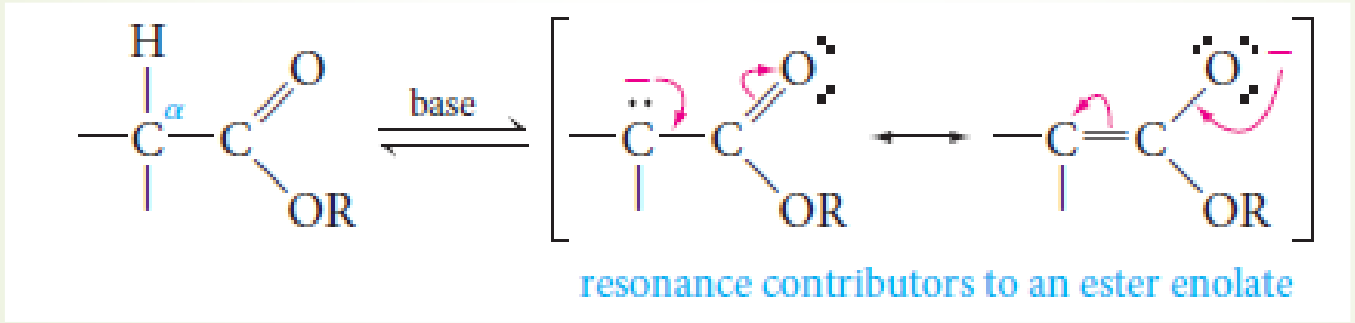
The Claisen Condensation

- **the α-hydrogens of an ester are weakly acidic and can be removed by a strong base. The product is an ester enolate.**

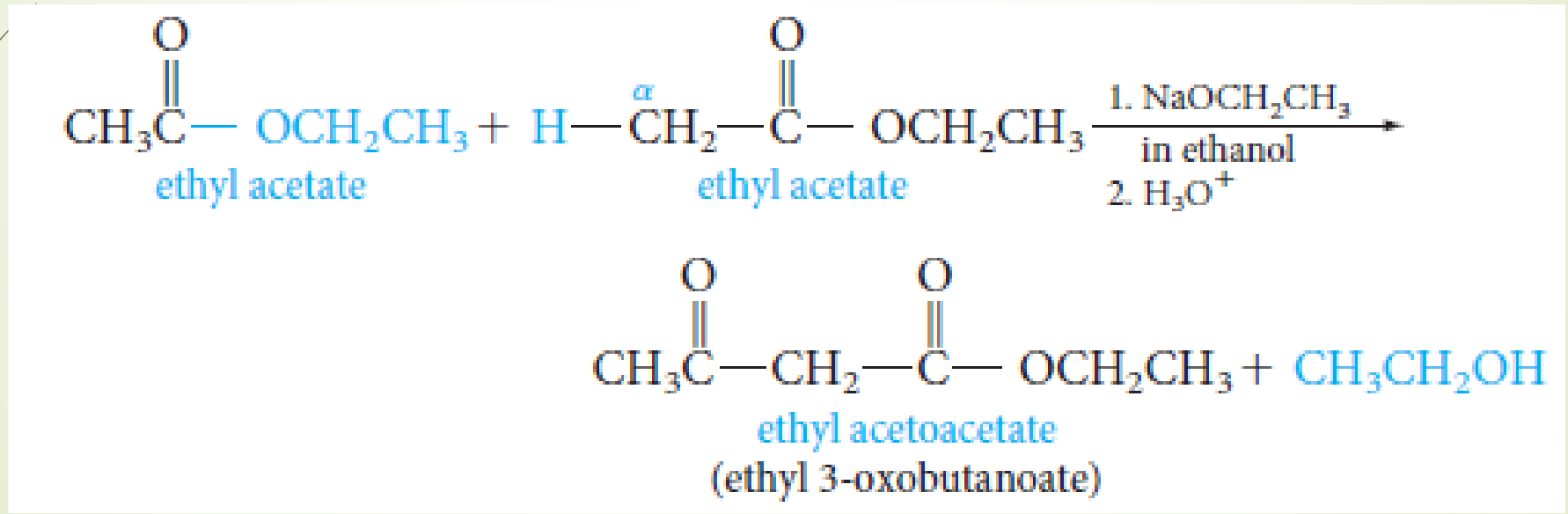


resonance contributors to an ester enolate

Common bases used for this purpose are sodium alkoxides (RO^- Na+). The ester enolate, once formed, can act as a carbon nucleophile and add to the carbonyl group of another ester molecule. This reaction is called the Claisen condensation. It is a way of making b-keto esters.

The Claisen Condensation

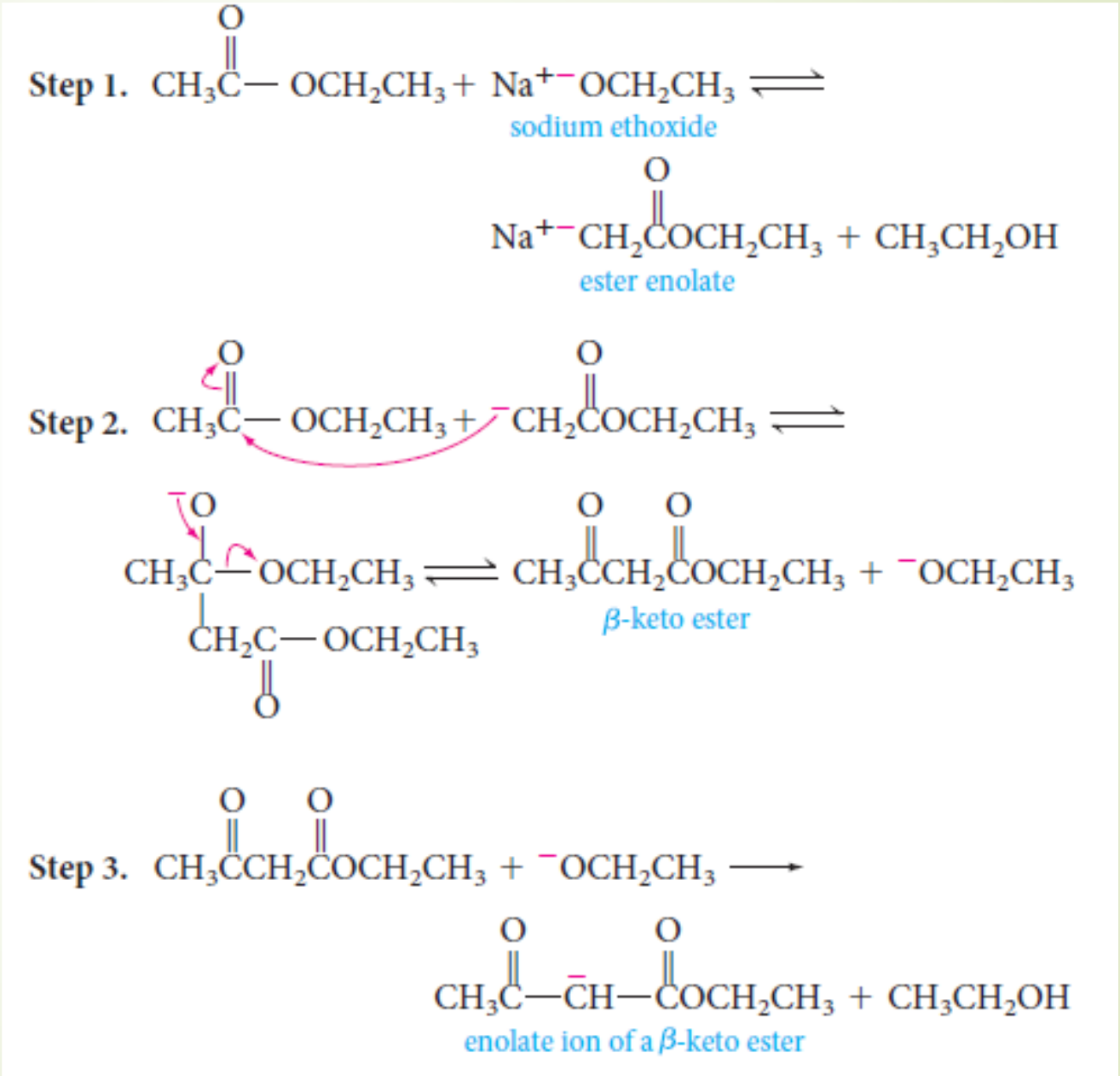
Treatment of ethyl acetate with sodium ethoxide in ethanol produces the *β*-keto ester, ethyl acetoacetate:



The Claisen Condensation

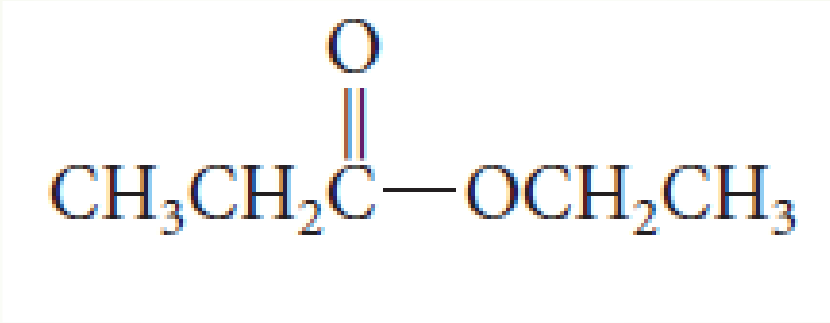
The Claisen condensation takes place in three steps (Mechanism)

To complete the Claisen condensation, the solution is acidified, to regenerate the *β*-keto ester from its enolate anion

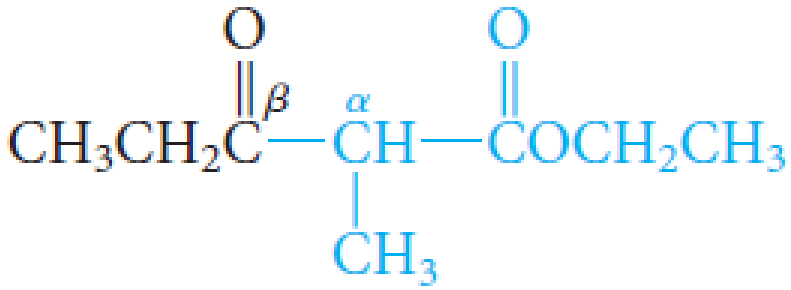


The Claisen Condensation

Example: Identify the product of the Claisen condensation of ethyl propanoate

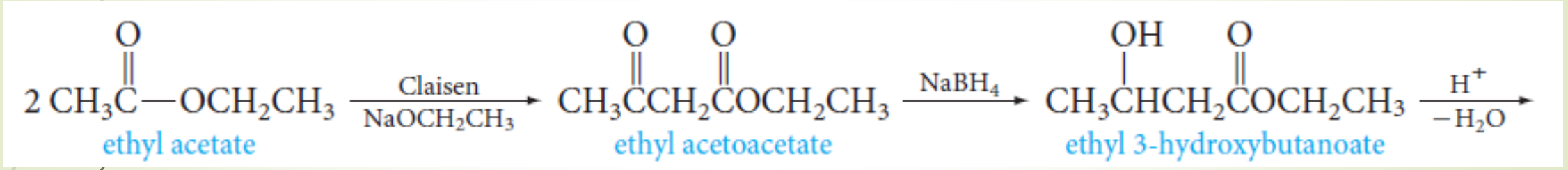


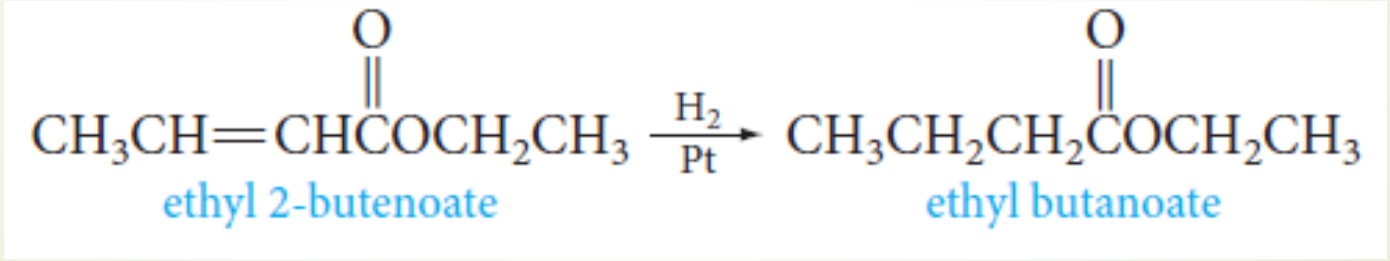
Solution The product is



The Claisen Condensation

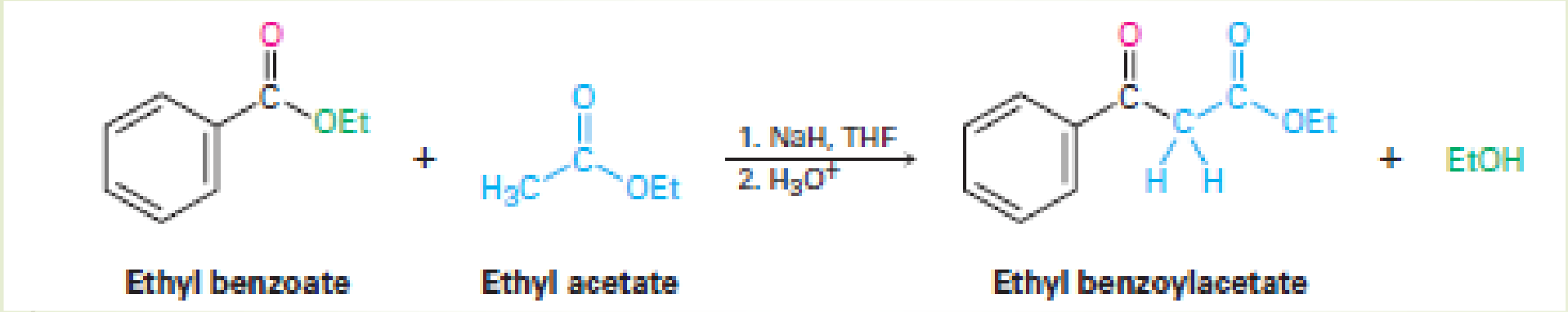
The Claisen condensation, like the aldol condensation, is useful for making new carbon–carbon bonds. The resulting β-keto esters can be converted to a variety of useful products. For example, ethyl acetate can be converted to ethyl butanoate by the following sequence





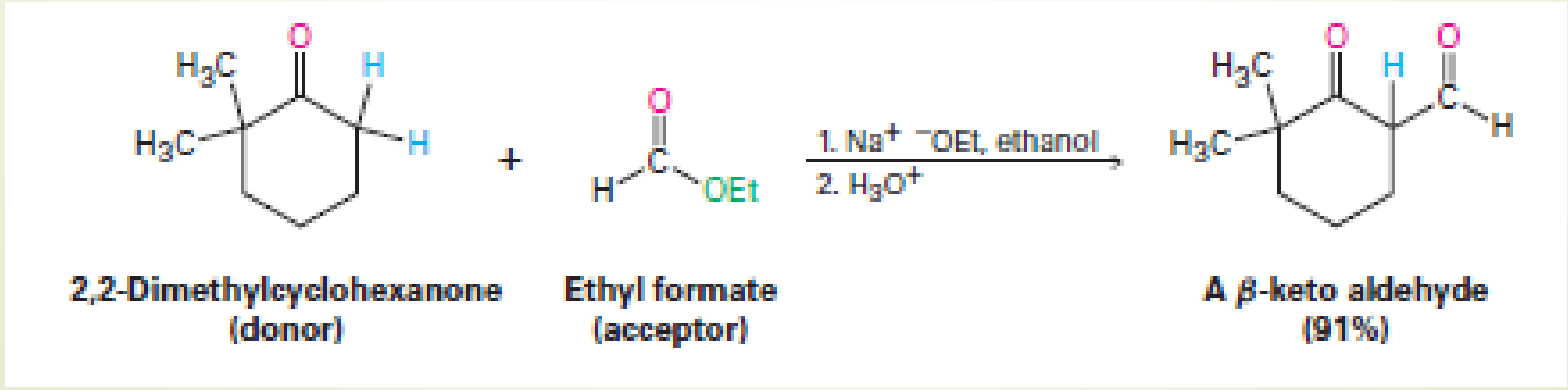
Mixed Claisen Condensations

The mixed Claisen condensation of two different esters



Ethyl benzoate + Ethyl acetate → Ethyl benzoylacetate + EtOH

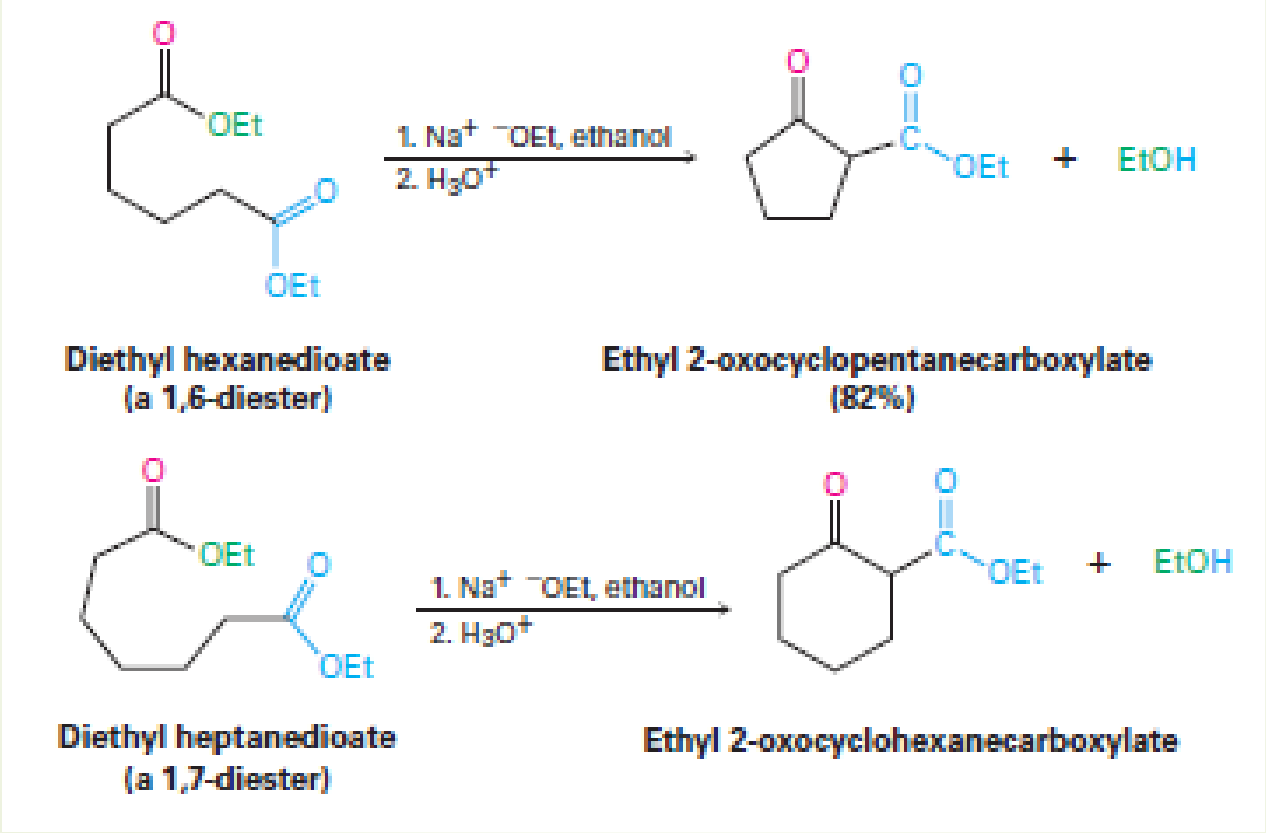
Mixed Claisen-like reactions can also be carried out between an ester and a ketone, resulting in the synthesis of a *b*-diketone.



2,2-Dimethylcyclohexanone (donor) + Ethyl formate (acceptor) → A β-keto aldehyde (91%)

Intramolecular Claisen Condensations: The Dieckmann Cyclization

Intramolecular Claisen condensations can be carried out with diesters



Dieckmann cyclization, the reaction works best on 1,6-diesters and 1,7-diesters. Intramolecular Claisen cyclization of a 1,6-diester gives a five-membered cyclic *b*-keto ester, and cyclization of a 1,7-diester gives a six-membered cyclic *b*-keto ester.

د. أحمد متنبي عبدالله

Mechanism of the Dieckmann cyclization of a 1,7-diester to yield a cyclic *b*-keto ester product.