Organic Chemistry 2
Third Examination
April 24, 2009
Prof. Malachowski

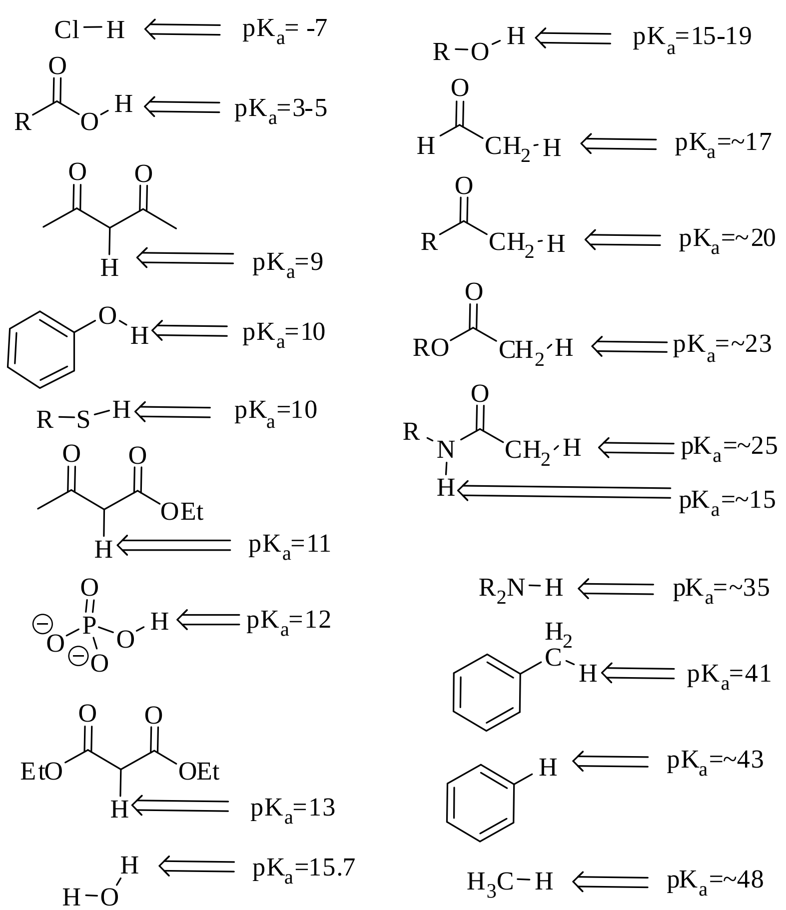
Name:_____Susan Boyle______________

The examination has six questions on four pages. The point values for each question are found with the question. Partial credit will be given where appropriate.

Read each question carefully before answering. Be certain you understand everything the question is requesting. Do the easy questions first. If questions appear confusing or exceedingly complex, then you may need to rethink the question. Keep in mind the intended examination topics.

In organic chemistry, hand-drawn pictures convey specific information. Be sure the drawing you have made conveys the essential information required to answer the question. Make certain that three-dimensional pictures display the correct atom arrangements. Don't forget to include lone pairs of electrons and formal charges when appropriate.

pKa information



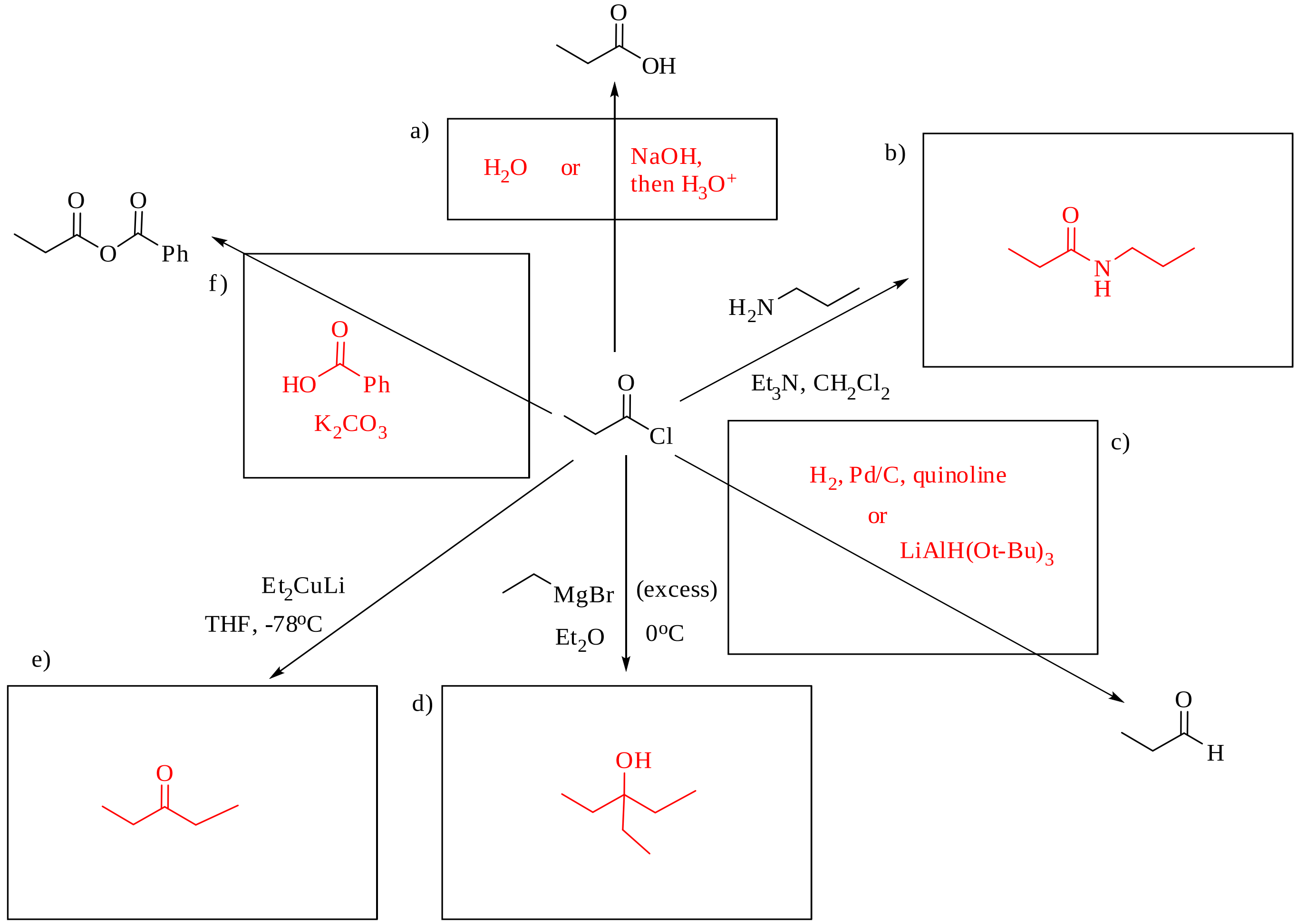
Note: R=alkyl

Portion of the Periodic Table:

C	N	O	F
Si	P	S	Cl

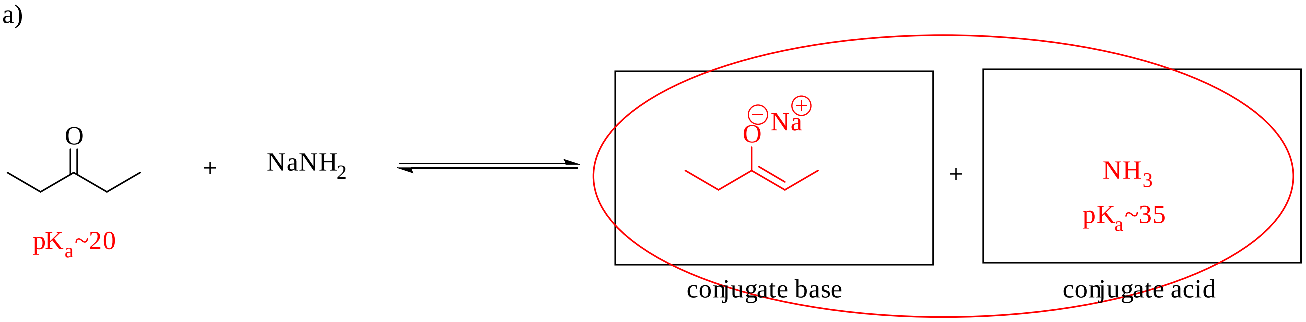
Electronegativity values:
O=3.6
Cl=2.9
S=2.6
C=2.5

1. Provide the necessary information, product or reagents, to complete the following reactions. (3 pts. per question)

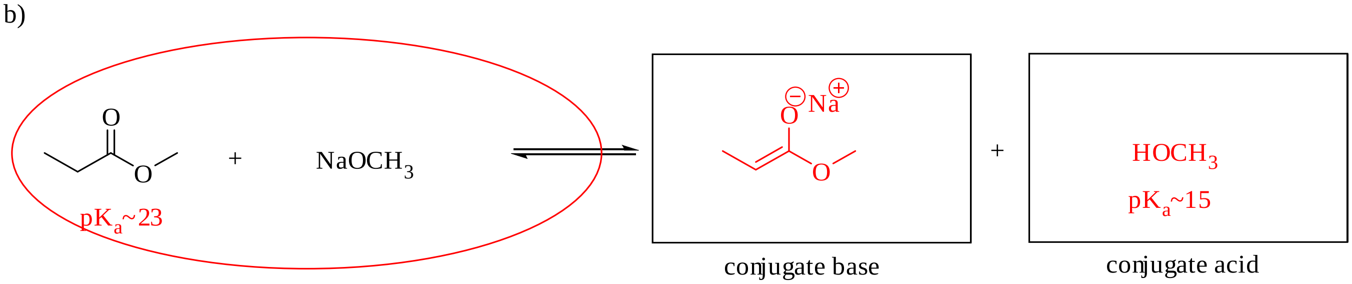


2. Complete the following acid-base equilibria by providing the conjugate base and acid products. Draw the most stable resonance form of all products and be sure to include formal charges and counter ions. Circle the side of the equilibria that will be favored. (5 pts. each)

a)

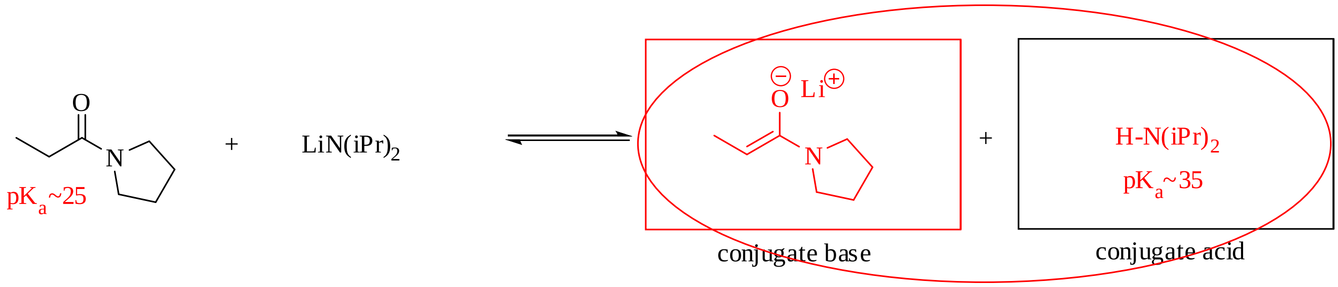


b)

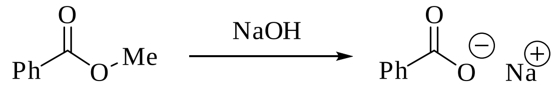


/28 pts.

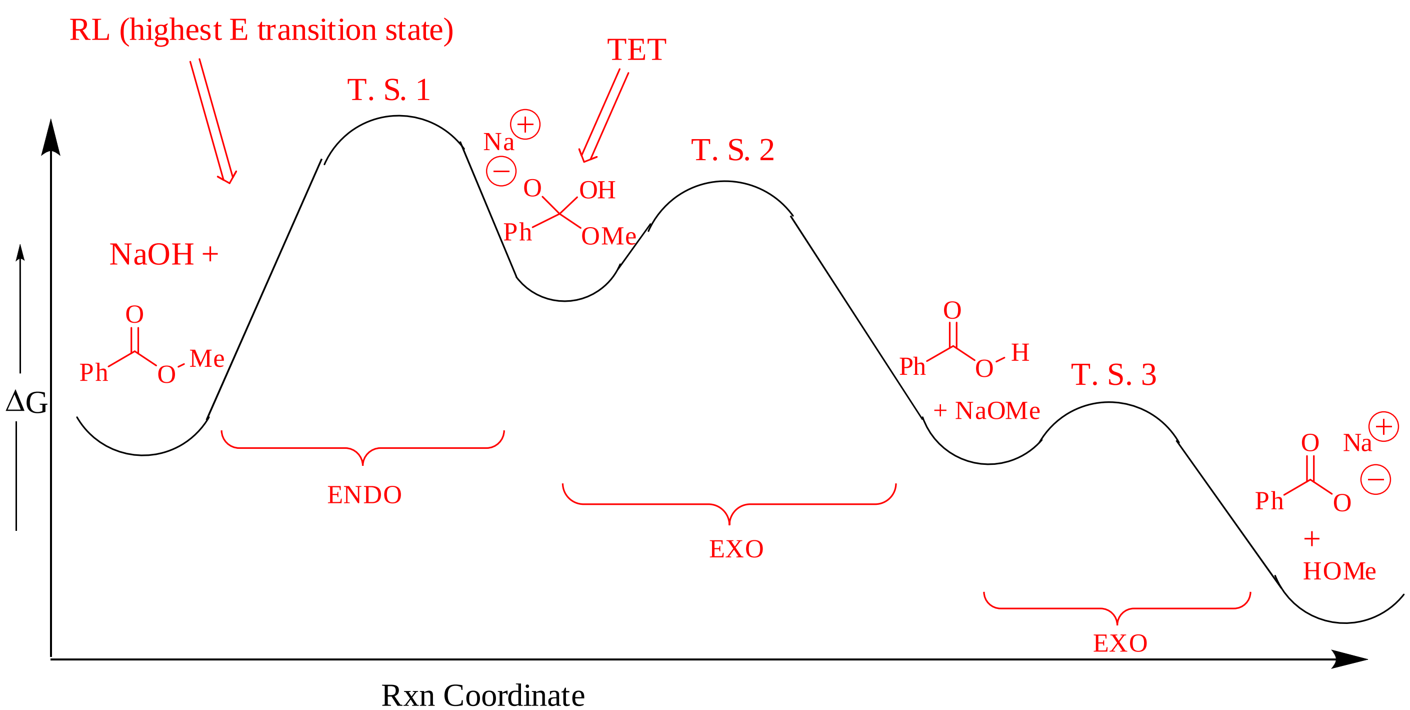
c)



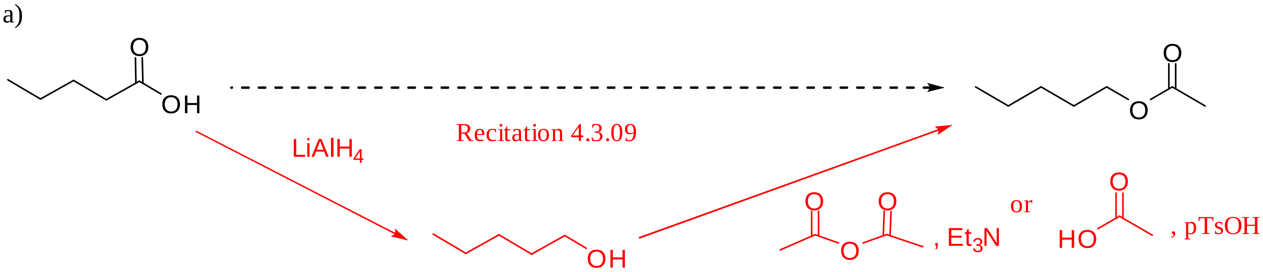
3. Answer the following questions about the reaction shown below. (14 pts.)



a) Draw the correct structures and place the starting materials, intermediates and products in the proper well of the energy diagram shown below. You do NOT need to show curved electron flow arrows.
b) Label all transtion states with TS. (You do NOT need to draw the transition state structures.)
c) Label the rate limiting step with RL.
d) Choose one step and label it as exothermic (EXO) or endothermic (ENDO).
e) Label the tetrahedral intermediate with TET.

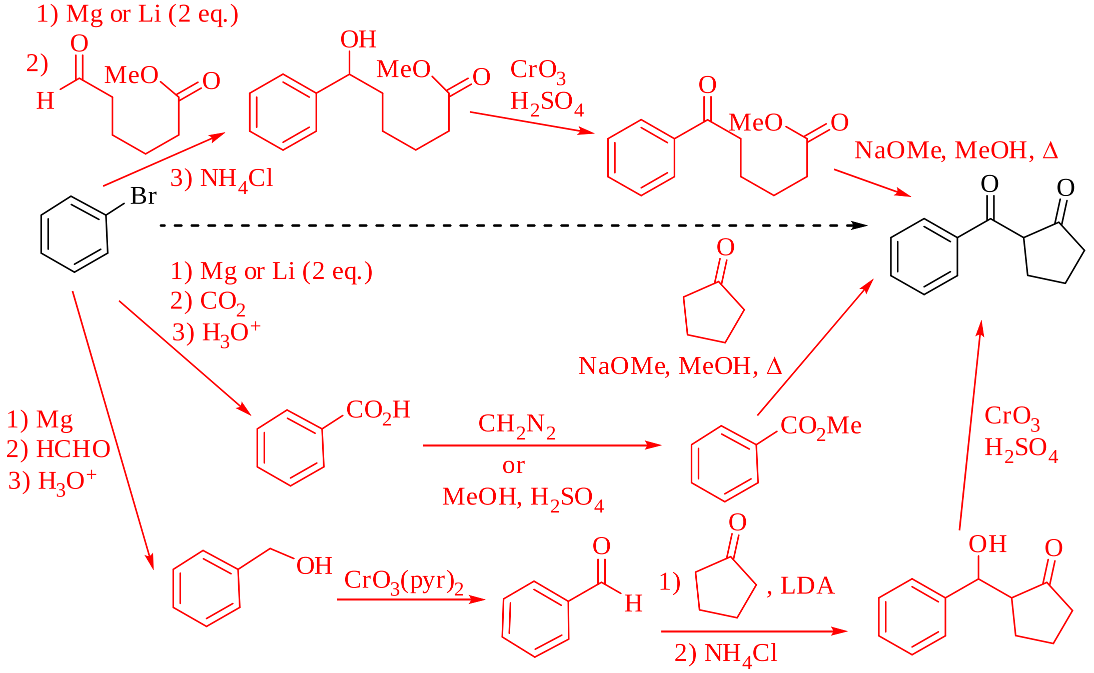


4. Suggest a synthesis to take the starting material on the left to the product on the right. This will require more than one step, but can be accomplished in three steps or less. You may use any inorganic or organic reagent. (9 pts. each)
a)

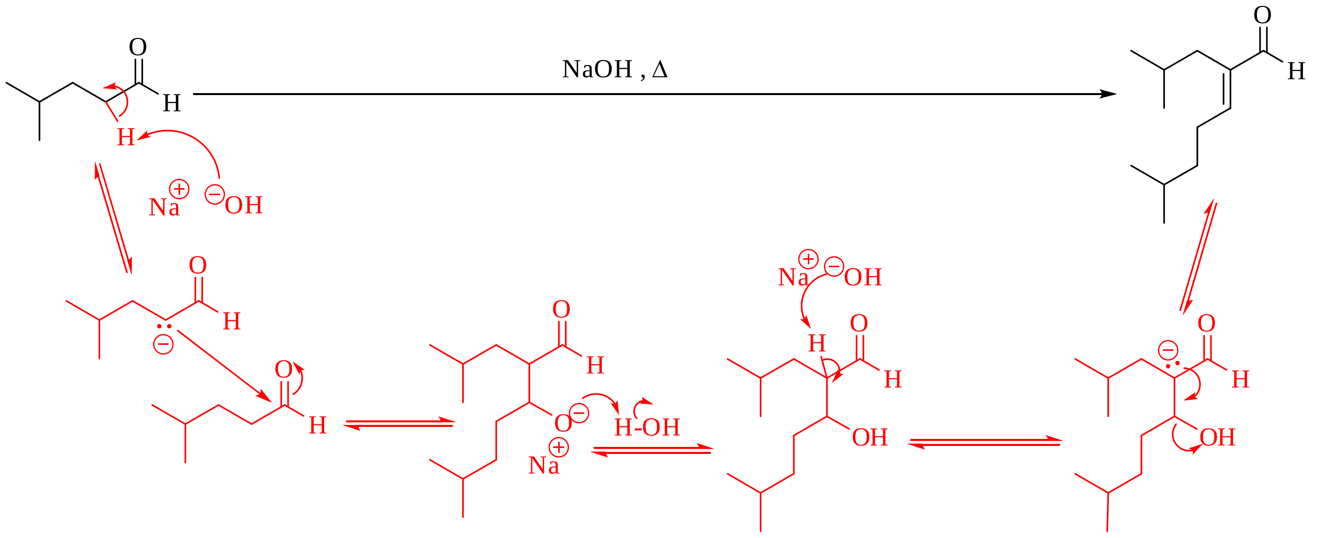


/28 pts.

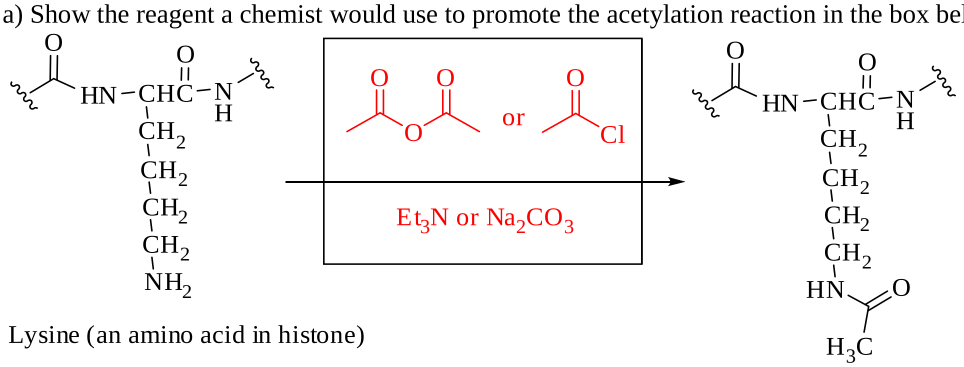
b)



5. Draw the mechanisms for the reaction shown below. Your mechanism should include formal charges and curved electron flow arrows. You do NOT need to draw important resonance structures. (10 pts.)



6. Histone acetylation and deacetylation has a key role in turning gene expression on and off. It therefore is a focus of many current cancer research studies. Answer the following questions about this reaction based on your knowledge of acid derivative reactions.
a) Show the reagent a chemist would use to promote the acetylation reaction in the box below. (3 pts.)



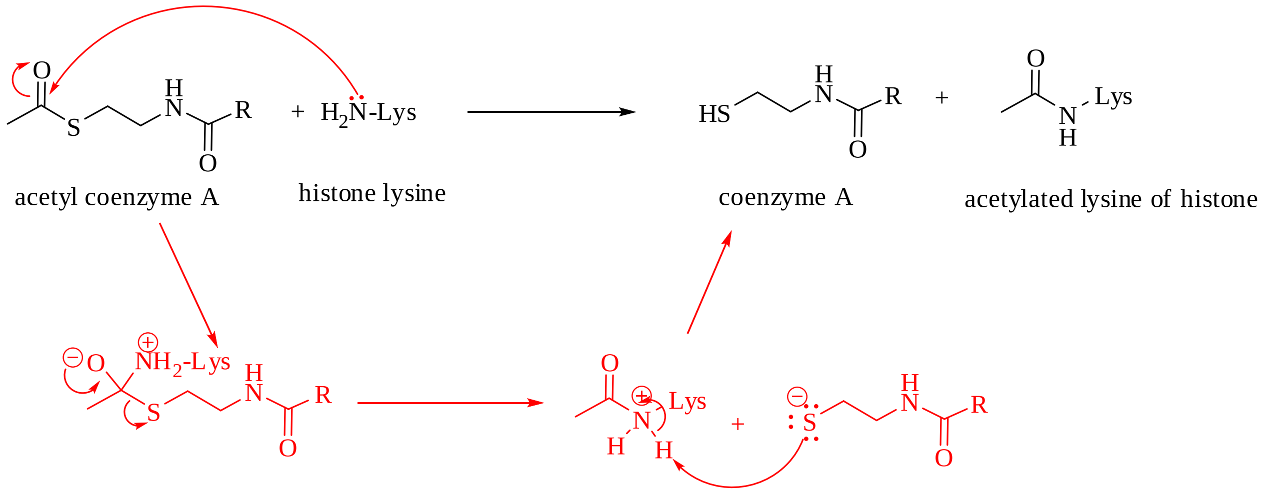
Lysine (an amino acid in histone)

/22 pts.

b) What type of functional group is reacting in the starting material and what type of functional group is formed in the product? Be as specific as possible. (2 pts. each)

starting material __primary amine___ **product** ___secondary amide_______

c) Nature acetylates the amine with acetyl coenzyme A. Show the curved electron flow arrows that depict the mechanism for the reaction of the amine of lysine with the thioester of acetyl coenzyme A. (8 pts.)



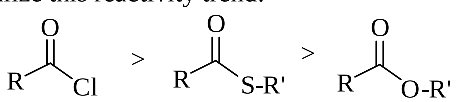
d) What type of mechanism is represented by this acetylation reaction? (2 pts.)

nucleophilic acyl substitution

e) Thioesters, such as in acetyl coenzyme A, are one of nature's acylating agents and they have reactivity intermediate between acid chlorides (chemist's acylating agent) and carboxylic esters. Rationalize this reactivity trend:

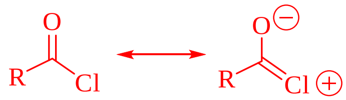
To receive full credit you must provide at least one good reason why thioesters have less reactivity than acid chlorides and more than esters. (8 pts.)

(Additional information is located on the cover page of the exam)

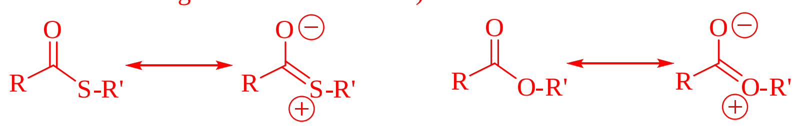


1. Reactivity of acid derivatives decreases with increasing resonance stabilization.

a) The resonance structure for the acid chloride (shown below) places a positive charge on a more electronegative Cl atom (versus S), therefore it is less likely to contribute than the resonance structure for a thioester. In addition, the acid chloride is more reactive than the thioester because the Cl is more electronegative than S and therefore creates a greater dipole moment between the C-Cl bond (than the C-S bond).



b) The thioester will be more reactive than the ester because S is a larger atom with valence electrons in the 3rd quantum level (see periodic table). This will prevent S from forming strong bonds with the smaller C atom (valence 2nd quantum level) in its resonance structure. The ester will have strong orbital overlap between the oxygen and carbon and the resonance structure should contribute more (despite oxygen being the most electronegative versus Cl and S).



2. Reactivity of acid derivatives decreases with more basic leaving groups.

The leaving groups for the acid chloride, thioester and ester are Cl^- , ^-SR , and ^-OR , respectively. Based on the pKa information for the conjugate acids of these three anions, the Cl^- is the weakest base and the ^-OR ion is the strongest base. Therefore, the acid chloride should be more reactive than the thioester, because the chloride ion is the weakest base and consequently, most stable leaving group. The ester should be less reactive than the thioester because it has the most basic and least stable leaving group.

(see Loudon 21.44 for similar example)

/22 pts.