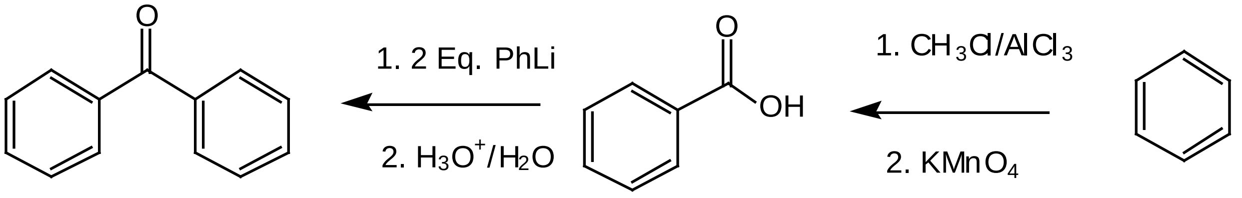
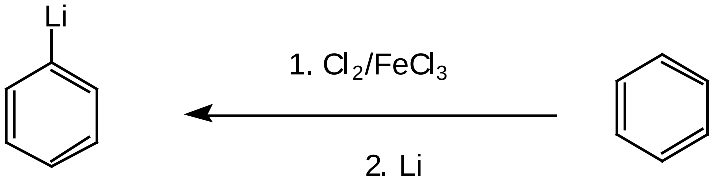
Answers to HT2, Chemistry 302-302A - 2004

1. There are many ways to do these problems - here is just one. For all three parts we can use diphenyl ketone (benzophenone) so let's make that first:

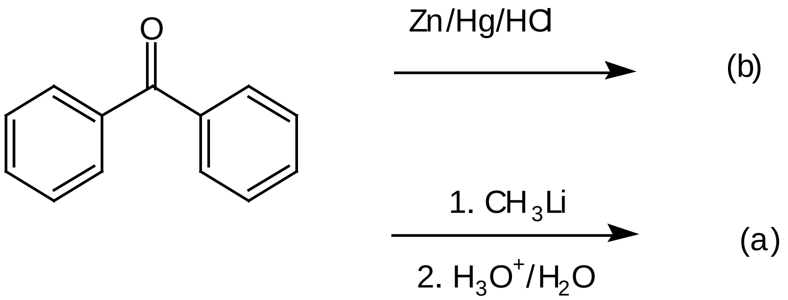


Phenyllithium and methyl chloride also have to be made:



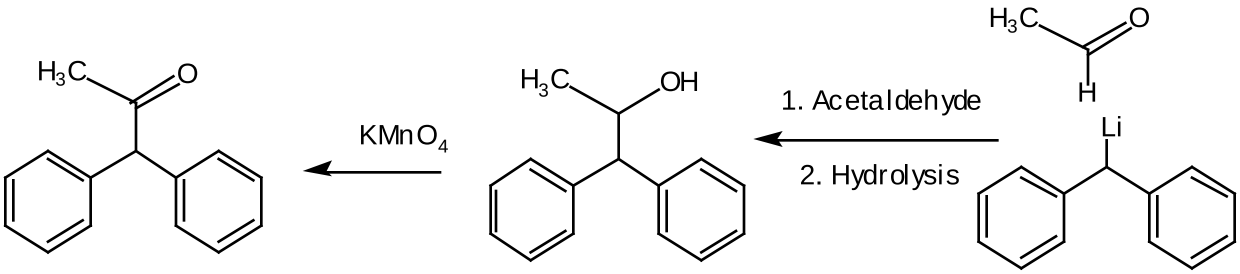
$CH_3Cl \xleftarrow{SOCl_2} CH_3OH$

Benzophenone can be used to make parts (a) and (b):

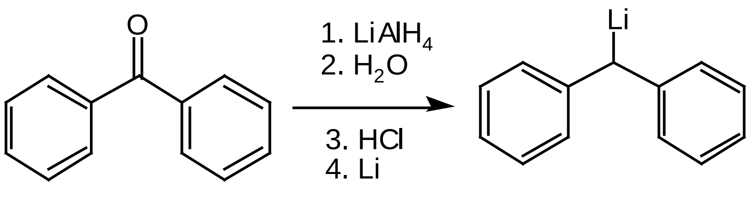


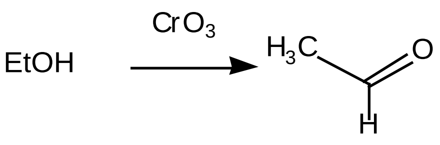
$CH_3Cl \xrightarrow{Li} CH_3Li$

Do part (c) through the usual deconstruction process:

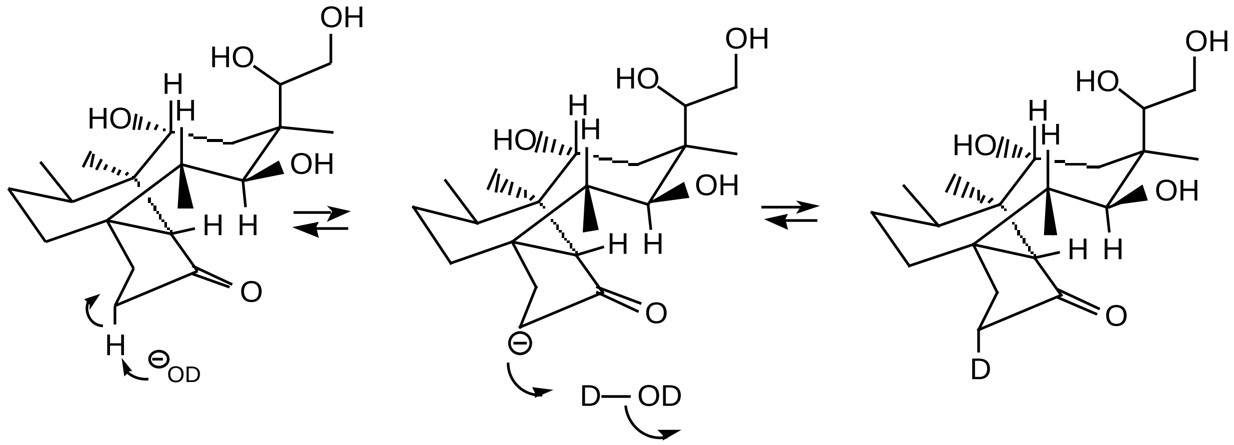


The necessary pieces come easily:

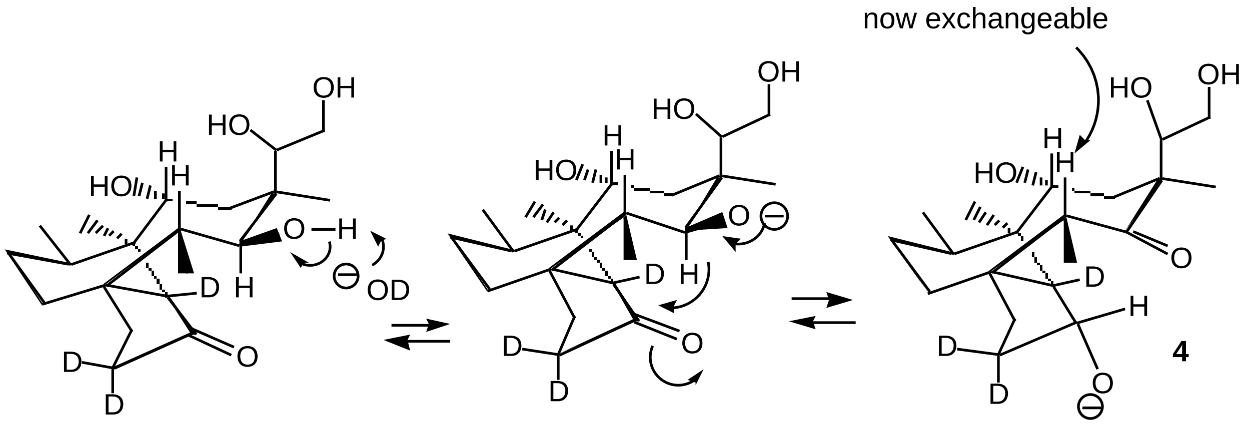




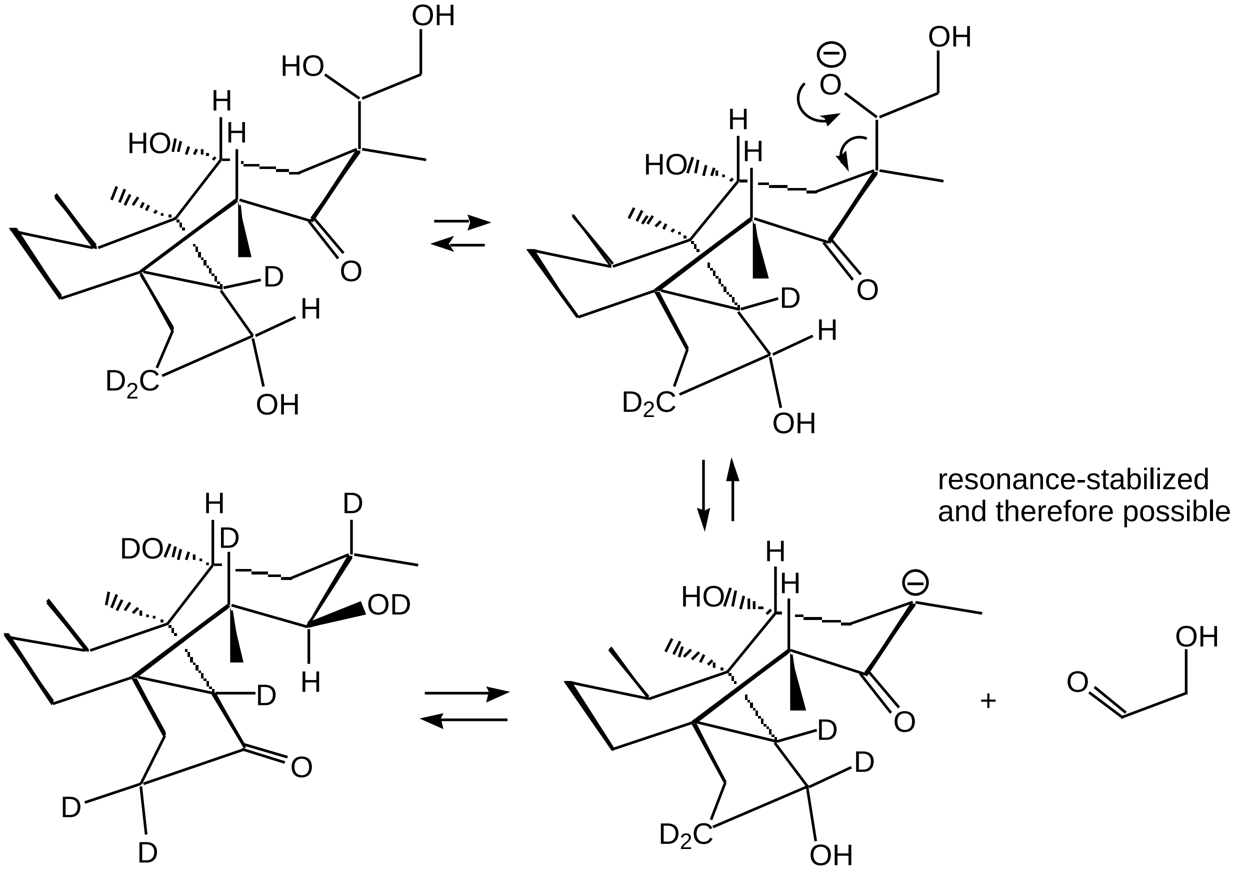
3. The three hydrogens a to the carbonyl group exchange in normal, base-catalyzed fashion (only one shown). Similarly, formation of the alkoxides and “protonation” by D_2O exchanges the OH groups.



That leaves the mysterious exchanges in the “upper” ring and the loss of the glycol. The critical step is hydride transfer from the upper ring to the carbonyl group in the lower ring. This produces **4**, and the “upper ring” a C-H bond can now exchange.



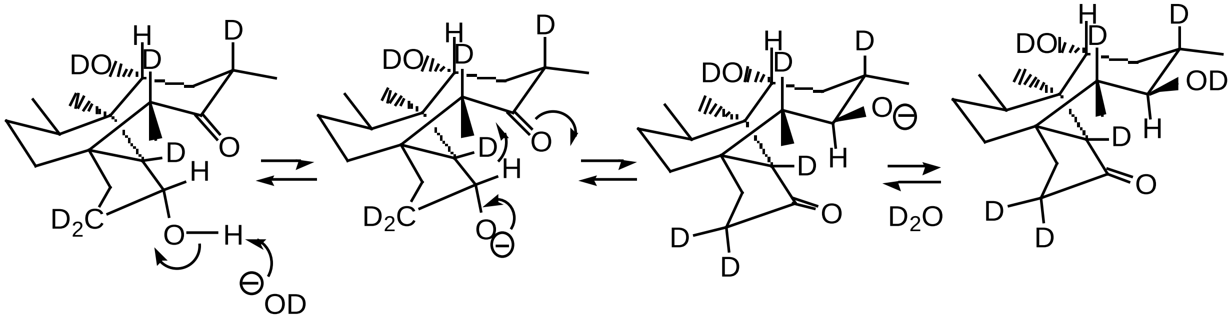
This also provides a means to lose the glycol:



resonance-stabilized
and therefore possible

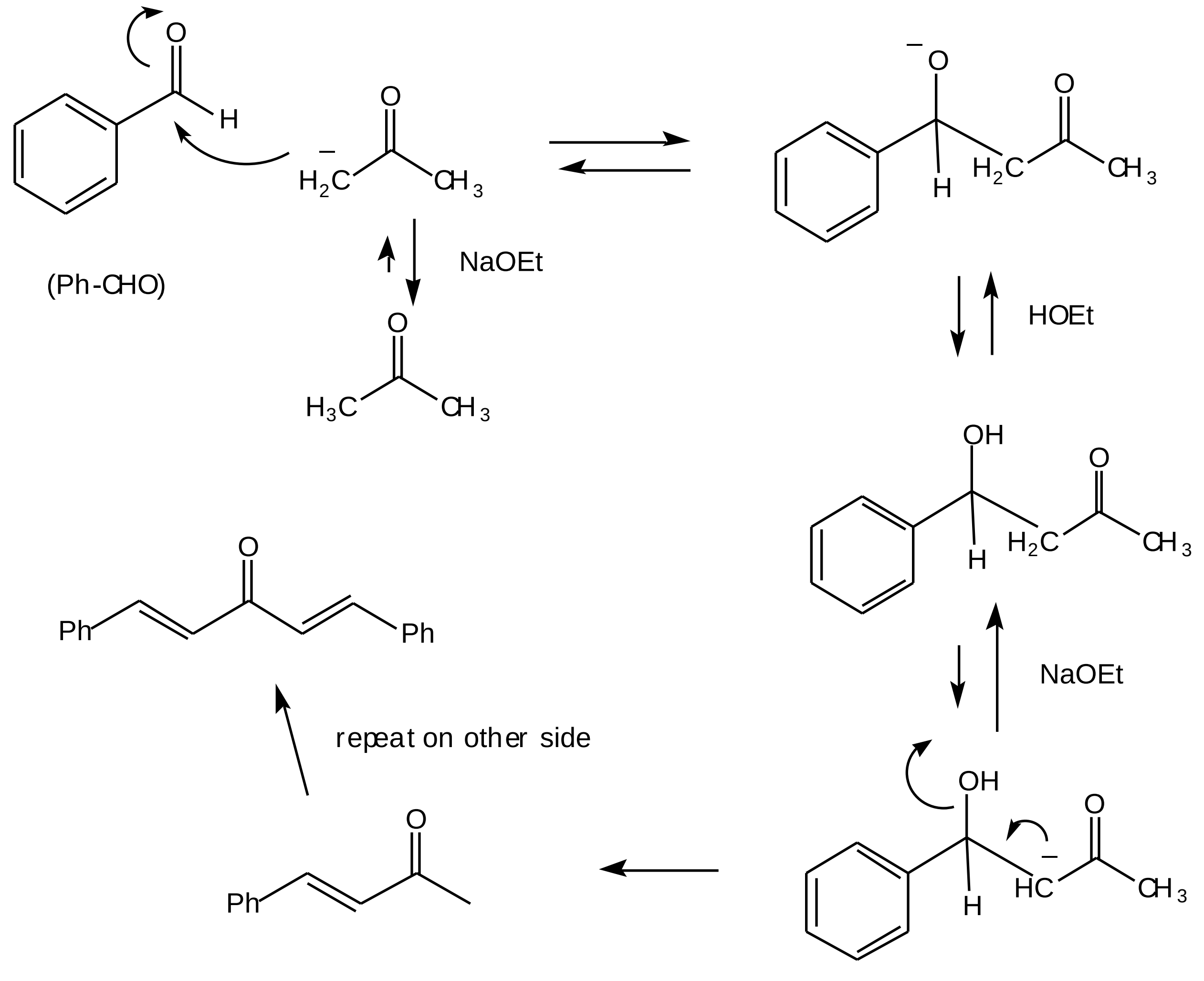
(after various exchanges)

A reverse hydride shift regenerates the ketone in the “lower” ring.

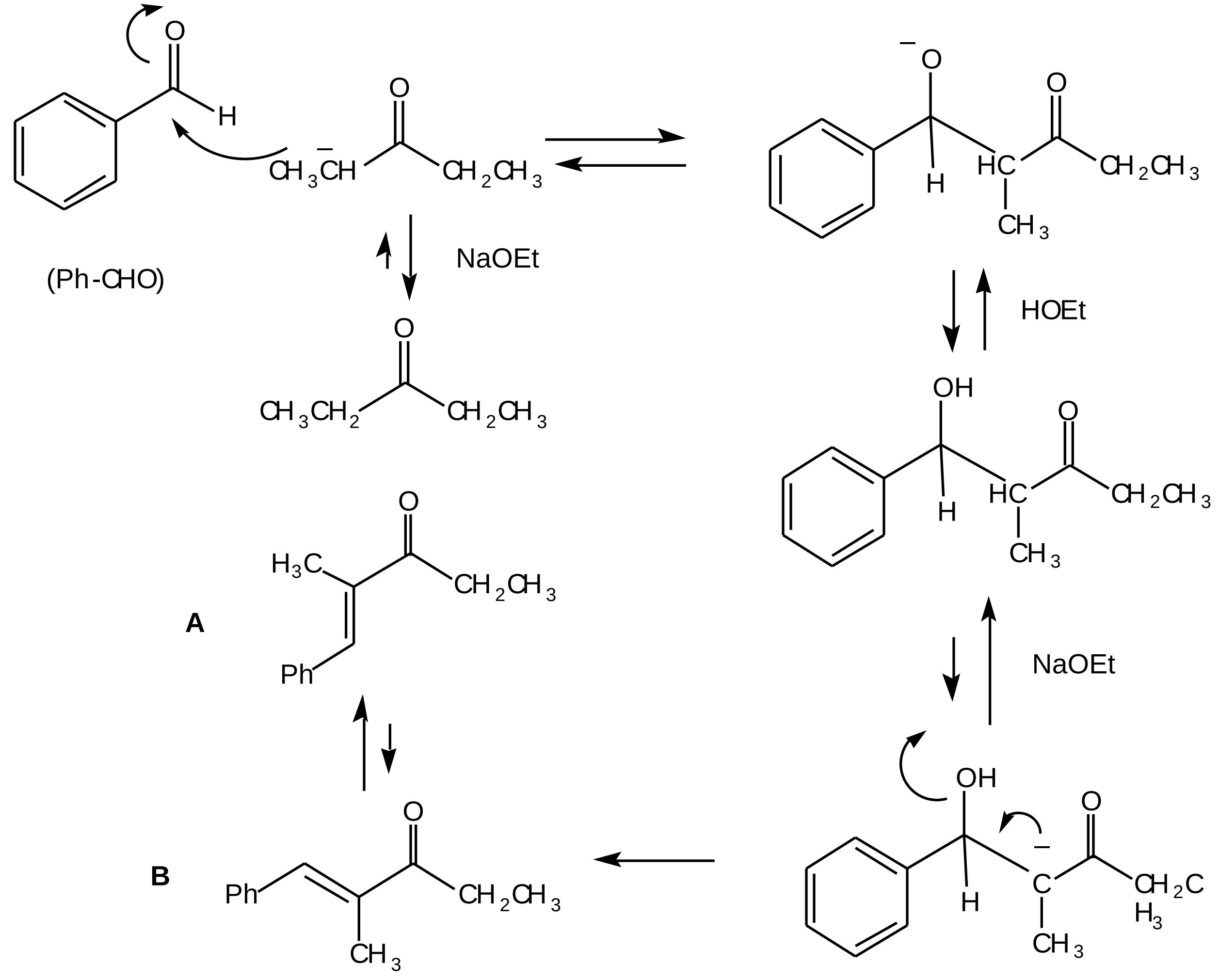


2(a).

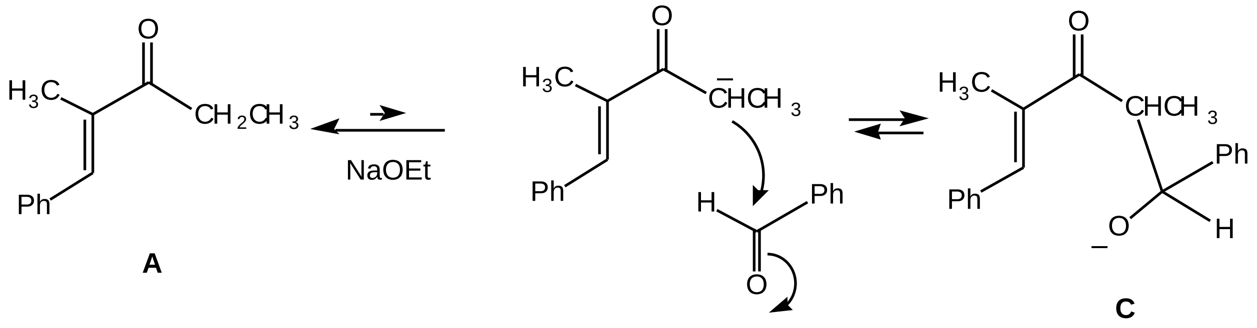
Analysis: We need two benzaldehydes and one acetone. There is only one kind of α hydrogen, so we need only consider the acetone enolate in base. Condensation is followed by dehydration. “All α,β-unsaturated ketones come from aldol condensations.”



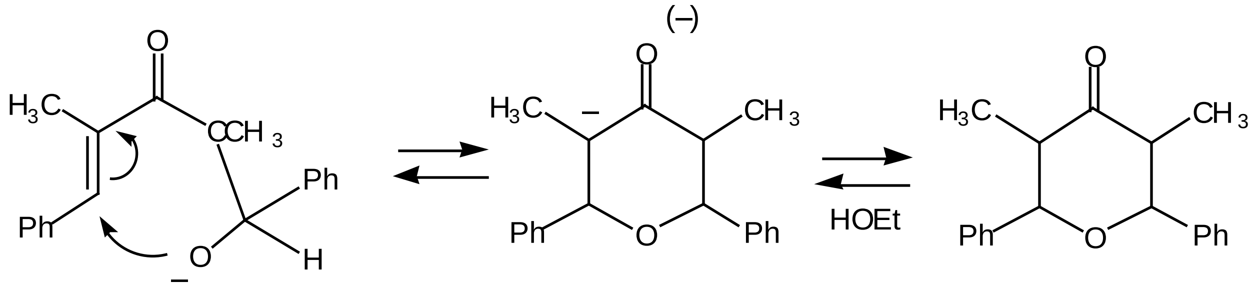
(b) Clearly something else has happened. The reaction starts just as in part (a):



Note that in contrast to the molecule in part (a), compound **A** will be relatively favored over **B** here because in **A** the “new” methyl group is far away from the ethyl group. Now start the second condensation:

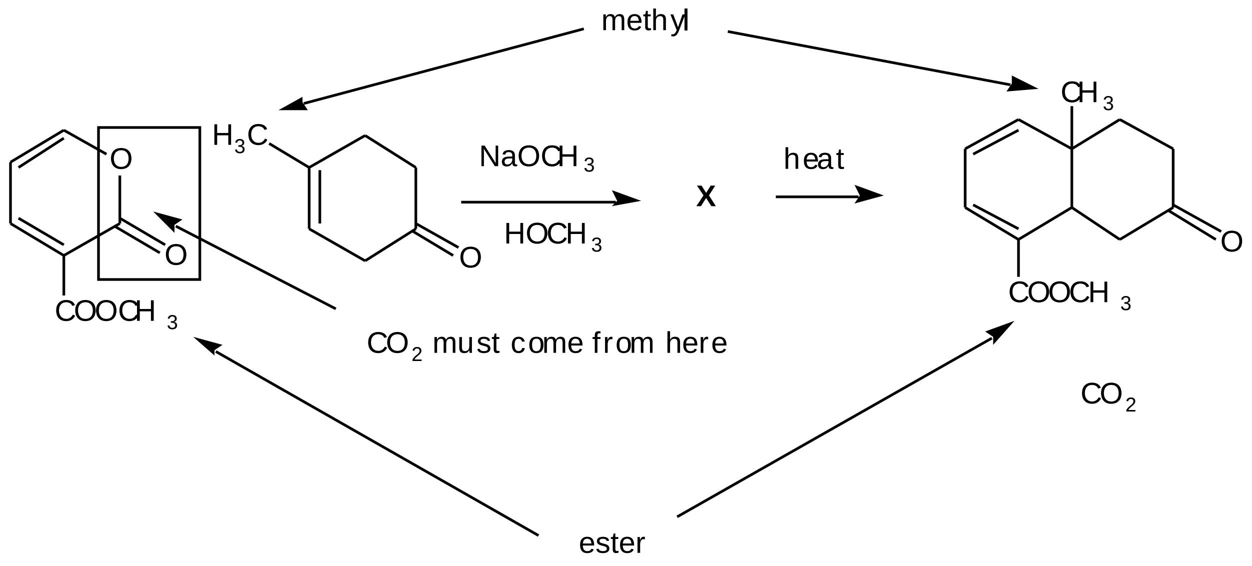


Notice that in **C** we are all set to close the new ring in a Michael reaction, and finish up part (b).

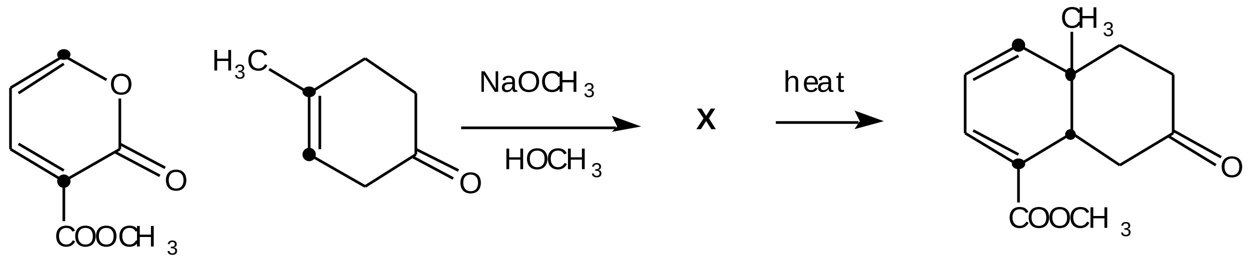


(c). We pretty much answered this part in the comments above. When diethyl ketone is used, there is a steric interaction that favors intermediate **A**, which is set up for the Michael. When that interaction is absent, as with acetone, an extended form such as **B** is favored and this form cannot do the Michael.

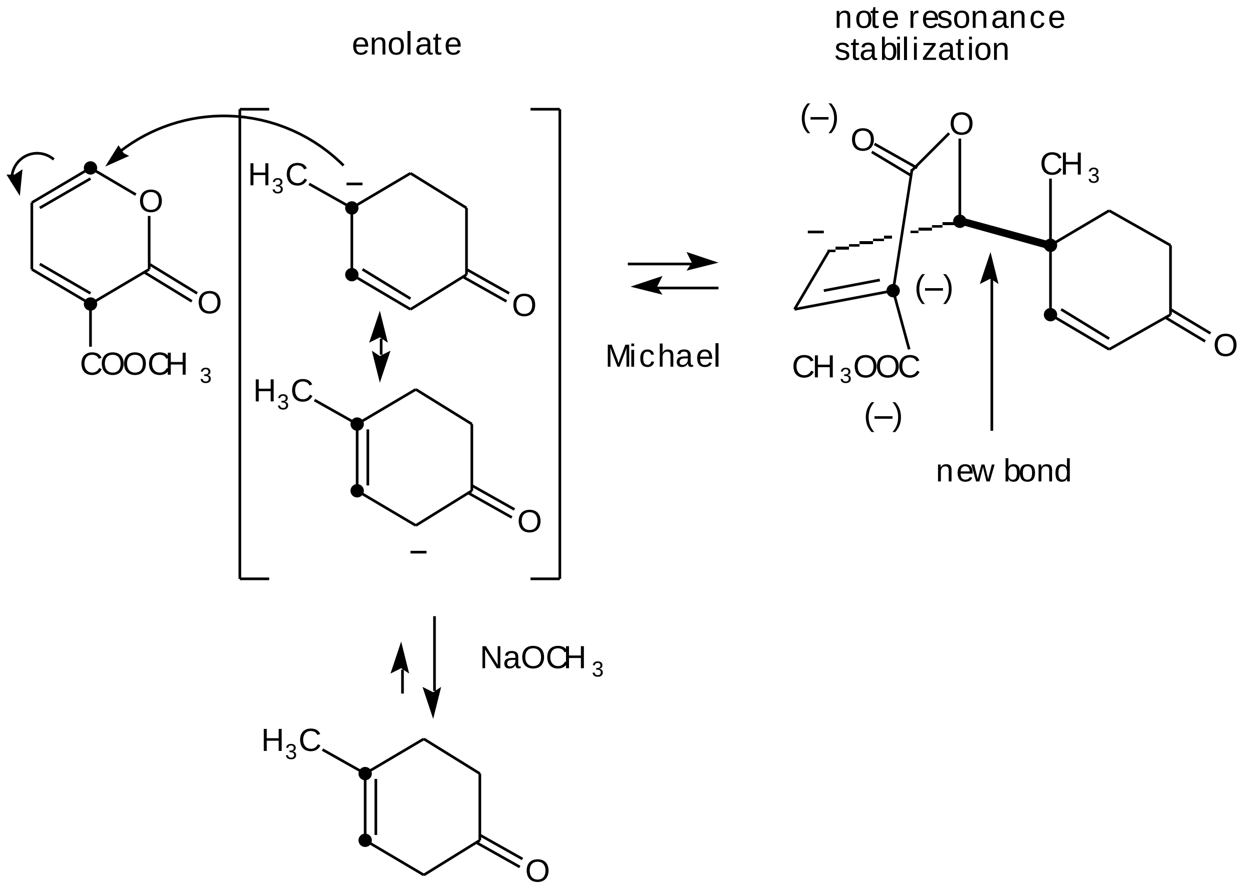
4. It must be clear where the CO_2 comes from, and the ester and methyl group provide nice markers for what winds up where. In turn that information allows you to see where the new bonds must be formed.



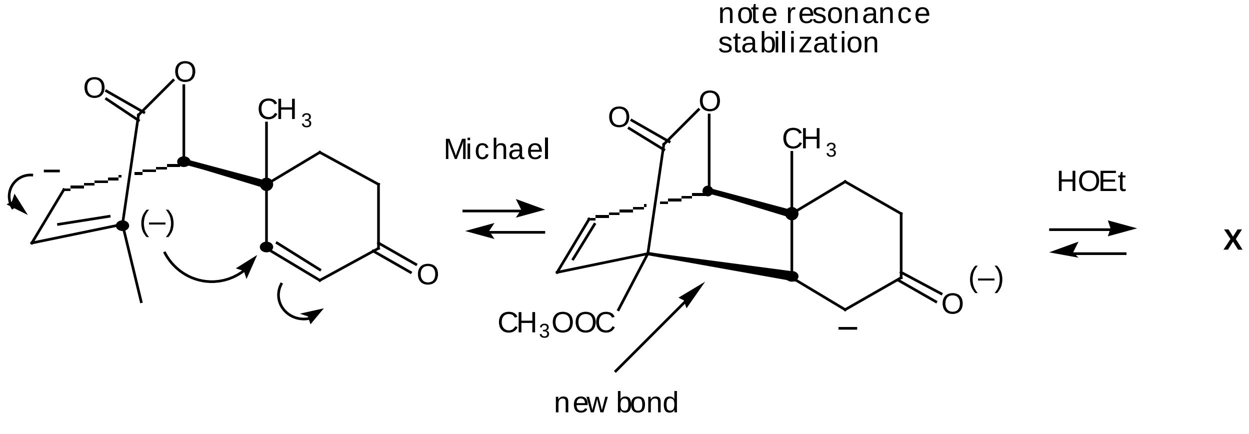
So the new bonds must form at the dots.



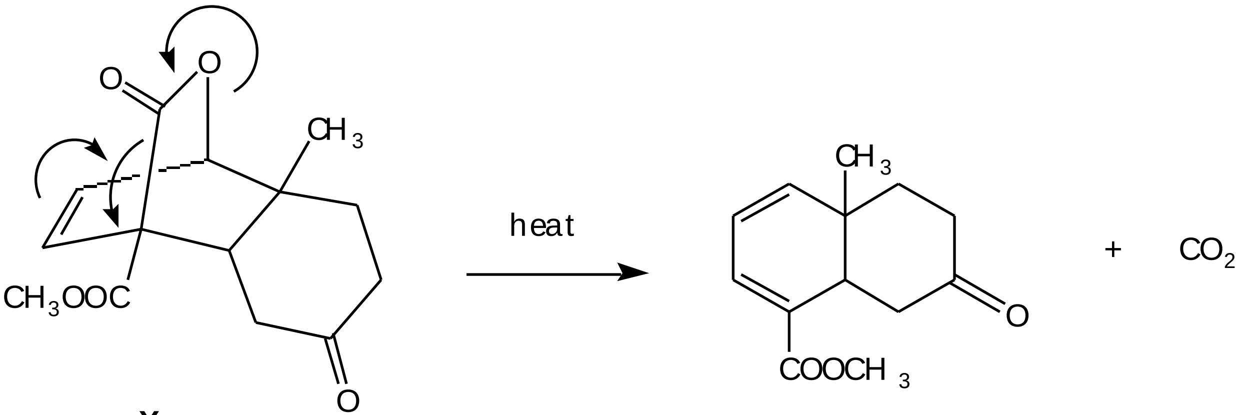
Let’s start by making the enolate that puts negative charge at one of the dotted positions, and do the Michael reaction:



Now we are all set to connect the next two dots and make **X** through another Michael reaction.



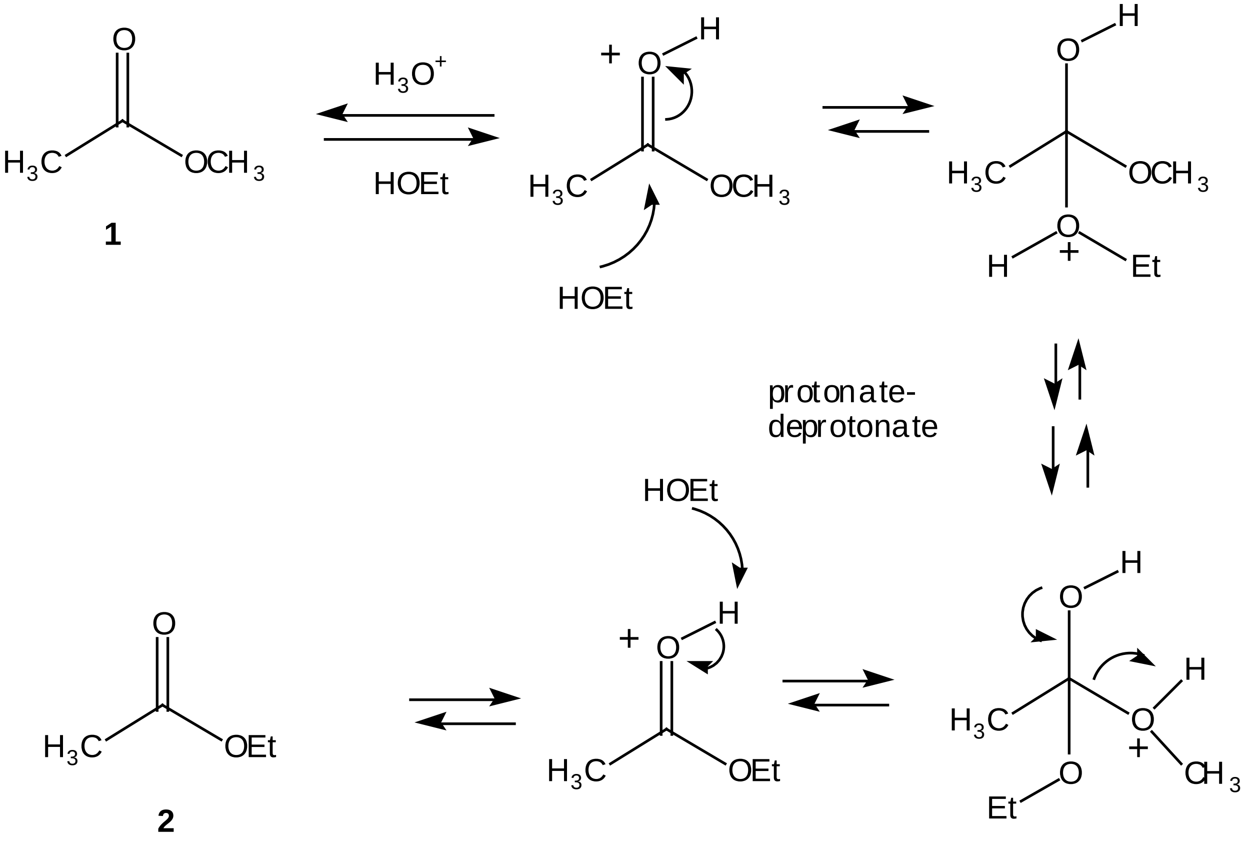
Loss of CO_2 (a sort of reverse Diels-Alder) finishes it off:



X

5.

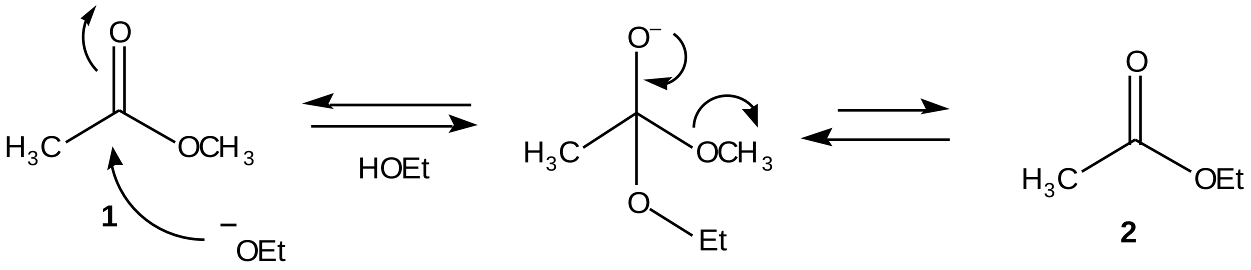
a, in acid:



1

2

In base:



(b,c) Acid works, base fails because the fastest possible reaction is deprotonation of the acid to give the carboxylate anion, which is the product of the reaction.