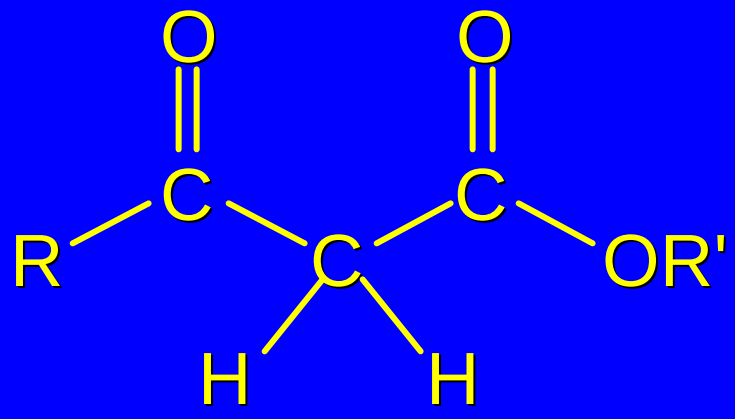
Chapter 21
Ester Enolates

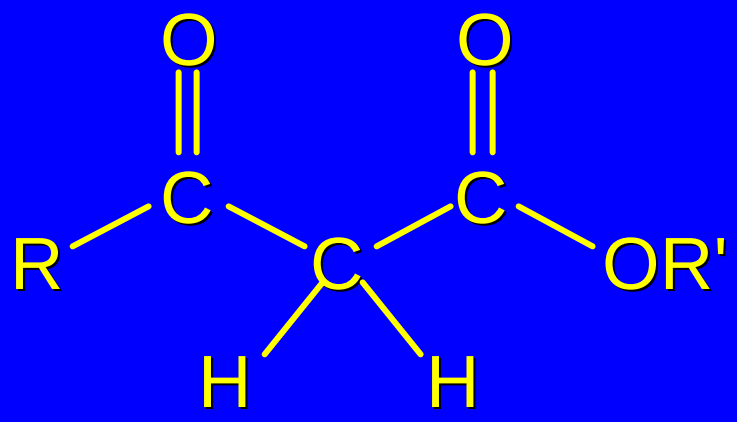
Introduction



The preparation and reactions of β-dicarbonyl compounds, especially β-keto esters, is the main focus of this chapter.

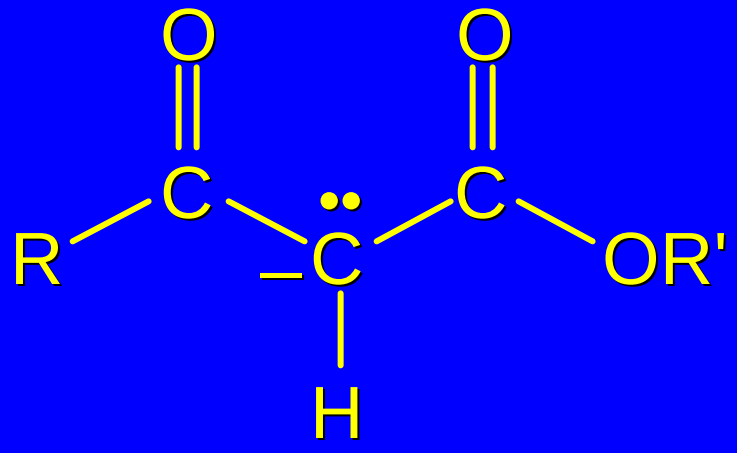
A proton on the carbon flanked by the two carbonyl groups is relatively acidic, easily and quantitatively removed by alkoxide ions.

Introduction

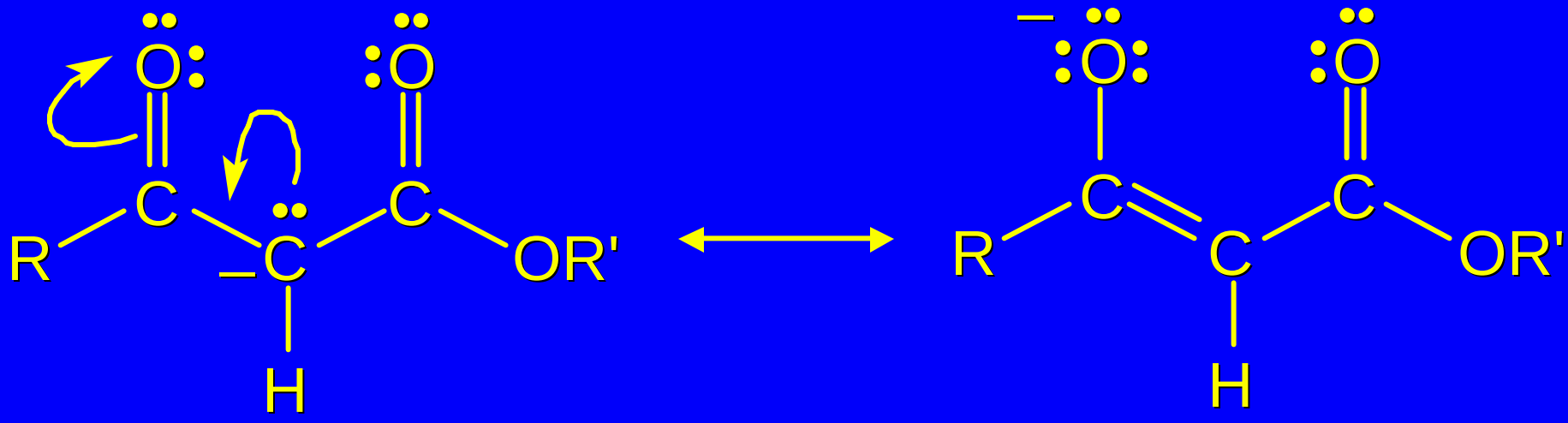


pK_a ~ 11

$CH_3CH_2O^-$

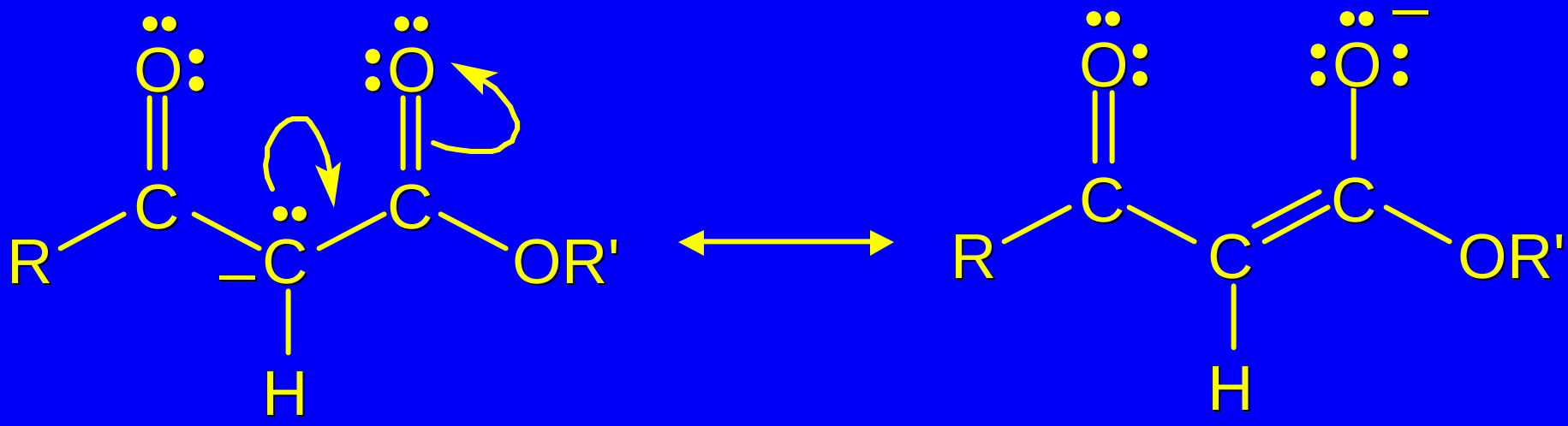


Introduction



The resulting carbanion is stabilized by enolate resonance involving both carbonyl groups.

Introduction

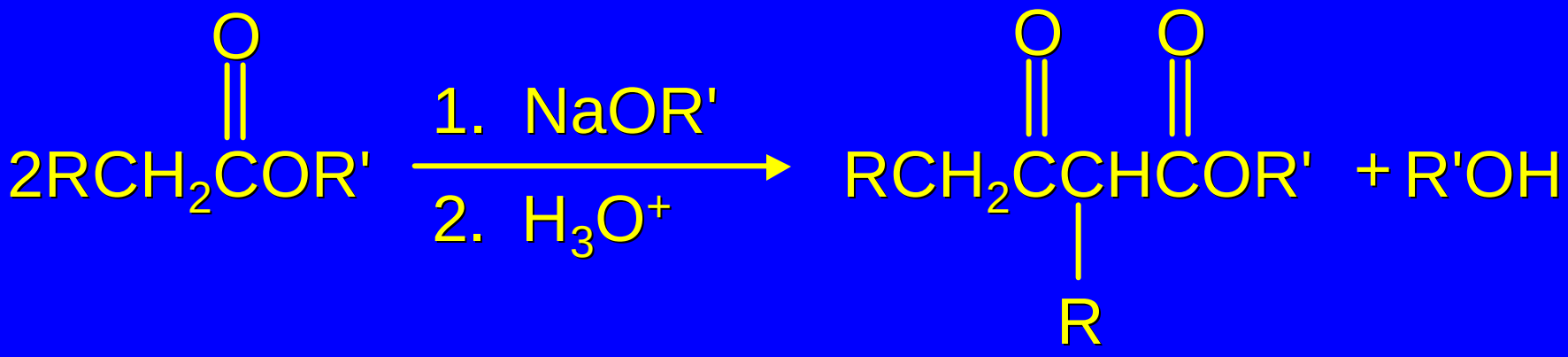


The resulting carbanion is stabilized by enolate resonance involving both carbonyl groups.

21.1

The Claisen Condensation

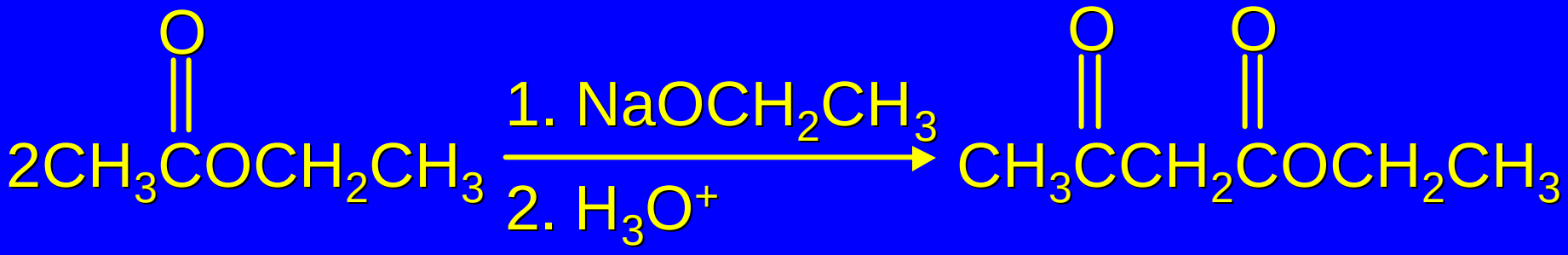
The Claisen Condensation



β-Keto esters are made by the reaction shown, which is called the Claisen condensation.

Ethyl esters are typically used, with sodium ethoxide as the base.

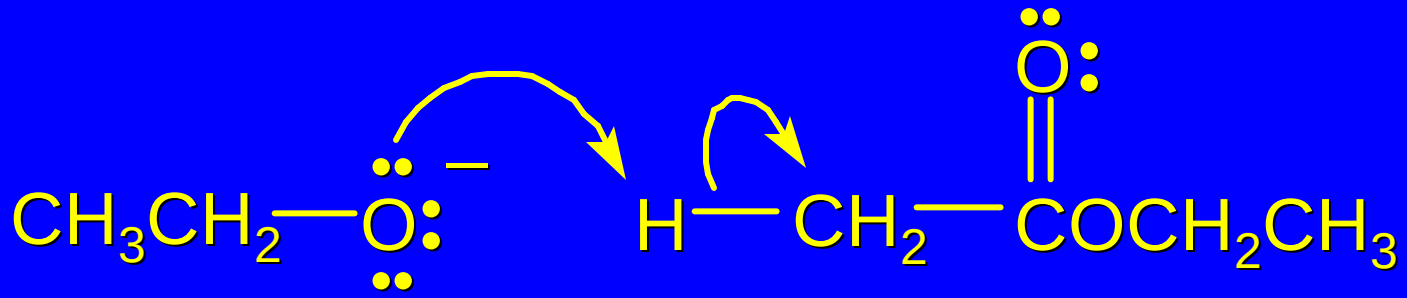
Example



Product from ethyl acetate is called *ethyl acetoacetate* or *acetoacetic ester.*

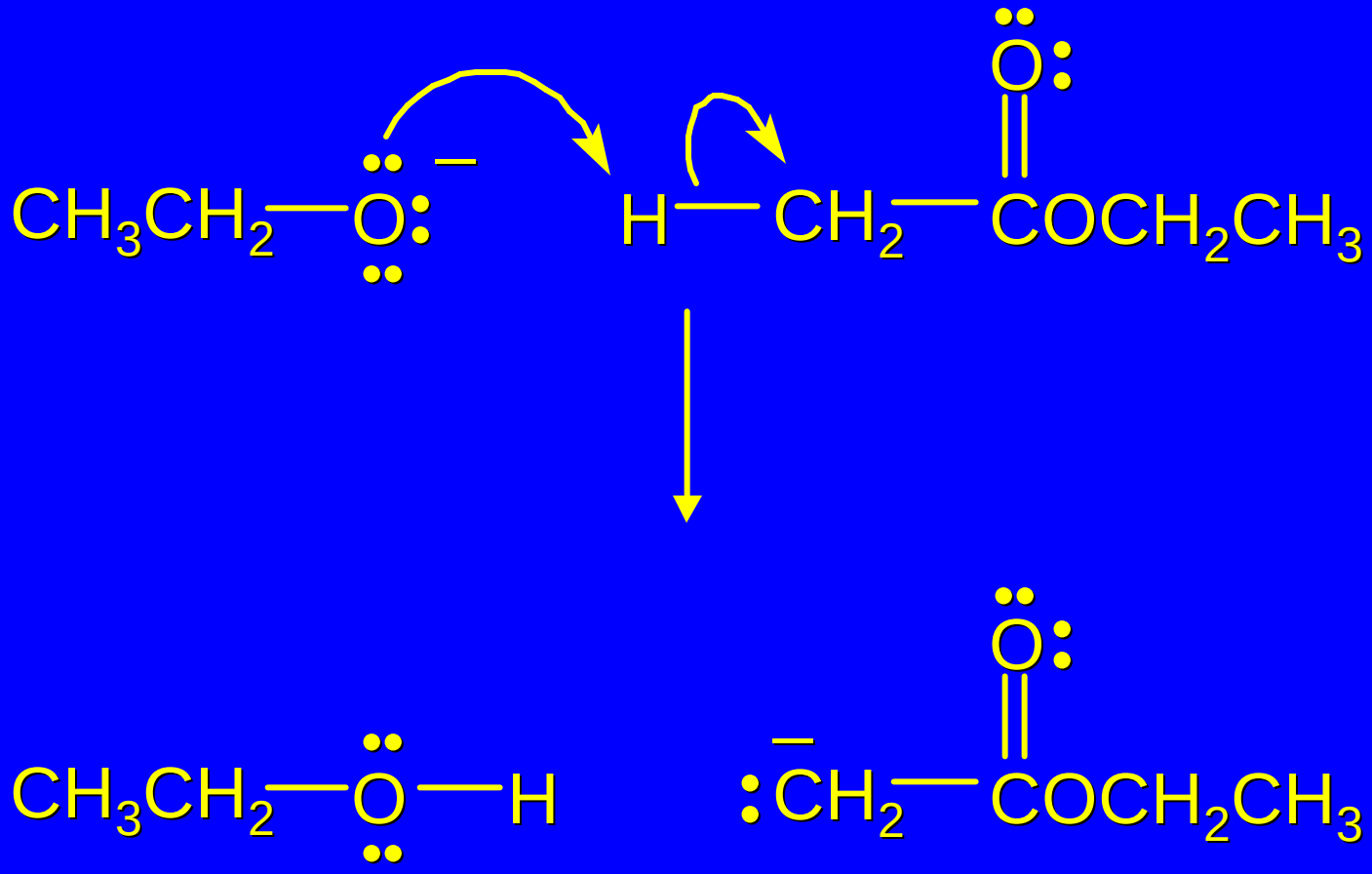
Mechanism

Step 1:



Mechanism

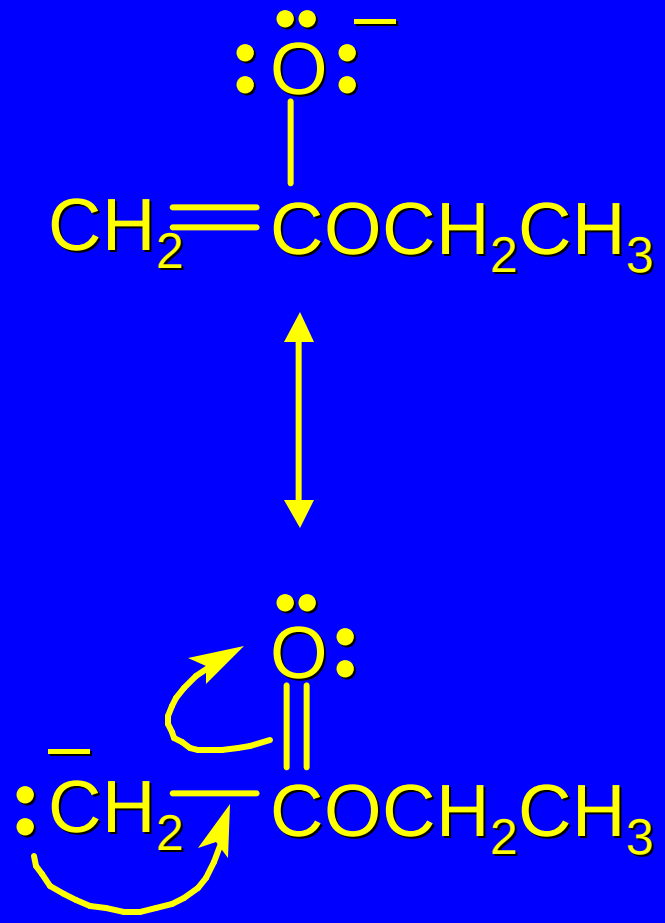
Step 1:



Mechanism

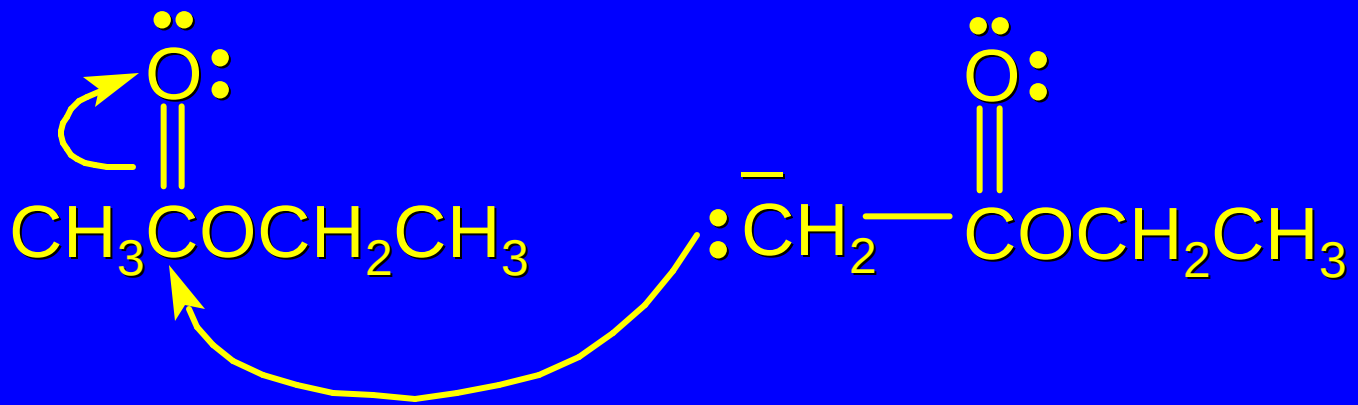
Step 1:

Anion produced is stabilized by electron delocalization; it is the enolate of an ester.



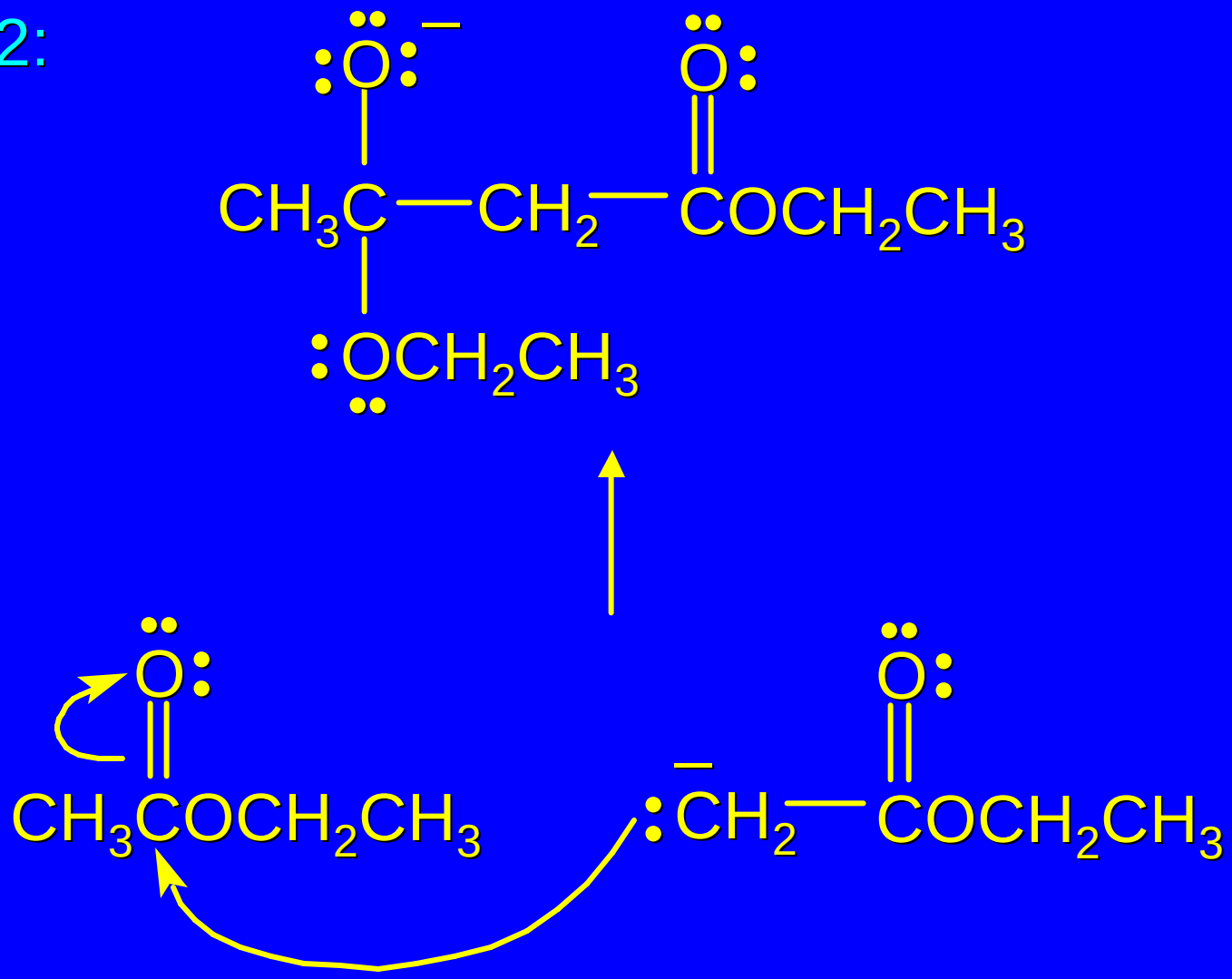
Mechanism

Step 2:



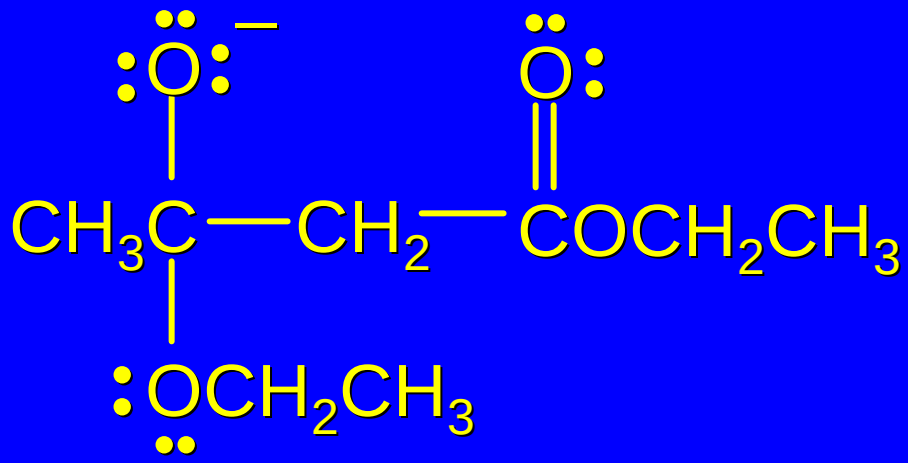
Mechanism

Step 2:



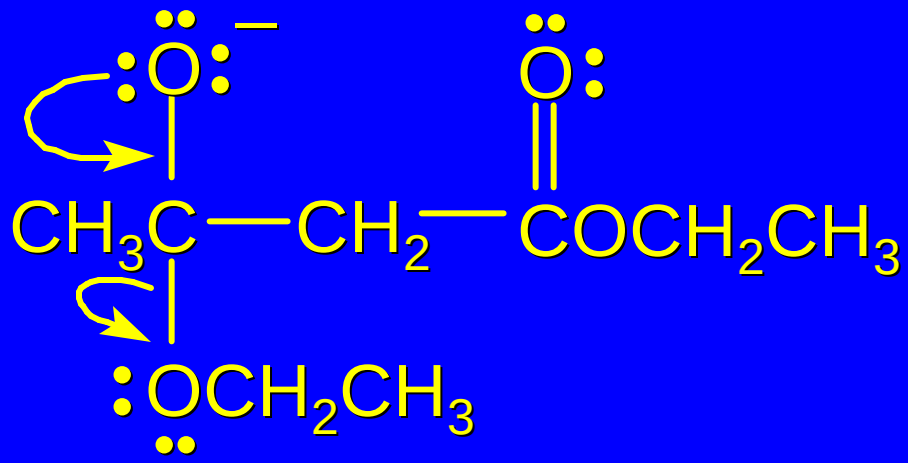
Mechanism

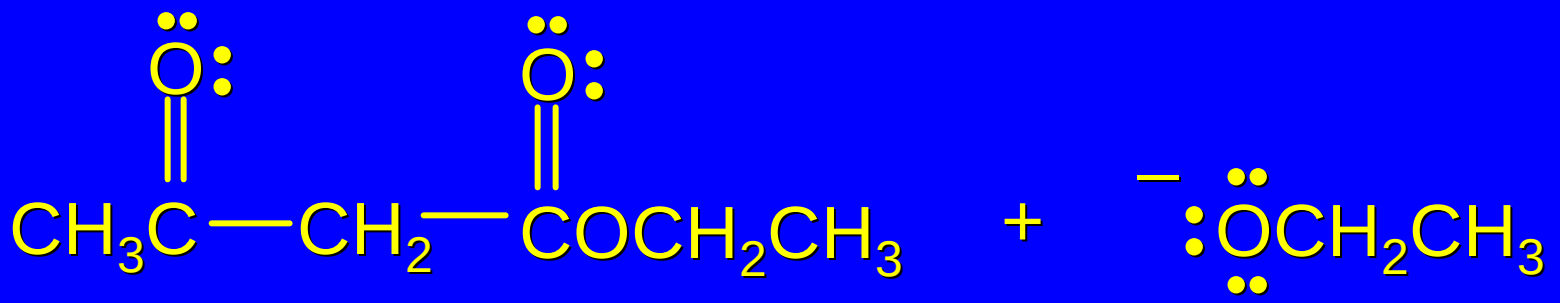
Step 2:



Mechanism

Step 3:





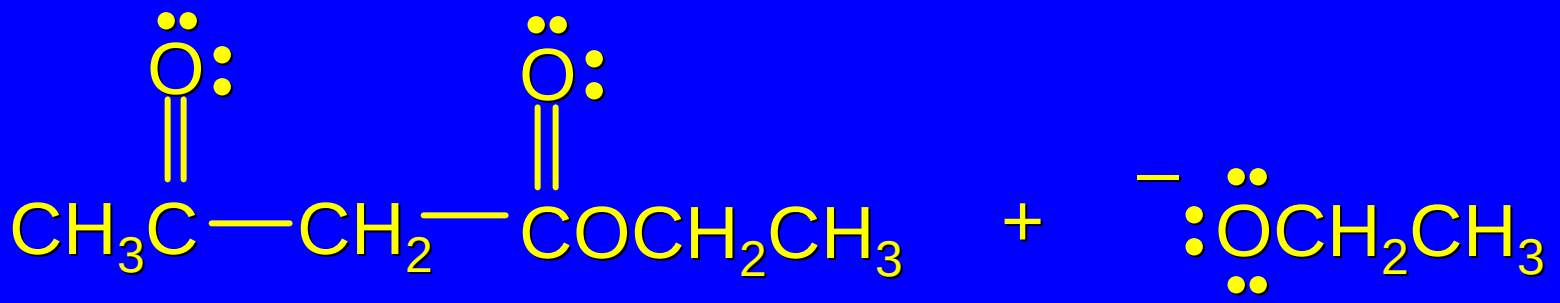
Mechanism

Step 3:

The product at this point is ethyl acetoacetate.

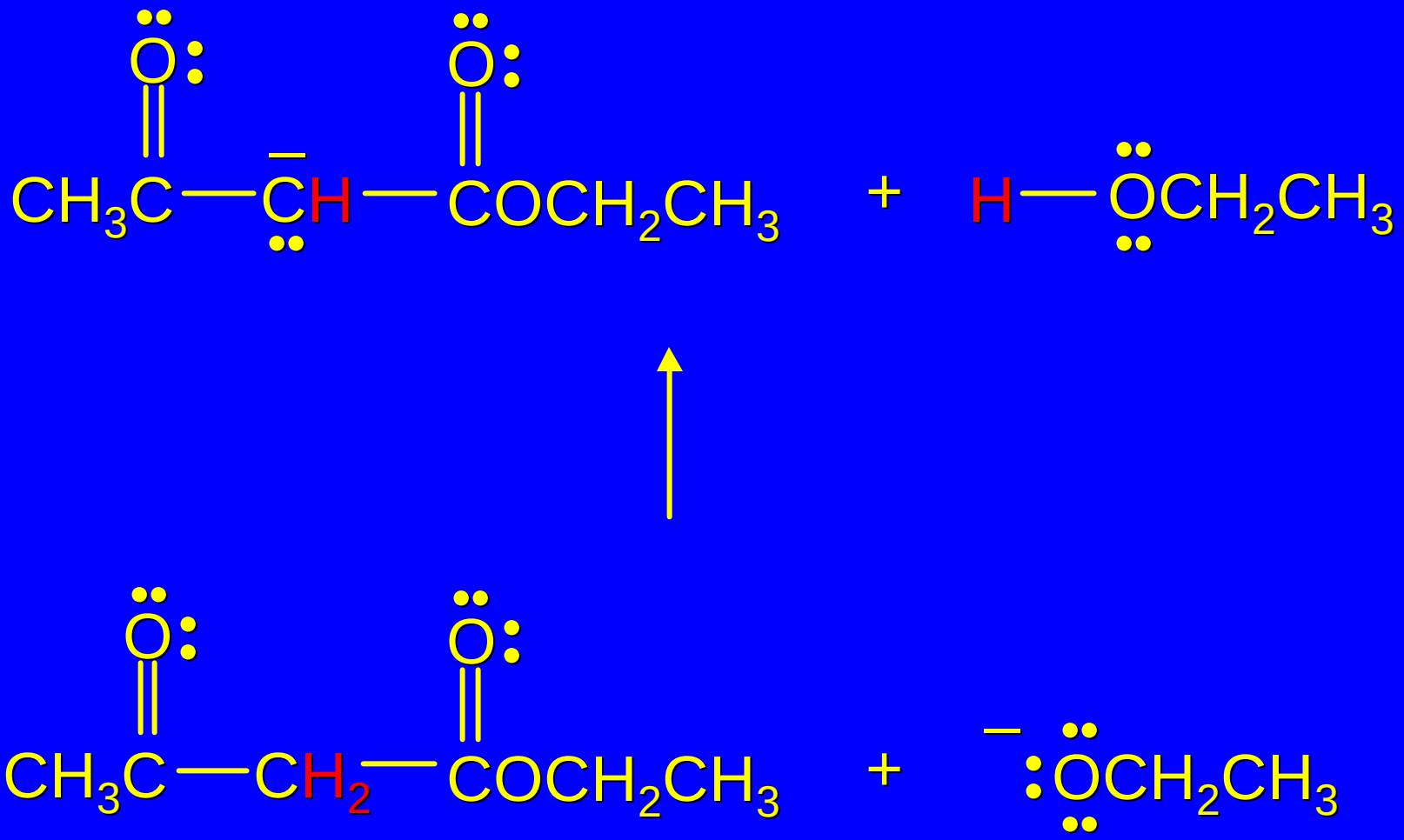
However, were nothing else to happen, the yield of ethyl acetoacetate would be small because the equilibrium constant for its formation is small.

Something else does happen. Ethoxide abstracts a proton from the CH_2 group to give a stabilized anion. The equilibrium constant for this reaction is favorable.



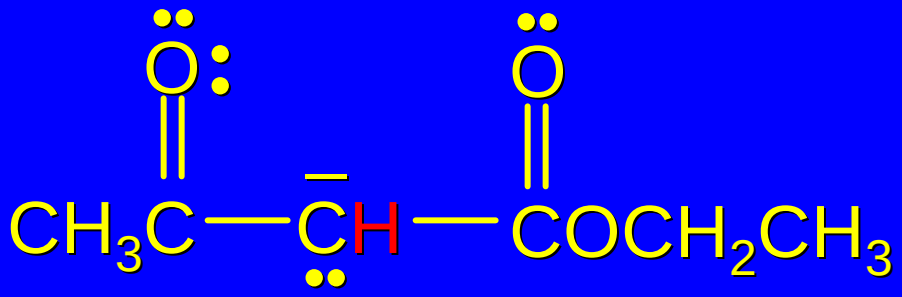
Mechanism

Step 4:



Mechanism

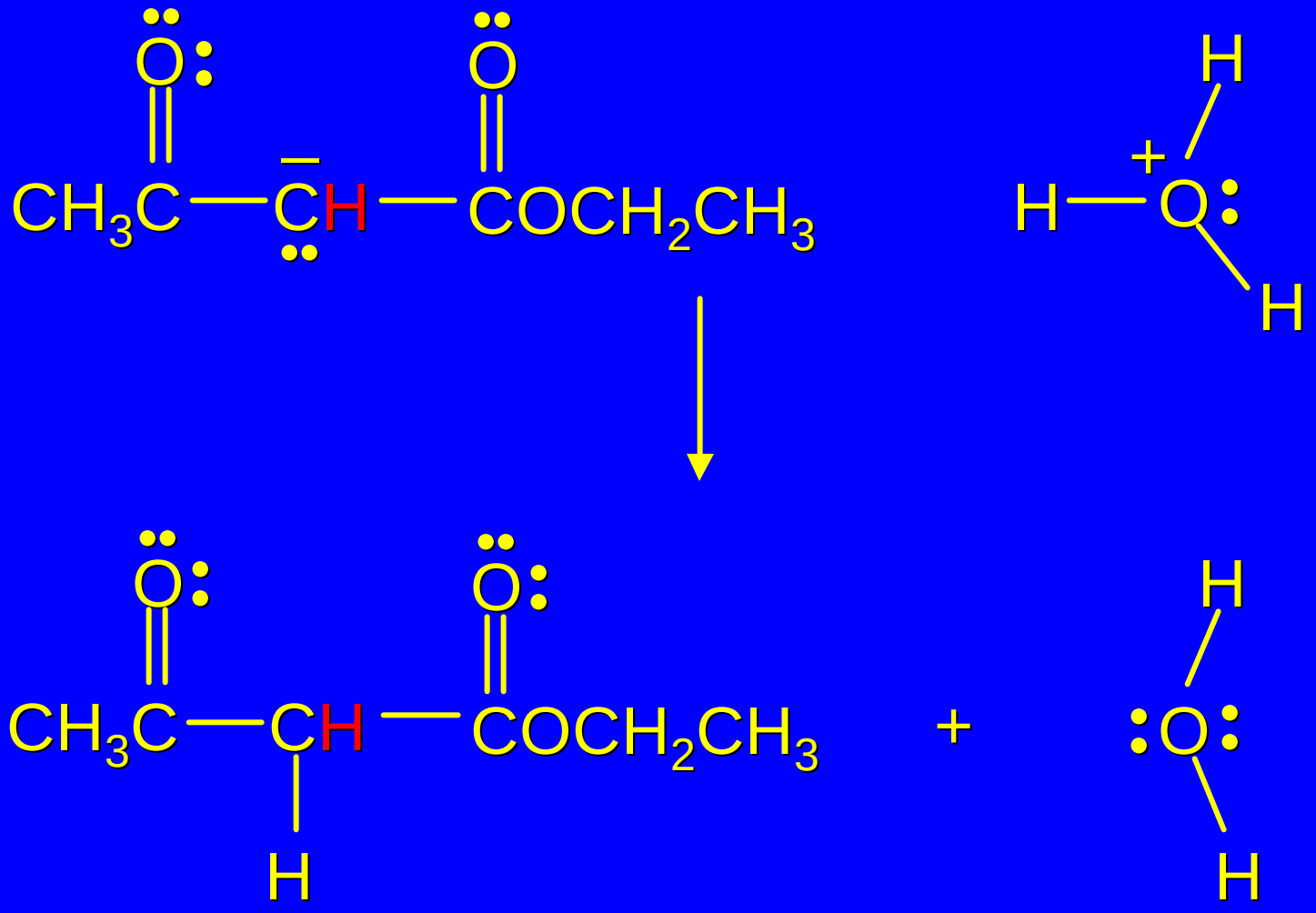
Step 5:



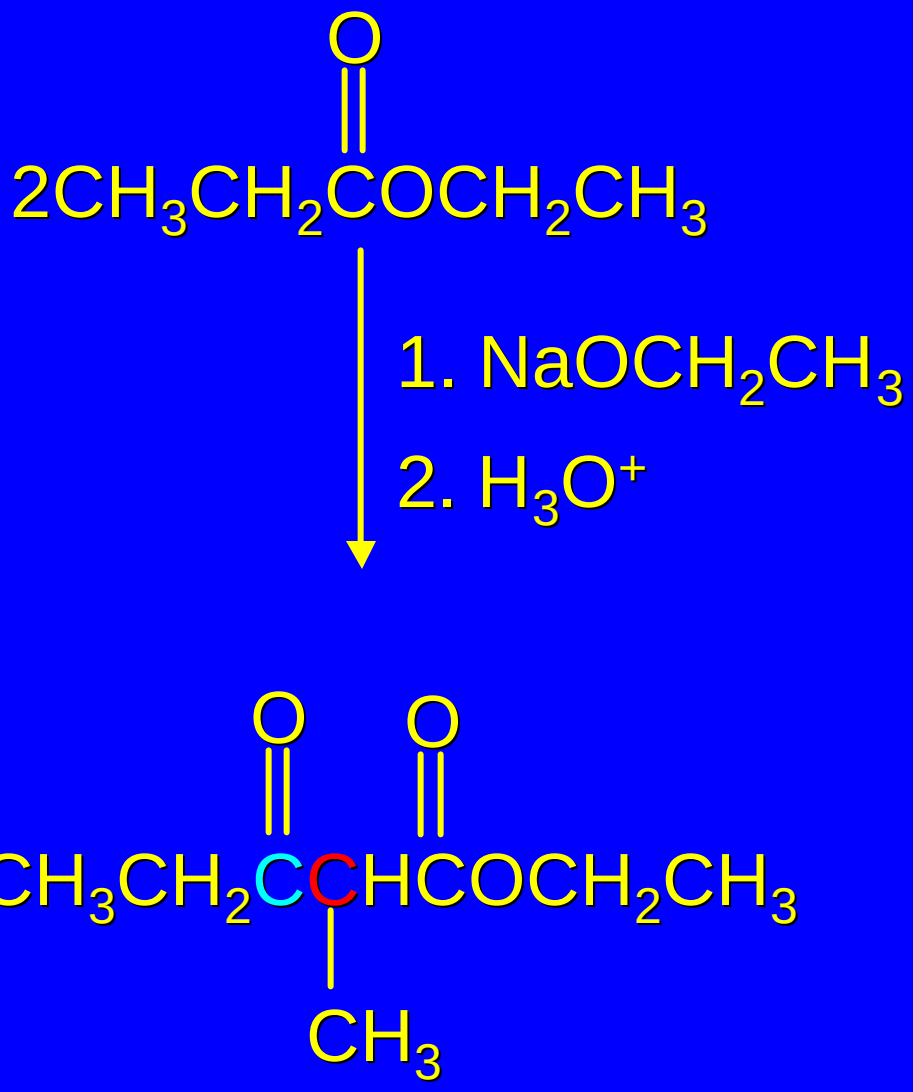
In a separate operation, the reaction mixture is acidified. This converts the anion to the isolated product, ethyl acetoacetate.

Mechanism

Step 5:



Another example

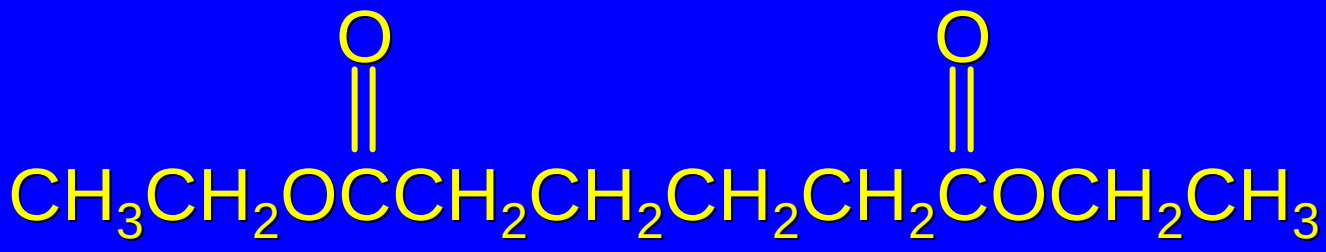


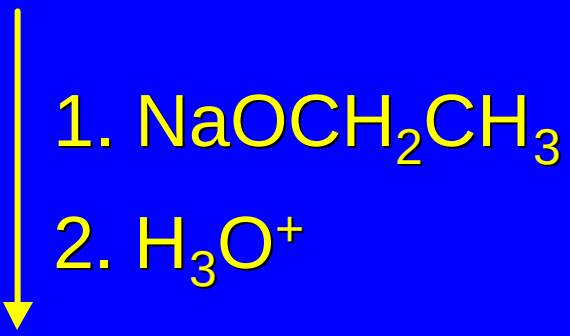
(81%)

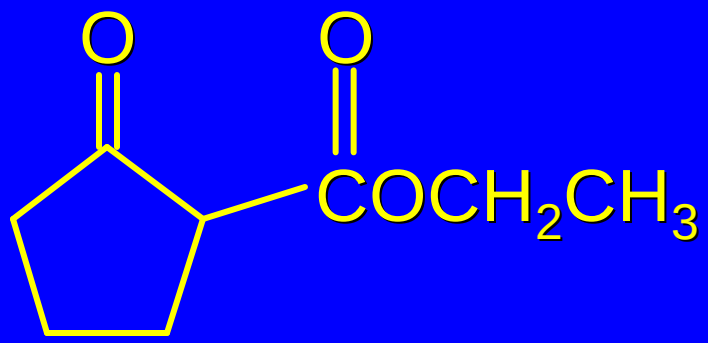
Reaction involves bond formation between the α-carbon atom of one ethyl propanoate molecule and the carbonyl carbon of the other.

21.2
Intramolecular Claisen Condensation: The Dieckmann Reaction

Example

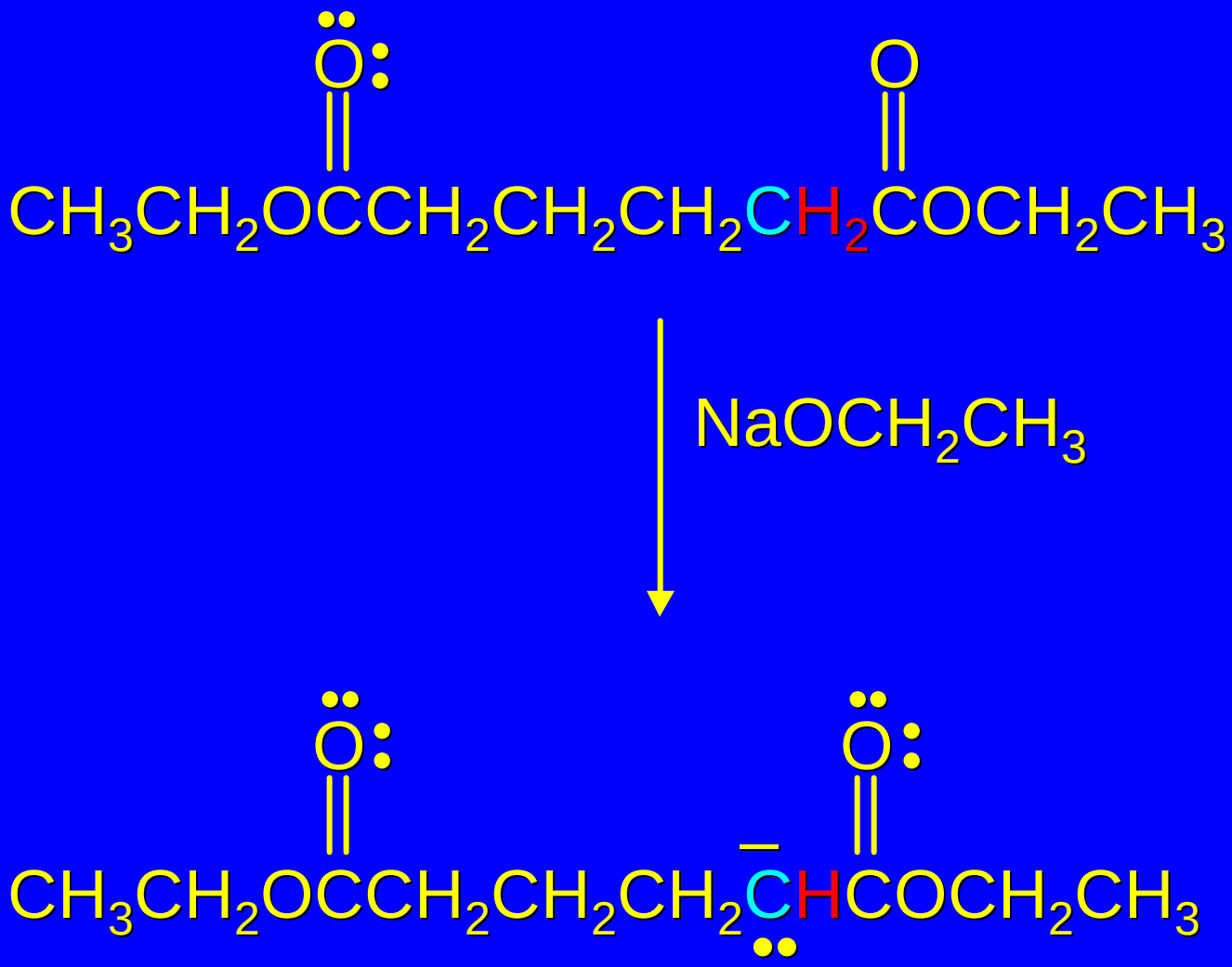




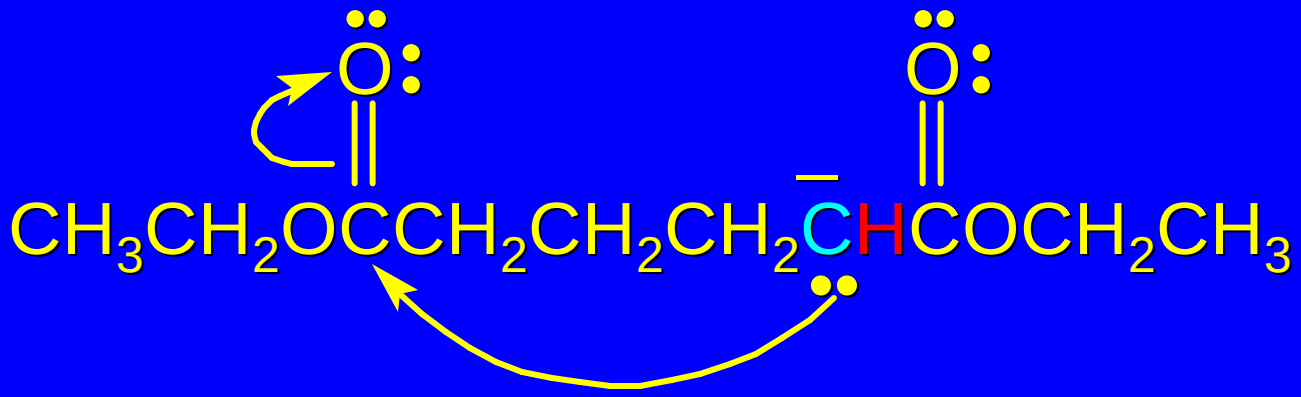


(74-81%)

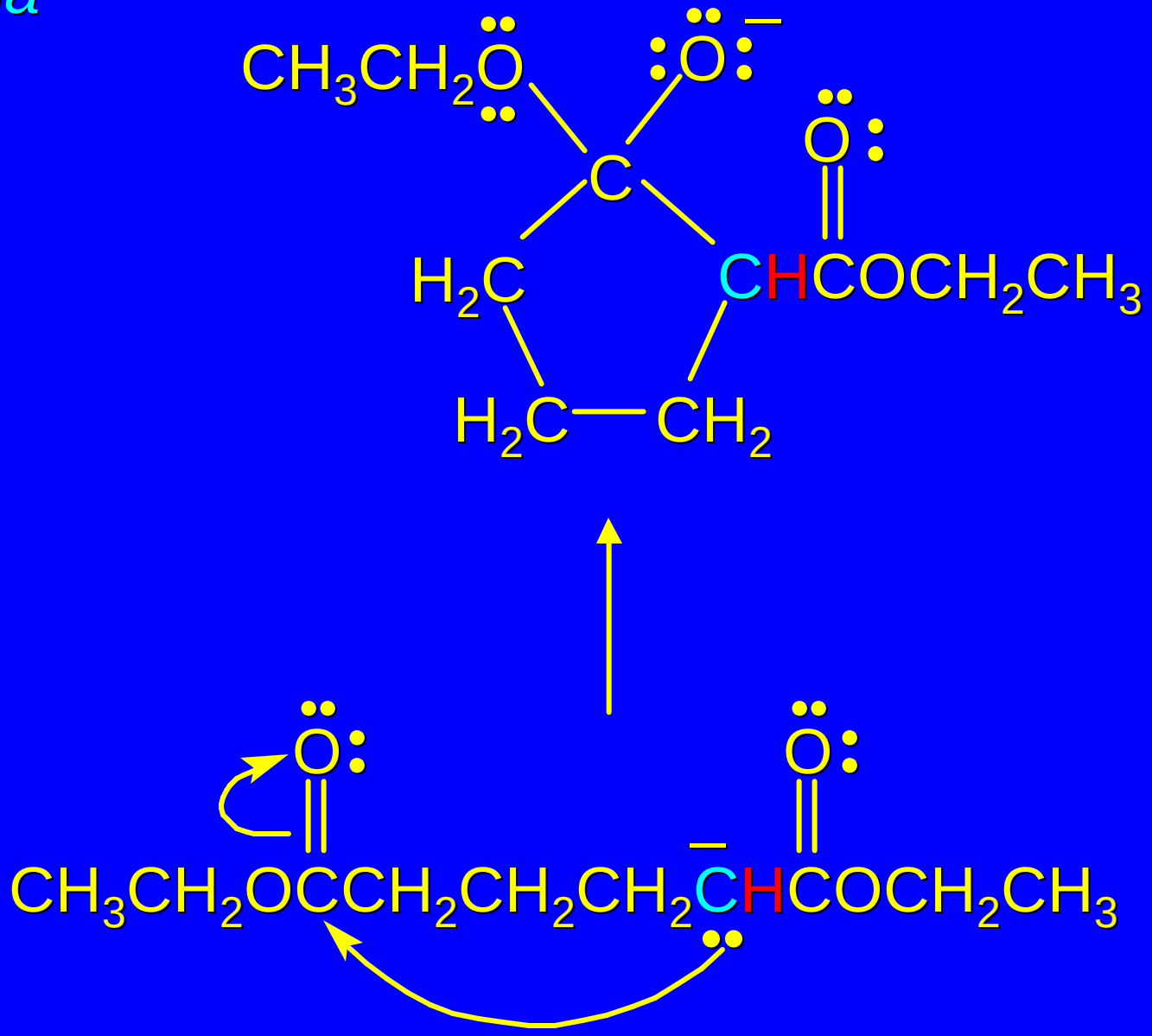
via


CH3CH2OCCH2CH2CH2CH2COCH2CH3
NaOCH2CH3
CH3CH2OCCH2CH2CH2CHCOCH2CH3

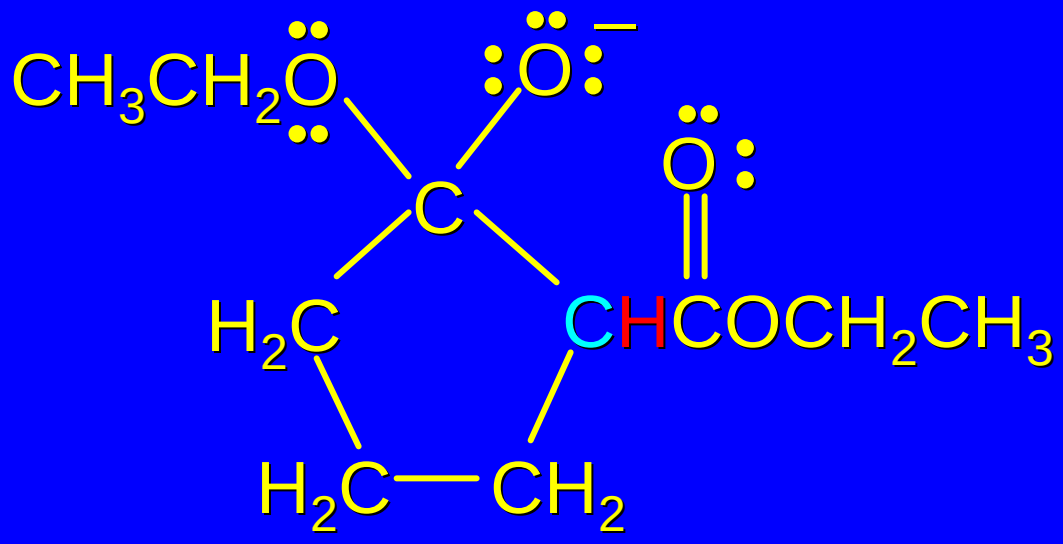
via



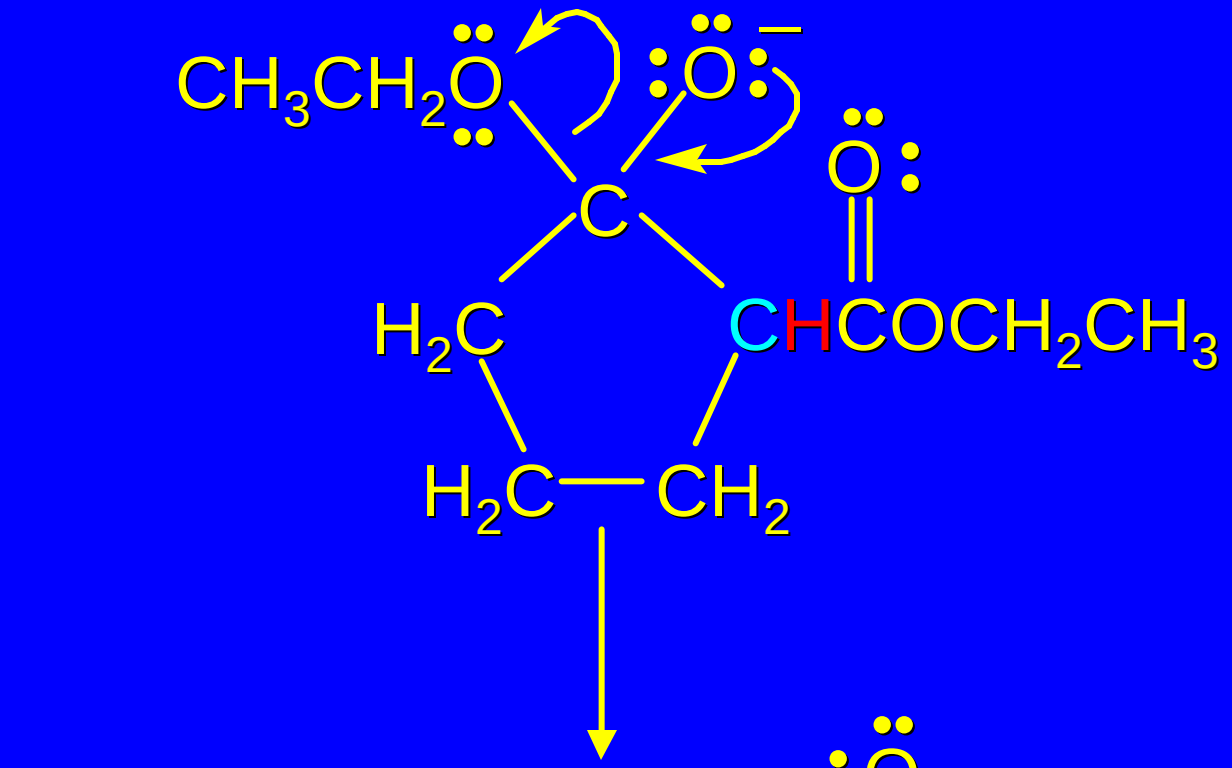
via

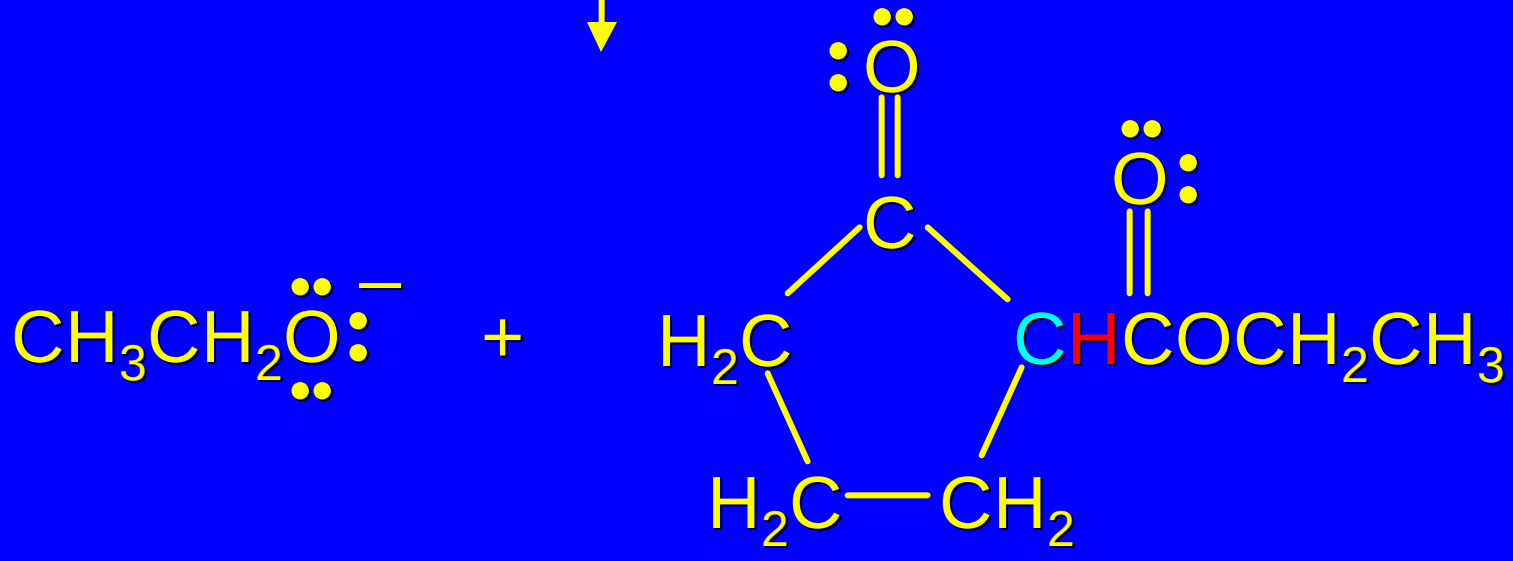

CH3CH2O
O
C
O
CHCOCH2CH3
H2C
H2C
CH2
O
O
CH3CH2OCCH2CH2CH2CHCOCH2CH3

via



via


CH3CH2O
O
C
O
H2C
CHCOCH2CH3
H2C
CH2


CH3CH2O
+
O
C
O
H2C
CHCOCH2CH3
H2C
CH2

21.3

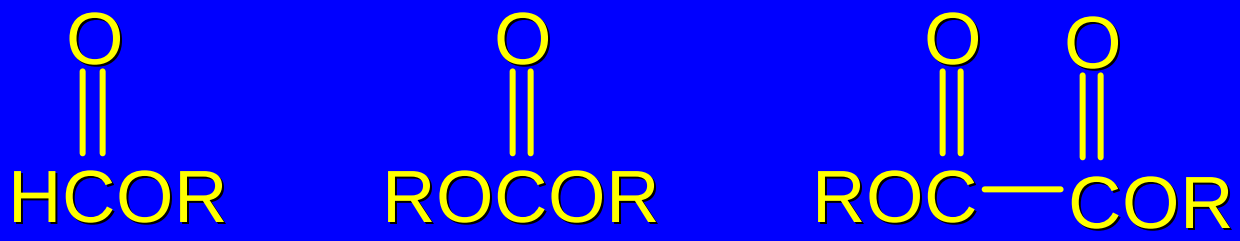
Mixed Claisen Condensations

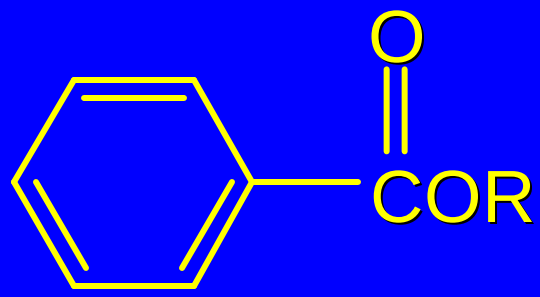
Mixed Claisen Condensations

As with mixed aldol condensations, mixed Claisen condensations are best carried out when the reaction mixture contains one compound that can form an enolate and another that cannot.

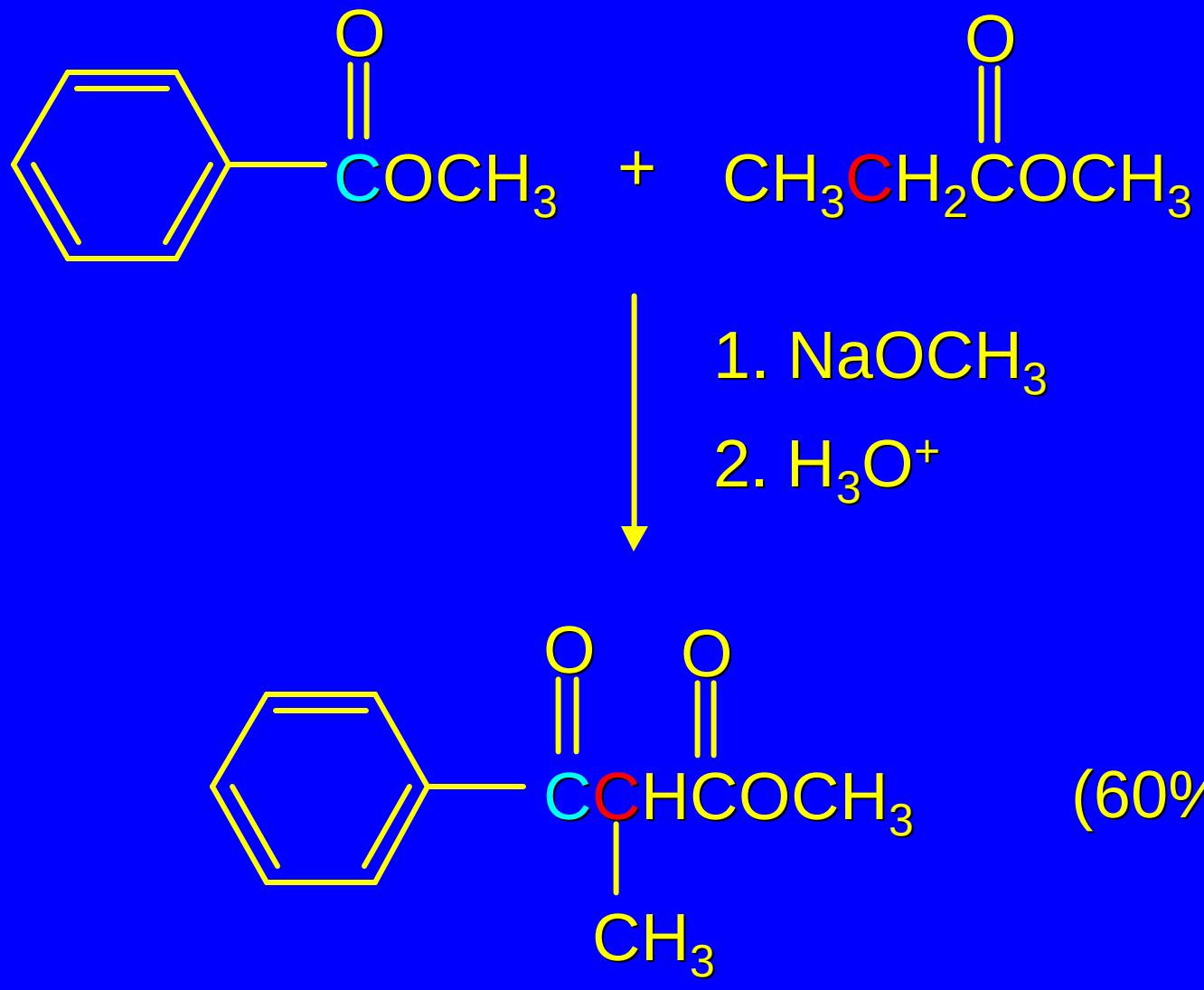
Mixed Claisen Condensations

These types of esters cannot form an enolate.





Example



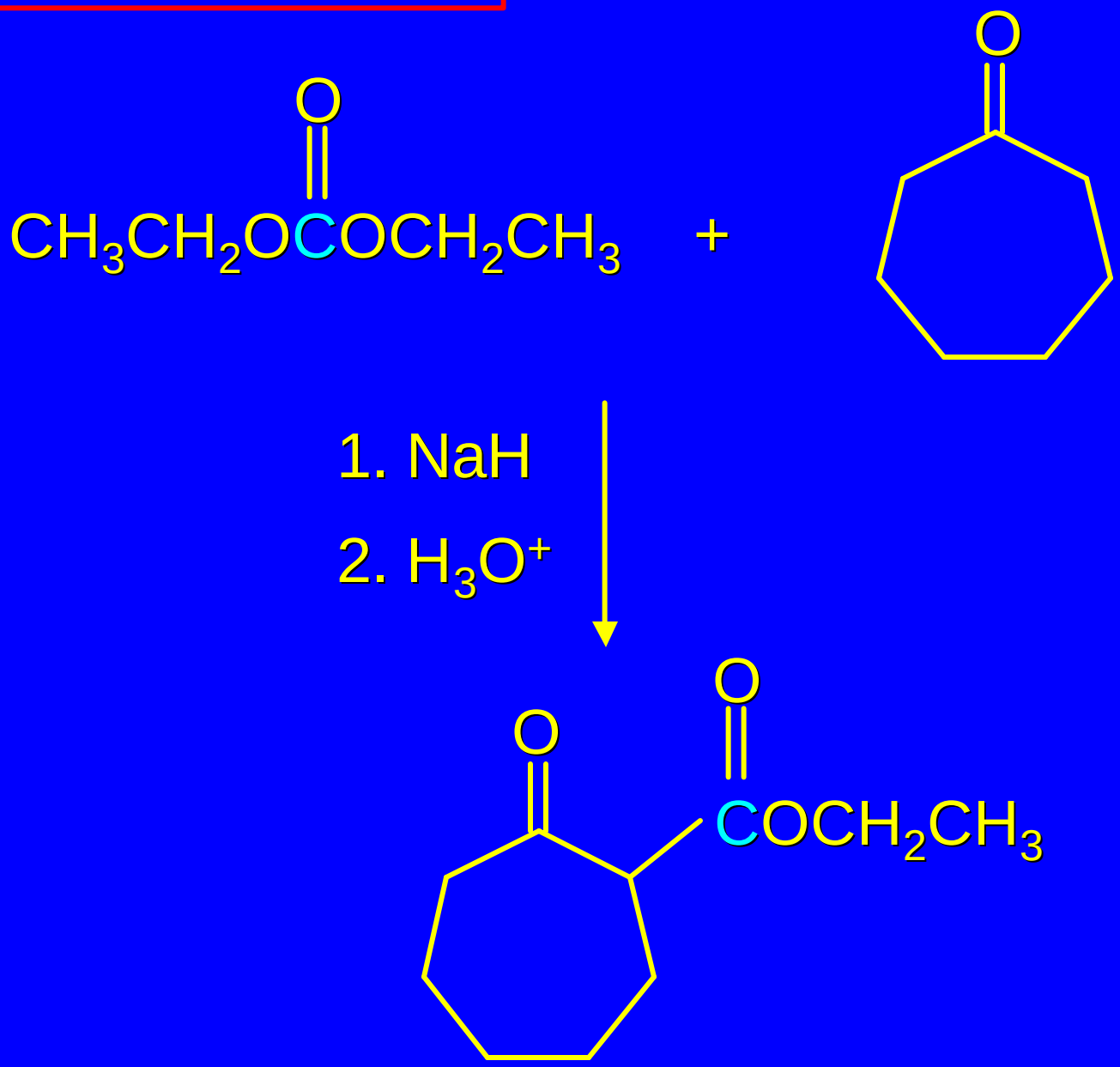
21.4

Acylation of Ketones with Esters

Acylation of Ketones with Esters

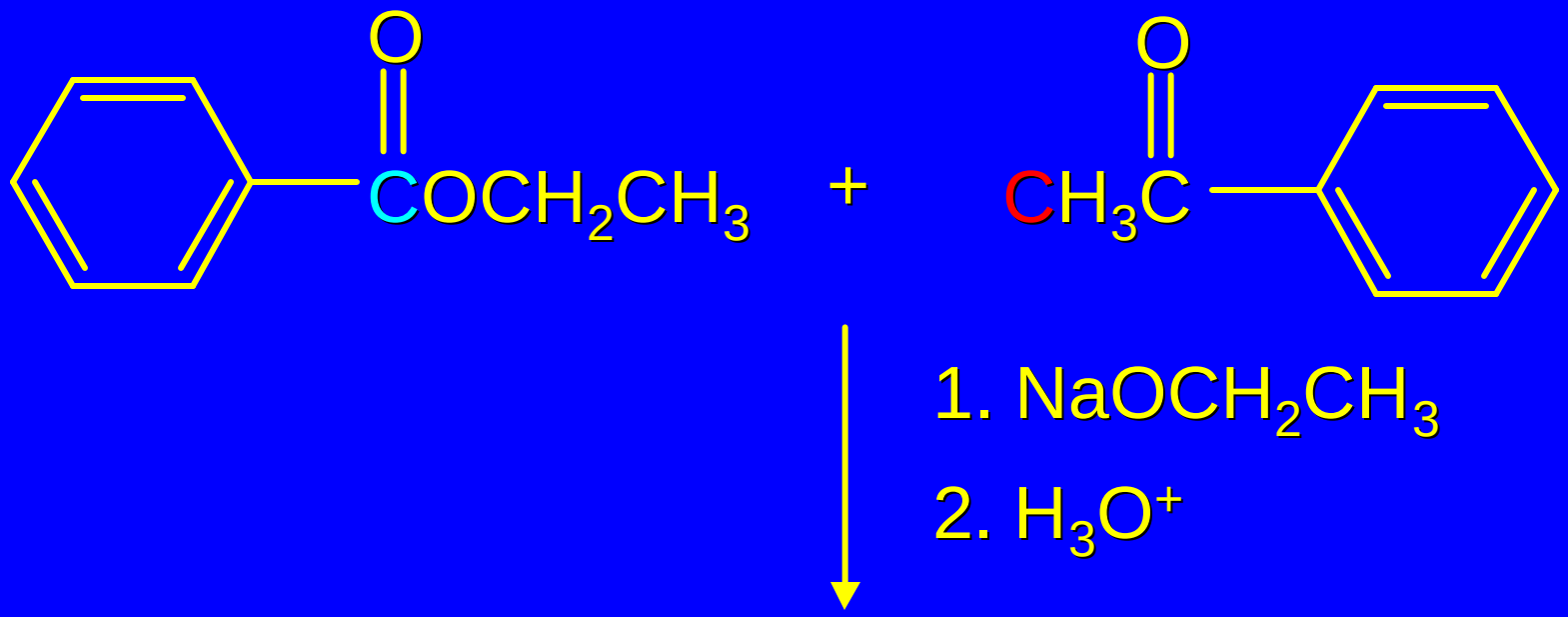
Esters that cannot form an enolate can be used to acylate ketone enolates.

Example



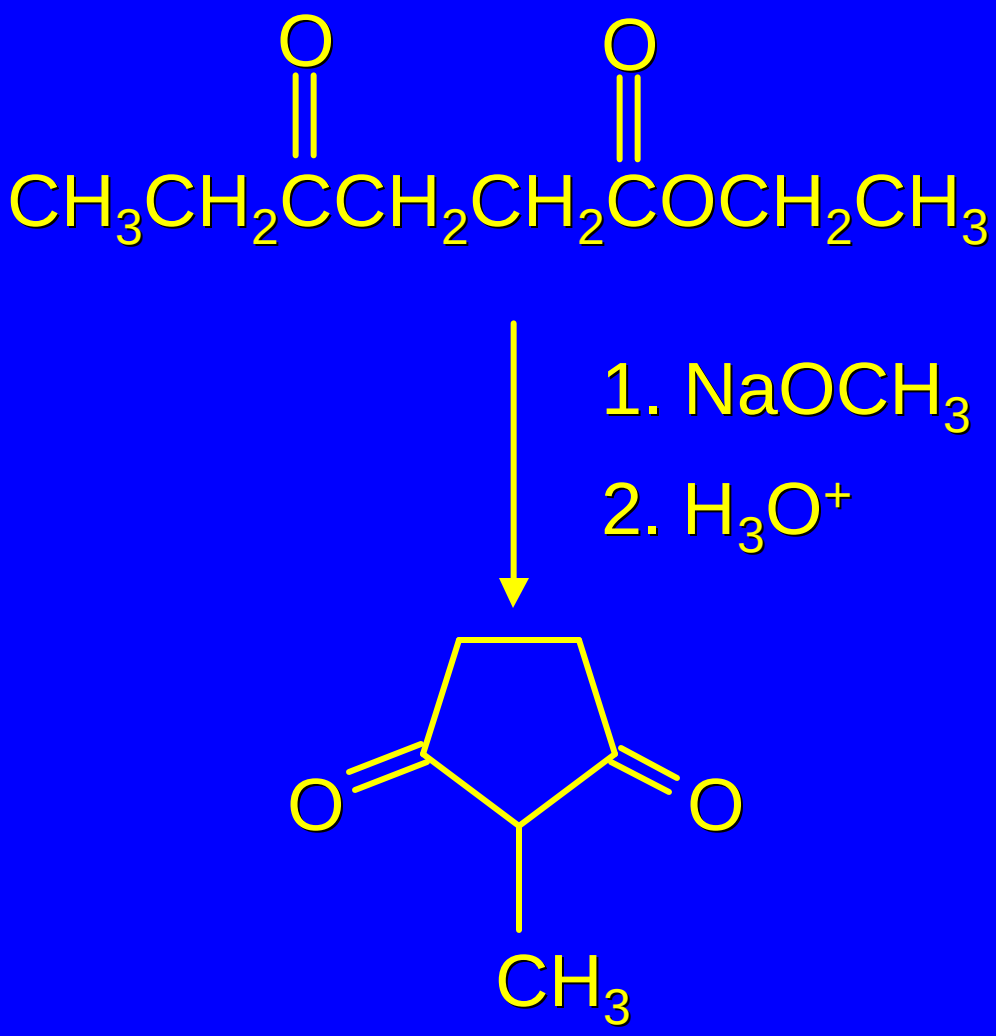
(60%)

Example



(62-71%)

Example

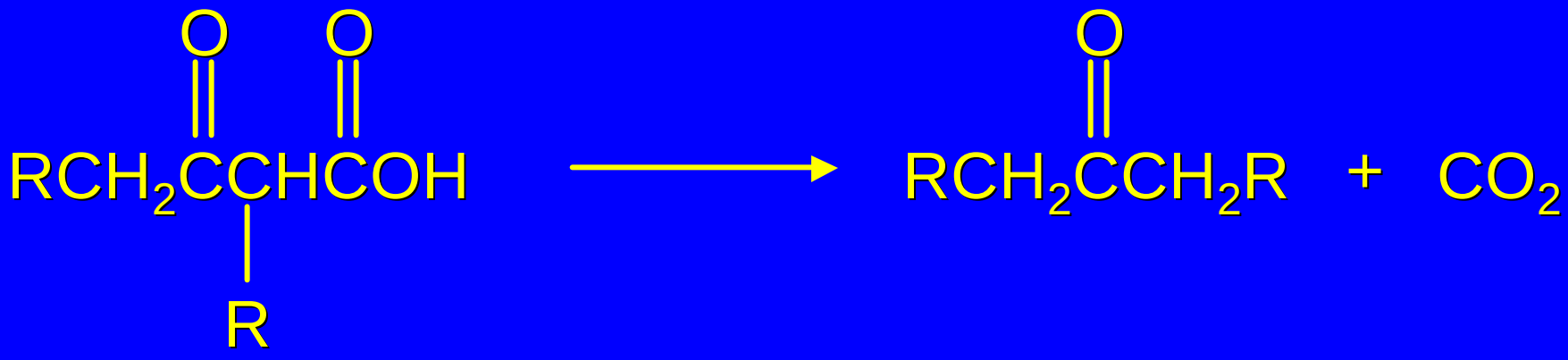


(70-71%)

21.5

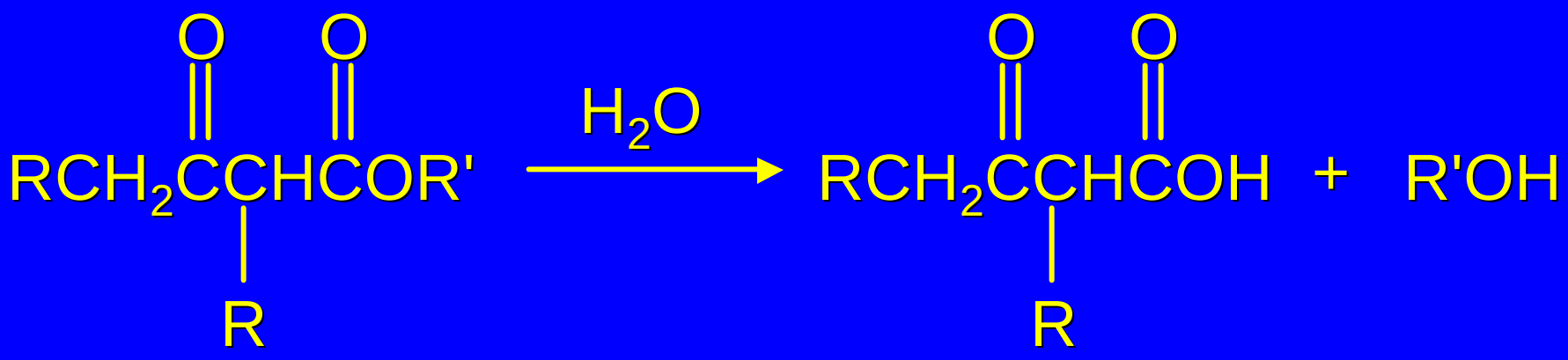
Ketone Synthesis via β-Keto Esters

Ketone Synthesis



β-Keto acids decarboxylate readily to give ketones (Section 19.17).

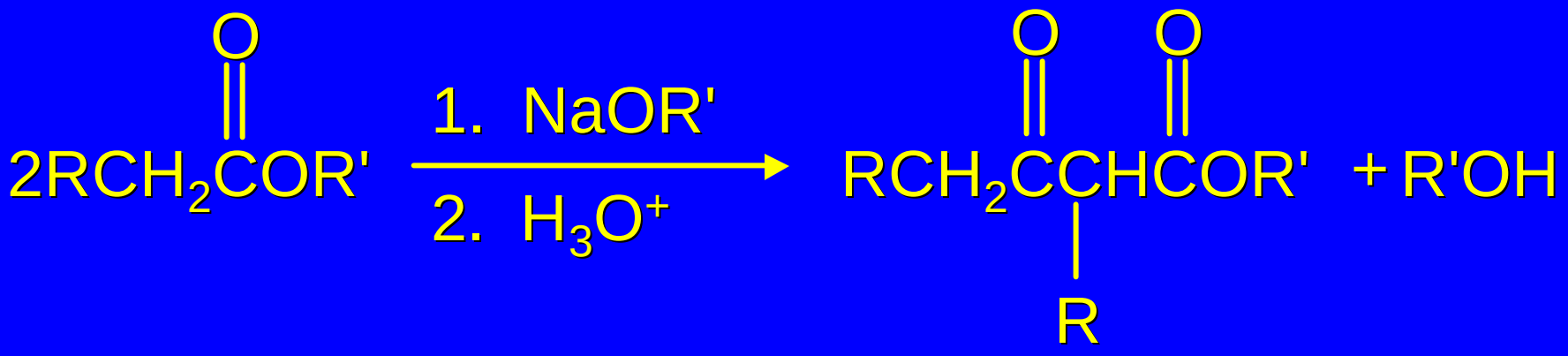
Ketone Synthesis



β-Keto acids decarboxylate readily to give ketones (Section 19.17).

β-Keto acids are available by hydrolysis of β-keto esters.

Ketone Synthesis

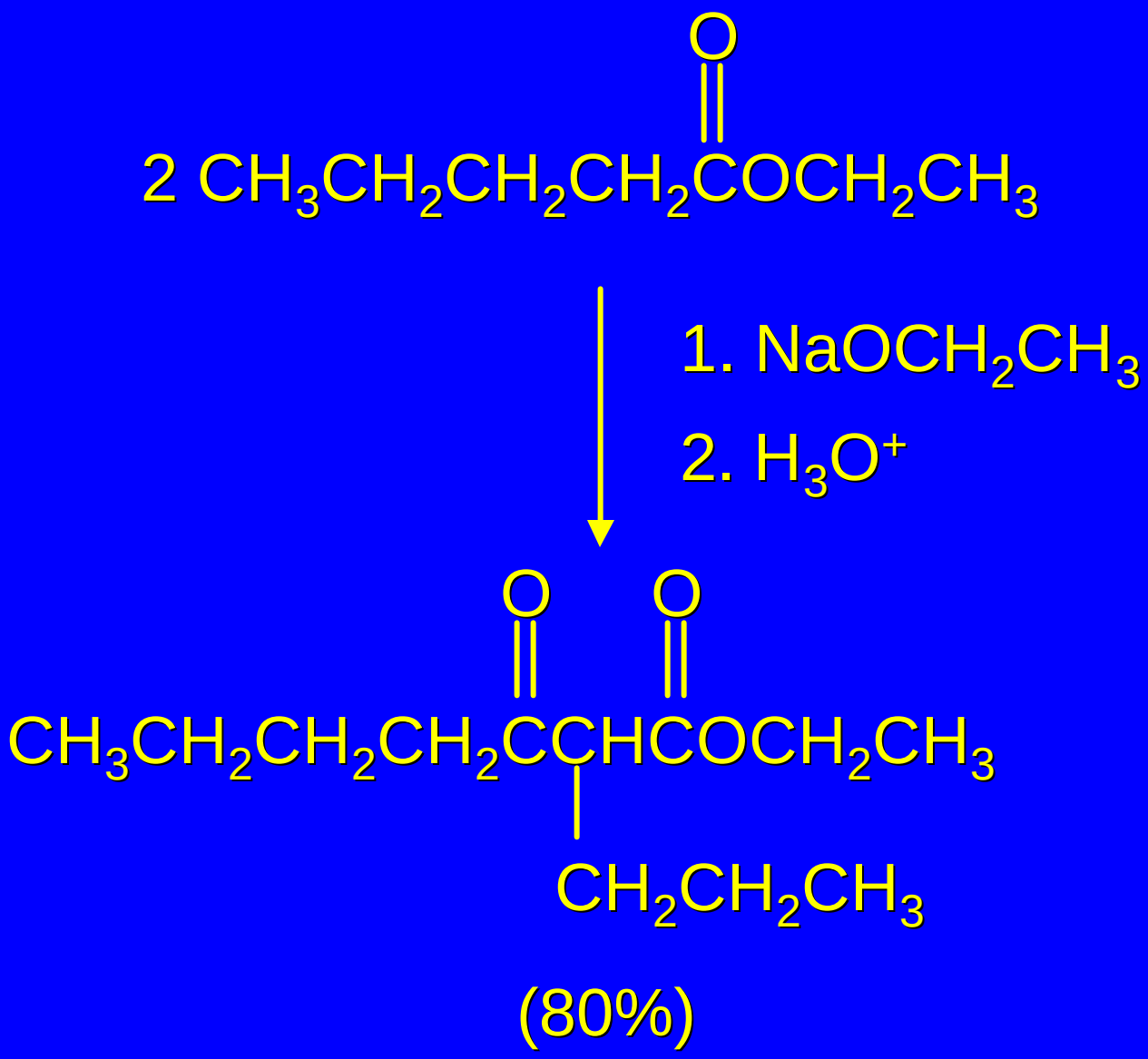


β-Keto acids decarboxylate readily to give ketones (Section 19.17).

β-Keto acids are available by hydrolysis of β-keto esters.

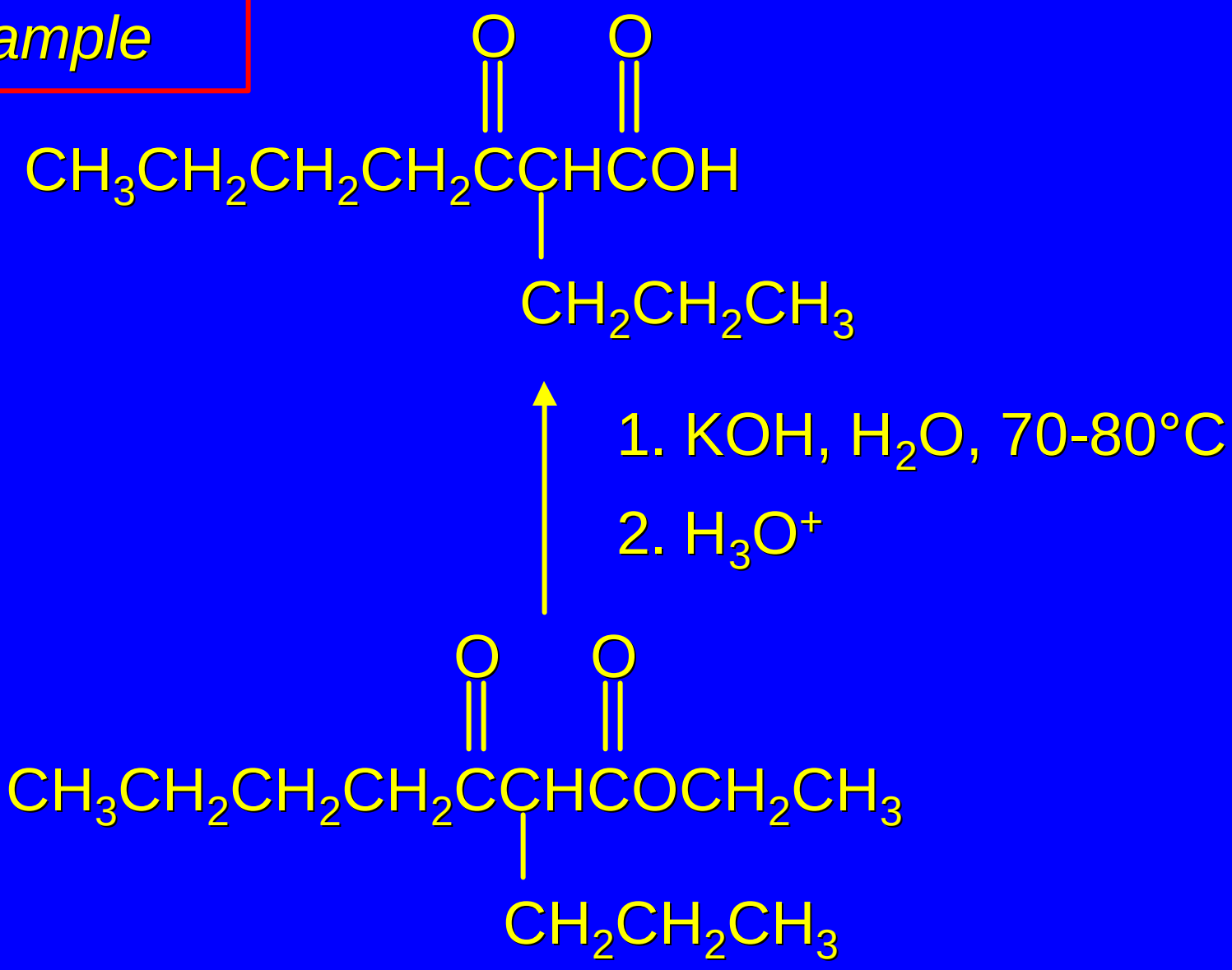
β-Keto esters can be prepared by the Claisen condensation.

Example

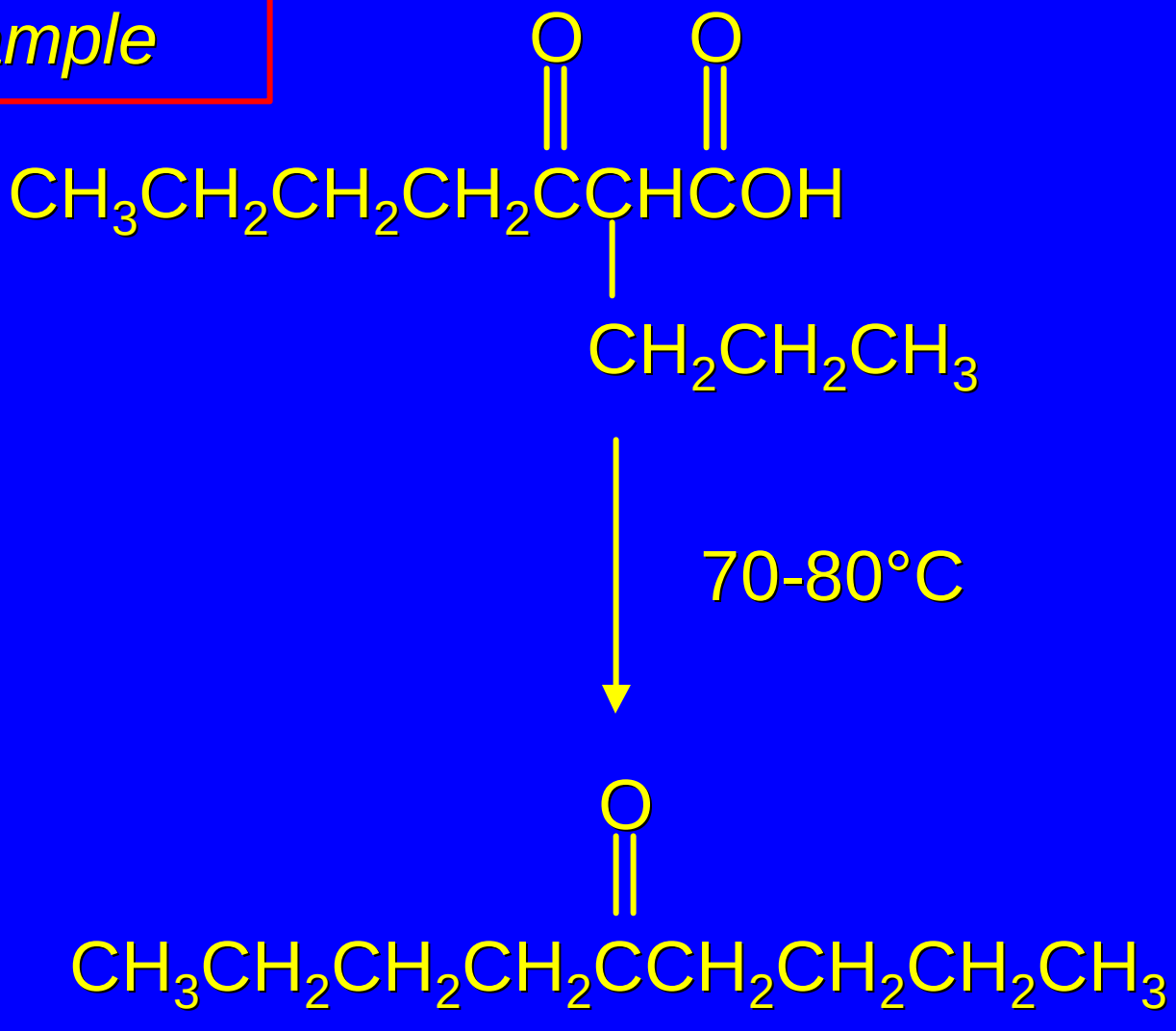

O
2 CH3CH2CH2CH2COCH2CH3
1. NaOCH2CH3
2. H3O+
O
O
CH3CH2CH2CH2CCHCOCH2CH3
CH2CH2CH3

(80%)

Example


O O
CH3CH2CH2CH2CCHCOH
CH2CH2CH3
1. KOH, H2O, 70-80°C
2. H3O+
O O
CH3CH2CH2CH2CCHCOCH2CH3
CH2CH2CH3

Example


O
O
CH3CH2CH2CH2CCHCOH
CH2CH2CH3
70-80°C
O
CH3CH2CH2CH2CCH2CH2CH2CH3

(81%)