Circle one: I wish to have my exam put in the rack. I wish to pick up my exam.

Printed Name Answer Key
(Please print clearly)

Signature _____

CHEMISTRY 262

Exam III
100 Points

March 27, 2013
6:30 – 8:30 PM

This exam has 8 problems on pages 2 through 8.

RULES

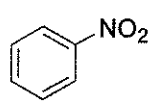
1. The use of a calculator and model kits are **not** permitted.
2. This exam is closed book and closed note. No aids other than writing implements are permitted.
3. Answer the questions in the spaces provided on this exam.
4. If you wish to ask a question about procedures or about a problem on the exam, raise your hand.

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____

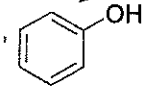
TOTAL: /100

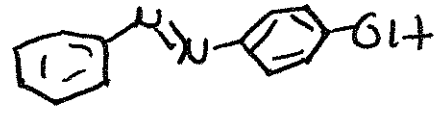
1. Predict the major product or products (be inclusive) that you would expect to be formed in **seven** of the following ten reactions (continued on the next page). If you feel that no reaction will occur, then answer no reaction. You may assume a workup step for each reaction. Be sure to answer **only** seven problems. If you answer more than seven, then *only your first seven will be graded.* (**21 points/ 3 pts. each**)

(a)

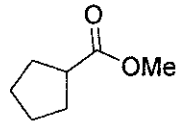


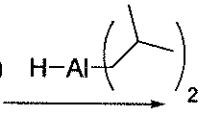
1) $LiAlH_4$
2) NaO-N=O, HCl
3) K_2CO_3,



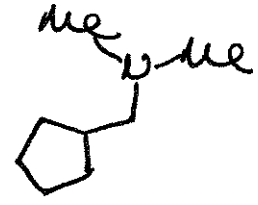


(b)

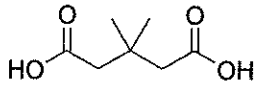


1) 

2) Me_2NH
H^+, $NaCNBH_3$

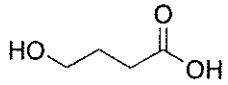


(c)

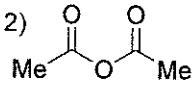


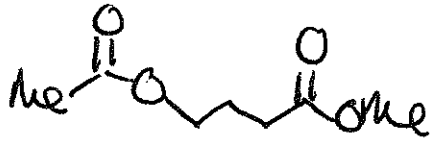
1) heat
2) $NaBH_4$

(d)

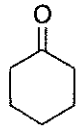


1) CH_2N_2
2)

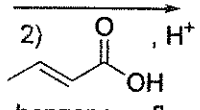




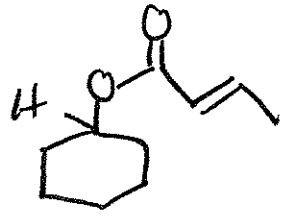
(e).



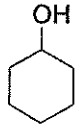
1) $LiAlH_4$
2)



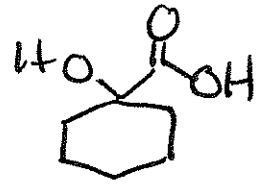
benzene, reflux
Dean-Stark trap



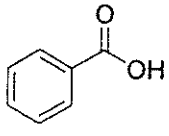
(f)



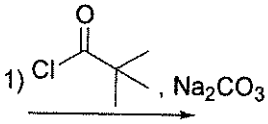
1) PCC, CH_2Cl_2
2) NaCN
3) H^+, H_2O



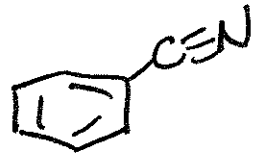
(g)

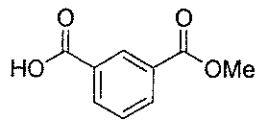


1)

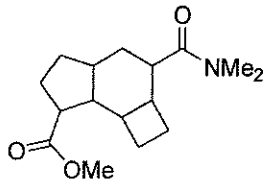


2) NH_3, Na_2CO_3
3) $POCl_3$

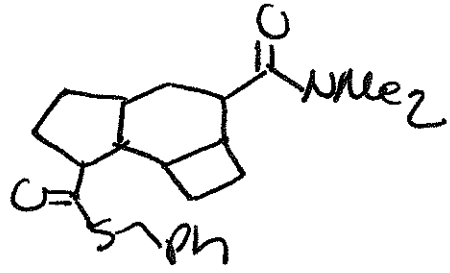


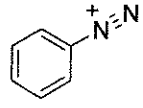
(h) 

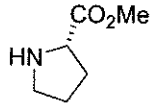
1) $BH_3 \cdot THF$
2) DIBAL-H
3) H^+, H_2O (workup)

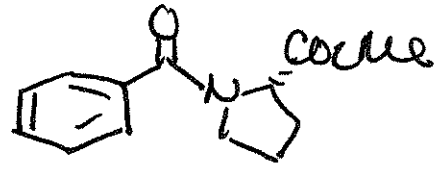
(i) 

1) NaOH (1 equiv.) MeOH
2) $(COCl)_2$, Na_2CO_3
3) $PhCH_2SH$, Na_2CO_3

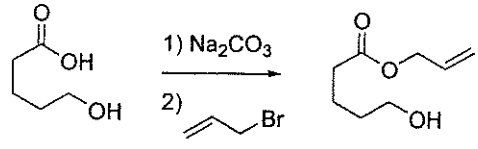


(j) 

1) CuBr
2) Mg(0)
3) CO_2 (followed by workup)
4) $SOCl_2$, heat
5) 



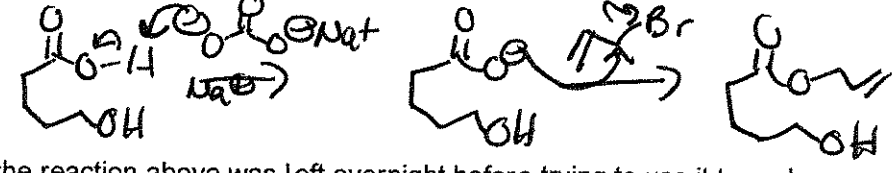
2. Consider the following reaction.



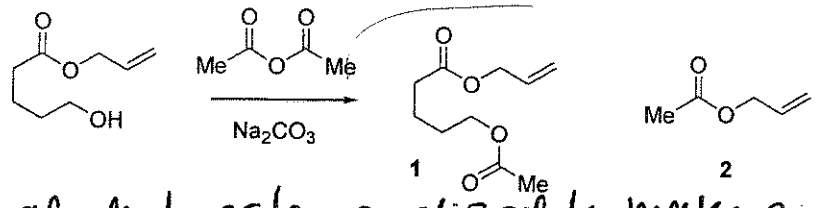
1) Na_2CO_3
2)

a. Why does this reaction lead to the formation of an ester product rather than an ether product derived from the alcohol. (**5 points**)

Because the base deprotonates the acid to make a carboxylate nucleophile.



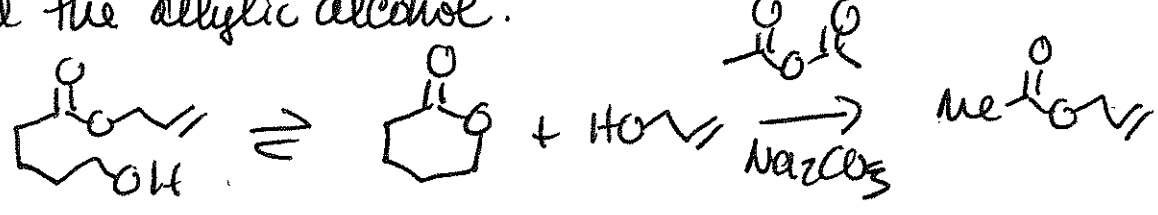
b. The product from the reaction above was left overnight before trying to use it to make product **1** as illustrated below. This led to the formation of product **2** instead of **1**. What happened? (**5 points**)



Na_2CO_3

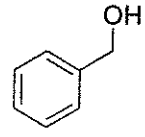
1 **2**

The alcohol ester cyclized to make a lactone and the allylic alcohol.

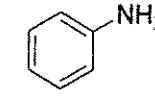


3. Fill in the reagents needed for accomplishing **three** of the five following transformations. More than one step may be required. Be sure to answer **only** three problems (**9 points/ 3 pts. each**)

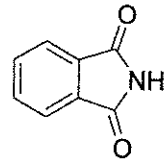
a)

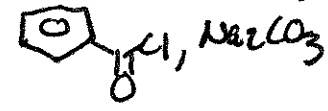


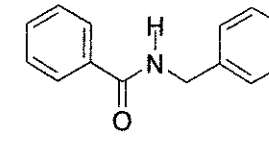
1. $H_2Cr_2O_7$, H_2SO_4
   H_2O, acetone
2. $(COCl)_2$, Na_2CO_3
   benzene.
3. $Na^{\oplus}\ ^{\ominus}N{=}N{=}N$
4. a) heat
   b) H_3, H_2O workup



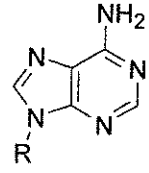
b)



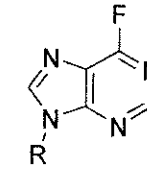
1. K_2CO_3, 
2. NH_2NH_2
3. 



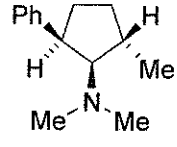
c)



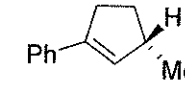
1) HCl, HO-N=O
2) HBF_4



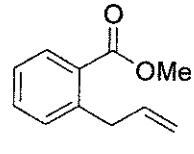
d)



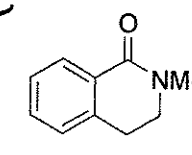
1) excess CH_3-I
2) Ag_2O
3) heat



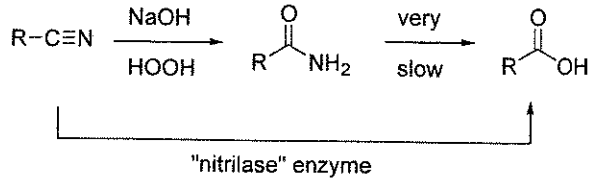
e)



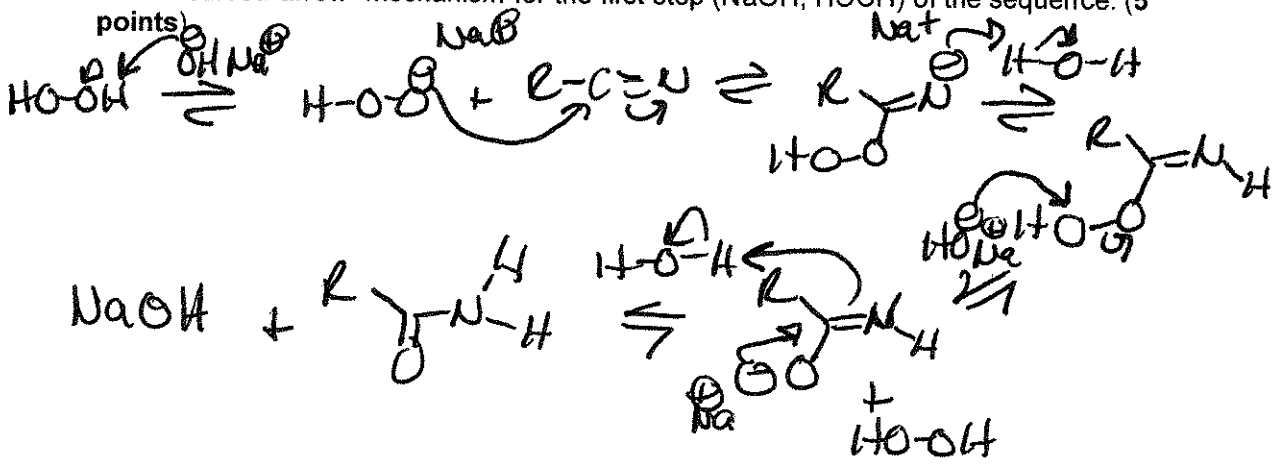
1) a) O_3 / MeOH / CH_2Cl_2
   b) Me_2S
2) $MeNH_2$, H+
   $NaCNBH_3$, MeOH



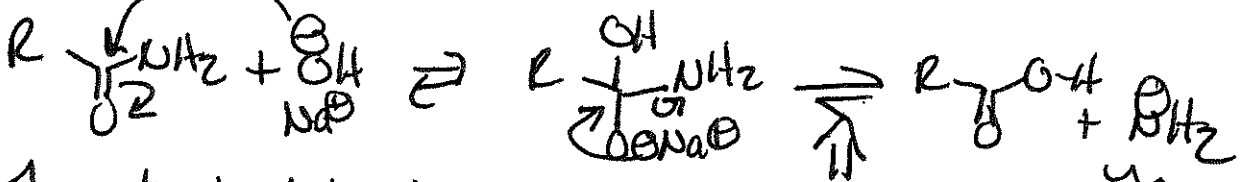
4. Consider the following:



a. Write a "curved-arrow" mechanism for the first step (NaOH, HOOH) of the sequence. (**5 points**)



b. The reaction can be used to make the amide because the second step leading to the acid is very slow. Why? Use a picture to help explain. (**5 points**)



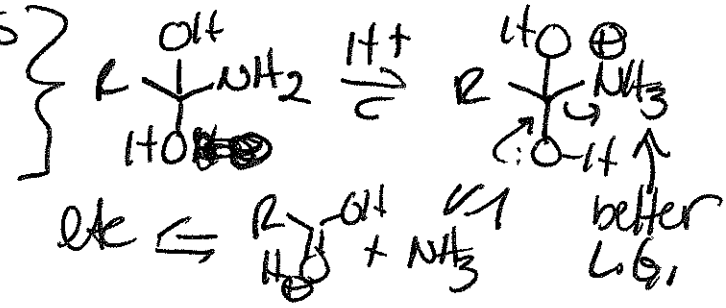
The elimination step is very slow because the $^{\ominus}NH_2$ is a bad leaving group.

very slow

terrible leaving group

c. Enzymes called nitrilases convert nitriles all the way to acids. What is present in their active sites that allows for this to happen readily at room temperature? Again, use a picture to help explain your answer (**5 points**)

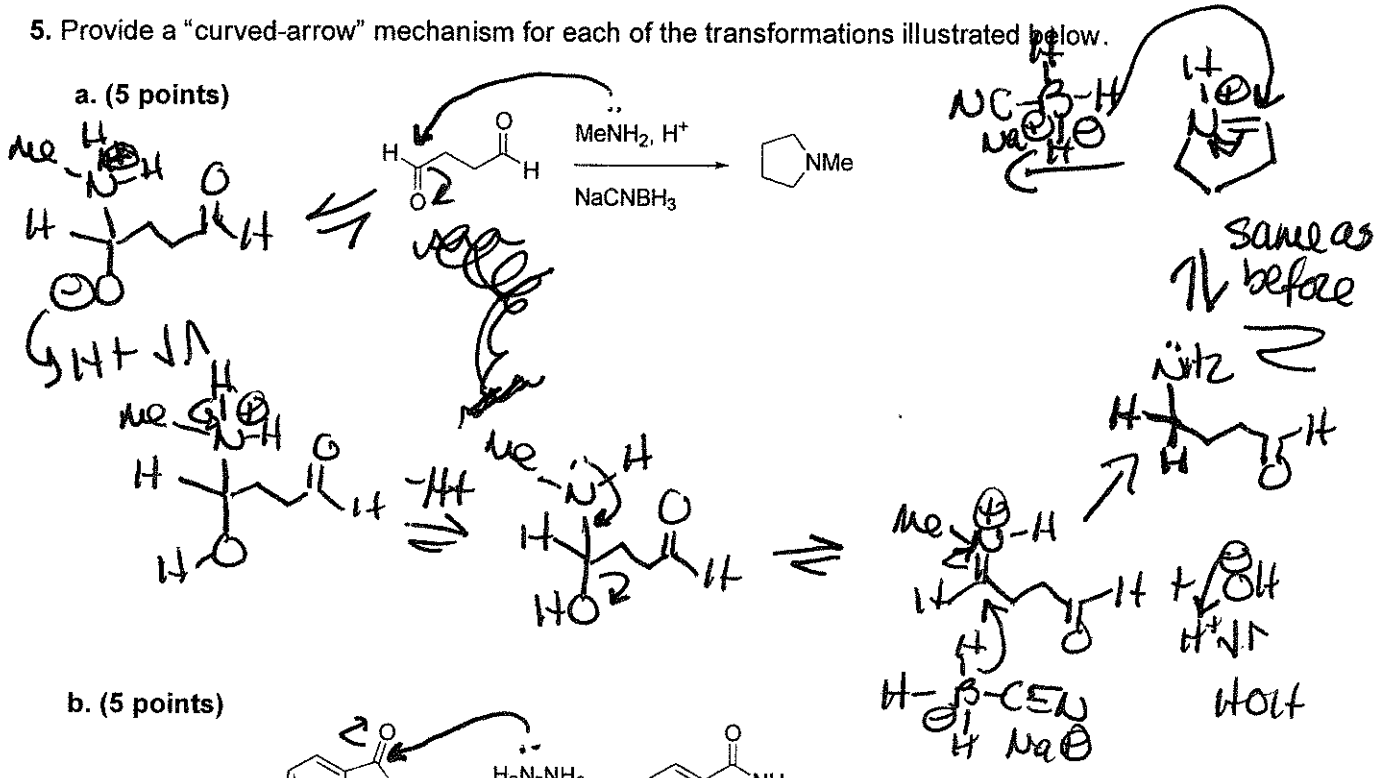
The enzymes have acid in their active sites. The acid protonates the amine in the tetrahedral intermediate and makes it a better leaving group.



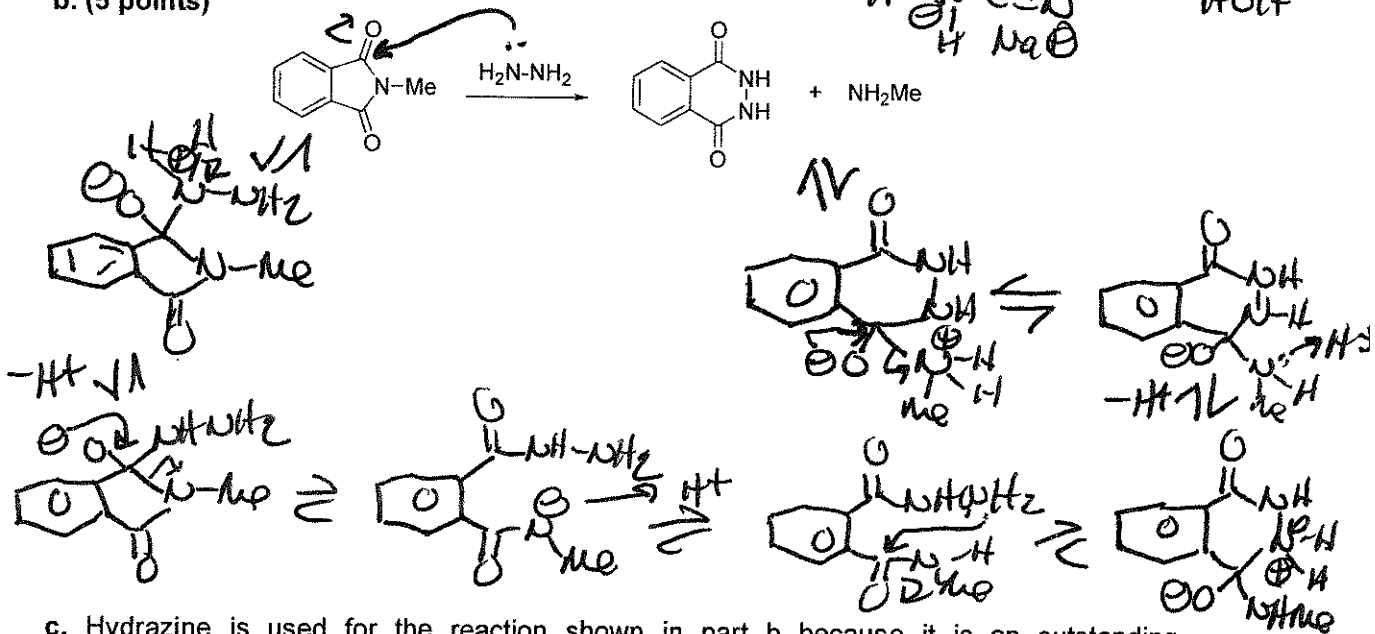
better L.G.

5. Provide a "curved-arrow" mechanism for each of the transformations illustrated below.

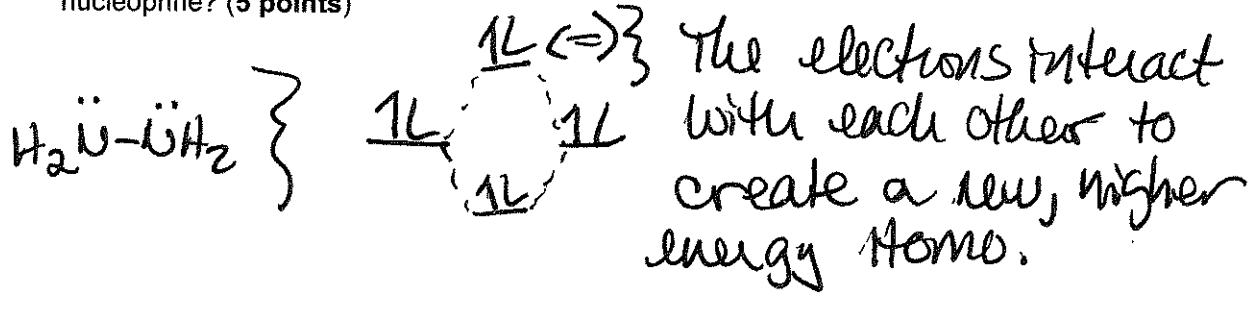
a. (5 points)



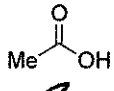
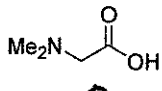
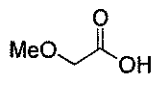
b. (5 points)

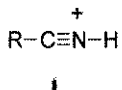
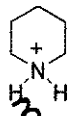
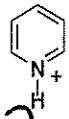


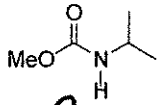
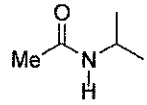
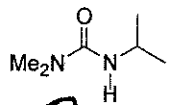
c. Hydrazine is used for the reaction shown in part b because it is an outstanding nucleophile; a much better nucleophile than ammonia. Why is hydrazine such a good nucleophile? **(5 points)**

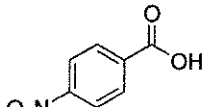
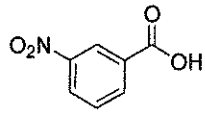
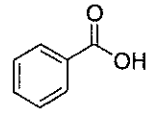


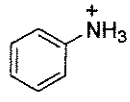
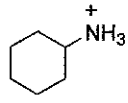
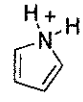
6. Rank the following molecules in terms of the acidity of the proton on either the oxygen or nitrogen. Rank the most acidic proton **1** and the least acidic proton **3**. (**10 points/ 2 pts each**)

a)  3  2  1

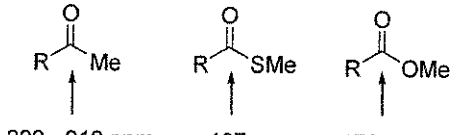
b)  1  3  2

c)  2  1  3

d)  1  2  3

e)  2  3  1

7. a. Nature often activates a carboxylic acid toward nucleophilic attack by converting it to a thioester. Use the NMR data provided below to explain why a thioester is more reactive toward a strong nucleophile than a normal ester. (**5 points**)

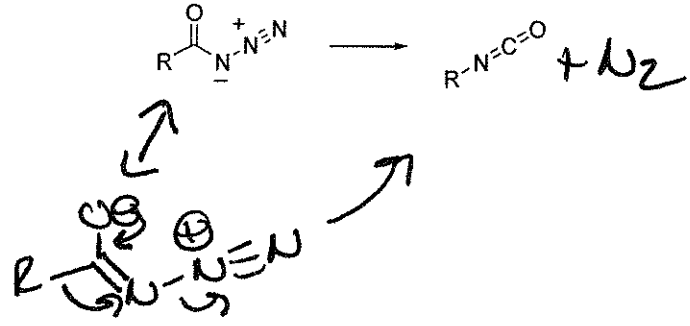


The ^{13}C-NMR data indicates that the (+)-charge character of the carbonyl carbon is more like the ketone than the ester. Hence the addition of a strong nucleophile to the thioester more closely resembles that of the more reactive ketone.

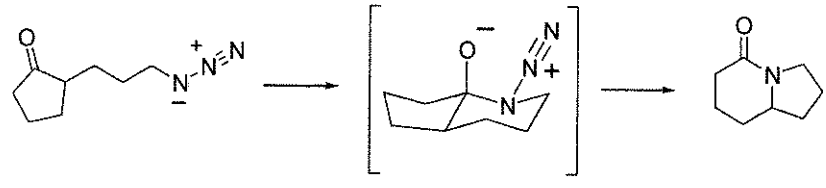
b. The thioester is also activated for reactions with weak nucleophiles. Why? (**5 points**)

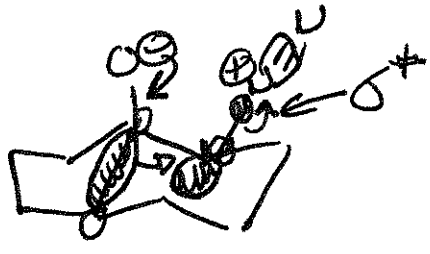
The more polarizable thiol (acid catalysis)/thiolate (base) group is a better leaving group than the alcohol/alkoxide group. This accelerates the leaving group elimination step for the reaction with a weak nucleophile.

8. a. In the Curtius rearrangement an acyl azide undergoes a bond migration to form an isocyanate. Use the reaction below and a "curved-arrow" mechanism to show how this happens. (**5 points**)



b. Jeff Aube' and coworkers commonly take advantage of a similar reaction (the Schmidt rearrangement) to make bicyclic alkaloids. The reaction (illustrated below) works because the ring amine in the key intermediate can invert an place the N_2-leaving group in an equatorial position. Use an orbital picture to explain why the N_2-leaving group needs to be equatorial for the reaction to work well. (**5 points**)





The equatorial leaving group has σ* aligned perfectly with the migrating σ-bond. It is the same overlap seen in the Curtius rearrangement.

Note that for an axial leaving group the alignment does not work so well.