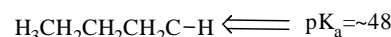
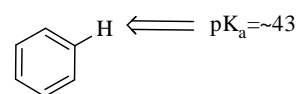
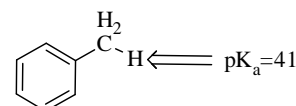
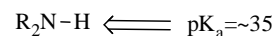
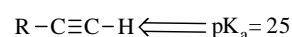
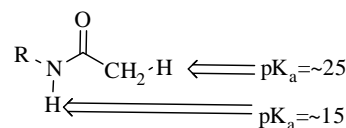
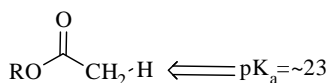
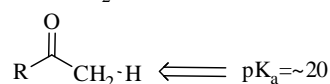
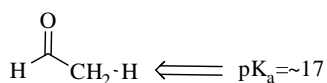
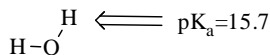
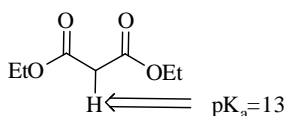
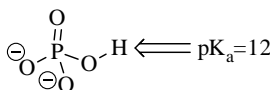
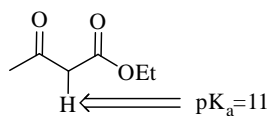
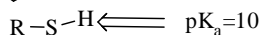
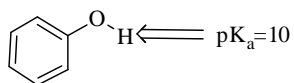
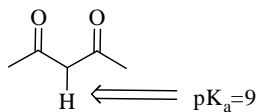
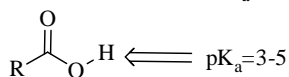
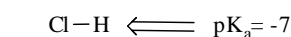


The examination has five questions on four pages. The point values for each question are found with the question. Partial credit will be given where appropriate.

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_a information



Note: R=alkyl

hydrogen 1 H 1.0079																	helium 2 He 4.0026	
lithium 3 Li 6.941	beryllium 4 Be 9.0122																	neon 10 Ne 20.180
sodium 11 Na 22.990	magnesium 12 Mg 24.305																	argon 18 Ar 39.948
potassium 19 K 39.098	calcium 20 Ca 40.078	scandium 21 Sc 44.956	titanium 22 Ti 47.867	vanadium 23 V 50.942	chromium 24 Cr 51.996	manganese 25 Mn 54.938	iron 26 Fe 55.845	cobalt 27 Co 58.933	nickel 28 Ni 58.693	copper 29 Cu 63.546	zinc 30 Zn 65.39	gallium 31 Ga 69.723	germanium 32 Ge 72.61	arsenic 33 As 74.922	selenium 34 Se 78.96	bromine 35 Br 79.904	krypton 36 Kr 83.80	
rubidium 37 Rb 85.468	strontium 38 Sr 87.62	yttrium 39 Y 88.906	zirconium 40 Zr 91.224	niobium 41 Nb 92.906	molybdenum 42 Mo 95.94	technetium 43 Tc [98]	ruthenium 44 Ru 101.07	rhodium 45 Rh 102.91	palladium 46 Pd 106.42	silver 47 Ag 107.87	cadmium 48 Cd 112.41	indium 49 In 114.82	tin 50 Sn 118.71	antimony 51 Sb 121.76	tellurium 52 Te 127.60	iodine 53 I 126.90	xenon 54 Xe 131.29	
caesium 55 Cs 132.91	barium 56 Ba 137.33	57-70 * Lu 174.97	hafnium 72 Hf 178.49	tantalum 73 Ta 180.95	tungsten 74 W 183.84	rhenium 75 Re 186.21	osmium 76 Os 190.23	iridium 77 Ir 192.22	platinum 78 Pt 195.08	gold 79 Au 196.97	mercury 80 Hg 200.59	thallium 81 Tl 204.38	lead 82 Pb 207.2	bismuth 83 Bi 208.98	polonium 84 Po [209]	astatine 85 At [210]	radon 86 Rn [222]	
francium 87 Fr [223]	radium 88 Ra [226]	89-102 ** Lr [262]	rutherfordium 104 Rf [261]	dubnium 105 Db [262]	seaborgium 106 Sg [263]	bohrium 107 Bh [264]	hassium 108 Hs [265]	meitnerium 109 Mt [266]	ununium 110 Uun [271]	ununium 111 Uuu [272]	ununium 112 Uub [277]	ununium 114 Uuq [289]						

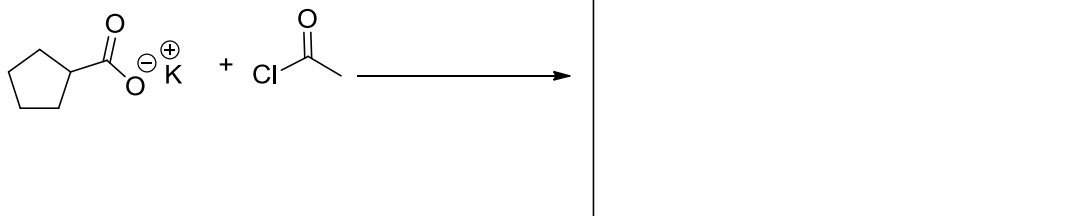
* Lanthanide series

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

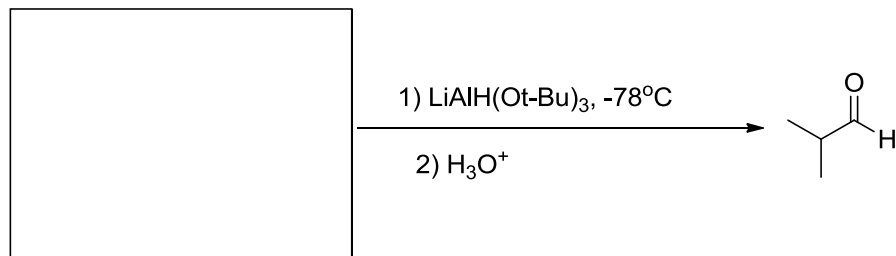
** Actinide series

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

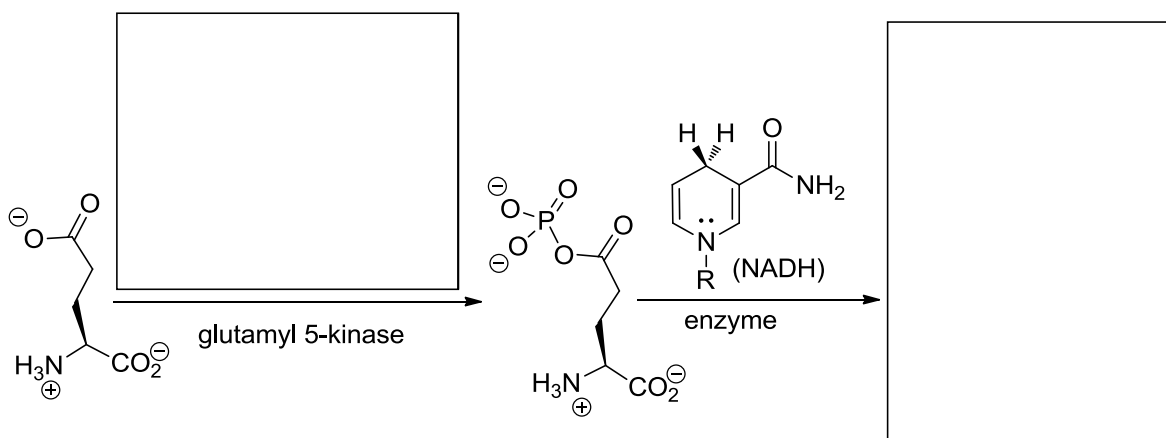
a)



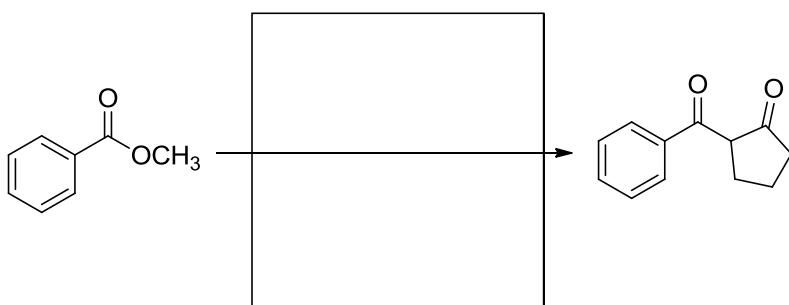
b)



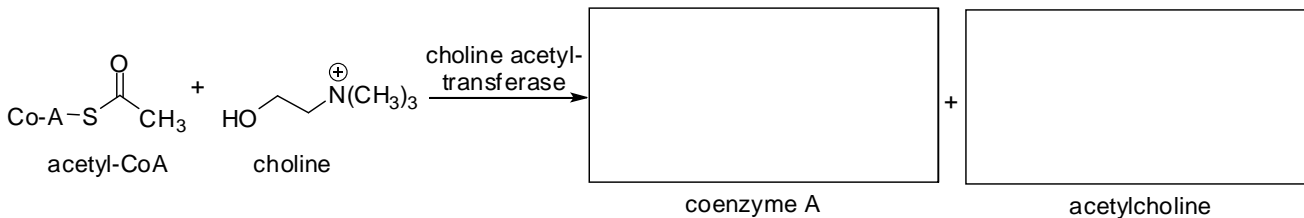
c)



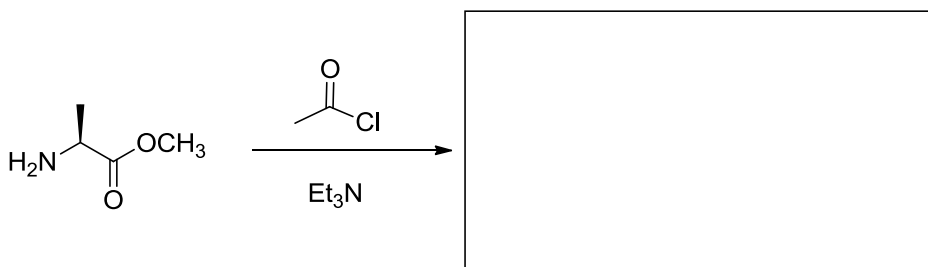
d)



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.

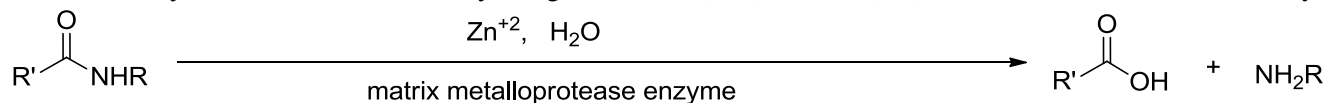


b)

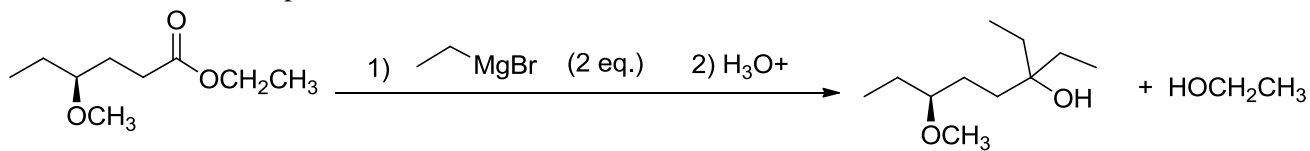


3. *Mechanism questions.* (33 pts.)

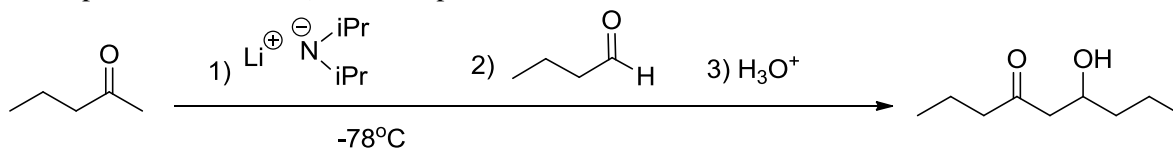
a) The matrix metalloproteases are an important class of enzymes which cancer cells use to cut through protein tissue and create space for more cancer growth. Matrix metalloproteases catalyze the following hydrolysis reaction (in a simplified format). Based on our related discussions in class and recitation, 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:-) conventions since this is an enzyme.



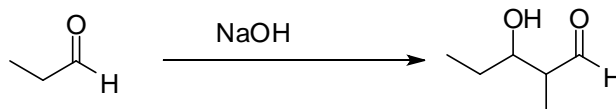
b) In addition to showing the mechanism, identify the nucleophile (Nu) and electrophile (E⁺) in the first step, and identify the type of reaction occurring (e.g. S_N2, electrophilic aromatic substitution, acid-base reaction, nucleophilic addition, etc.) for all steps.



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_N2, electrophilic aromatic substitution, acid-base reaction, nucleophilic addition, etc.) for all steps.



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

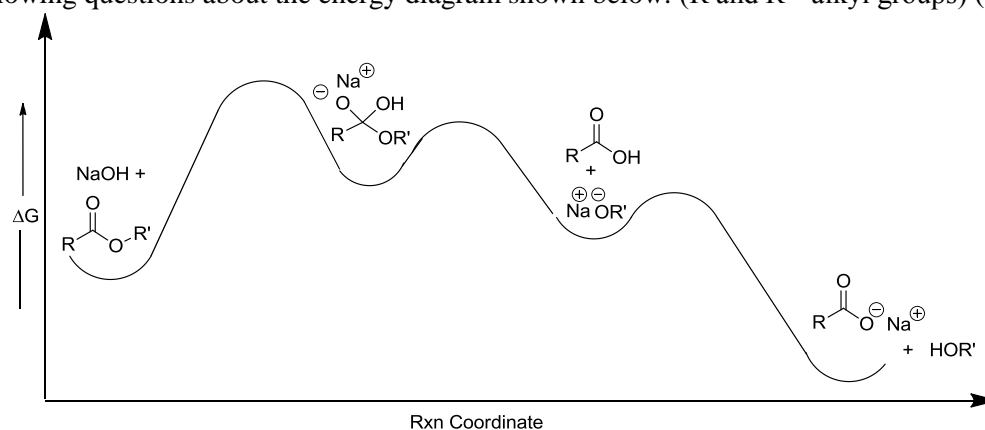


a) Draw the acid-base equilibrium that is the first step of the aldol addition shown above. You do NOT need to draw curved electron flow arrows. You should draw the most stable resonance form of all structures.

- 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.
- c) Based on your pK_a assignments, what will be the K_{eq} and the approximate ratio of [aldehyde]:[conjugate base].
- d) Show the next step of the aldol addition after the acid-base equilibrium.

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)?

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.
- b) Place a RDS at the point along the energy path of the reaction that is the 'rate determining step'.
- c) How many steps are in this reaction?
- d) Which statement best explains why the strong base RO⁻ can act as a leaving group?
- Since the reaction is run in HO⁻ (hydroxide) there is no problem with RO⁻, a weaker base, leaving in the reaction.
 - The step involved is exothermic and, according to Hammond's postulate, this means there will be little formation of RO⁻ at the transition state.
 - 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.

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.

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.