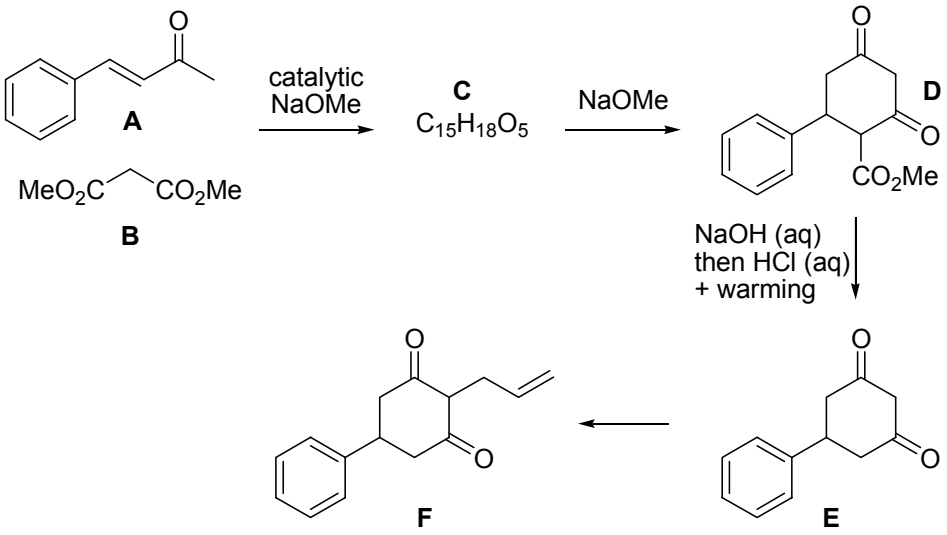
Bifunctional Chemistry, Semester 2, 2006 (06522)

1. Consider the following reaction scheme and answer **all** of the following parts.



(a) Draw an enol tautomer for both **A** and **E** and state why the most stable enol form of **E** is more stable than that of a simple ketone.

(*3 marks*)

(b) The ^{1}H-NMR spectrum of **E** in $CDCl_3$ changes when treated with a few drops of D_2O. What happens and why?

(*2 marks*)

(c) Give the mechanism of the reaction of **B** with NaOMe to form an enolate.

(*2 marks*)

(d) Compound **A** can be prepared from acetone and benzaldehyde using an aldol reaction. Give the mechanism of this reaction and state what by-product might be formed if a slight excess of aldehyde is employed.

(*5 marks*)

(e) Using a mechanism explain why in the reaction between **A** and **B** a catalytic amount of NaOMe can be employed in making **C**. State clearly the structure of **C** in your answer.

(*5 marks*)

(f) What by-product is formed in the conversion of **D** into **E**? Give the intermediates formed in this reaction.

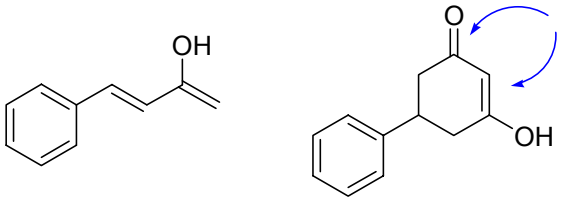
(*3 marks*)

(g) State the reagents needed to convert **E** into **F** and show a mechanism for this conversion.

(*5 marks*)

Bifunctional Chemistry, Semester 2, 2006 (06522)
MODEL ANSWER

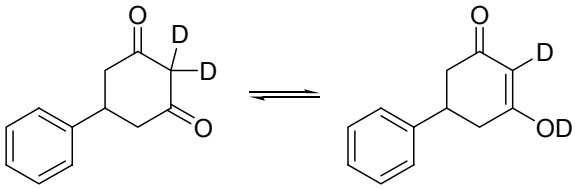
1(a)



conjugation makes enol more stable

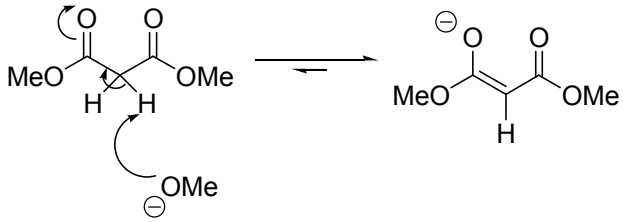
(but no intramolecular H-bonding possible in this cyclic example)

1(b)

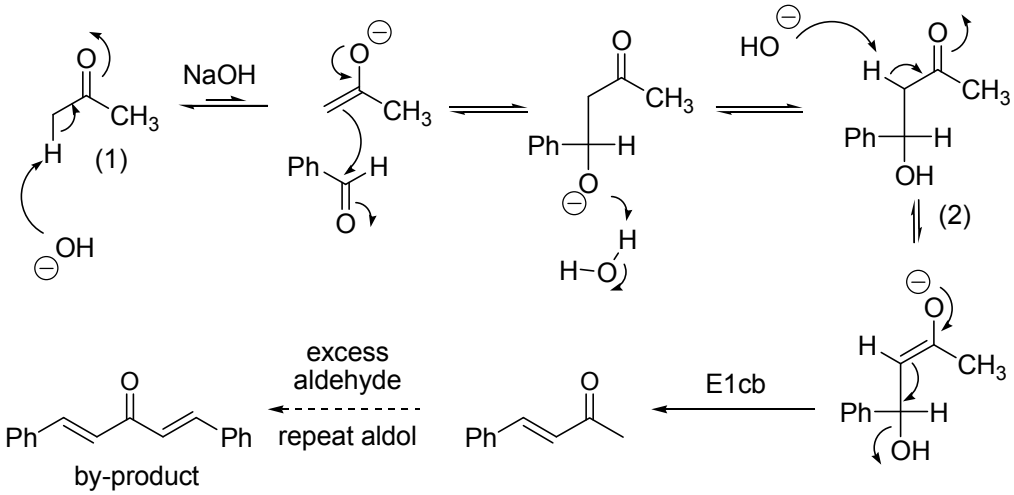


During enolisation the acidic OH and CH will be exchanged with D (from the D_2O). The NMR will be simplified and the CH/CH_2 and OH signals will eventually disappear.

1(c)



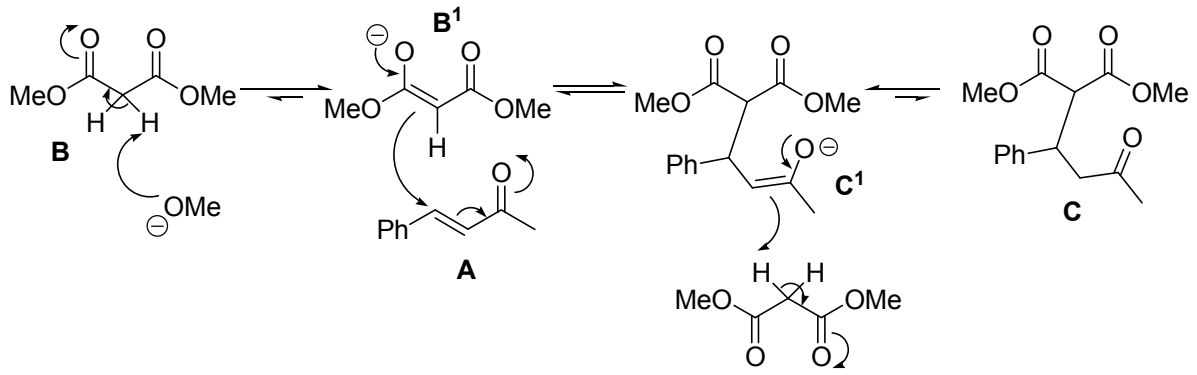
1(d)



(1) Only acetone has acidic α-hydrogens, but benzaldehyde is a more reactive electrophile so a crossed condensation takes place.

(2) E2 elimination is slower (-OH is a poor leaving group) than enolate formation (α-deprotonation) so E1cb elimination takes place. Loss of water is essentially irreversible.

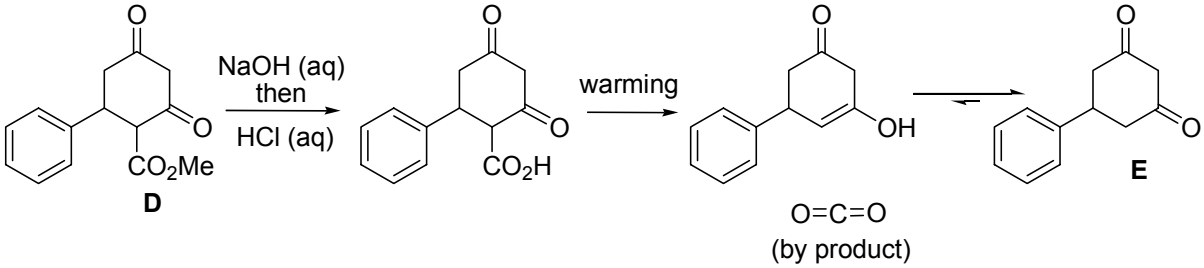
1(e)



Methoxide deprotonates the malonate **B** (MeOH pKa ~16; dimethyl malonate pKa ~12) producing the enolate $\mathbf{B^1}$ which then undergoes conjugate addition to the α,β-unsaturated ketone **A** producing enolate $\mathbf{C^1}$. This keto enolate, $\mathbf{C^1}$, is much more basic than methoxide and so can easily deprotonate **B** and thus perpetuate the cycle.

N.B. $\mathbf{C^1}$ may also deprotonate the solvent, which of course is present in higher concentration than **B**. E.g. if the reaction is performed in methanol, this would produce more methoxide. Also, you may have spotted that there is an acidic α-CH in the malonate portion of the product **C**. If deprotonated however this would make a much less reactive nuclophile due to steric hindrance. This enolate can then easily exchange with unsubsituted dimethyl malonate to keep the reaction going.

1(f)



1(g)