

I. β -dicarbonyl compounds

By virtue of their acidity, β -dicarbonyl compounds are useful for alkylation reactions.

A. The Malonic Ester synthesis

The malonic ester synthesis is a classical procedure for ester enolate alkylation prior to the advent of LDA. Malonate ester alkylation is followed by hydrolysis to the diacid and subsequent decarboxylation (loss of CO_2). Note that malonate ions can be alkylated in $\text{S}_{\text{N}}2$ fashion with alkyl halides or tosylates. In effect, the second ester group heightens the acidity of the alpha position so alkylation can take place with weaker bases such as hydroxide or alkoxides.

Note that multiple substitutions may be carried out by performing two sequential alkylations on the malonate ester:

Ring synthesis may also be accomplished using malonate ester alkylation of dibromides:

B. The acetoacetic ester synthesis

Analogous alkylation of β -keto esters, followed by hydrolysis and decarboxylation results in the formation of substituted ketones; dialkylation is also possible.

Show how you could prepare the following molecule using the above procedure:

II. α,β -unsaturated carbonyl compounds

α,β -Unsaturated carbonyl compounds possess electrophilic β -carbon atoms, as can be seen from their resonance structures:

The 1,4 addition of a stabilized enolate nucleophile is termed Michael addition. The enone electrophile is the **Michael acceptor**, and the enolate nucleophile is the Michael donor. See the following list of typical Michael donors and acceptors:

Hydrolysis and decarboxylation of the 1,4-addition product leads to a δ -keto acid or δ -diketone:

Note the following relationships:

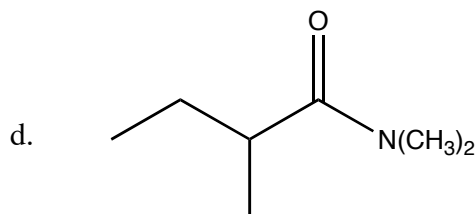
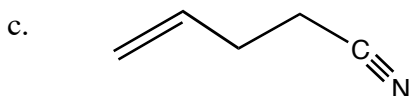
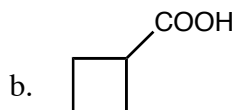
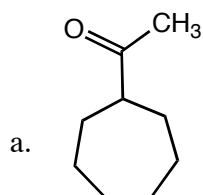
III. The Robinson Annulation

The Robinson annulation is simply a Michael addition followed by an intramolecular aldol condensation. This is an effective strategy for forming carbocyclic rings from ketones and enones :

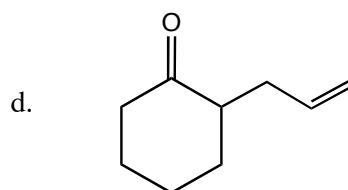
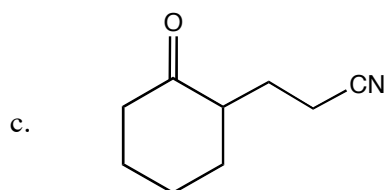
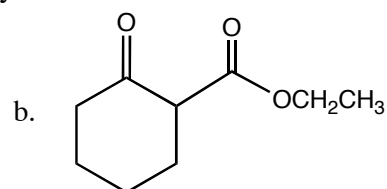
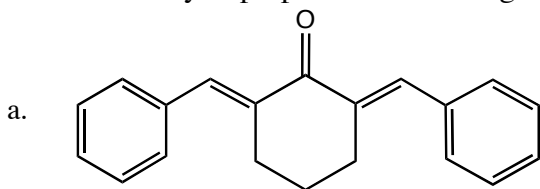
See the following representative examples:

Additional Problems for Practice:

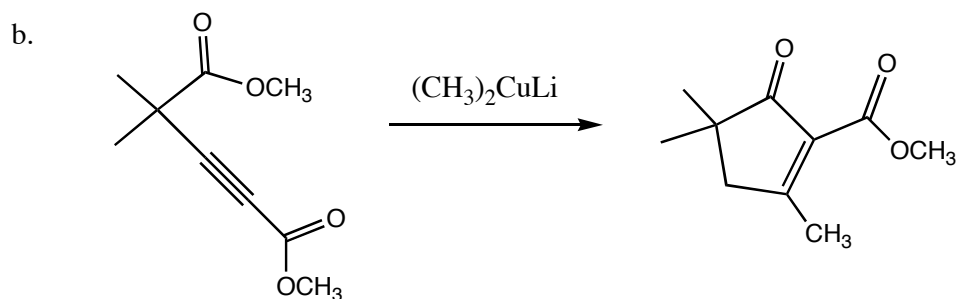
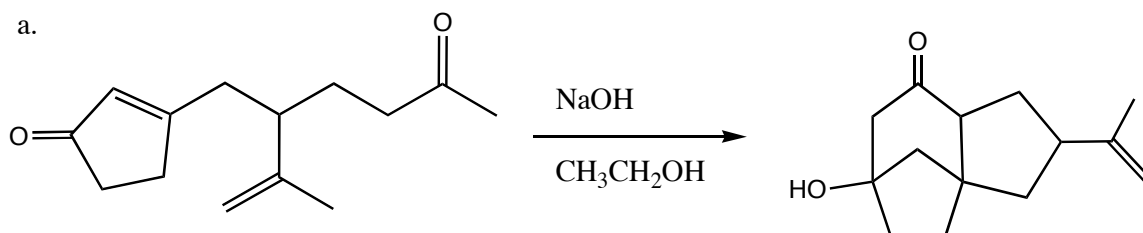
1. How would you prepare these compounds using either an acetoacetic ester synthesis or a malonic ester synthesis?



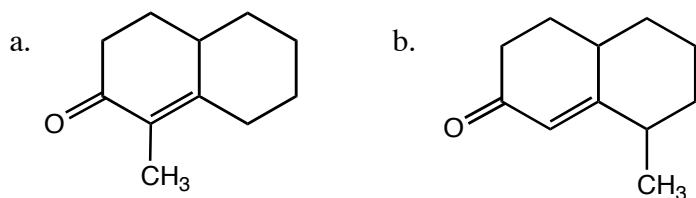
2. How would you prepare the following compounds from cyclohexanone?



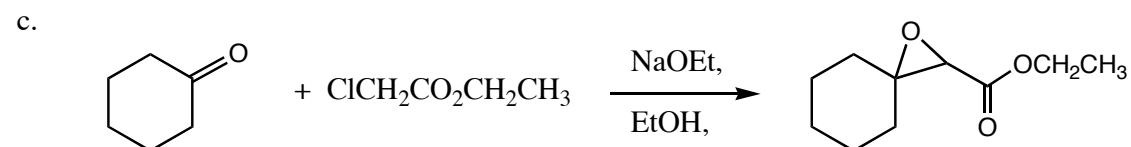
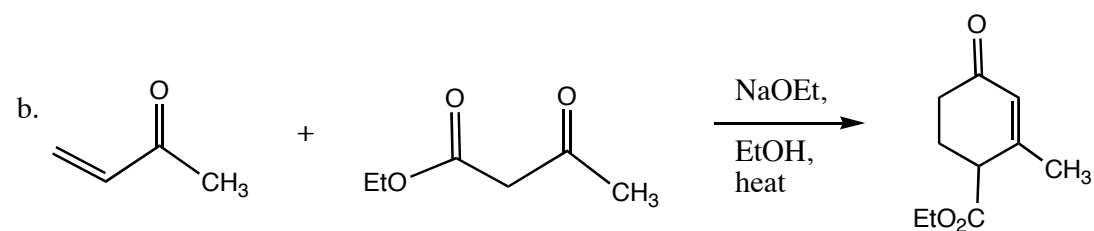
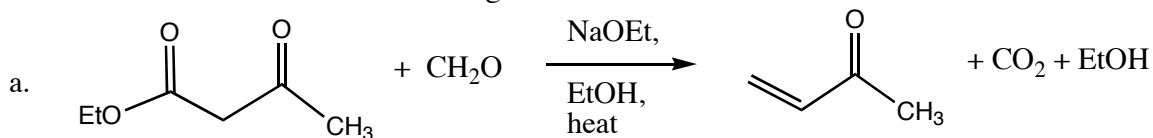
3. Propose a mechanism to account for the following reactions:



4. How could you prepare the following cyclohexenones by combining a Stork reaction with an intramolecular aldol condensation?



5. Show a mechanism for the following reactions:



6. Double Michael additions have been used to prepare spirocyclic compounds such as the one below. Show a mechanism for the formation of **B**.

