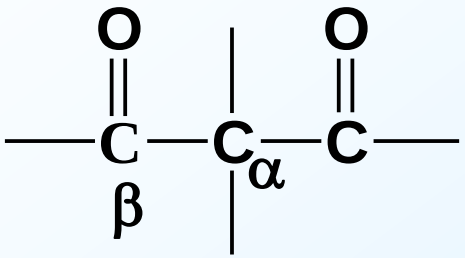
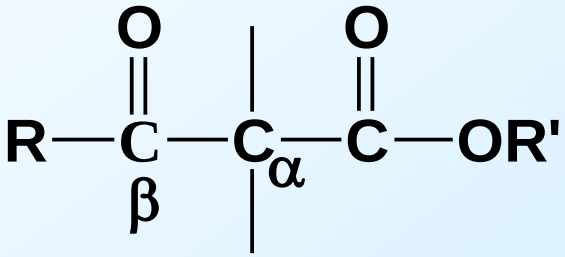
β-Dicarbonyl compounds

Compounds having two carbonyl groups separated by an intervening carbon atom are called β-dicarbonyl compounds, and these compounds are highly versatile reagents for organic synthesis.

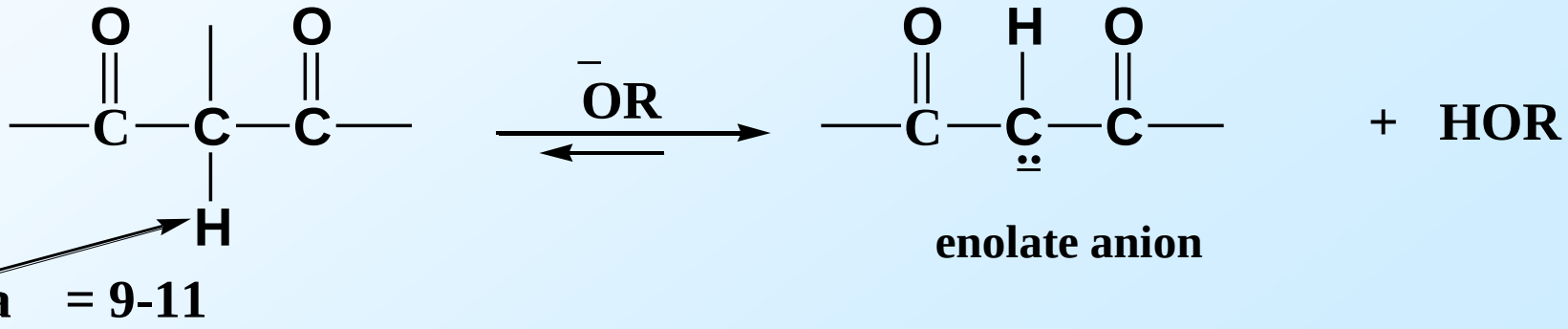


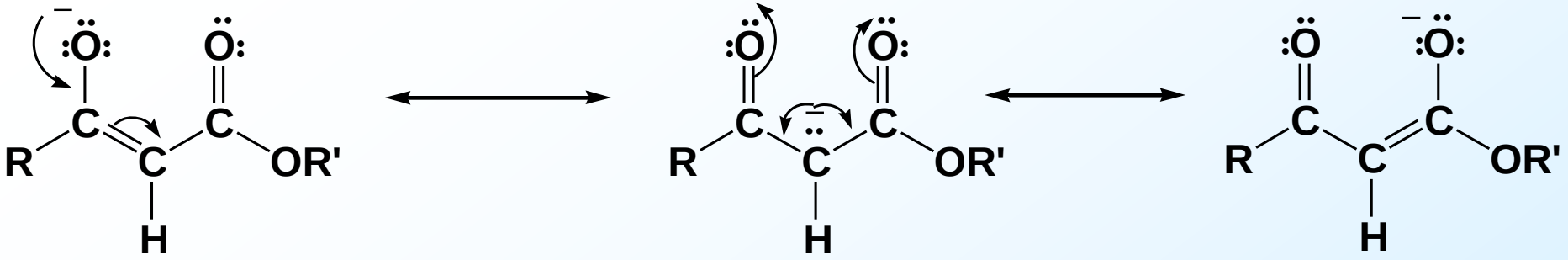
β-Dicarbonyl system



β-Keto ester

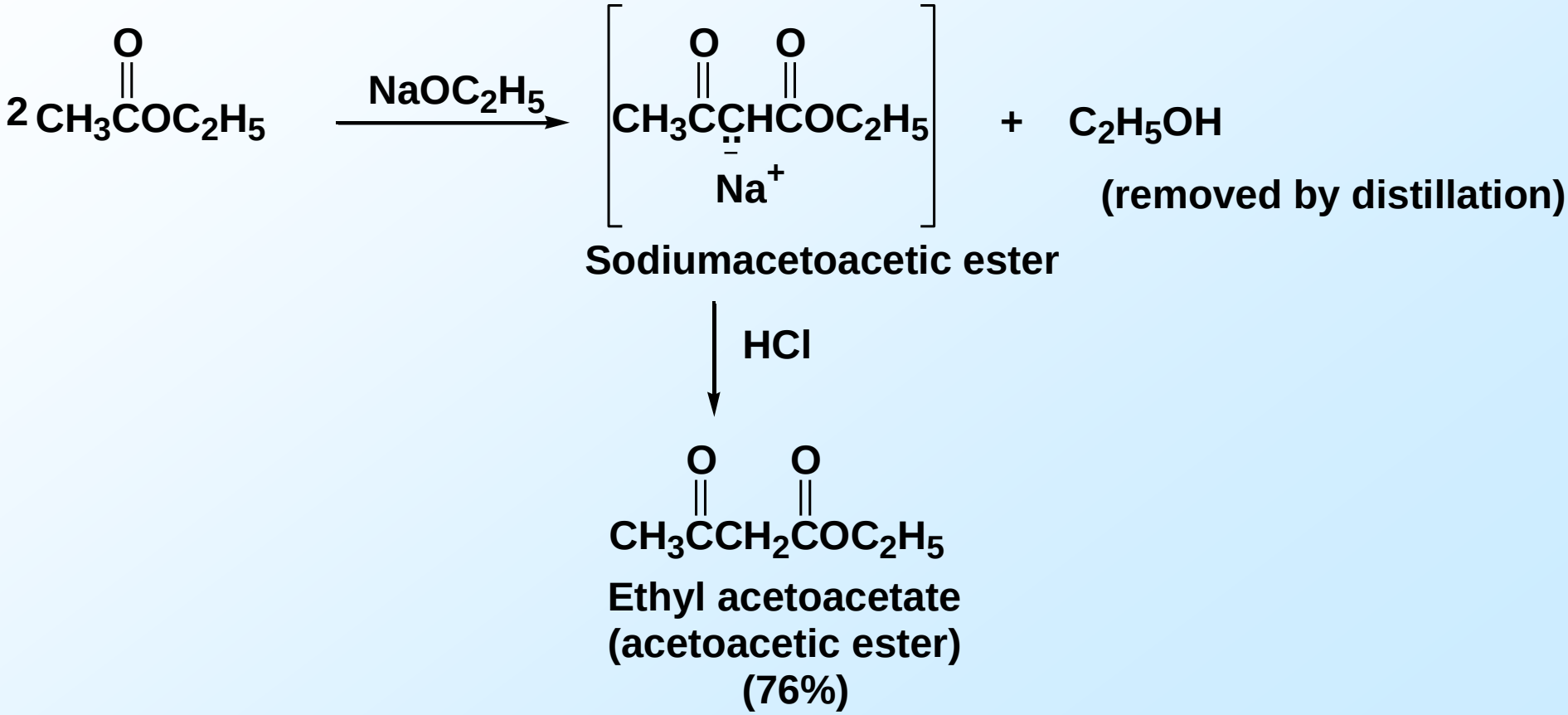
** The p*K*a for such a proton is in the range 9-11, acidic enough to be removed easily by an alkoxide base to form an enolate.

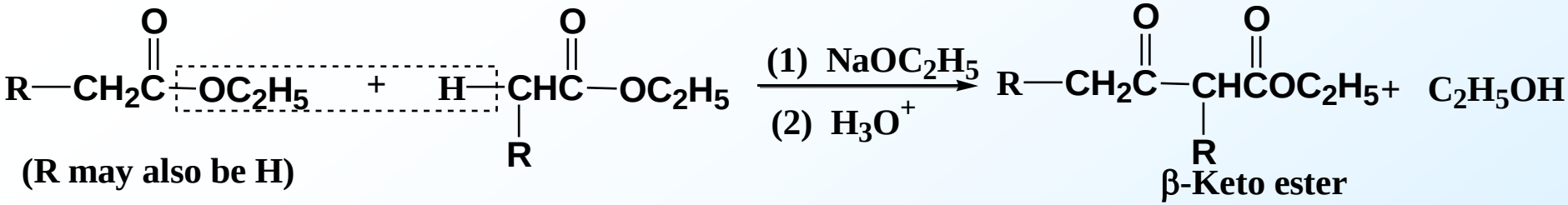




Resonance structure of the anion of a β-keto ester

Synthesis of β-keto ester (Claisen condensation)



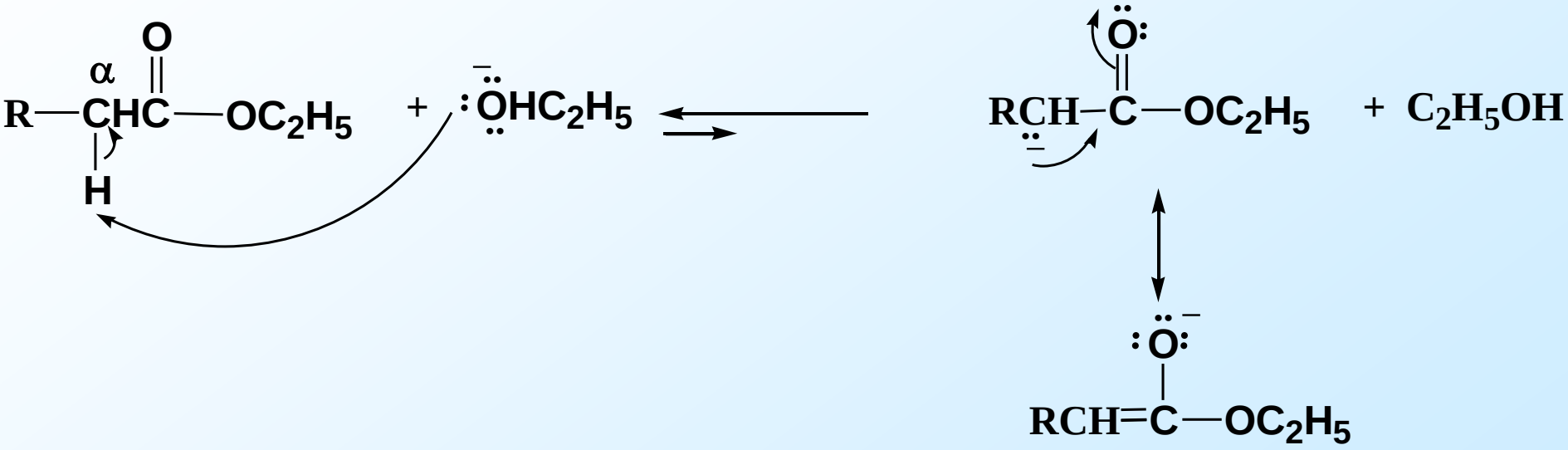


(R may also be H)

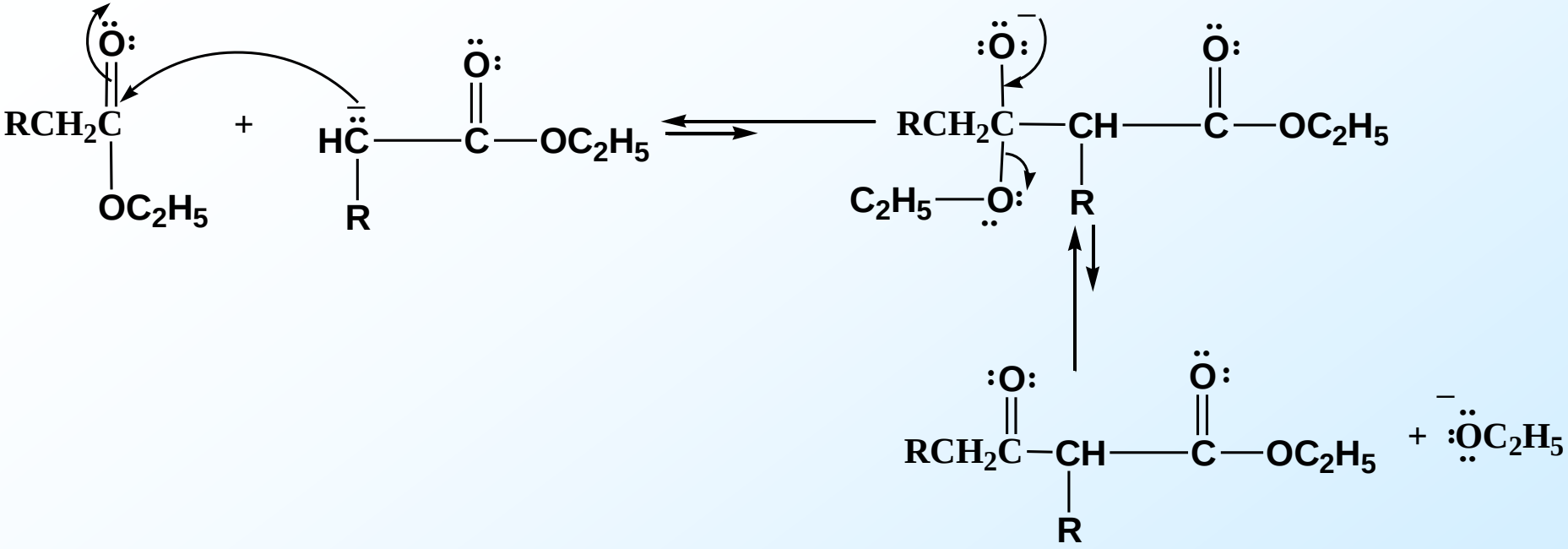
β-Keto ester

Mechanism

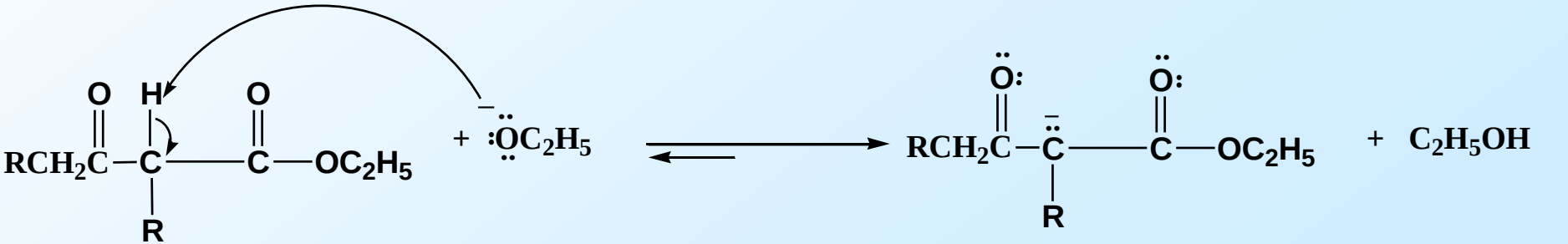
Step1



Step 2



Step 3

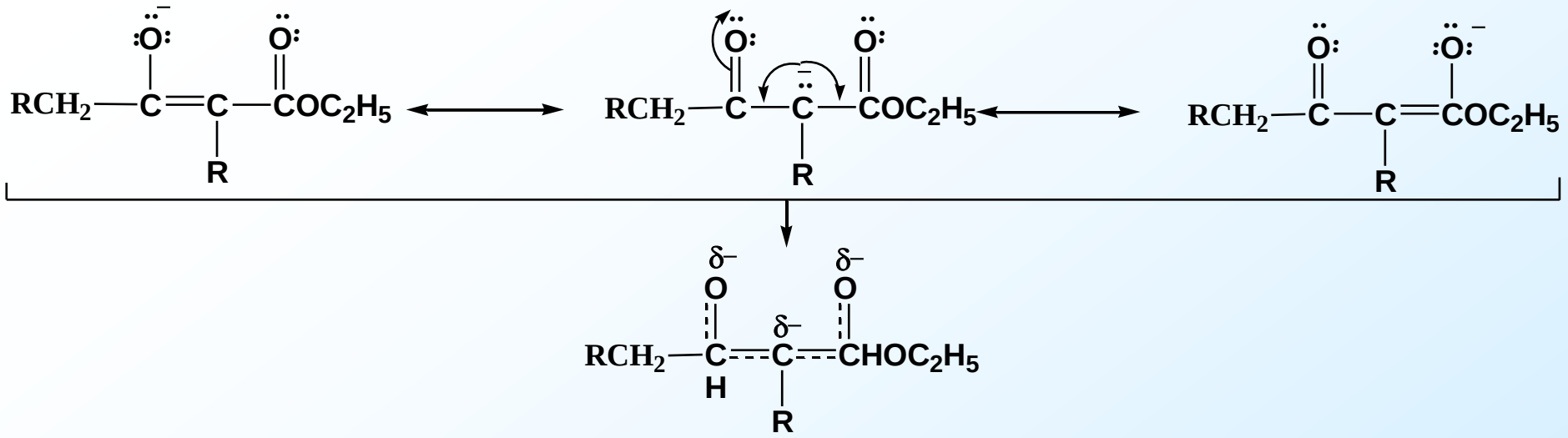


β-Keto ester (strong acid)

Ethoxide ion (stronger base)

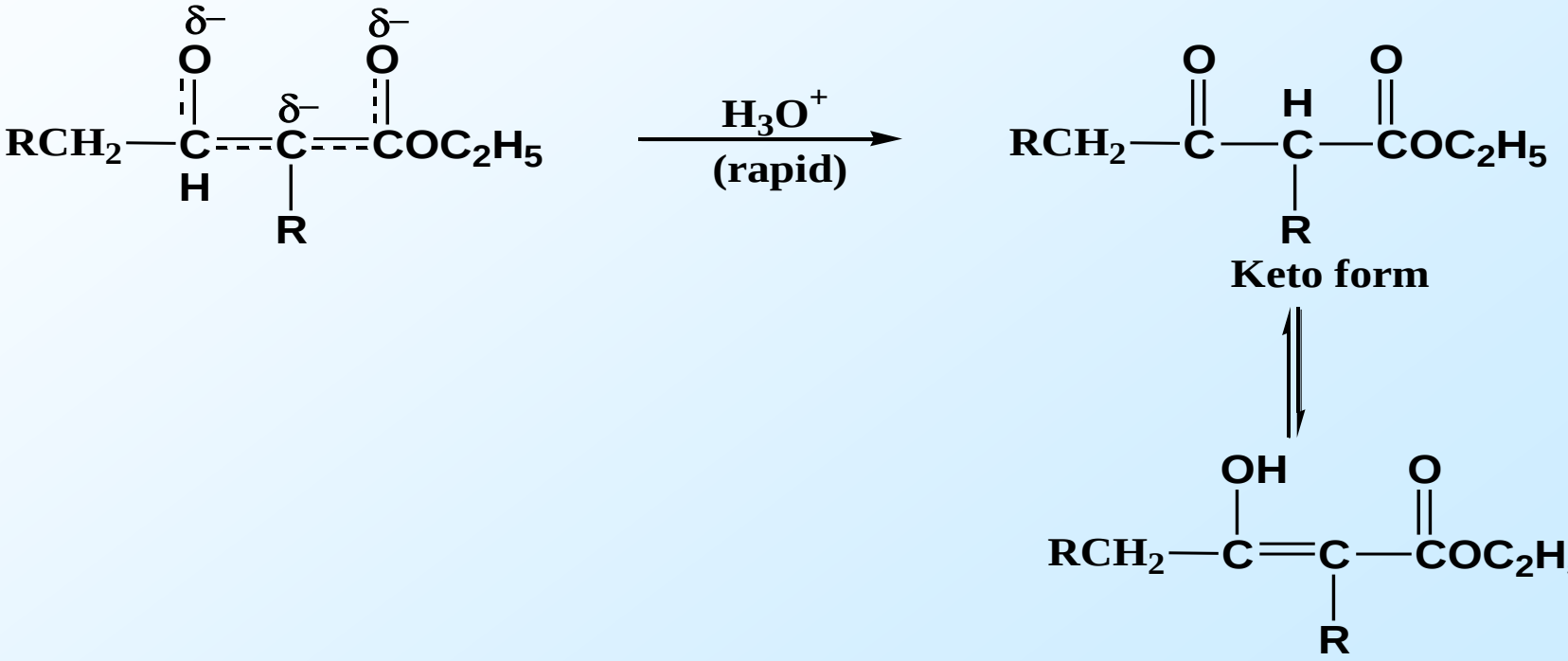
β-Keto ester anion (weaker base)

Ethanol (weaker acid)



Step 4

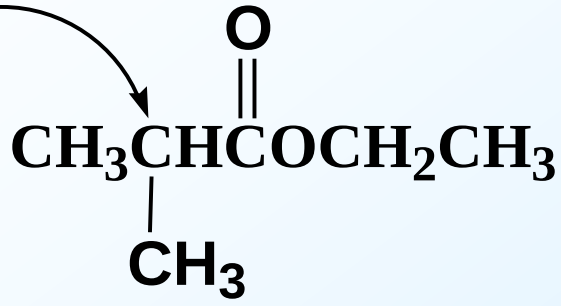
Resonance hybrid



Keto form

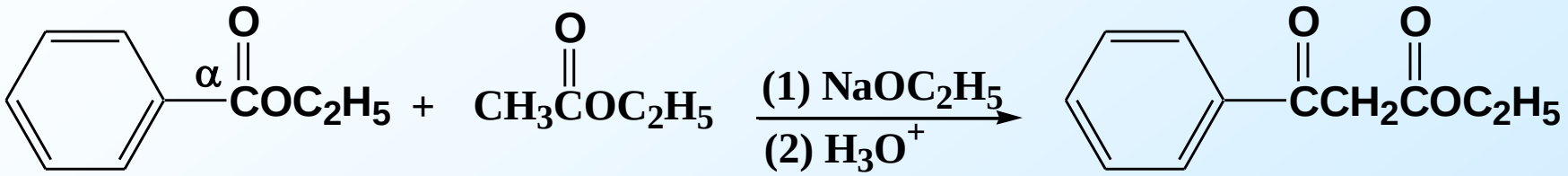
Enol form

Only one α hydrogen



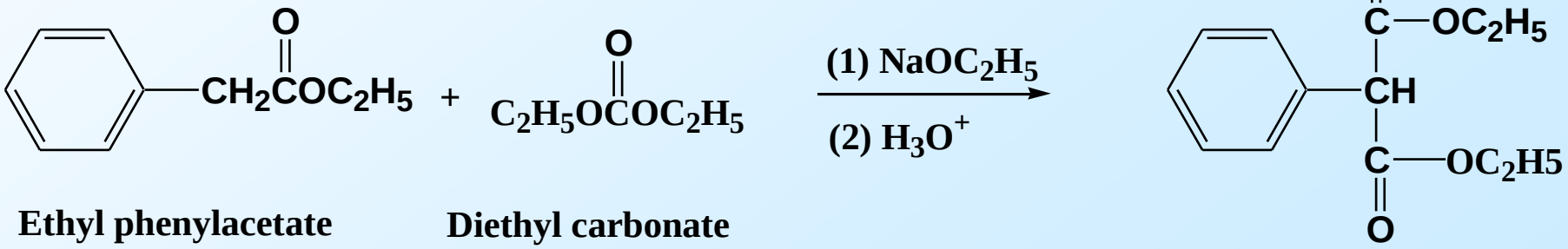
Ethyl-2-methylpropanoate

Crossed Claisen condensations



Ethyl benzoate
(no α hydrogen)

Ethyl benzoylacetate (60%)



Ethyl phenylacetate

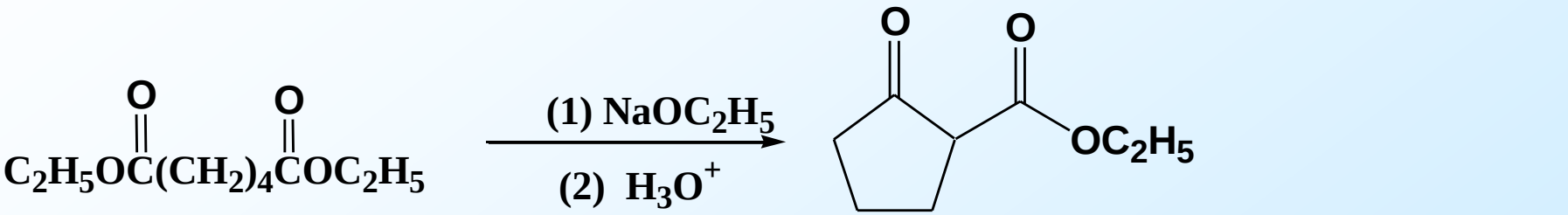
Diethyl carbonate
(no α carbon)

Diethyl phenylmalonate
(65%)

Dieckmann condensation

It is an intramolecular Claisen condensation. The α carbon atom and the ester group for the condensation come from the same molecule.

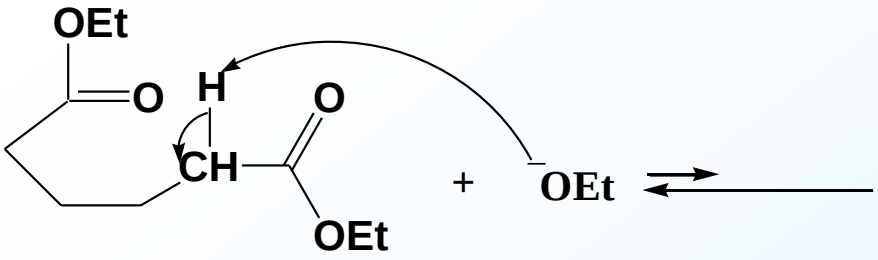
**** In general, Dieckmann condensation is useful only for the preparation of five- and six-membered rings.**



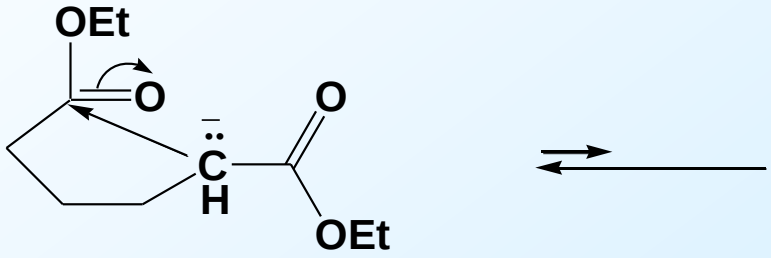
Diethyl hexanedioate (diethyl adipate)

Ethyl 2-oxocyclopentanecarboxylate (74-81%)

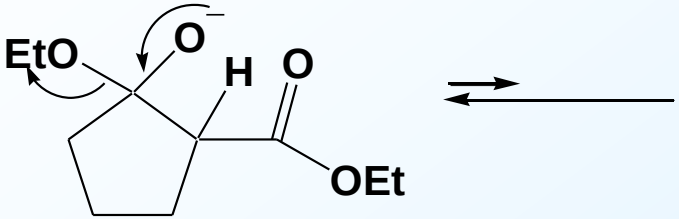
Mechanism



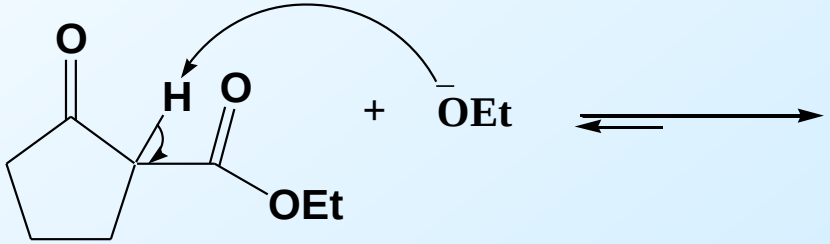
Ethoxide anion removes an α hydrogen



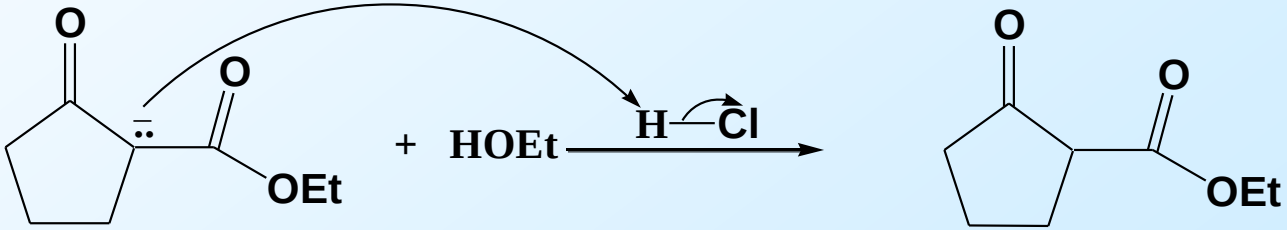
The enolate anion attacks the carbonyl group at the other end of the chain



An ethoxide anion is expelled



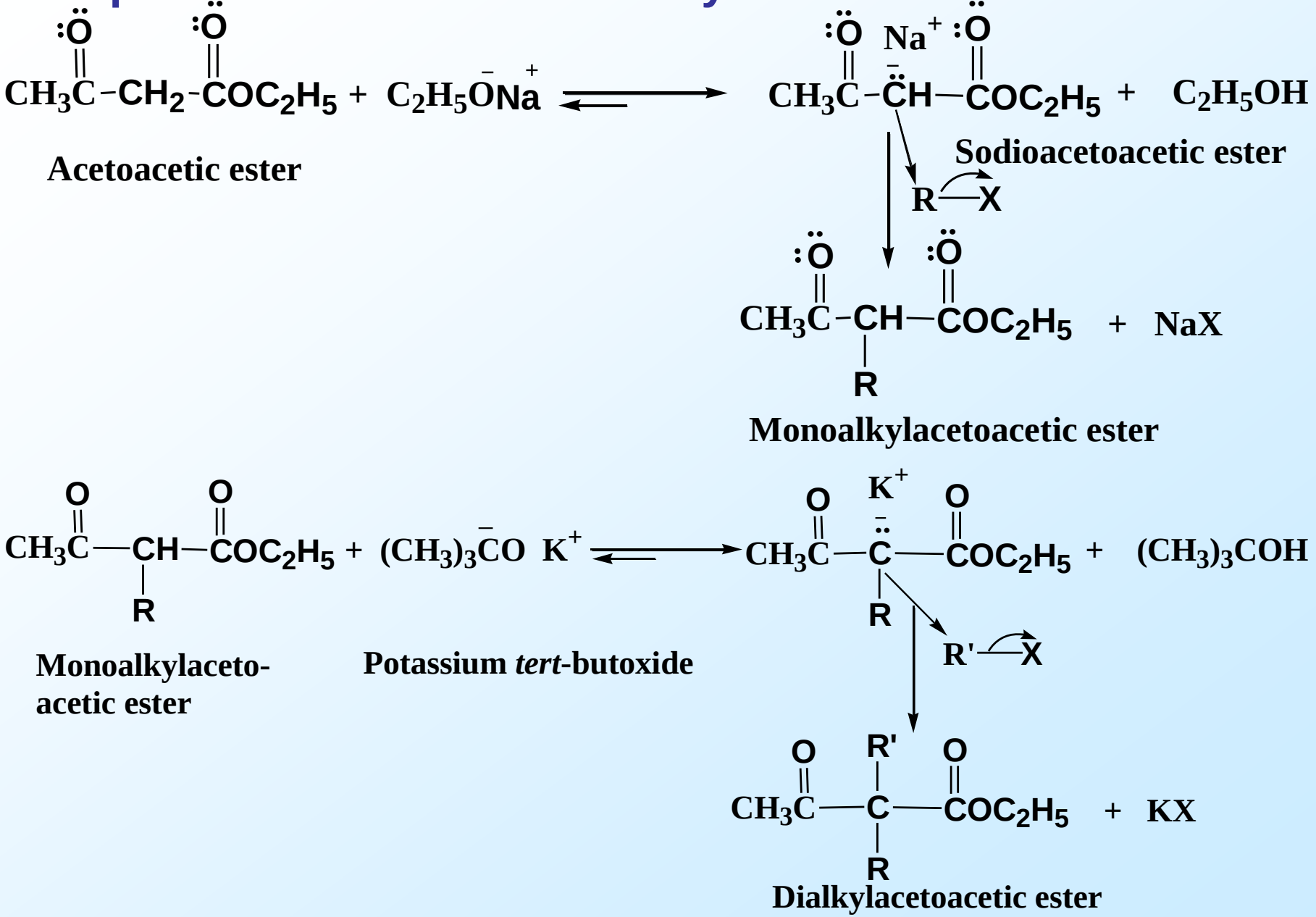
The ethoxide anion removes the acidic hydrogen located between two carbonyl groups. This favorable equilibrium drives the reaction.



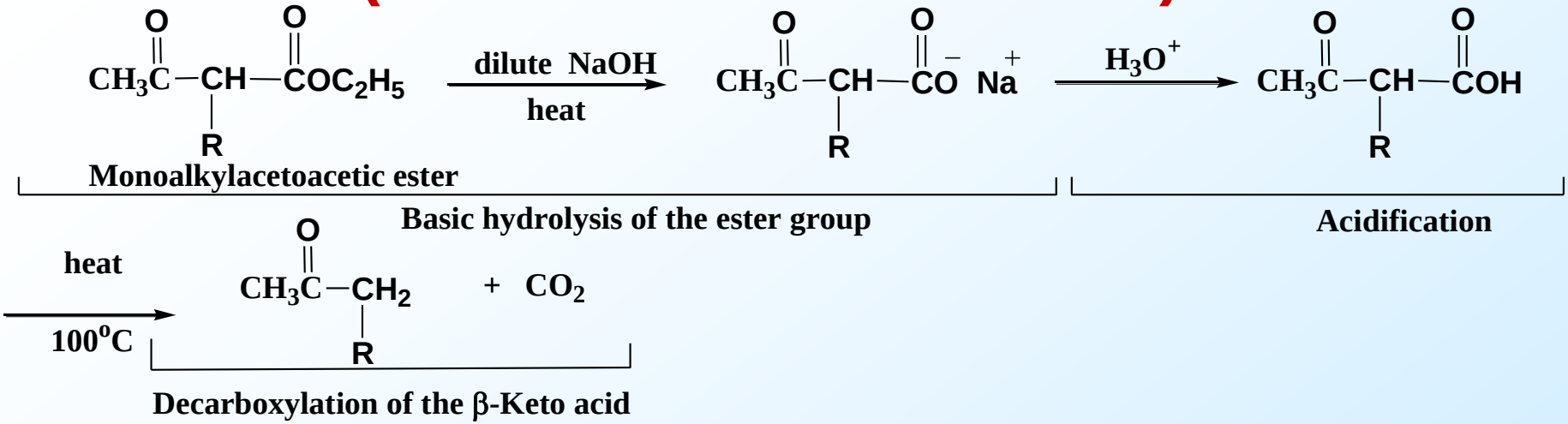
Addition of HCl rapidly protonates the anion, giving the final product.

Acetoacetic ester synthesis utility

1- Preparation of mono and dialkylacetoacetic ester

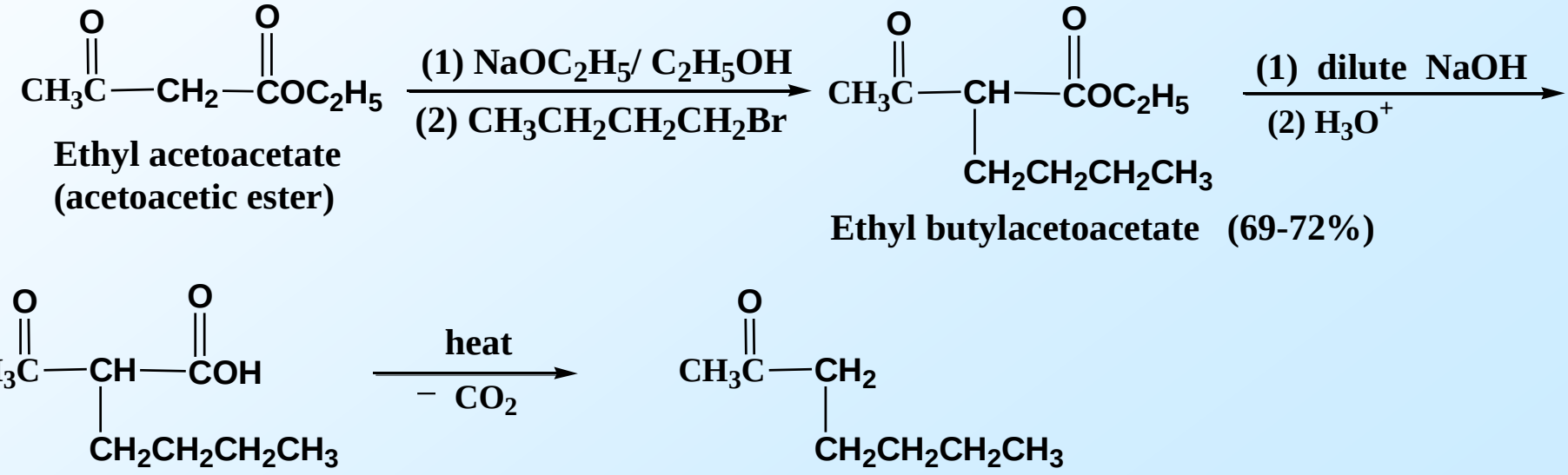


2- Synthesis of monosubstituted methyl ketone (monosubstituted acetone)



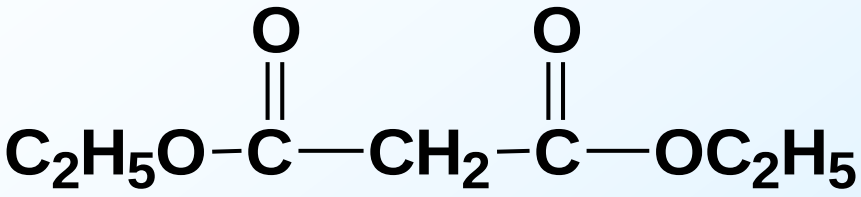
Specific examples

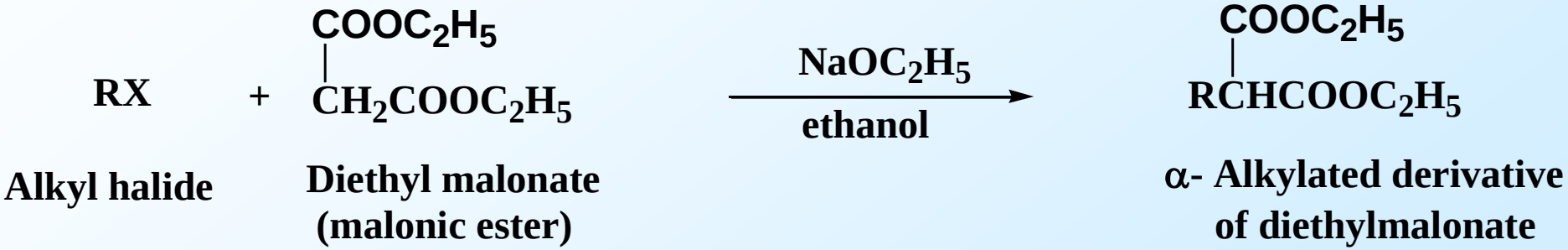
Synthesis of 2-heptanone:

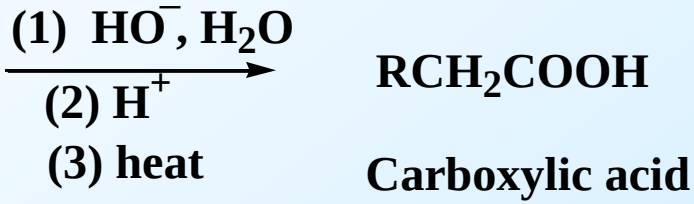


Utility of malonic ester synthesis (synthesis of substituted acetic acid)

1- Preparation of carboxylic acid (mono and dialkylacetic acid)

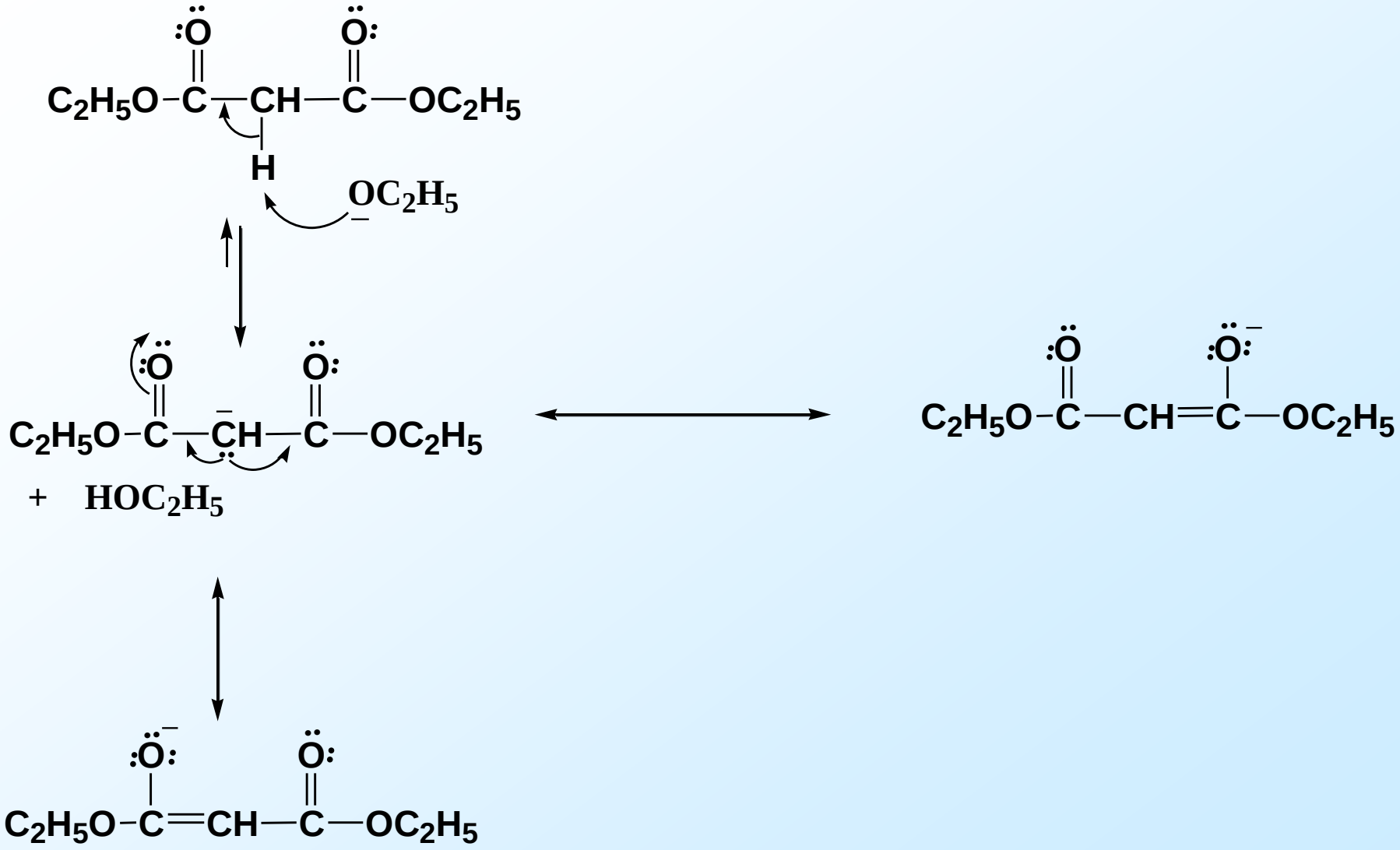




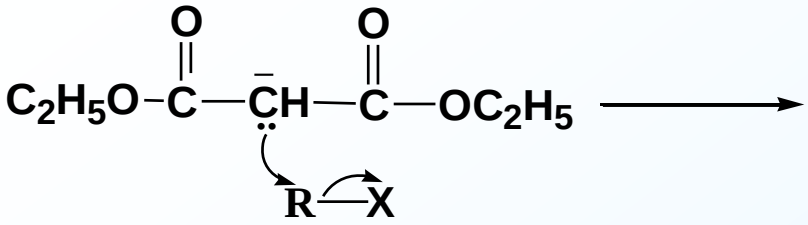


Mechanism

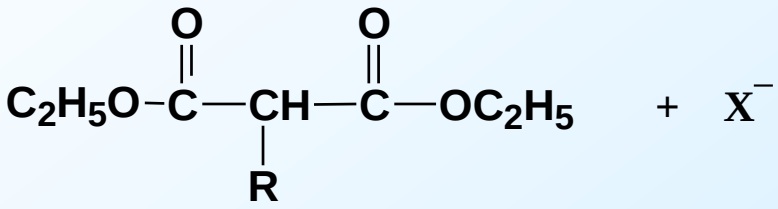
Step 1 Diethyl malonate, the starting compound, forms a relatively stable enolate anion:



Step2 This enolate anion can be alkylated in an S_N2 reaction,

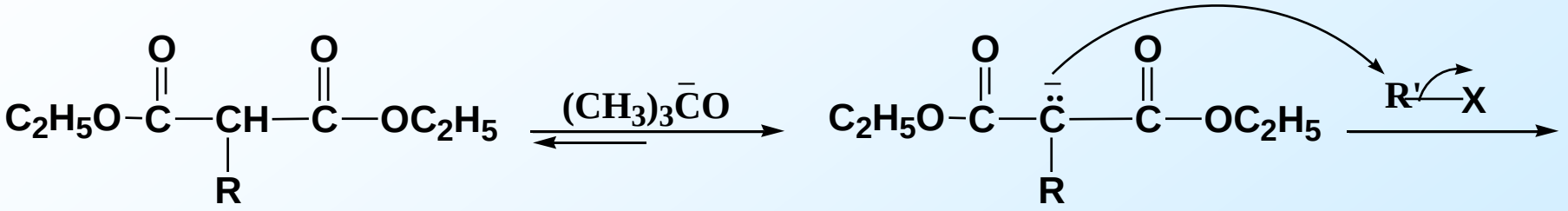


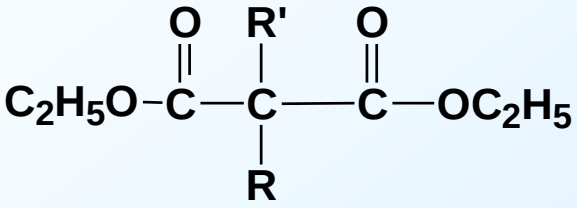
Enolate ion



Monoalkylmalonic ester

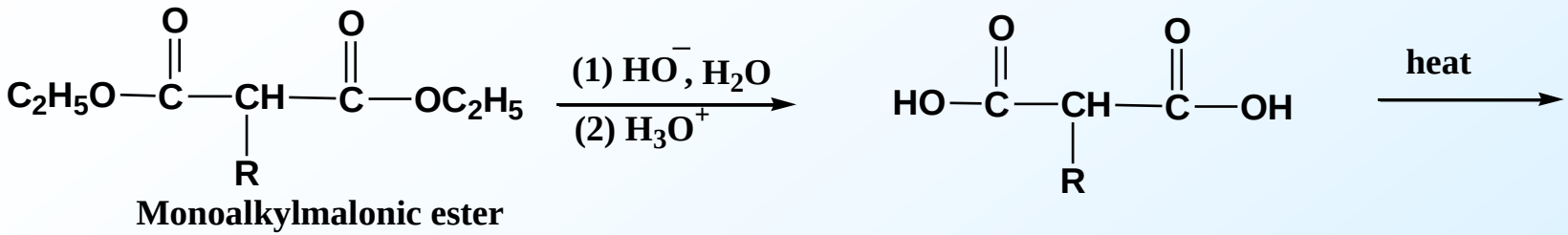
and the product can be alkylated again if our synthesis requires it:



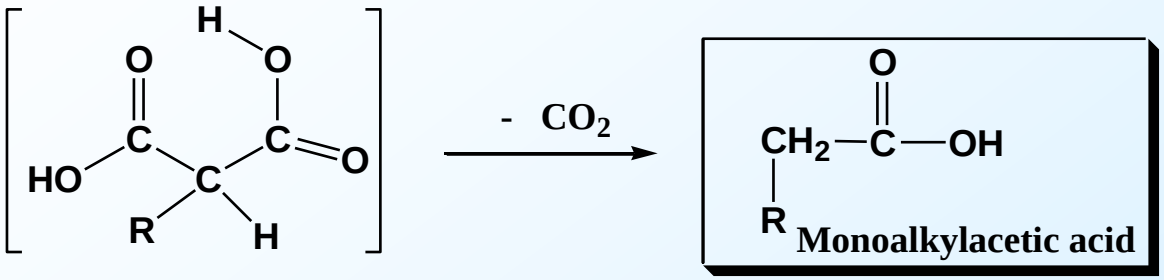


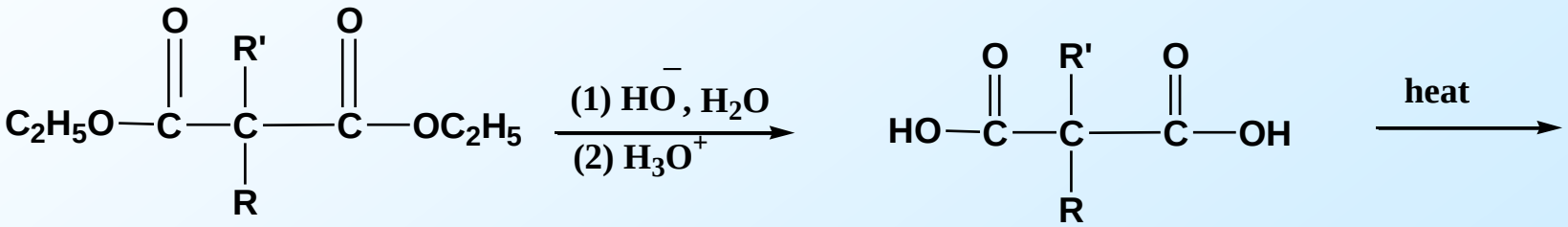
Dialkylmalonic ester

Step 3 The mono- or dialkylmalonic ester can then be hydrolyzed to a mono- or dialkylmalonic acid, and substituted malonic acids decarboxylate readily. Decarboxylation gives a mono- or disubstituted acetic acid.

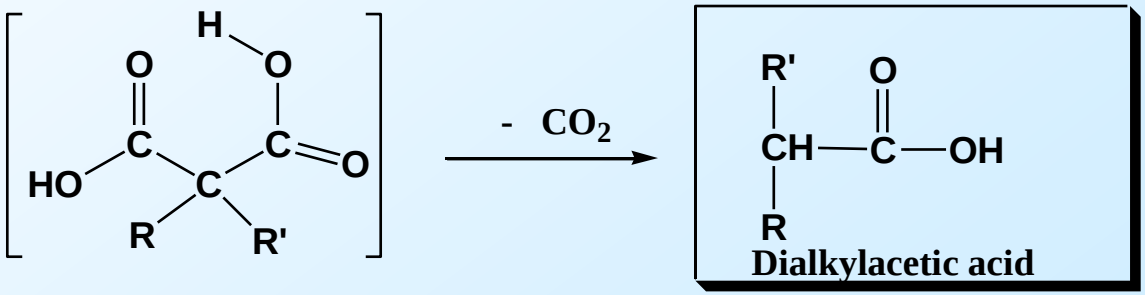


Monoalkylmalonic ester



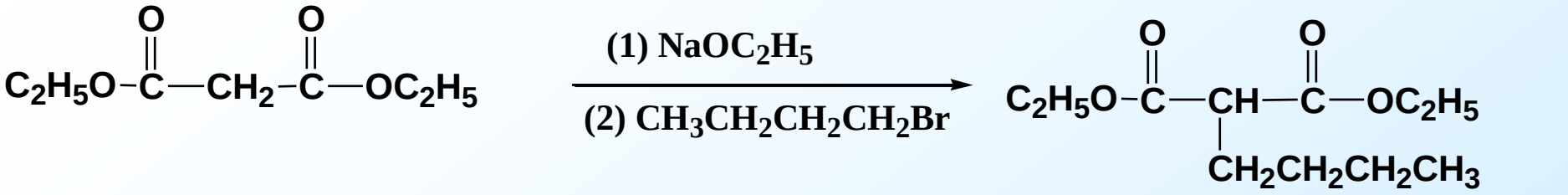


Dialkylmalonic ester

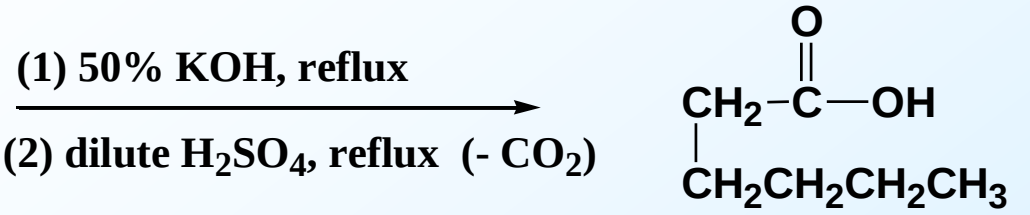


Specific examples of the malonic ester synthesis utility

1) A malonic ester utility in synthesis of hexanoic acid

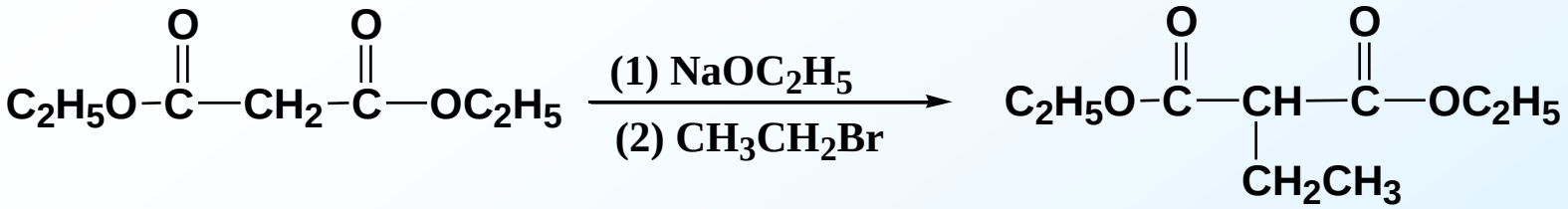


Diethyl butylmalonate (80 - 90%)

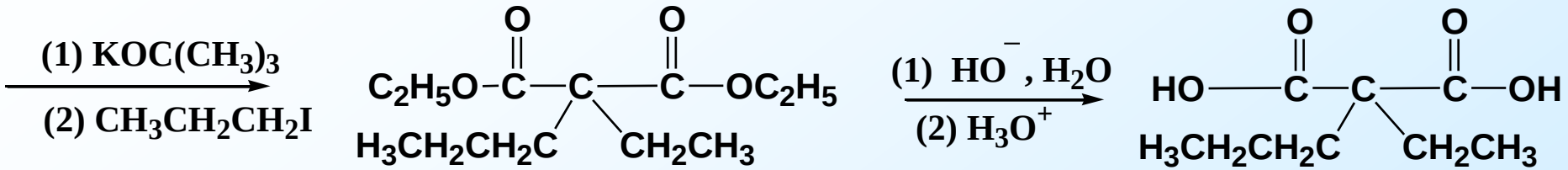


Hexanoic acid (75%)

2) A malonic ester utility in synthesis of 2-ethylpentanoic acid

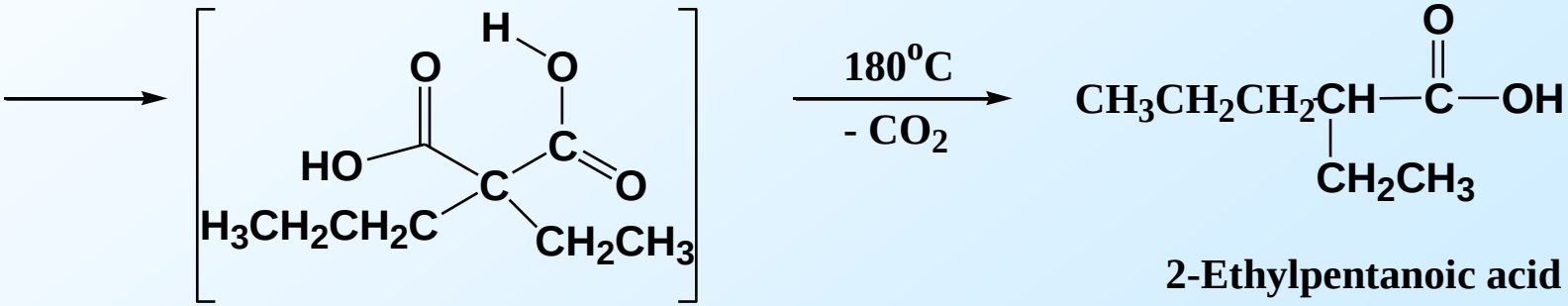


Ethyldiethylethylmalonate (80 - 90%)



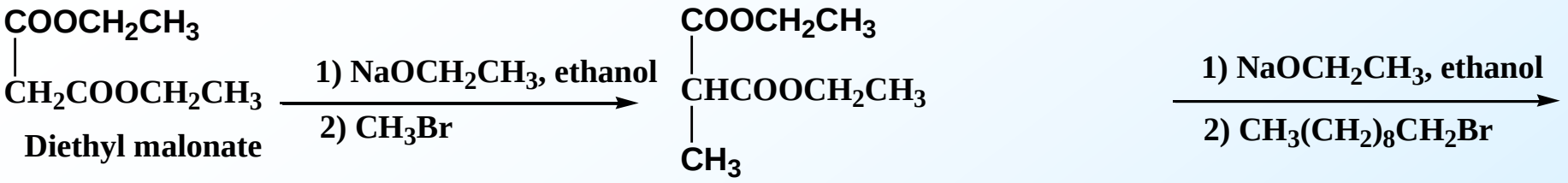
Diethyl ethylpropylmalonate

Ethylpropylmalonic acid

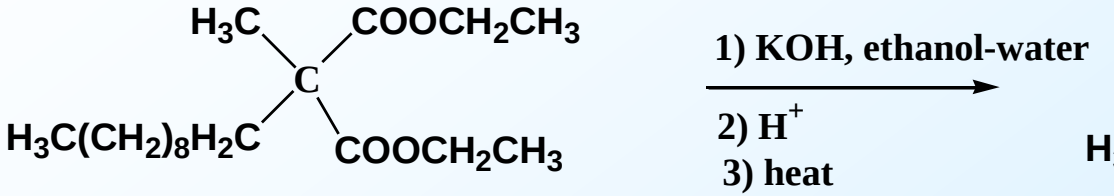


2-Ethylpentanoic acid

3) A malonic ester utility in synthesis of 2-methyldodecanoic acid



Diethyl -2-methyl-1,3-propanedioate (79-83%)



Diethyl-2-decyl-2-methyl-1,3-propanedioate

2- Methyldodecanoic acid (61-74%)