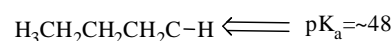
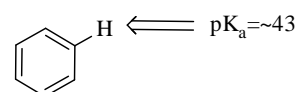
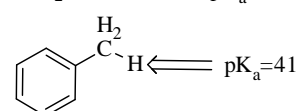
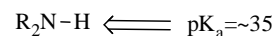
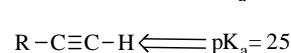
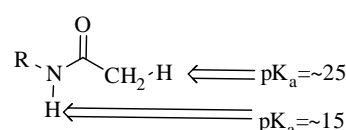
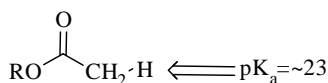
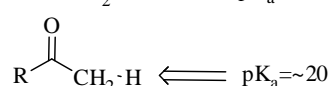
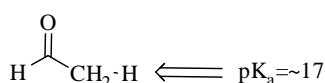
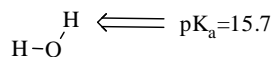
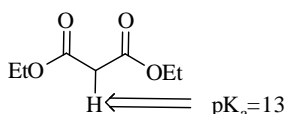
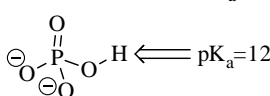
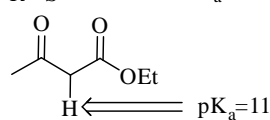
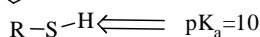
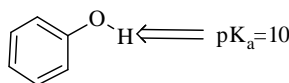
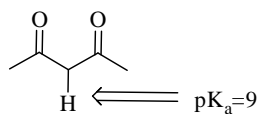
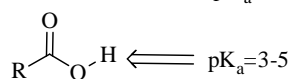
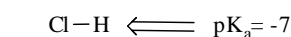


The examination has five questions on four pages. The point values for each question are found with the question. Partial credit will be given where appropriate.

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. Don't forget to include lone pairs of electrons and formal charges when appropriate.

pK<sub>a</sub> information



Note: R=alkyl

hydrogen 1 <b>H</b> 1.0079																	helium 2 <b>He</b> 4.0026						
lithium 3 <b>Li</b> 6.941	beryllium 4 <b>Be</b> 9.0122																	boron 5 <b>B</b> 10.811	carbon 6 <b>C</b> 12.011	nitrogen 7 <b>N</b> 14.007	oxygen 8 <b>O</b> 15.999	fluorine 9 <b>F</b> 18.998	neon 10 <b>Ne</b> 20.180
sodium 11 <b>Na</b> 22.990	magnesium 12 <b>Mg</b> 24.305																	aluminum 13 <b>Al</b> 26.982	silicon 14 <b>Si</b> 28.086	phosphorus 15 <b>P</b> 30.974	sulfur 16 <b>S</b> 32.065	chlorine 17 <b>Cl</b> 35.453	argon 18 <b>Ar</b> 39.948
potassium 19 <b>K</b> 39.098	calcium 20 <b>Ca</b> 40.078	scandium 21 <b>Sc</b> 44.956	titanium 22 <b>Ti</b> 47.867	vanadium 23 <b>V</b> 50.942	chromium 24 <b>Cr</b> 51.996	manganese 25 <b>Mn</b> 54.938	iron 26 <b>Fe</b> 55.845	cobalt 27 <b>Co</b> 58.933	nickel 28 <b>Ni</b> 58.693	copper 29 <b>Cu</b> 63.546	zinc 30 <b>Zn</b> 65.39	gallium 31 <b>Ga</b> 69.723	germanium 32 <b>Ge</b> 72.61	arsenic 33 <b>As</b> 74.922	selenium 34 <b>Se</b> 78.96	bromine 35 <b>Br</b> 79.904	krypton 36 <b>Kr</b> 83.80						
rubidium 37 <b>Rb</b> 85.468	strontium 38 <b>Sr</b> 87.62	yttrium 39 <b>Y</b> 88.906	zirconium 40 <b>Zr</b> 91.224	niobium 41 <b>Nb</b> 92.906	molybdenum 42 <b>Mo</b> 95.94	technetium 43 <b>Tc</b> [98]	ruthenium 44 <b>Ru</b> 101.07	rhodium 45 <b>Rh</b> 102.91	palladium 46 <b>Pd</b> 106.42	silver 47 <b>Ag</b> 107.87	cadmium 48 <b>Cd</b> 112.41	indium 49 <b>In</b> 114.82	tin 50 <b>Sn</b> 118.71	antimony 51 <b>Sb</b> 121.76	tellurium 52 <b>Te</b> 127.60	iodine 53 <b>I</b> 126.90	xenon 54 <b>Xe</b> 131.29						
caesium 55 <b>Cs</b> 132.91	barium 56 <b>Ba</b> 137.33	57-70 *	lutetium 71 <b>Lu</b> 174.97	hafnium 72 <b>Hf</b> 178.49	tantalum 73 <b>Ta</b> 180.95	wolfram 74 <b>W</b> 183.84	reuterium 75 <b>Re</b> 186.21	osmium 76 <b>Os</b> 190.23	iridium 77 <b>Ir</b> 192.22	platinum 78 <b>Pt</b> 195.08	gold 79 <b>Au</b> 196.97	mercury 80 <b>Hg</b> 200.59	thallium 81 <b>Tl</b> 204.38	lead 82 <b>Pb</b> 207.2	bismuth 83 <b>Bi</b> 208.98	polonium 84 <b>Po</b> [209]	astatine 85 <b>At</b> [210]	radon 86 <b>Rn</b> [222]					
francium 87 <b>Fr</b> [223]	radium 88 <b>Ra</b> [226]	89-102 **	lawrencium 103 <b>Lr</b> [262]	rutherfordium 104 <b>Rf</b> [261]	dubnium 105 <b>Db</b> [262]	seaborgium 106 <b>Sg</b> [269]	bohrium 107 <b>Bh</b> [264]	hassium 108 <b>Hs</b> [269]	meitnerium 109 <b>Mt</b> [269]	ununium 110 <b>Uun</b> [271]	ununium 111 <b>Uuu</b> [272]	ununium 112 <b>Uub</b> [272]	ununium 114 <b>Uuq</b> [289]										

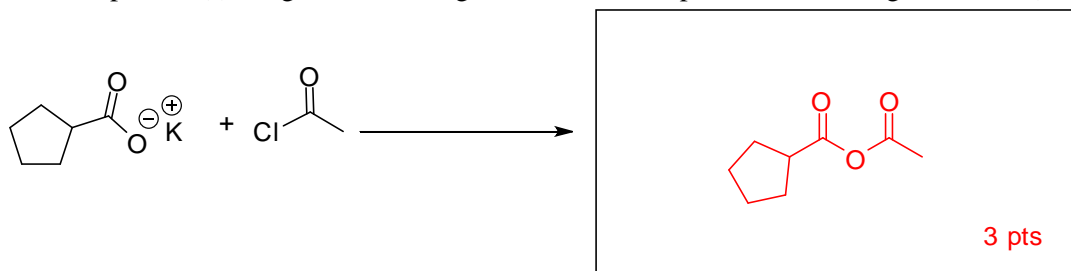
\* Lanthanide series

lanthanum 57 <b>La</b> 138.91	cerium 58 <b>Ce</b> 140.12	praseodymium 59 <b>Pr</b> 140.91	neodymium 60 <b>Nd</b> 144.24	promethium 61 <b>Pm</b> [145]	samarium 62 <b>Sm</b> 150.36	europium 63 <b>Eu</b> 151.96	gadolinium 64 <b>Gd</b> 157.25	terbium 65 <b>Tb</b> 158.93	dysprosium 66 <b>Dy</b> 162.50	holmium 67 <b>Ho</b> 164.93	erbium 68 <b>Er</b> 167.26	thulium 69 <b>Tm</b> 168.93	ytterbium 70 <b>Yb</b> 173.04
actinium 89 <b>Ac</b> [227]	thorium 90 <b>Th</b> 232.04	protactinium 91 <b>Pa</b> 231.04	uranium 92 <b>U</b> 238.03	neptunium 93 <b>Np</b> [237]	plutonium 94 <b>Pu</b> [244]	americium 95 <b>Am</b> [243]	curium 96 <b>Cm</b> [247]	berkelium 97 <b>Bk</b> [247]	californium 98 <b>Cf</b> [251]	einsteinium 99 <b>Es</b> [252]	fermium 100 <b>Fm</b> [257]	mendelevium 101 <b>Md</b> [258]	nobelium 102 <b>No</b> [259]

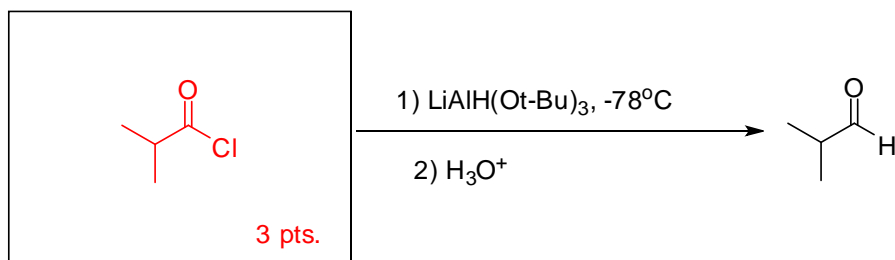
\*\* Actinide series

1. Provide the product(s), reagents or starting materials, to complete the following reactions. (20 pts.)

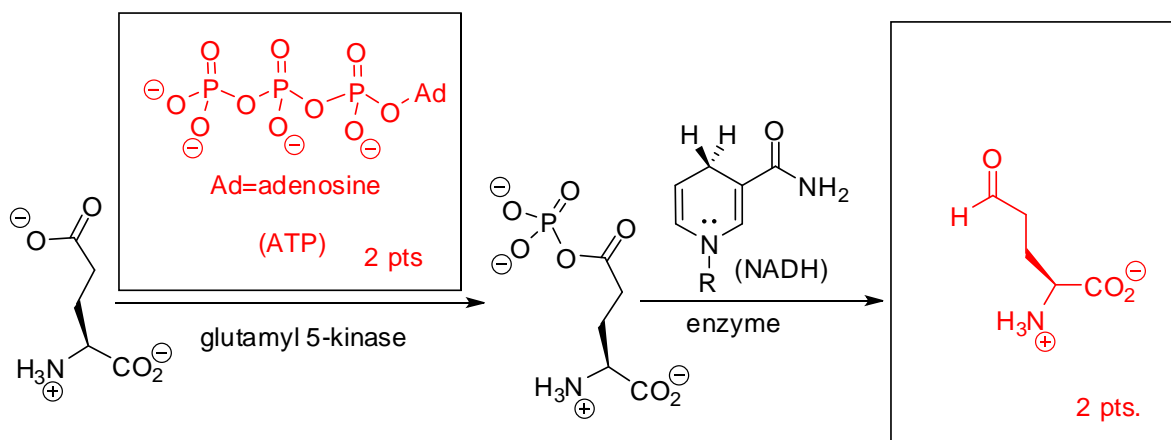
a)



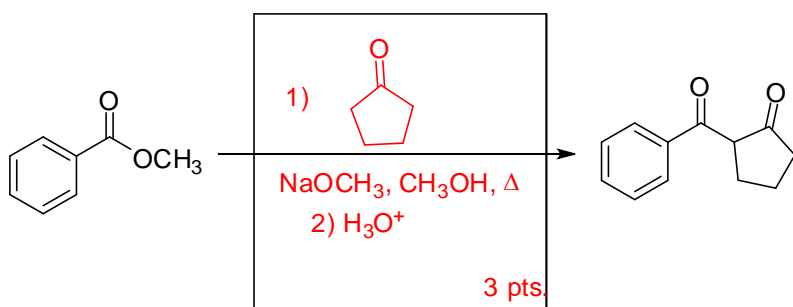
b)



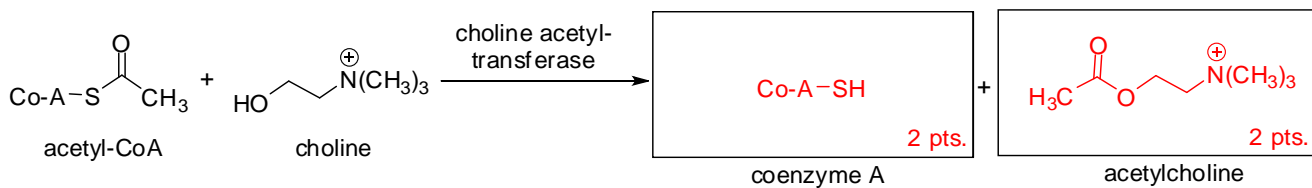
c)



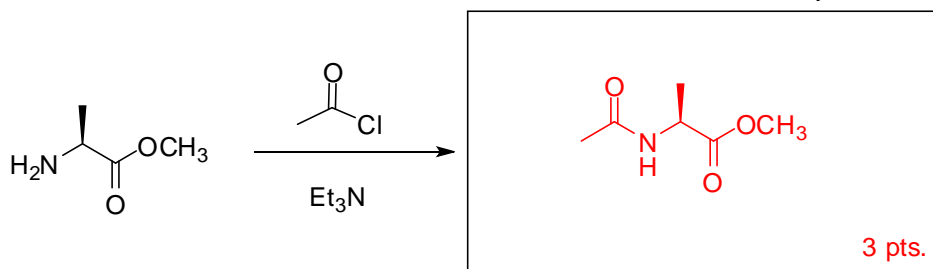
d)



e)

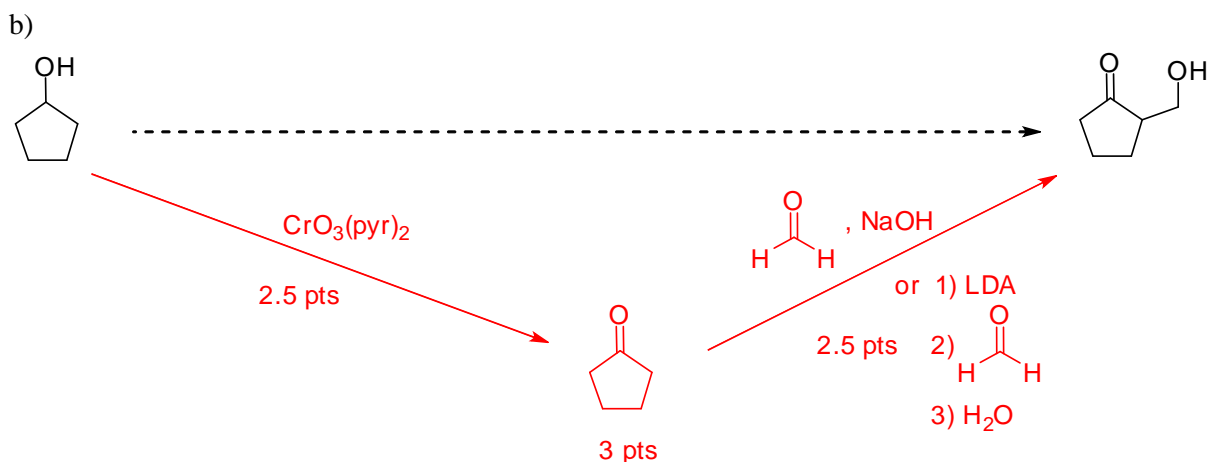
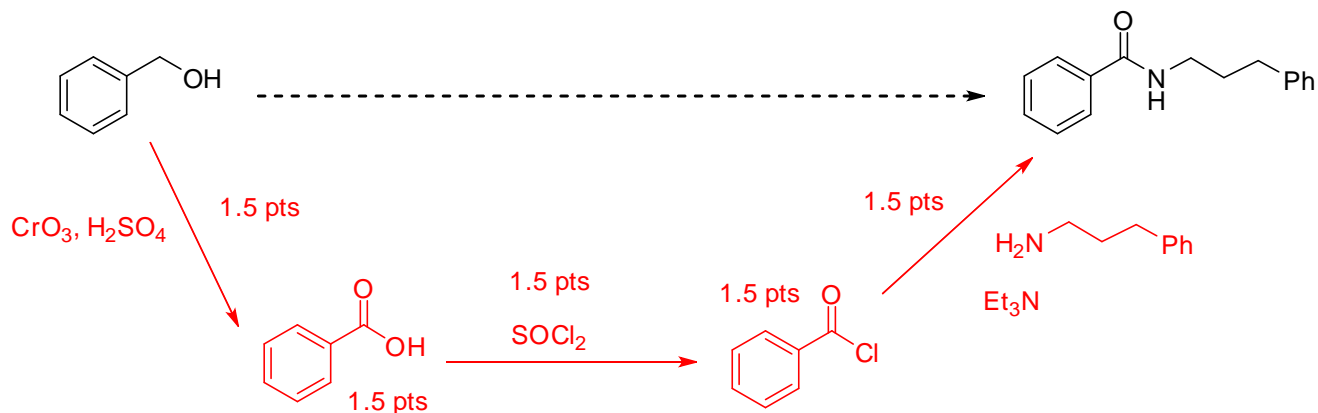


f)



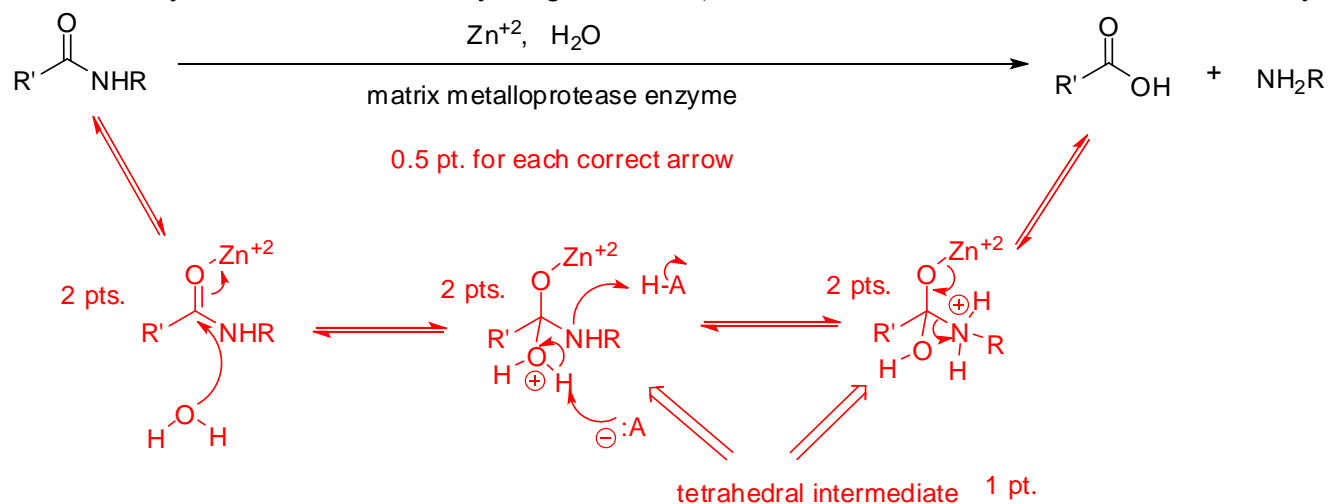
2. *Synthesis questions.* (16 pts.)

a) Suggest a series of reactions to take the starting material on the left to the product on the right. This will require two or three steps. You may use any inorganic or organic reagents.

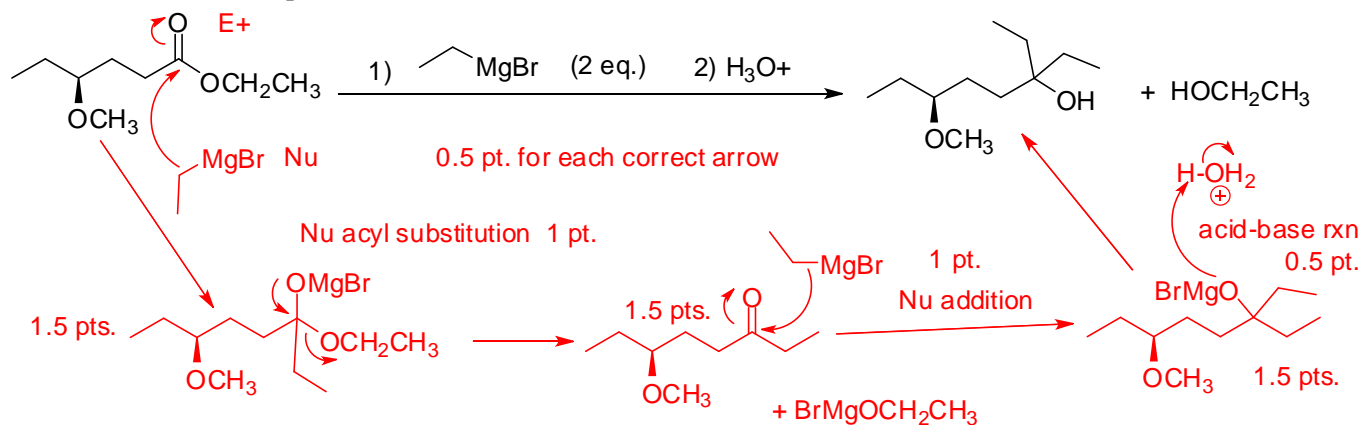


3. *Mechanism questions.* (33 pts.)

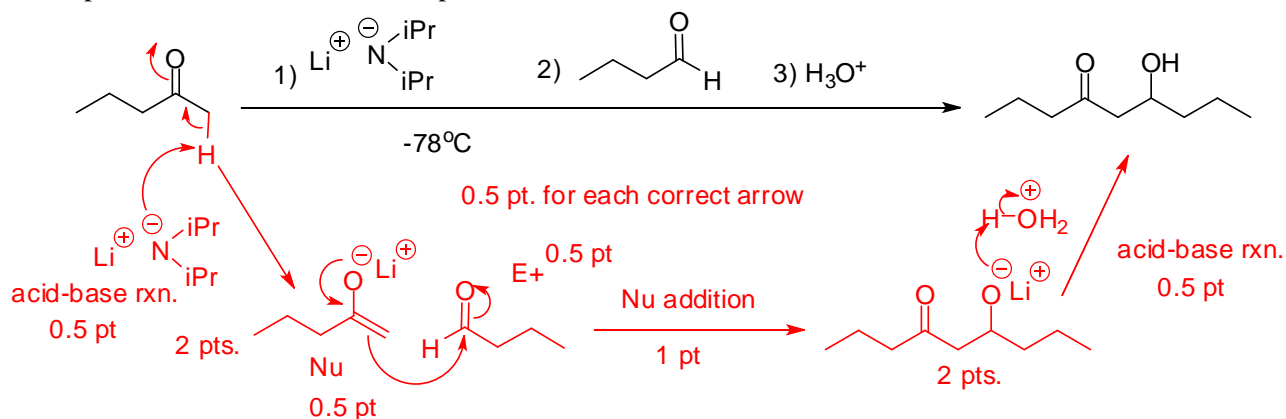
a) The matrix metalloproteases are an important class of enzymes which cancer cells use to cut through protein tissue and create space for more cancer growth. Matrix metalloproteases catalyze the following hydrolysis reaction (in a simplified format). Based on our related discussions in class and recitation, draw a mechanism for this process. Your mechanism should include the following: A role for zinc, curved electron flow arrows, and the identification of “special” or “noteworthy” intermediates. You may use general acid (H-A) or base (A<sup>-</sup>) conventions since this is an enzyme.



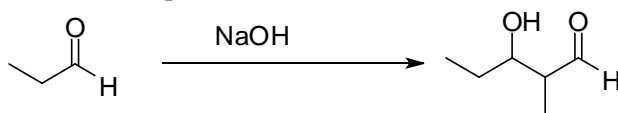
b) In addition to showing the mechanism, identify the nucleophile (Nu) and electrophile (E+) in the first step, and identify the type of reaction occurring (e.g. S<sub>N</sub>2, electrophilic aromatic substitution, acid-base reaction, nucleophilic addition, etc.) for all steps.



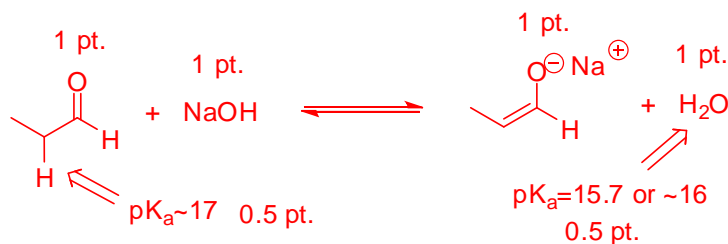
c) In addition to showing the mechanism, identify the nucleophile (Nu) and electrophile (E+) in the C-C bond forming step, and identify the type of reaction occurring (e.g. S<sub>N</sub>2, electrophilic aromatic substitution, acid-base reaction, nucleophilic addition, etc.) for all steps.



4. Analyze the aldol addition shown below. (16 pts.)



a) Draw the acid-base equilibrium that is the first step of the aldol addition shown above. You do NOT need to draw curved electron flow arrows. You should draw the most stable resonance form of all structures.

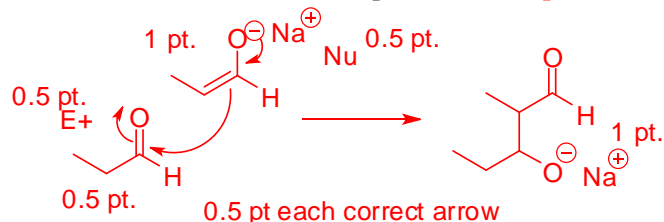


b) Identify the acids on both sides of the equilibrium by drawing an arrow to the acidic proton and writing the approximate  $pK_a$  of each proton. (1 pt. see above)

c) Based on your  $pK_a$  assignments, what will be the  $K_{eq}$  and the approximate ratio of [aldehyde]:[conjugate base].

$pK_{eq} = 17 - 16 = 1$ ; therefore  $K_{eq} = 10^{-1}$  or 0.1 The ratio of [aldehyde]:[conjugate base] will be approximately 10/1. (3 pts.)

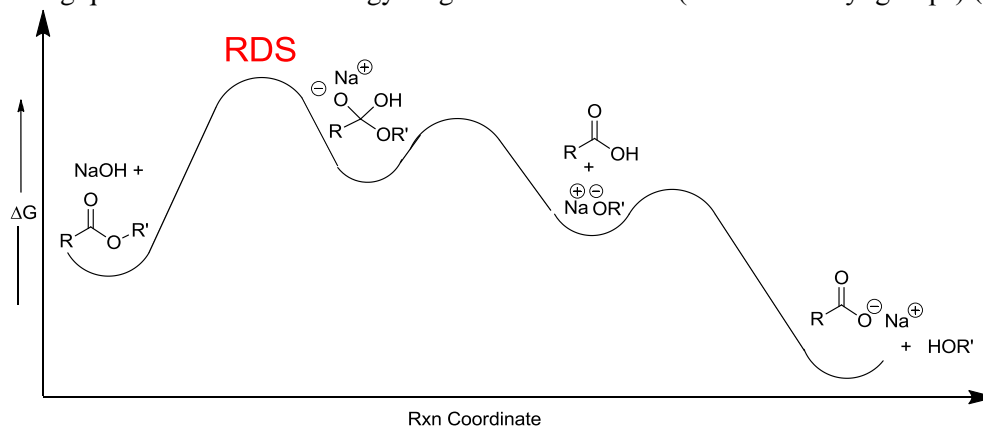
d) Show the next step of the aldol addition after the acid-base equilibrium. (5 pts.)



e) Combining the information you provided in step d with your analysis in step c, why might the use of NaOH as the base be optimum? For example, what problem might there be with using a stronger base such as NaH or lithium diisopropylamide (LDA)?

With NaOH, there is still plenty of aldehyde available to act as an electrophile. With a stronger base, there would be complete deprotonation and there would be no aldehyde electrophile remaining. (3 pts.)

5. Answer the following questions about the energy diagram shown below. (R and R'=alkyl groups) (15 pts.)



a) What reaction is shown in this diagram? Be as specific as possible. (2 pts.)

The saponification reaction

b) Place a RDS at the point along the energy path of the reaction that is the 'rate determining step'. (1.5 pt.)

c) How many steps are in this reaction? 3 (1.5 pt.)

d) Which statement best explains why the strong base  $RO^-$  can act as a leaving group?

(i) Since the reaction is run in  $HO^-$  (hydroxide) there is no problem with  $RO^-$ , a weaker base, leaving in the reaction.

(ii) The step involved is exothermic and, according to Hammond's postulate, this means there will be little formation of  $RO^-$  at the transition state.

(iii) The final step is exothermic and this allows the process to be thermodynamically favorable.

(iv) The formation of a strong C-OH bond allows the reaction to overcome the liabilities of the strong base  $RO^-$  leaving group.

(v) The sodium cation binds to the  $RO^-$  and helps reduce the negative effects of  $RO^-$  as a leaving group.

(3 pts.)

e) Select the reason that best explains why the reaction is thermodynamically favorable for product formation.

(i) The first step is completed early and the rest of the reaction has low energy transition states.

(ii) A more reactive ester functional group is converted to a less reactive carboxylic acid and that makes the process energetically favorable.

(iii) A tetrahedral intermediate forms which is always the sign of a spontaneous process.

(iv) The carbonyl bond is one of the most stable bonds known and the formation of it in multiple steps of the reaction makes the overall process highly favorable.

(v) The final step is a highly favorable acid-base reaction that shifts the overall equilibrium to the products.

(3 pts.)

f) Circle all the reasons that explain why thioesters ( $R'-C(=O)-SR$ ) are more reactive than esters ( $R'-C(=O)-OR$ ).

(i) Thioesters have weaker resonance stabilization due to the poor overlap between sulfur's 3p orbitals and carbon's 2p orbitals.

(ii) The thioalkoxide ( $RS^-$ ) leaving group is a weaker base and therefore better leaving group than the alkoxide ( $RO^-$ ) leaving group.

(iii) Esters have better resonance stabilization due to oxygen's higher electronegativity and willingness to donate electrons.

(iv) Alkoxides are immediately protonated and therefore are made good leaving groups through this protonation event.

(v) Oxygen is more electronegative than sulfur, so the C-O bond is more polarized than the C-S bond.

2 pts. each correct; -0.5 pt. for extra circled