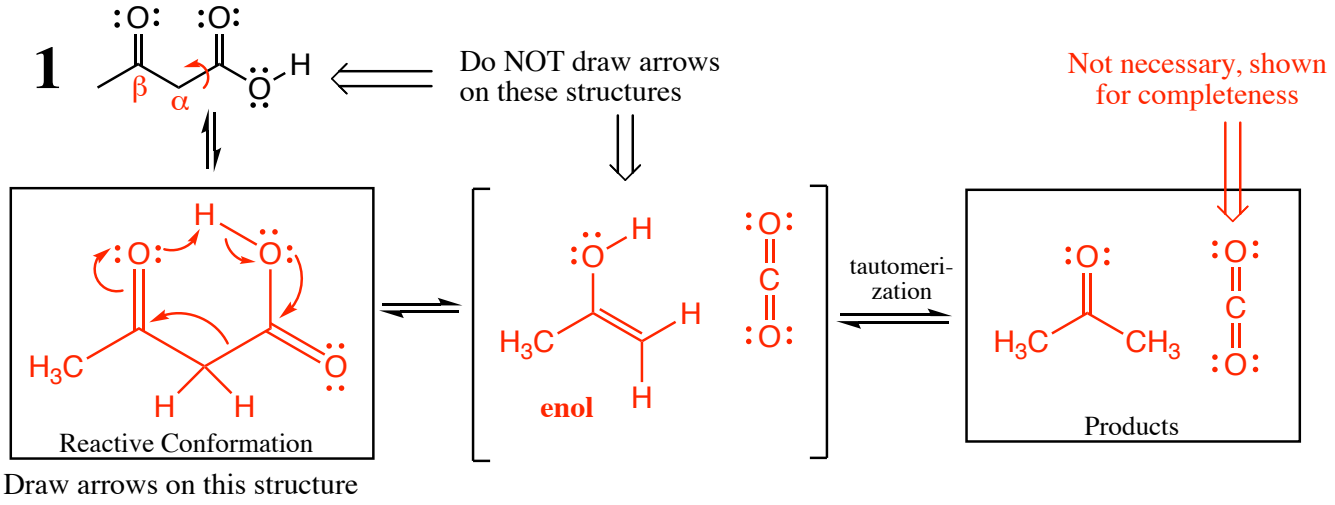
**isopropyl (*R*)-2-hydroxy-4-pentenoate**



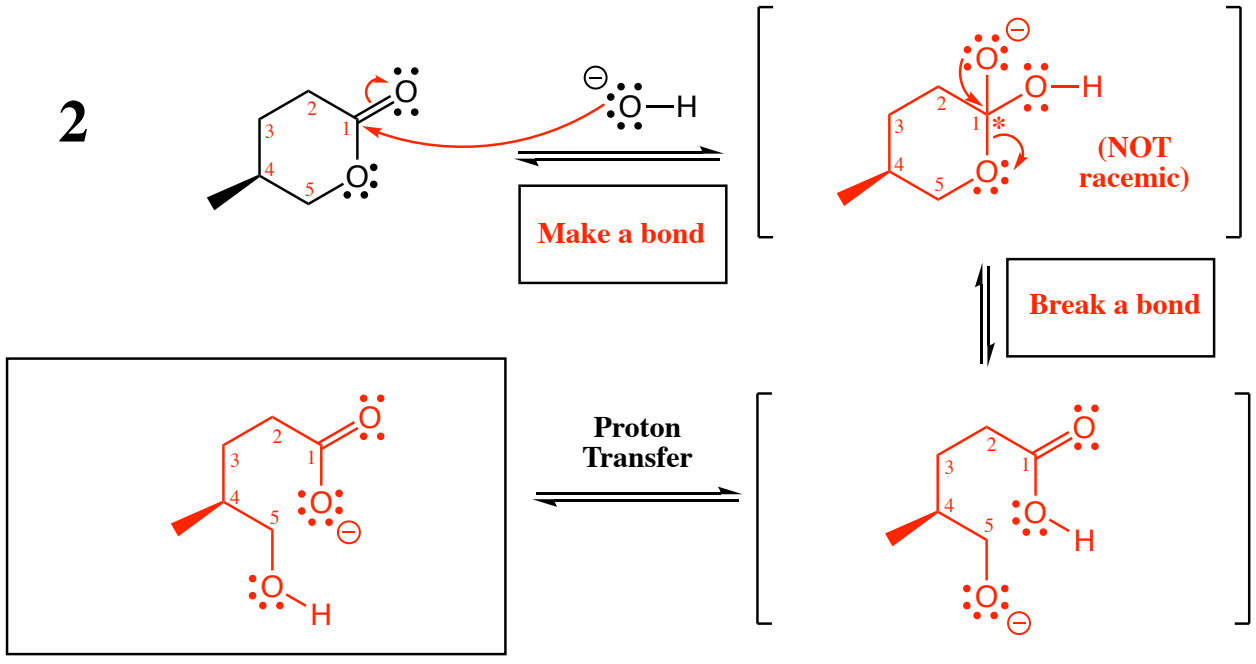

**Latin Name: (3*Z*,4a*Z*,6*Z*,11a*Z*,13*Z*,14*Z*)-3,8,10,15-tetra-*tert*-butyl-9-hexyl-1a,1b,1c,2a,15a,16a,16b,16c-octahydro-1*H*,9*H*-cyclohepta[9,10]octaleno[3,4-*b*]cyclopropa[3',4']cyclobuta[1',2':3,4]cyclobuta[1,2-*e*][1,4]dioxine**

**13.** (12 pts) Complete the mechanism for the following decarboxylation reaction. **Be sure to show arrows to indicate movement of <u>all</u> electrons on the "Reactive Conformation", 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 PRODUCT, MARK IT WITH AN ASTERISK AND LABEL THE MOLECULE AS RACEMIC IF APPROPRIATE.**



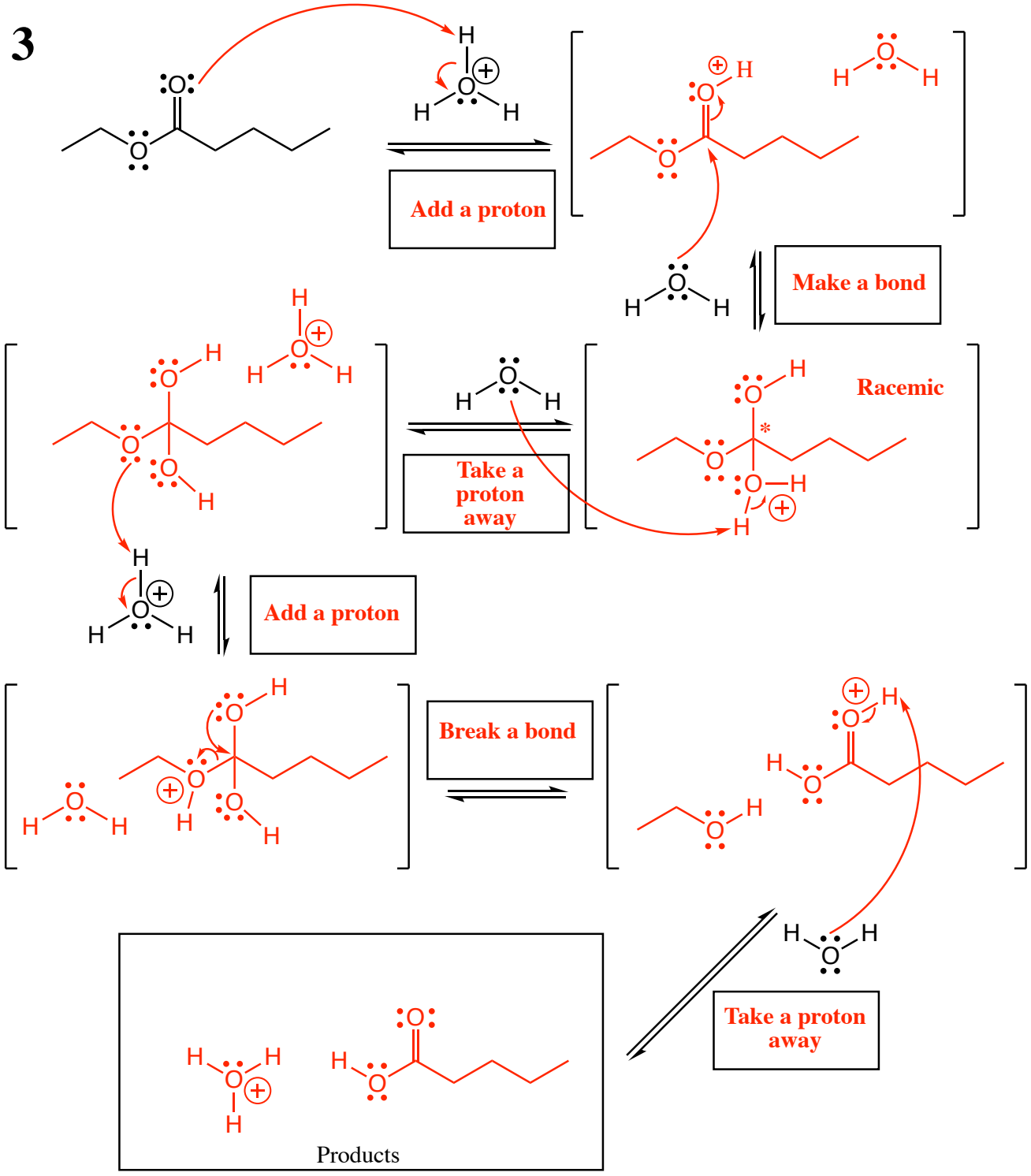

***Note you will have to write a balanced equation for the above mechanism on page 11***

**14**. (12 pts) Complete the mechanism for the following reaction a lactone and hydroxide. **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 PRODUCT, MARK IT WITH AN ASTERISK AND LABEL THE MOLECULE AS RACEMIC IF APPROPRIATE. In the boxes provided, write which of the 4 mechanistic elements describes each step (make a bond, break a bond, etc.).**




***Note you will have to write a balanced equation for the above mechanism on the page 11***

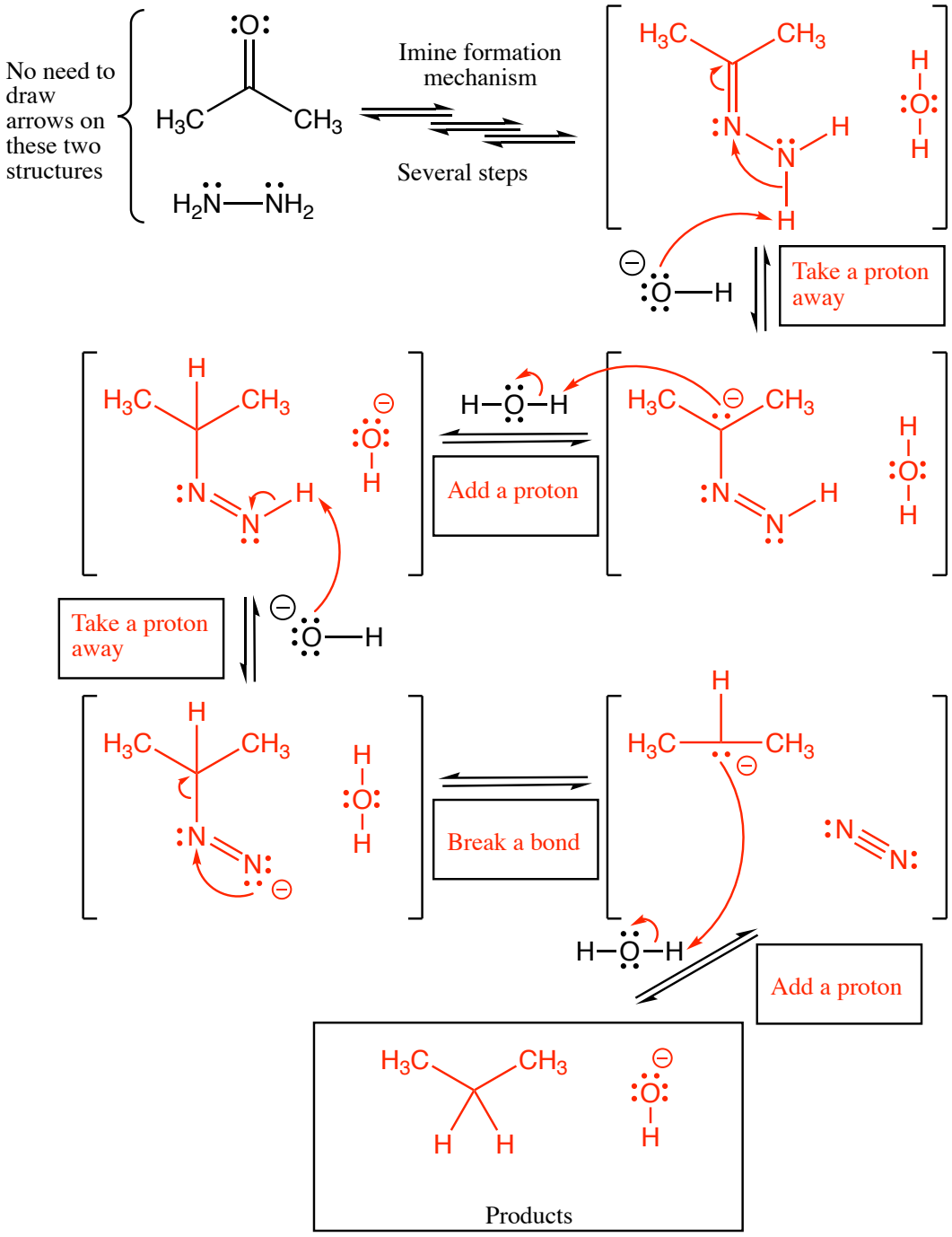
15. (35 pts) Complete the mechanism for the following ester hydrolysis reaction. **Be sure to show arrows to indicate movement of <u>all</u> electrons, write <u>all</u> lone pairs, <u>all</u> formal charges, and <u>all</u> the products for each step.** Remember, I said <u>all</u> the products for each step. **IF A NEW CHIRAL CENTER IS CREATED IN AN INTERMEDIATE OR PRODUCT, MARK IT WITH AN ASTERISK AND LABEL THE MOLECULE AS RACEMIC IF APPROPRIATE. In the boxes provided, write which of the 4 mechanistic elements describes each step (make a bond, break a bond, etc.).**




*Note you will have to write a balanced equation for the above mechanism on PAGE 11*

16. (34 pts) Complete the mechanism for the following Wolff-Kishner 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 PRODUCT, MARK IT WITH AN ASTERISK AND LABEL THE MOLECULE AS RACEMIC IF APPROPRIATE. In the boxes provided, write which of the 4 mechanistic elements describes each step (make a bond, break a bond, etc.).**

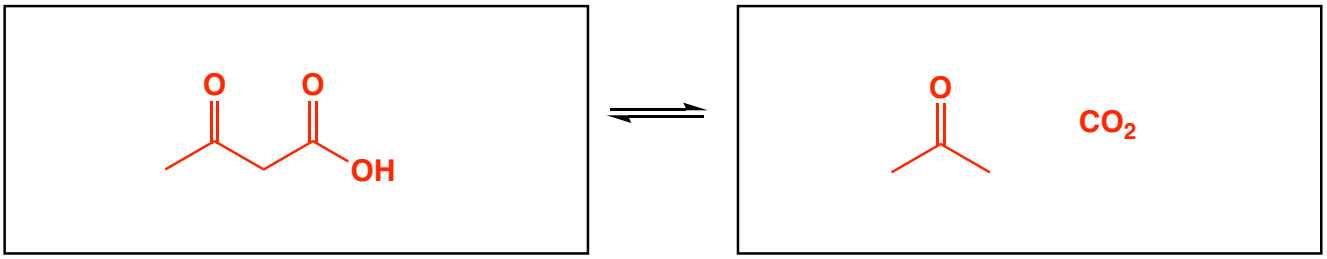
**4**



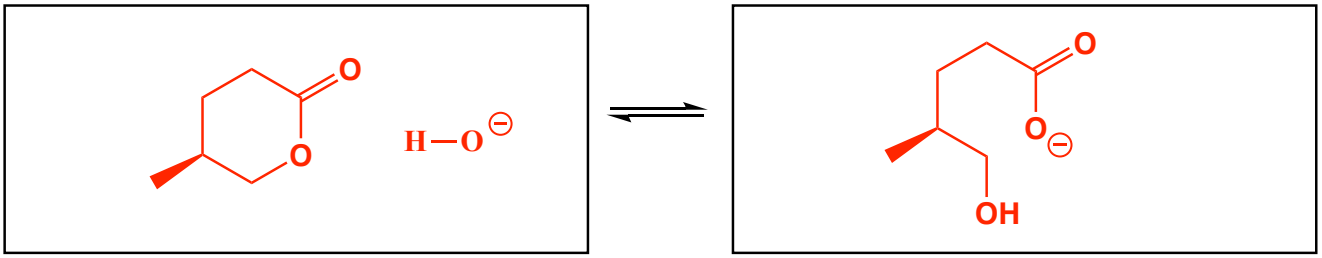

***Note you will have to write a balanced equation for the above mechanism on PAGE 11***

17. (14 pts) Write BALANCED equations for the four mechanisms, 1-4, that you drew on the last three pages. Only include molecules consumed or created during the reactions. In other words, DO NOT SHOW CATALYSTS IN EITHER BOX!

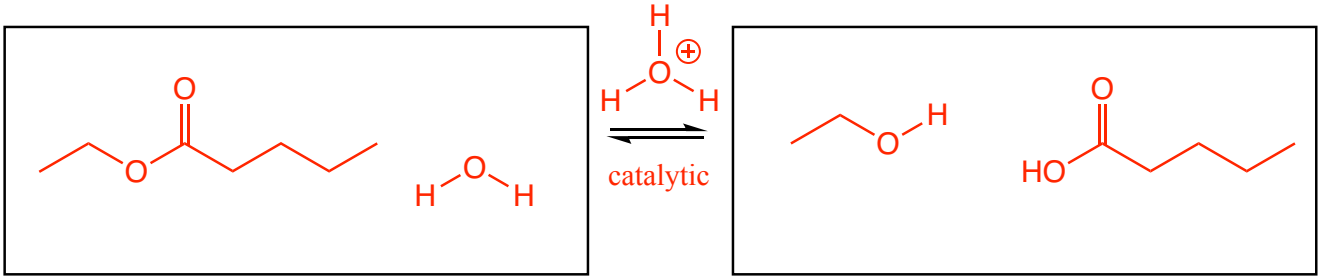
**Write a balanced equation for the overall process described by mechanism 1 from page 8**



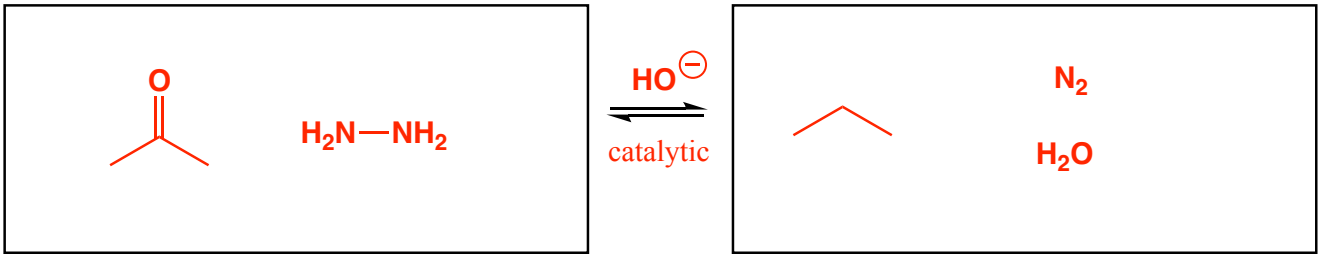

**Write a balanced equation for the overall process described by mechanism 2 from page 8**



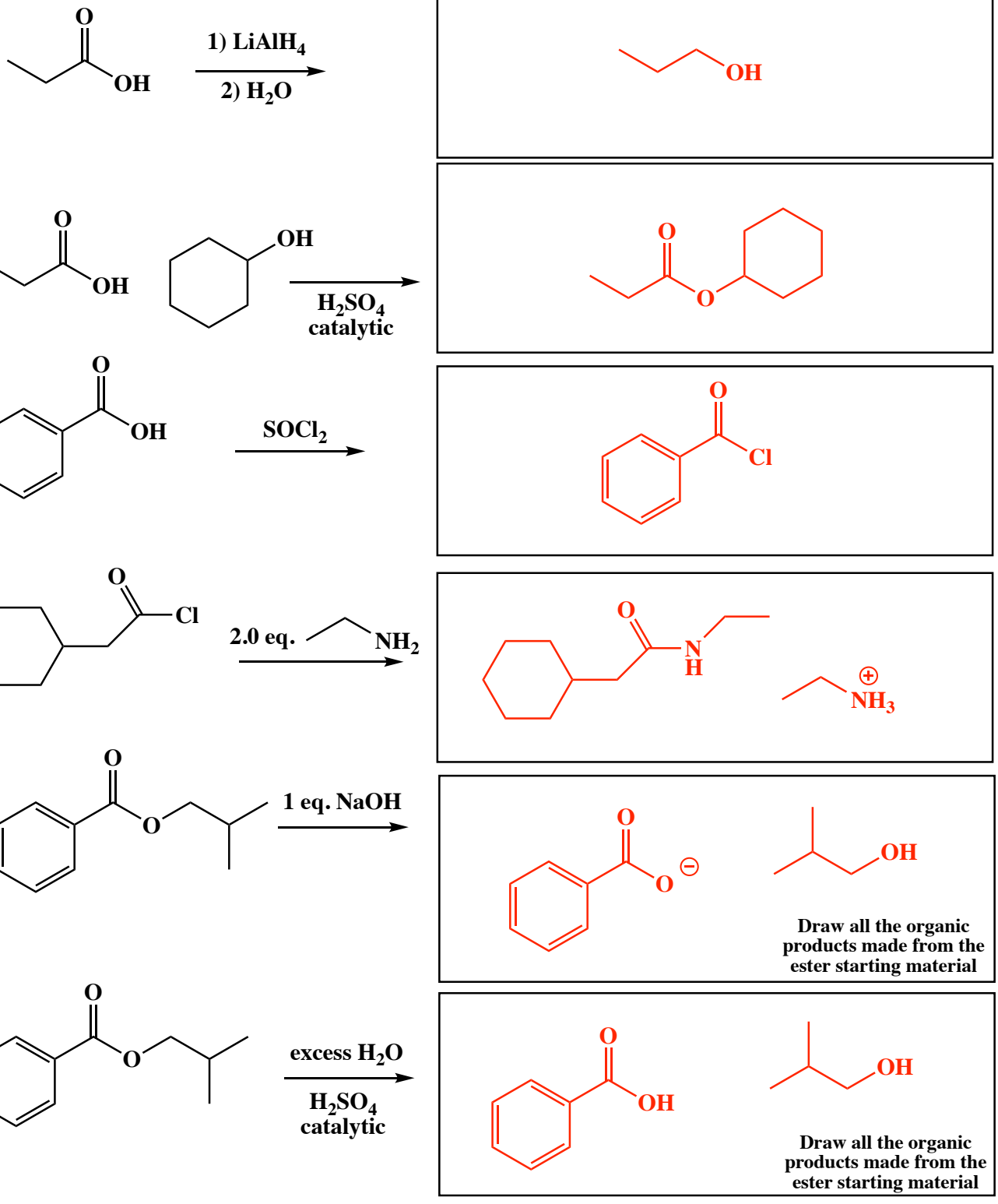

**Write a balanced equation for the overall process described by mechanism 3 from page 9**



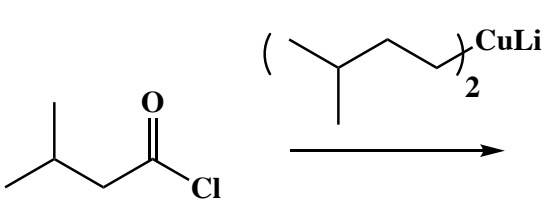

**Write a balanced equation for the overall process described by mechanism 4 from page 10**

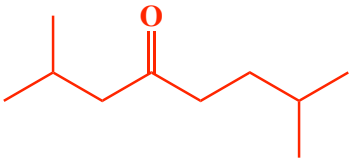


**18. (3 or 5 pts.)** Write the predominant **carbon containing** product or products that will occur for each transformation. **If there are two carbon containing products, WRITE THEM BOTH. If a new chiral center is created and a racemic mixture is formed, label the chiral center with an asterisk (*) and write racemic. No need for wedges and dashes. Also, do not worry about balancing these equations, you just need to show us the major carbon-containing products of these transformations.**

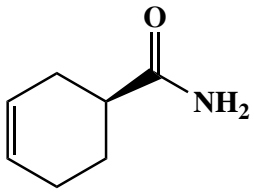


**19. (3 or 5 pts.)** Write the predominant **carbon containing** product or products that will occur for each transformation. **If there are two carbon containing products, WRITE THEM BOTH. If a new chiral center is created and a racemic mixture is formed, label the chiral center with an asterisk (*) and write racemic. No need for wedges and dashes. Also, do not worry about balancing these equations, you just need to show us the major organic products of these transformations.**



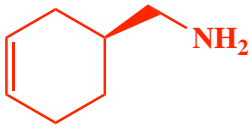



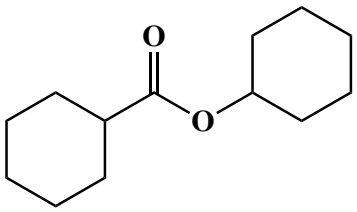

Cu Salts




1) $LiAlH_4$

2) $H_2O$

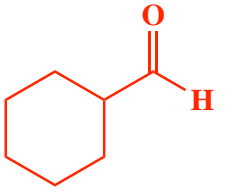


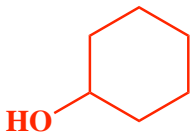




1) DIBALH

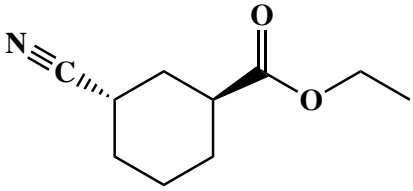
2) $H_2O$/HCl

mild acid



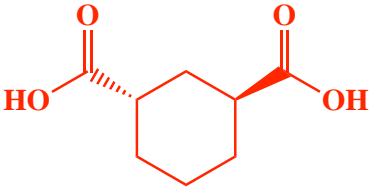

**Draw all the carbon containing products made from the ester starting material**

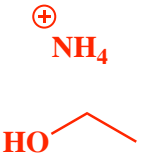



excess

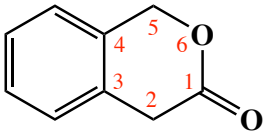
$H_2SO_4$ / $H_2O$

(high heat)




**Draw all the carbon containing products made from the ester starting material**

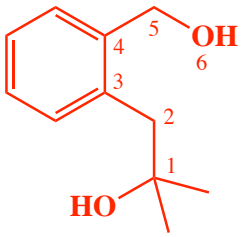



1) 2 eq.

$CH_3MgBr$

2) HCl / $H_2O$

(mild acid)



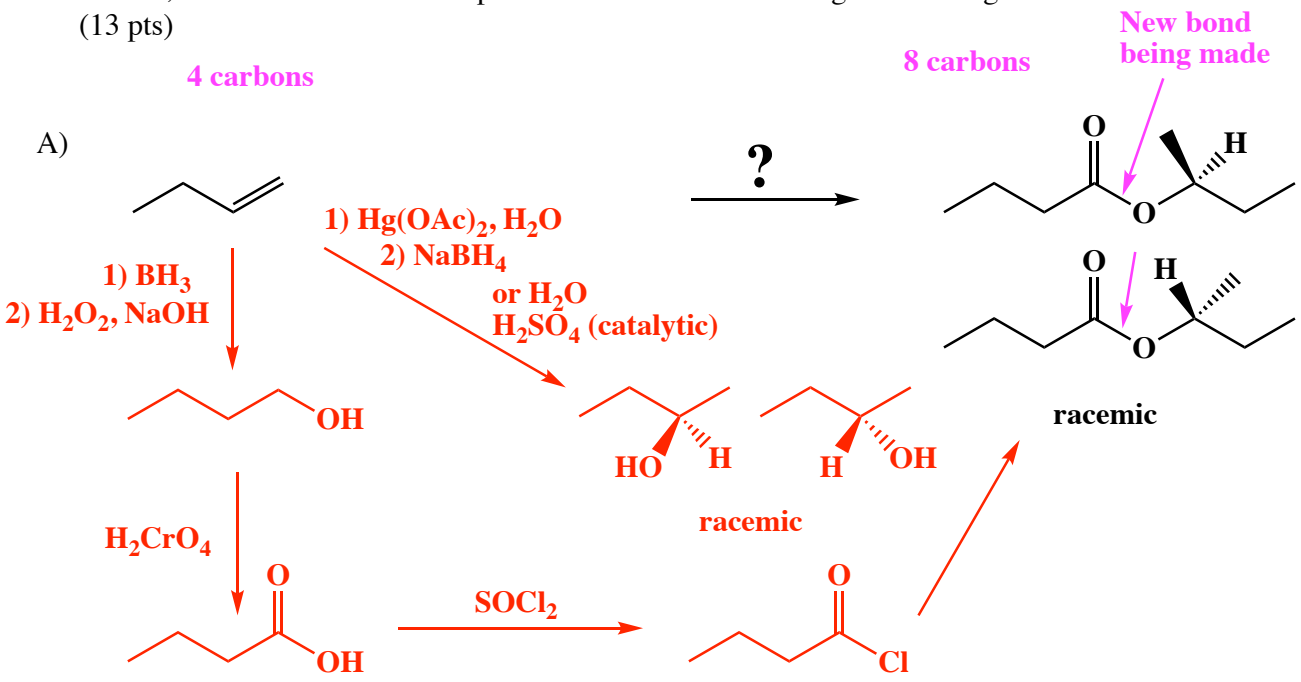

**Draw all the carbon containing products made from the ester starting material**

**19.** Using any reagents turn the starting material into the indicated product. All carbon atoms inthe product must come from the starting material. Draw all molecules synthesized along the way. When in doubt, draw the molecule! Label all chiral centers with an asterisk (*) and make sure to write "Racemic" where appropriate. Hint: this should look familiar as a homework problem.

Remember, all of the carbons of the product must come from the given starting material.

(13 pts)

A)



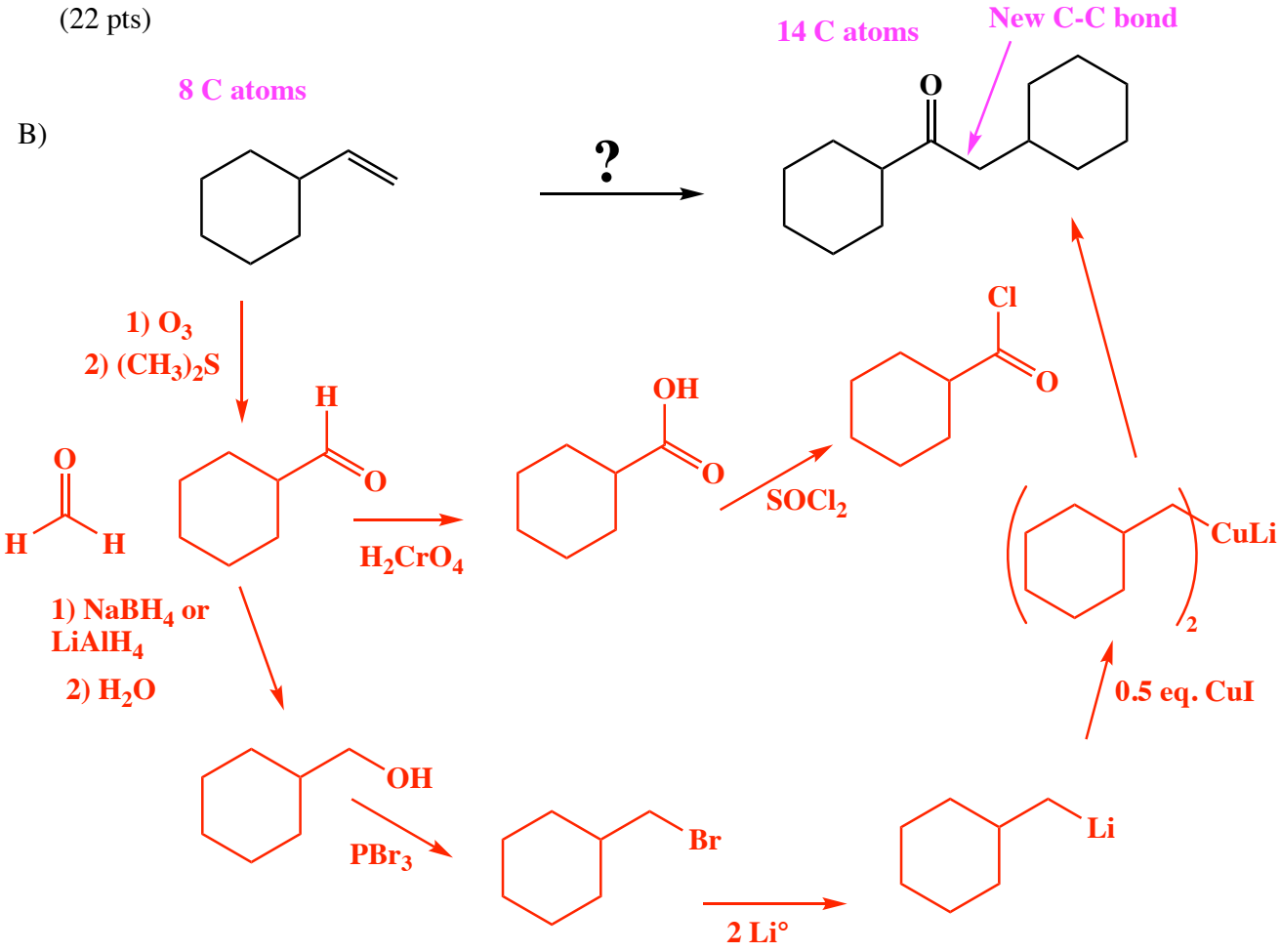

**Recognize** there are 8 carbons in the product, but 4 carbons in the starting material so two starting material units must be used to make the product. Further, the product is an ester. Therefore, the new bond being made to produce the product must be the one shown by the arrow. **Recognize** further that the ester is derived from an acid chloride and secondary alcohol as shown. The acid chloride is produced from the corresponding carboxylic acid, which is the result of a Jones oxidation of the primary alchol (1-butanol) as shown. The only way to make 1-butanol from 1-butene is through the hydroboration/oxidation route because this adds the -OH according to non-Markovnikov (less substituted) regiochemistry. **Recognize** that the secondary alcohol needed for the ester is made in a single step from the starting 1-butene via the Markovnikov addition of water using either the mercury reagent or simple acid-catalyzed hydration. It would be prefectly acceptable to use a Fischer esterification reaction between the secondary alcohol and carboxylic acid instead of the acid chloride approach illustrated above.

**19.** Using any reagents turn the starting material into the indicated product. All carbon atoms inthe product must come from the starting material. Draw all molecules synthesized along the way. When in doubt, draw the molecule! Label all chiral centers with an asterisk (*) and make sure to write "Racemic" where appropriate. Hint: this should look familiar as a homework problem.

Remember, all of the carbons of the product must come from the given starting material.

(22 pts)

B)



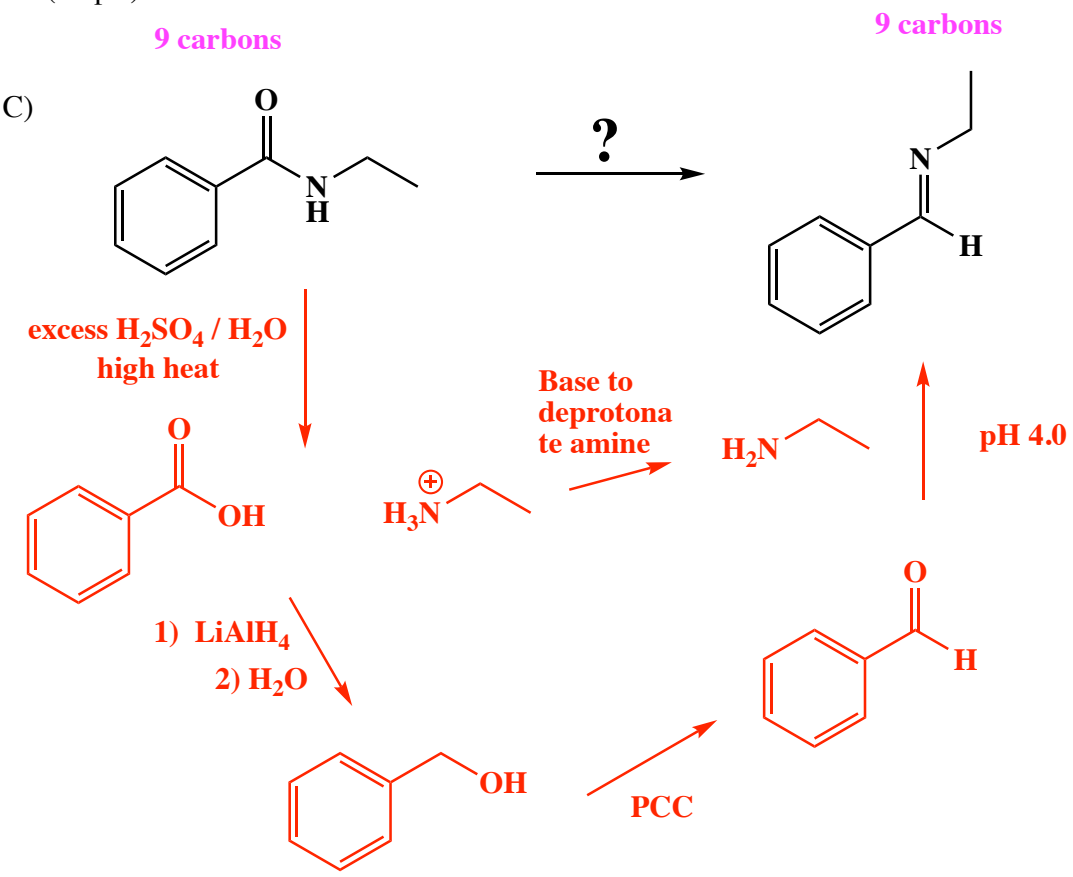

**Recognize** there are 8 C atoms in the starting material, but 14 in the product, with the new C-C bond being the one shown in the middle of the molecule. Therefore one carbon must be removed prior to assembling the final product bond from two 7-carbon pieces. **Recognize** that the product has a ketone group adjacent to the new C-C bond, the KRE for a Gilman reagent reacting with an acid chloride. The required acid chloride is derived from a 7-carbon carboxylic acid as shown. **Recognize** that the only way to make a 7-carbon fragment from the starting alkene is to use ozonolysis to generate a 7-carbon aldehyde. Therefore, the 7-carbon carboxylic acid can be made from Jones oxidation of the 7-carbon aldehyde as shown. The Gilman reagent can be made from the 7 carbon alkyl lithium, which comes from the 7-carbon bromoalkane using 2 equivalents of Li°. The 7-carbon bromoalkane is derived from the corresponding alcohol, which is the product of hydride reduction of the 7-carbon aldehyde produced in the ozonolysis reaction of the starting alkene. Note that the product could also have been made in fewer overall steps from the reaction of a 7-carbon Grignard reagent with the 7-carbon aldehyde shown above followed by Jones or PCC oxidation.

**19.** Using any reagents turn the starting material into the indicated product. All carbon atoms inthe product must come from the starting material. Draw all molecules synthesized along the way. When in doubt, draw the molecule! Label all chiral centers with an asterisk (*) and make sure to write"Racemic" where appropriate. Hint: this should look familiar as a homework problem.

Remember, all of the carbons of the product must come from the given starting material.

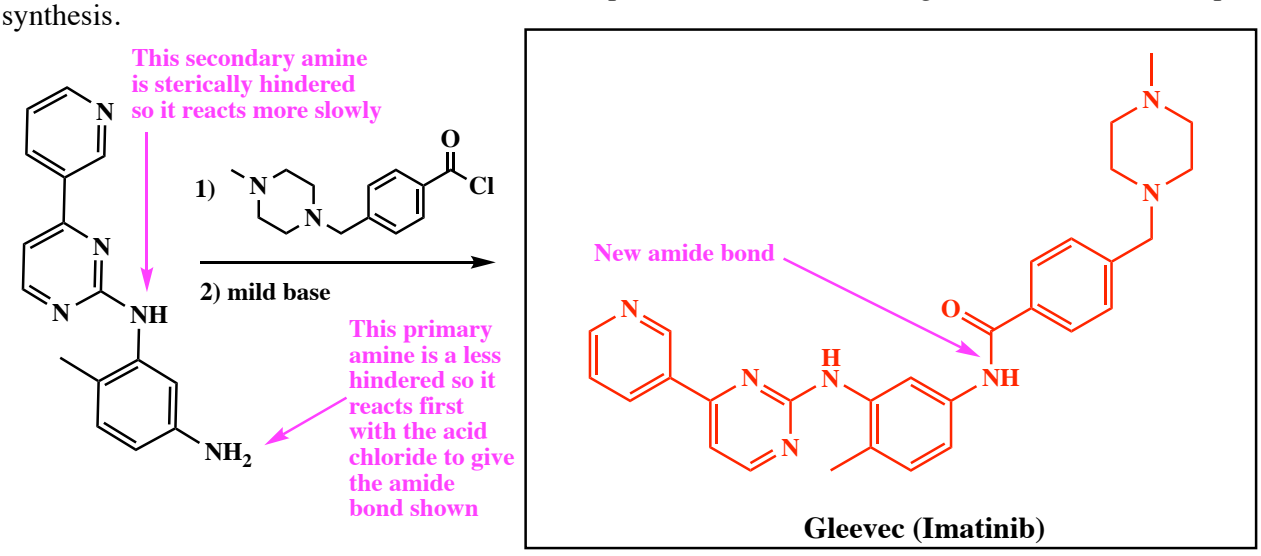
(13 pts)

C)




**Recognize** there are 9 carbons in the product and 9 carbons in the starting material. **Recognize** the product as an imine (AKA Schiff base) so assume the last reaction consists of an aldehyde reacting with a primary amine. **Recognize** the starting material as an amide, that can be hydrolyzed to give a carboxylic acid and protonated amine. The required aldehyde can be made from the carboxylic acid through a two-step process of hydride reduction to give the primary alcohol followed by PCC oxidation. The amine can be deprotonated in base then used to make the imine at pH 4.0.

**20.** Gleevec (also called imatinib) is the first example of a class of drugs known as TKI's, which stands for tyrosine kinase inhibitors. TKI's inhibit rogue enzymes that enable the "out of control" growth of certain cancers, such as several kinds of leukemia. The last step in the synthesis of Gleevec involves chemistry you know. Draw the structure of Gleevec in the box provided based on the reagents used in the last step of its synthesis.




**21.** As part of his research in my laboratory, your TA Chris needs to make an interesting molecule using the chemistry shown below. You know all the chemistry involved, or at least chemistry that is similar. Draw the product of the following step, which produces the molecule Chris will need to make what we hope will be an entirely new class of responsive liquid crystals. **You only need to show the main (largest) carbon containing product, not all of the products of this process.** Hint: Four reactions take place under these conditions and the product is a racemic mixture.