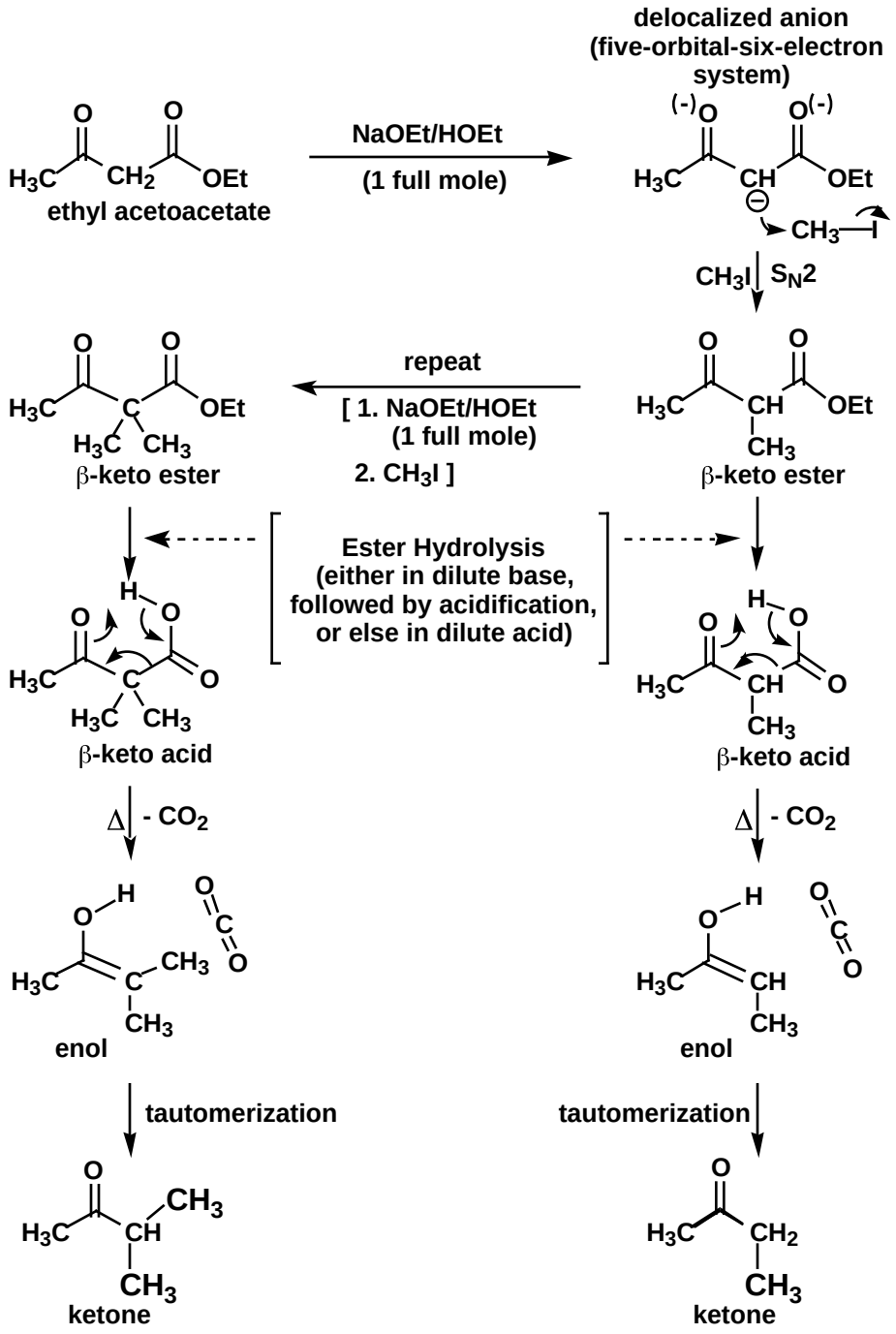
**Text Related to Segments 20.06 & 20.07 ©2002 Claude E. Wintner**

Because β-keto ester anions are so stable, they can be alkylated via $S_N2$ reactions, using simple alkylating agents:



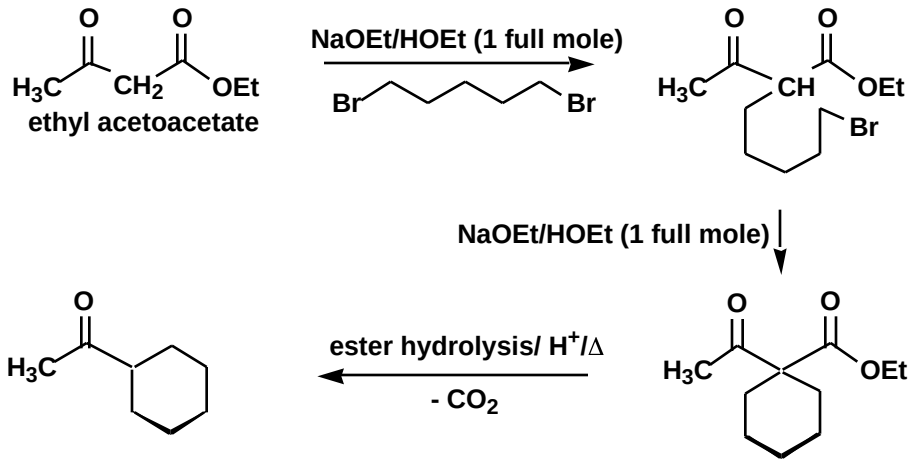

**alkylation of ethyl acetoacetate**

**hydrolysis of β-keto esters**

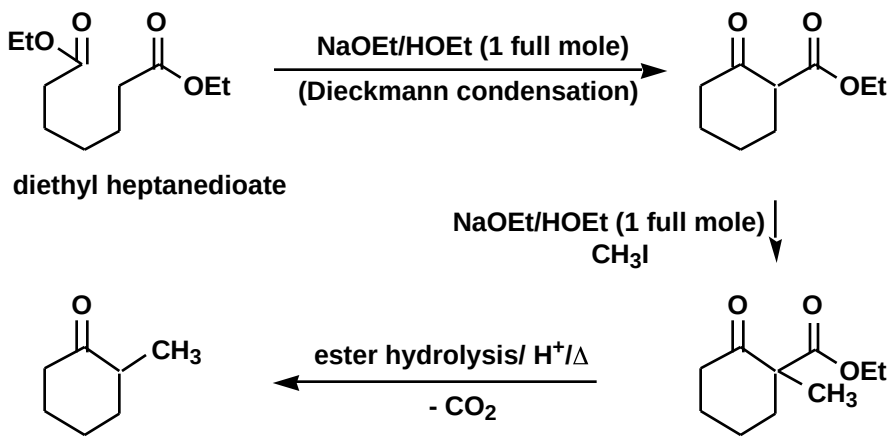
**thermal decarboxylation of β-keto acids to form ketones**

For example, as above, ethyl acetoacetate can be methylated or dimethylated readily. The great value of these alkylation reactions becomes apparent when they are coupled with another reaction sequence applicable to β-keto esters: hydrolysis in dilute base (saponification) to the corresponding β-keto acid anions, followed in turn by acidification and then thermal decomposition of the resulting β-keto acids to ketones, with concomitant loss of carbon dioxide via the mechanism indicated in the figure. These steps also are illustrated in the figure above.

Alternatively, a molecule such as 1,5-dibromopentane can be employed in the alkylation sequence, leading in two steps to ring formation. Again, after hydrolysis and decarboxylation, a ketone, now cyclic, is the result:

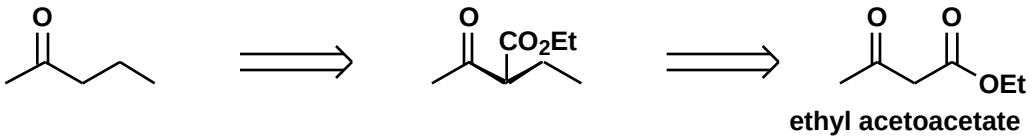



A cyclic β-keto ester such as 2-carboethoxy cyclohexanone can be alkylated as well, leading to yet another constitutional pattern:



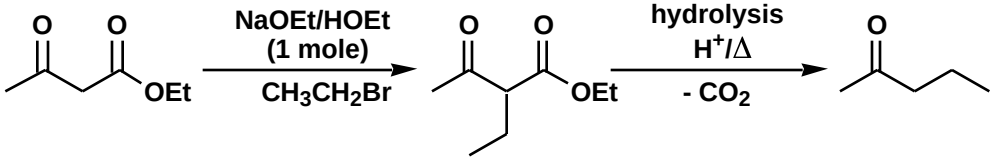

It is instructive to return here to the method of retrosynthetic analysis. By means of this technique, syntheses of 2-pentanone from ethyl acetoacetate, of acetyl cyclobutanone from the same starting material, or of 2-ethylcyclohexanone from 2-carboethoxy cyclohexanone all can be envisioned readily, once one has focused on the trick of imagining in retrospect the group (carboethoxy) that must have been lost as a result of the β-keto ester hydrolysis and decarboxylation steps:

retrosynthetic analysis:




ethyl acetoacetate

synthetic route:

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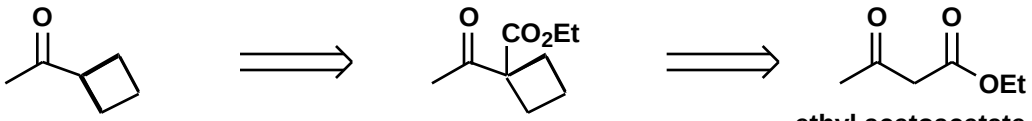
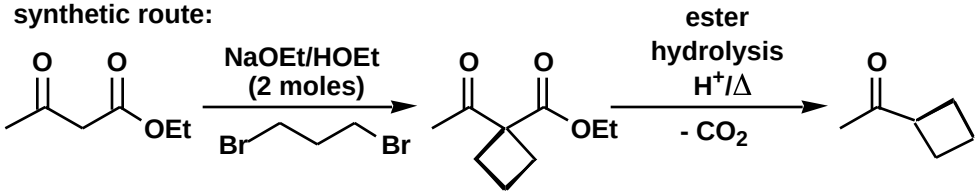
retrosynthetic analysis:




ethyl acetoacetate

synthetic route:

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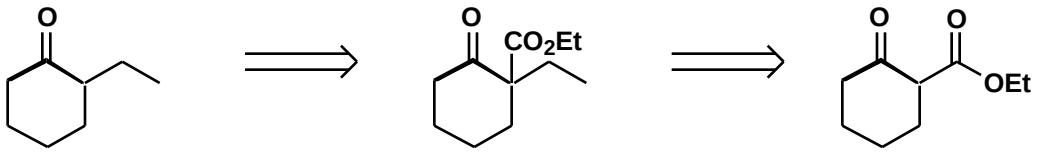
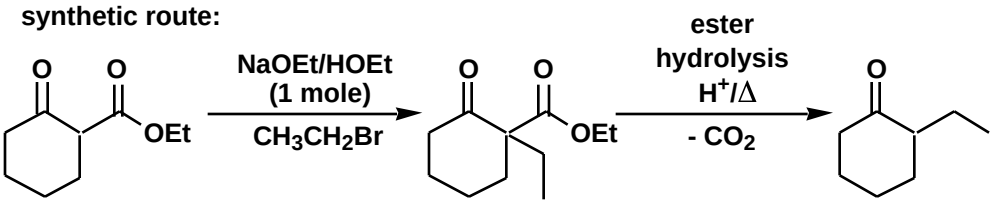
retrosynthetic analysis:




from diethyl
heptanedioate
(by Dieckmann)

synthetic route:




**retrosynthetic analyses and corresponding synthetic routes for representative ketones, based on β-keto ester alkylation, hydrolysis, and decarboxylation**

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