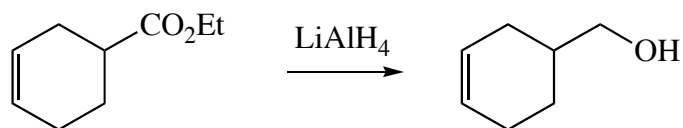
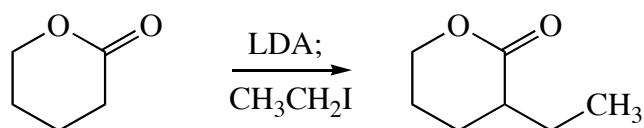


1. (5 pts. each, 30 pts. total.) Draw the *major* product of each of the following reactions, including the stereochemistry, if appropriate. **Assume aqueous workup in each case, so your product should be neutral and should not contain any metals. Do not draw mechanisms!**

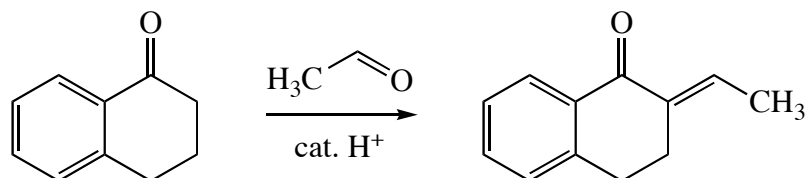
(a)



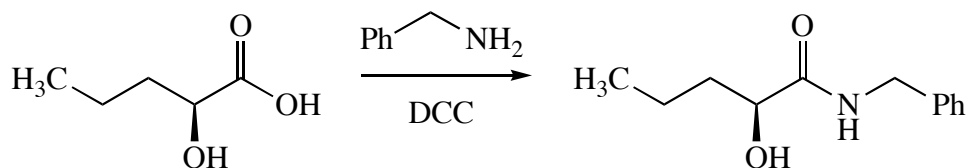
(b)



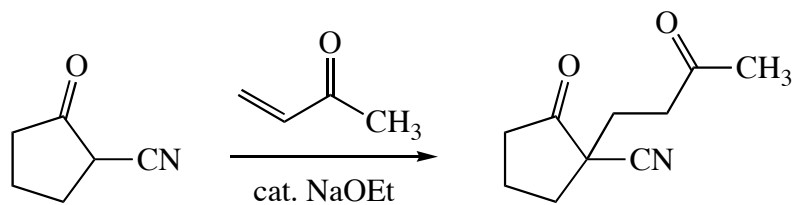
(c)



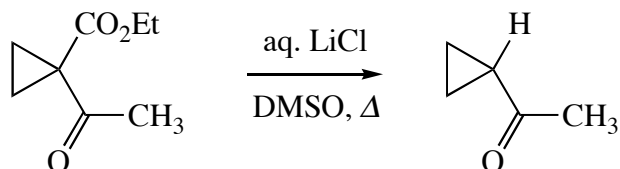
(d)



(e)

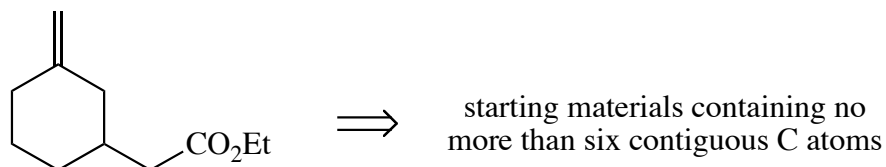


(f)

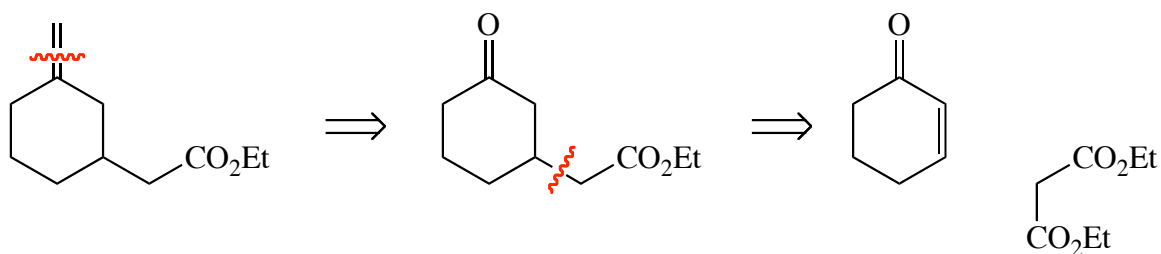


2. (15 pts. each, 30 pts. total) Design syntheses of each product from the given starting materials. Show all reagents you will need for each step. **Do not draw mechanisms!** You are strongly advised to do a retrosynthetic analysis first.

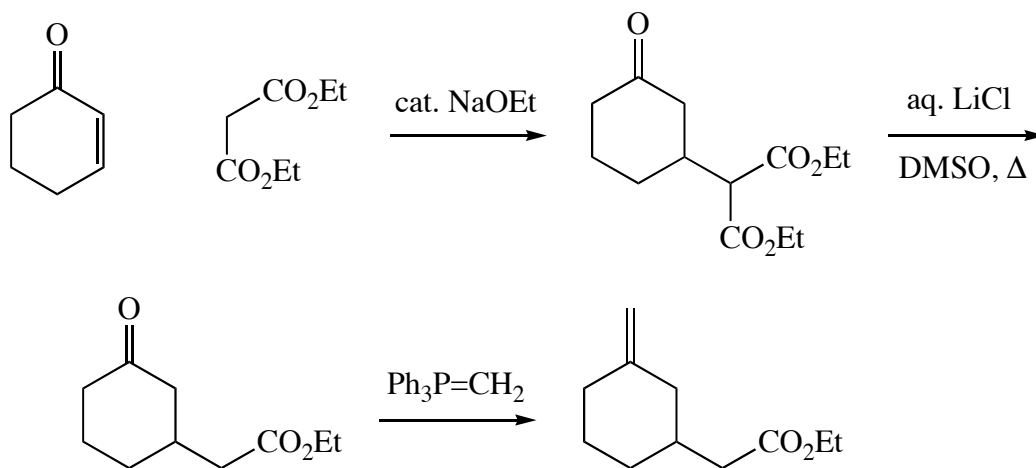
(a)



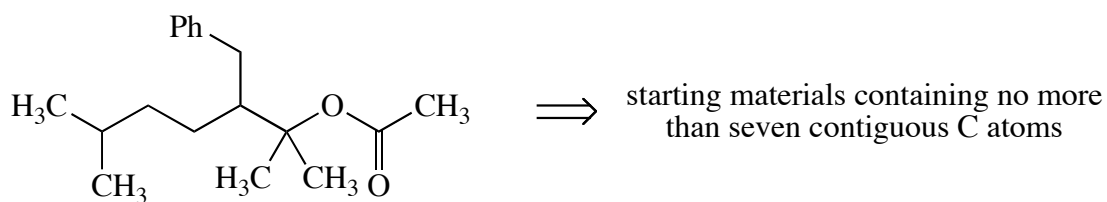
Retrosynthesis:



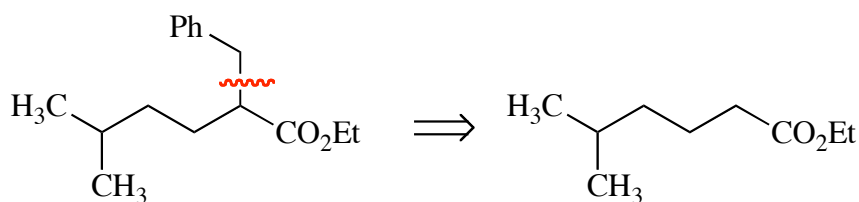
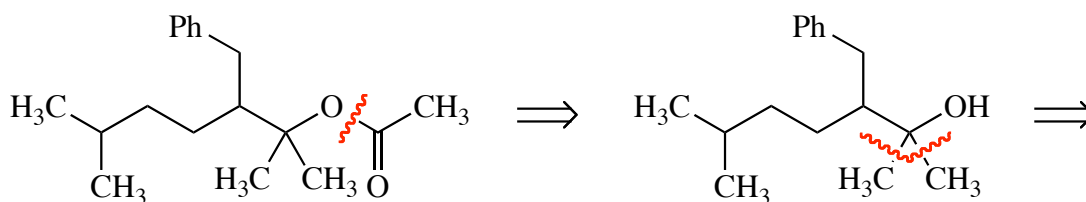
Forward synthesis:



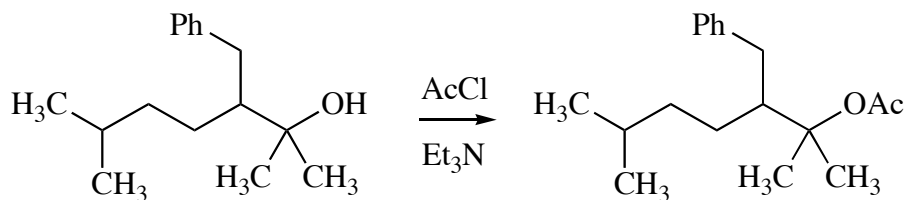
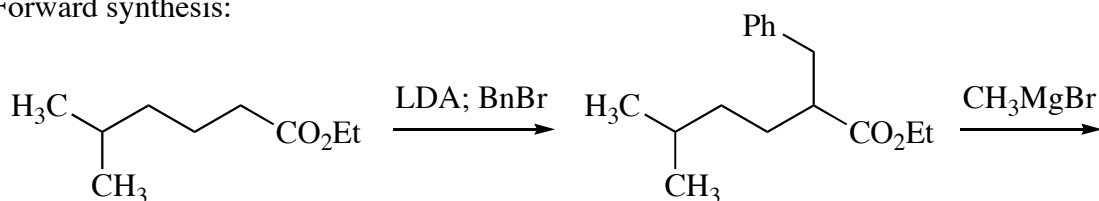
(b)



Retrosynthesis:

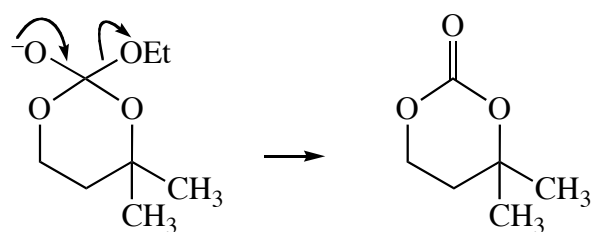
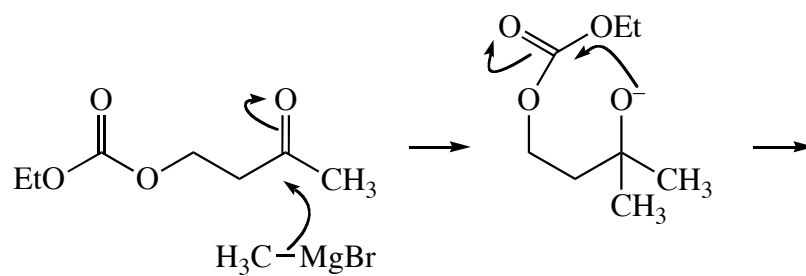
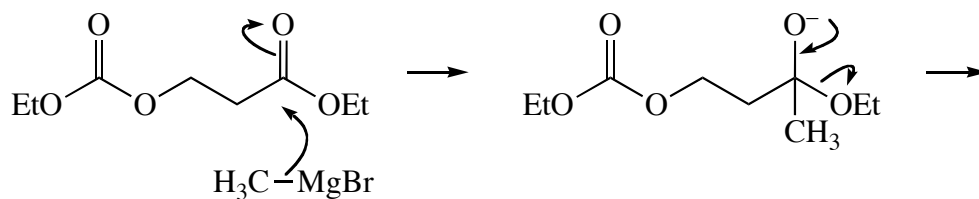
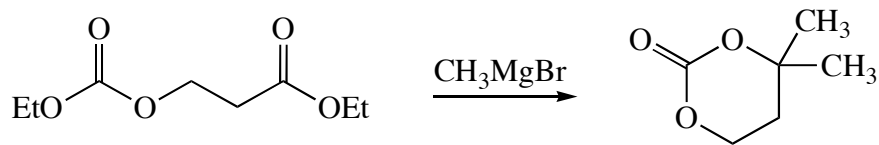


Forward synthesis:

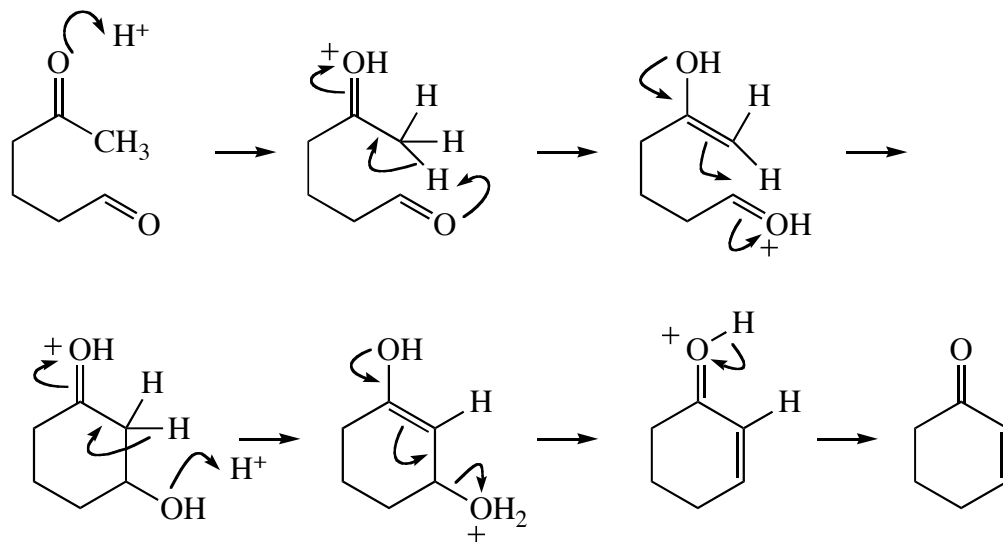
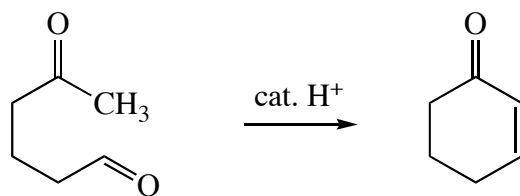


3. (15 pts. each, 30 pts. total) Draw reasonable mechanisms for each of the following reactions.

(a)



(b)

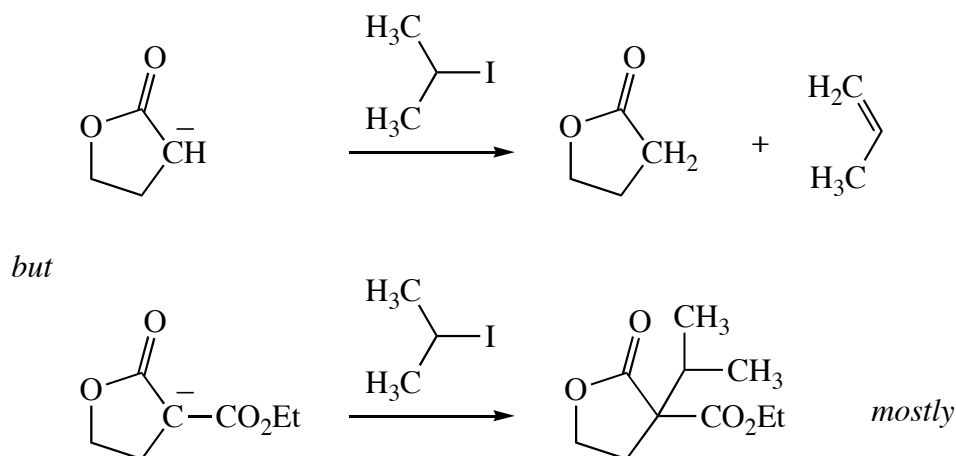


4. (5 pts. each, 30 pts. total.) Answer each of the following questions in one or two coherent, grammatically correct English sentences. Drawings to illustrate your point are encouraged.

(a) Why are higher-energy carbonyl compounds (such as acyl chlorides) *more acidic* at the α -carbon atom than lower-energy carbonyl compounds (such as esters)?

When a carbonyl compound converts to an enol, the stabilization (or destabilization) of the $\overset{\pm}{\text{C}}-\bar{\text{O}}$ resonance form is lost, so the conversion to an enol for lower-energy carbonyls is more unfavorable than that for higher-energy carbonyls.

(b) Explain the difference in the courses of the two reactions below.

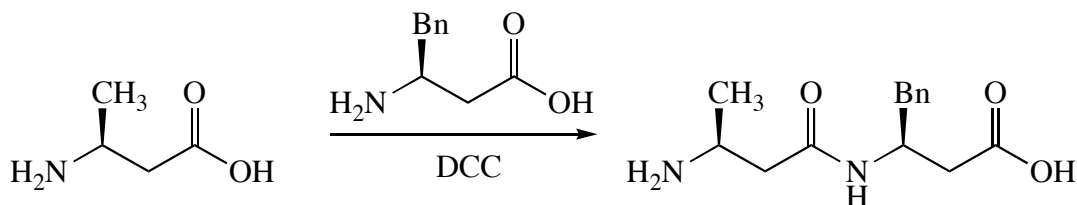


Enolates are good nucleophiles and good bases, so their reaction with 2° alkyl halides can proceed via substitution or elimination. Adding an electron-withdrawing group like CO_2Et to the enolate reduces its nucleophilicity and its basicity, but its basicity is reduced more, so a greater proportion of substitution occurs.

(c) Primary amines (RNH_2) react rapidly with esters at room temperature to make amides, but they do not react rapidly with carboxylic acids at room temperature to make amides, even though carboxylic acids and esters have the same energy.

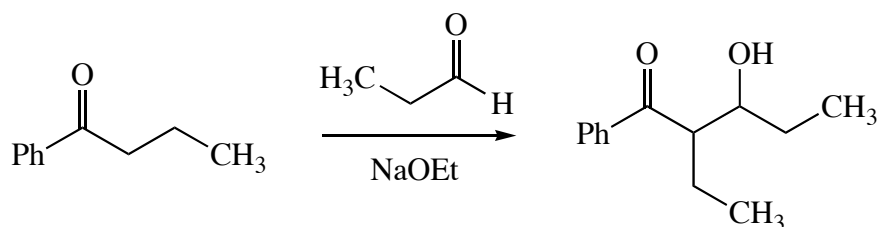
Amines are bases, so they simply deprotonate carboxylic acids to give carboxylates, which are fairly inert.

(d) The following reaction does not proceed as shown. Why not, and what can be done to make it proceed as shown?



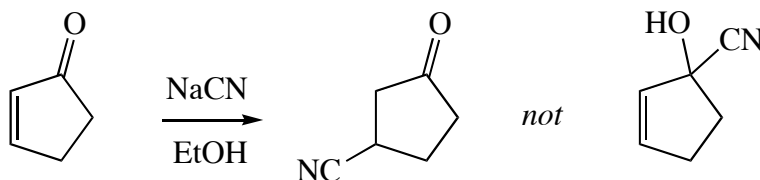
Either NH_2 can condense with either CO_2H , and the product can react with more starting material. The solution is to protect the NH_2 group on one starting material and the CO_2H group on the other, and then, after the reaction, deprotect both groups.

(e) The following reaction does not cleanly give the product shown. Why not, and what can be done to make it do so?



The aldehyde can react with itself, the ketone can react with itself (not as likely), and the aldol product is likely to undergo dehydration to give the α,β -unsaturated carbonyl compound under these weakly basic conditions. The solution is to use LDA to deprotonate the ketone, then add the aldehyde.

(f) Explain why the product isolated from the following reaction is the β -cyano ketone, not the α -cyano alcohol (cyanohydrin).



The reaction of ^-CN at the carbonyl C is faster, but it is reversible, and the reaction at the β -carbon is thermodynamically preferred, so the reaction funnels over to the β -cyano ketone.