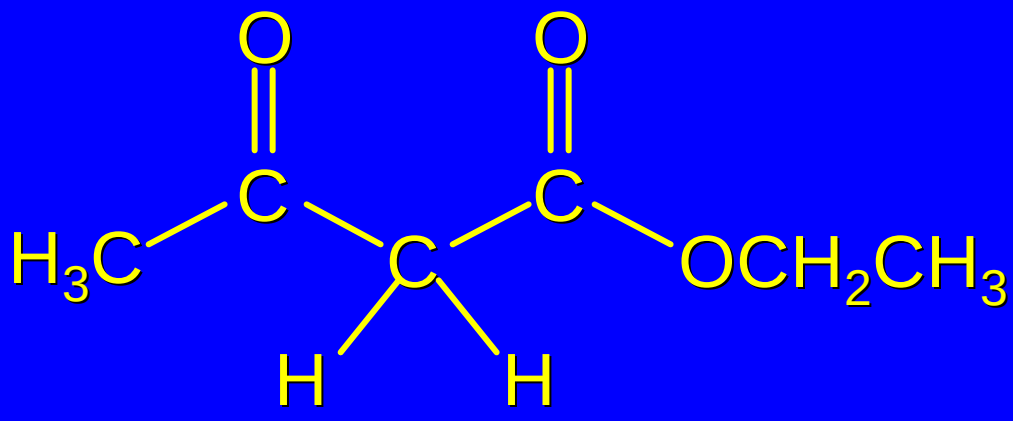
21.6

The Acetoacetic Ester Synthesis

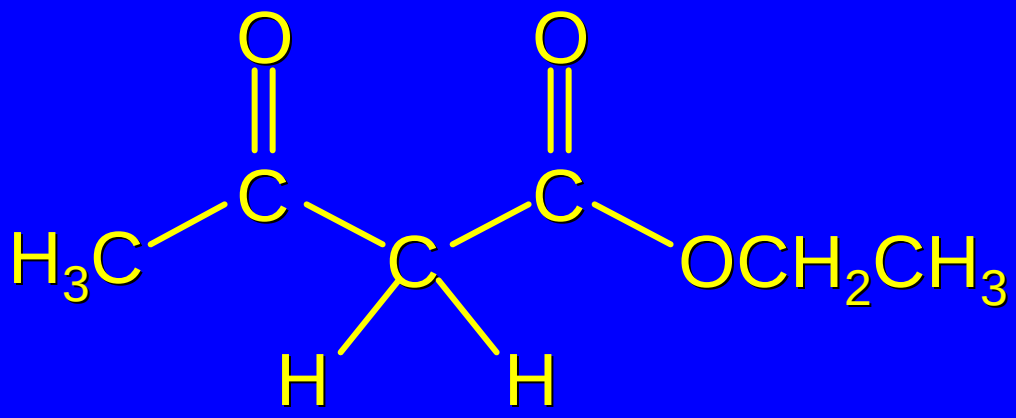
Acetoacetic Ester



Acetoacetic ester is another name for *ethyl acetoacetate*.

The "acetoacetic ester synthesis" uses acetoacetic ester as a reactant for the preparation of ketones.

Deprotonation of Ethyl Acetoacetate

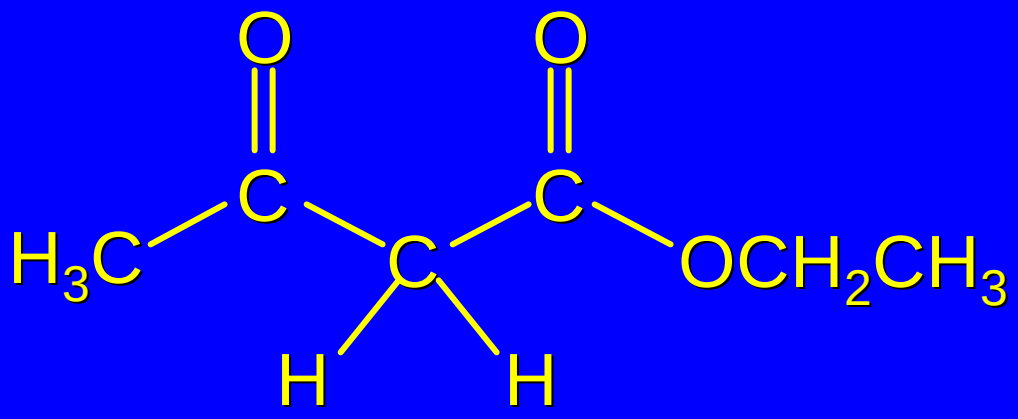


pK_a ~ 11

+ $CH_3CH_2O^-$

Ethyl acetoacetate can be converted readily to its anion with bases such as sodium ethoxide.

Deprotonation of Ethyl Acetoacetate

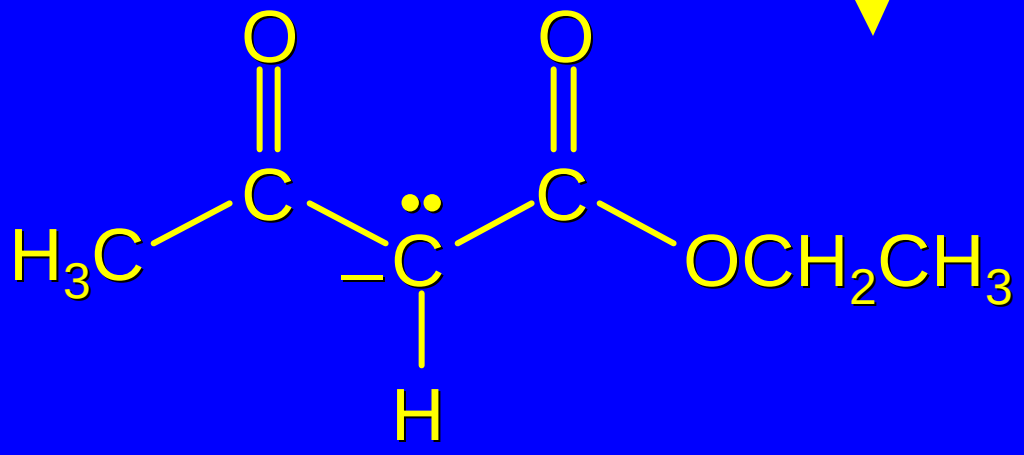


+ $CH_3CH_2O^-$

pK_a ~ 11

$K \sim 10^5$

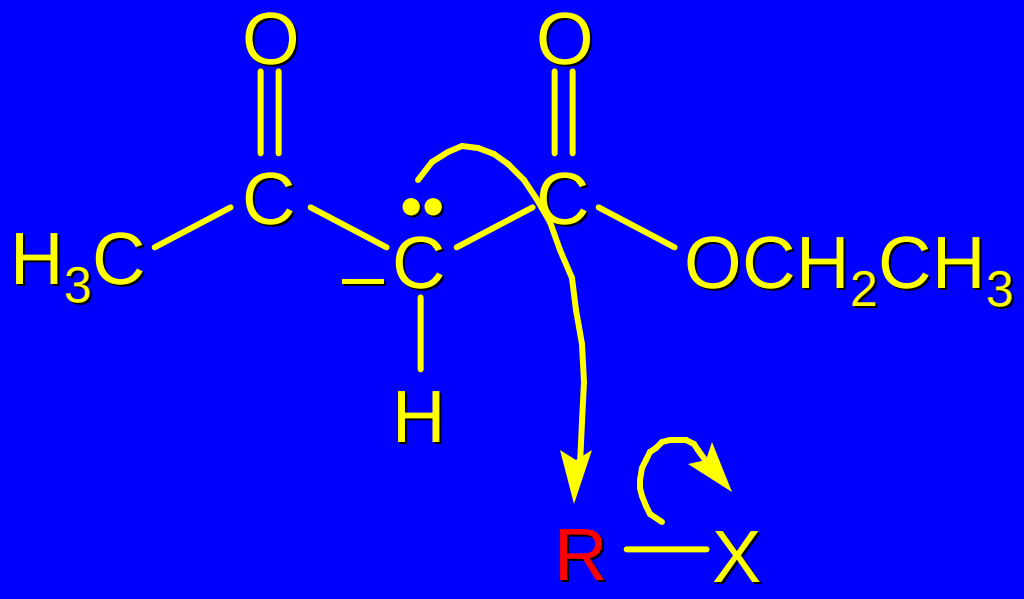
Ethyl acetoacetate can be converted readily to its anion with bases such as sodium ethoxide.



+ CH_3CH_2OH

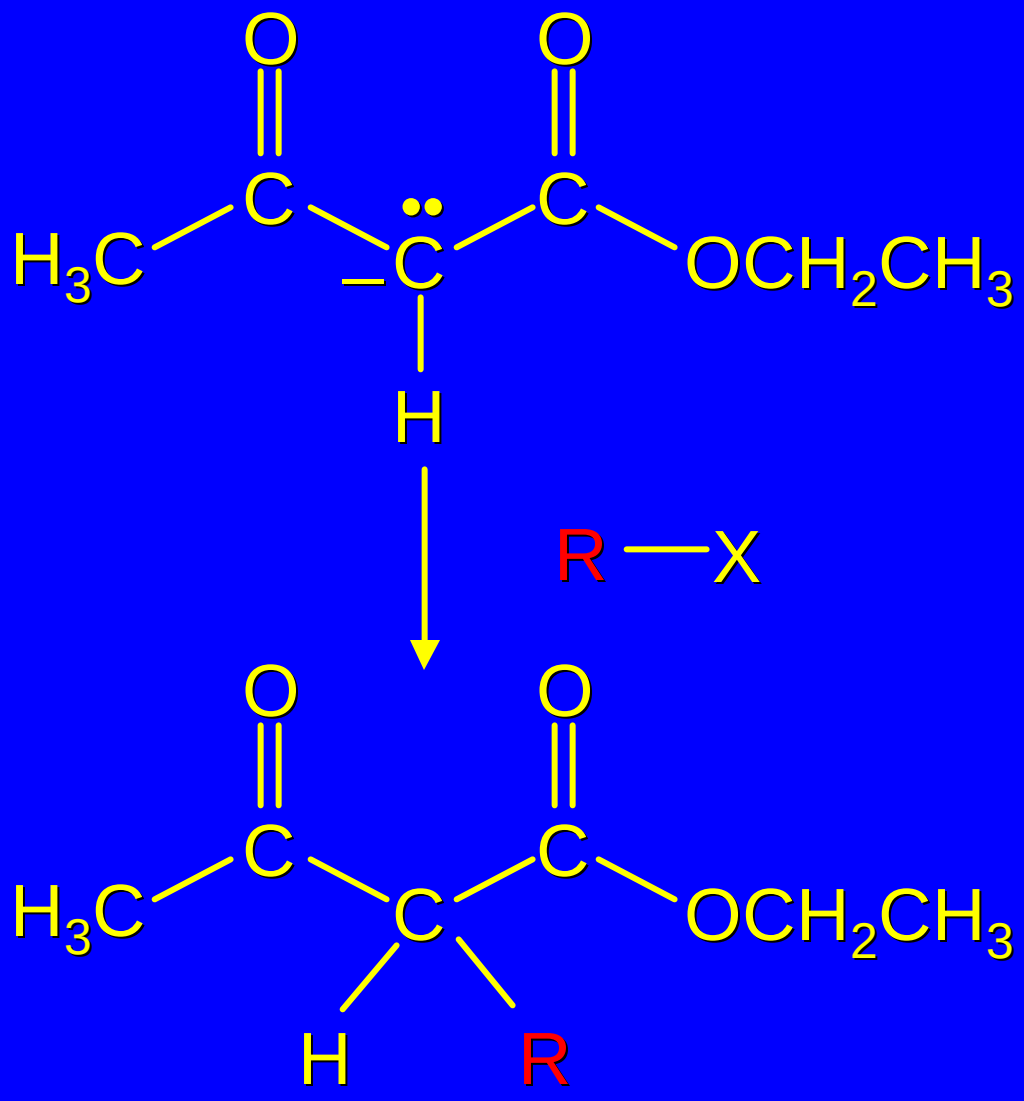
pK_a ~ 16

Alkylation of Ethyl Acetoacetate



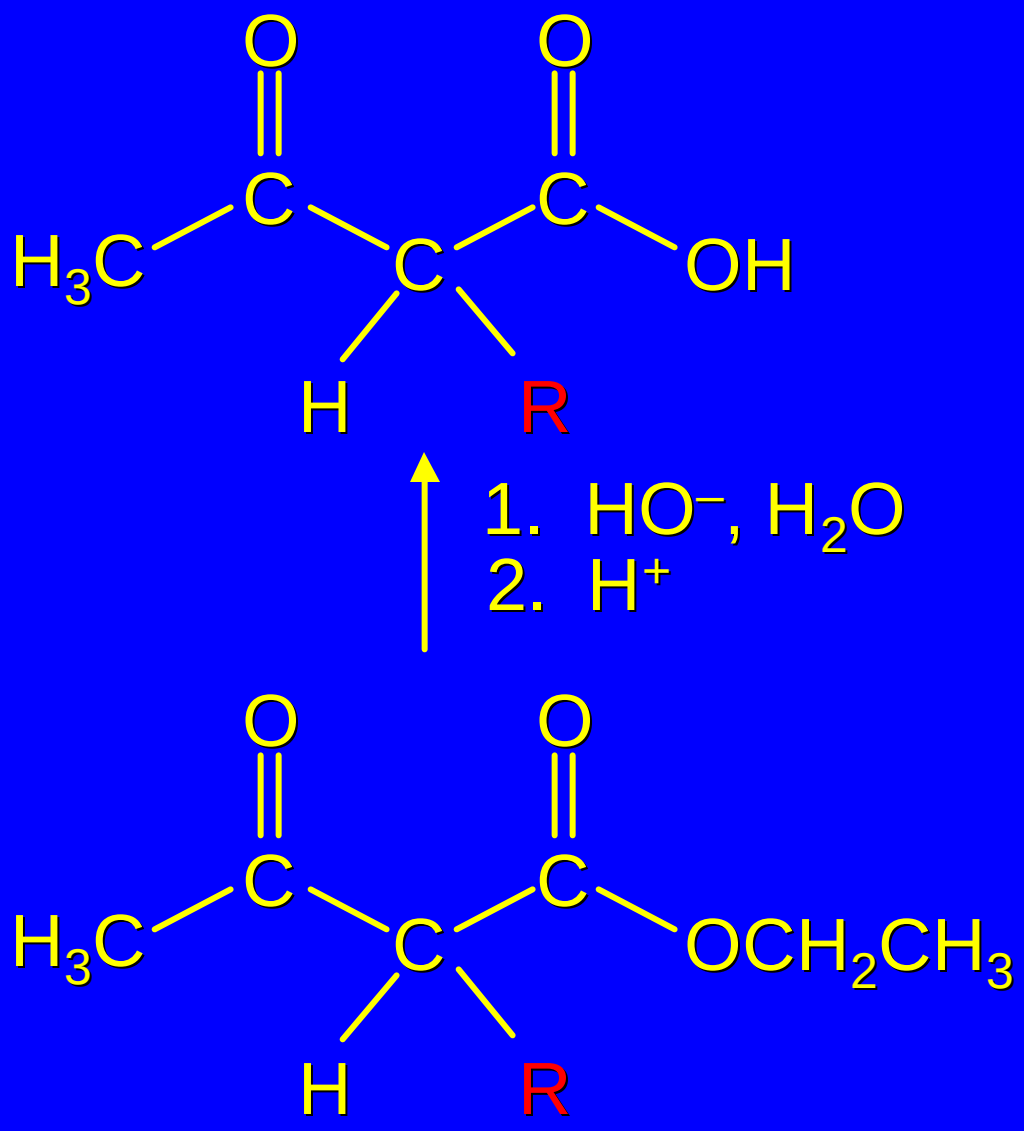
The anion of ethyl acetoacetate can be alkylated using an alkyl halide (S_N2: primary and secondary alkyl halides work best; tertiary alkyl halides undergo elimination).

Alkylation of Ethyl Acetoacetate



The anion of ethyl acetoacetate can be alkylated using an alkyl halide (S_N2: primary and secondary alkyl halides work best; tertiary alkyl halides undergo elimination).

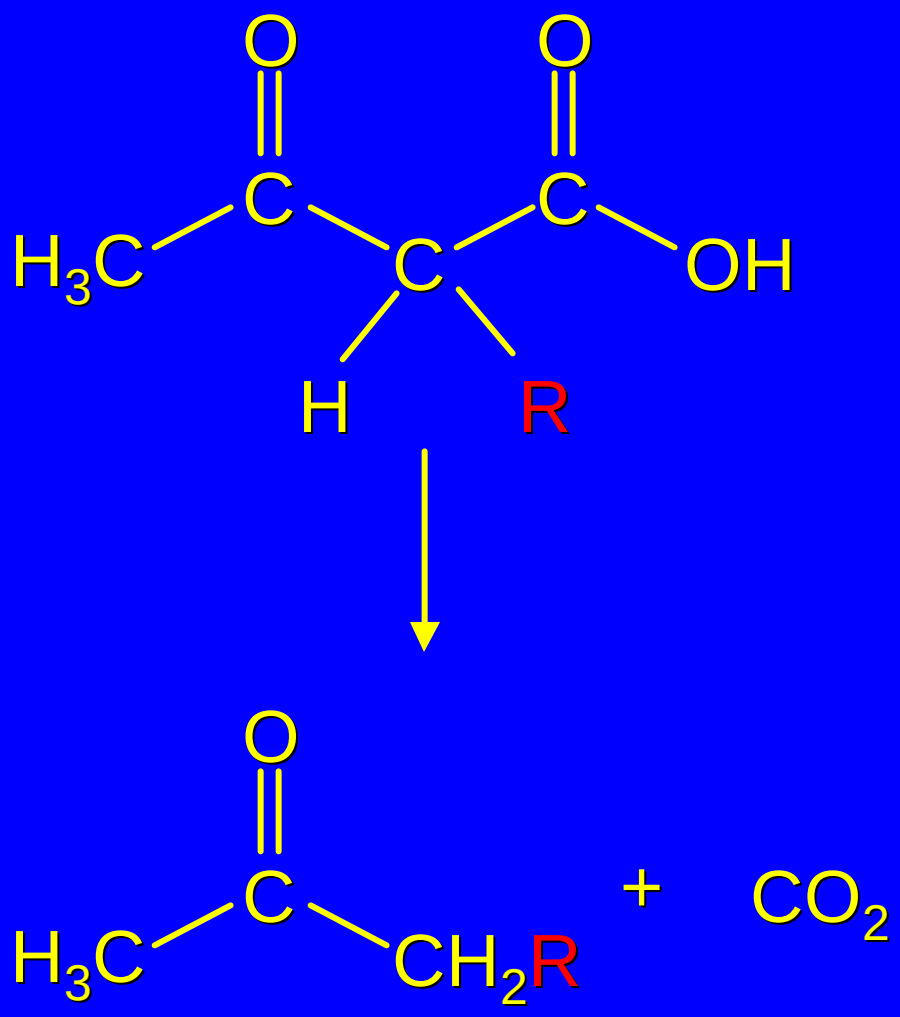
Conversion to Ketone



Saponification and acidification convert the alkylated derivative to the corresponding β-keto acid.

The β-keto acid then undergoes decarboxylation to form a ketone.

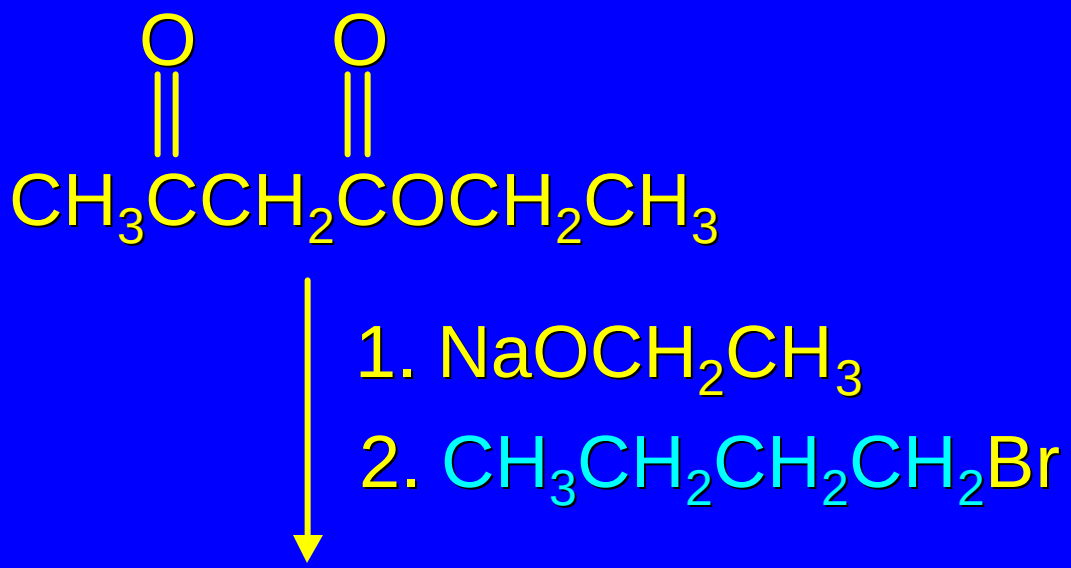
Conversion to Ketone



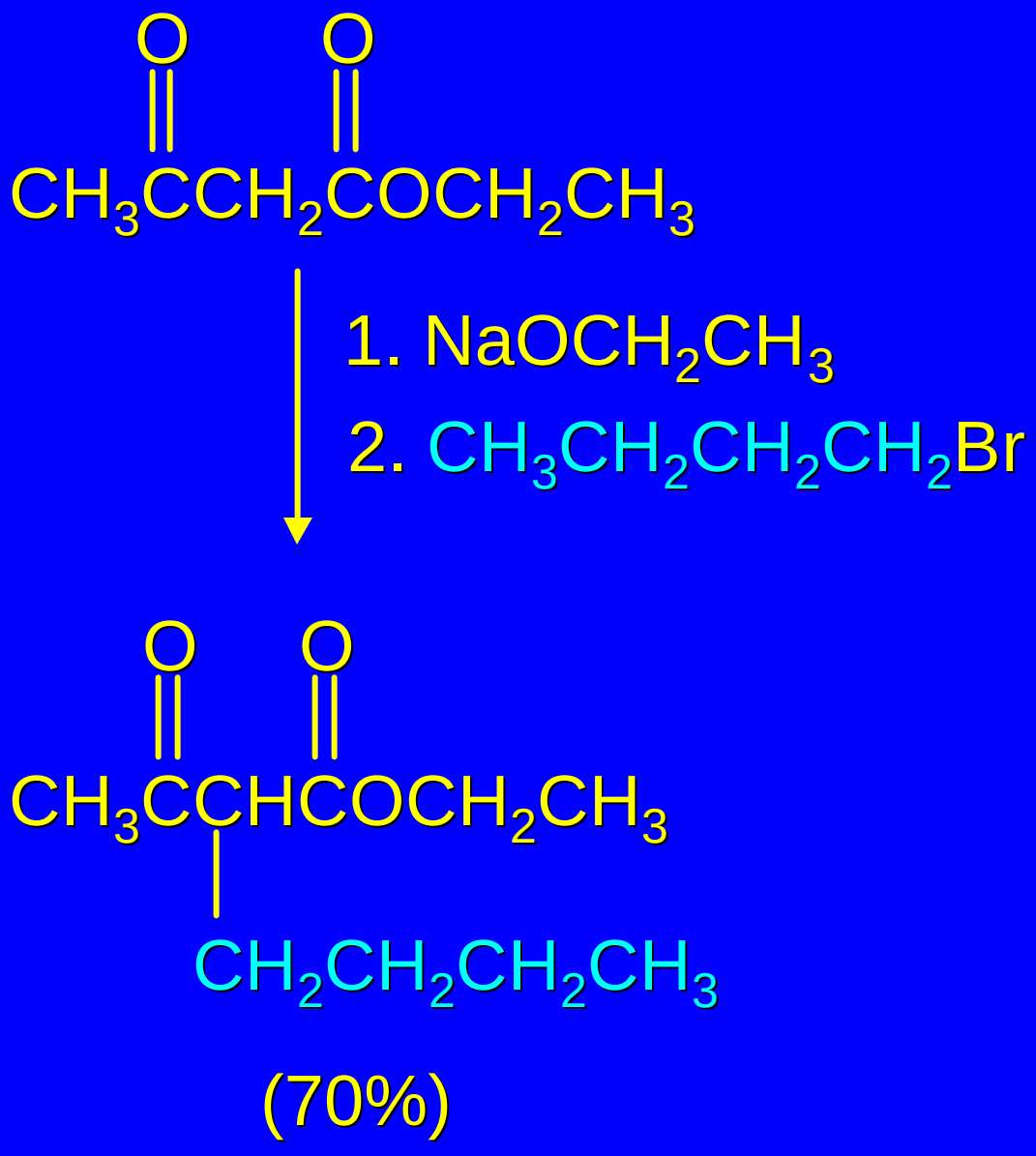
Saponification and acidification convert the alkylated derivative to the corresponding β-keto acid.

The β-keto acid then undergoes decarboxylation to form a ketone.

Example

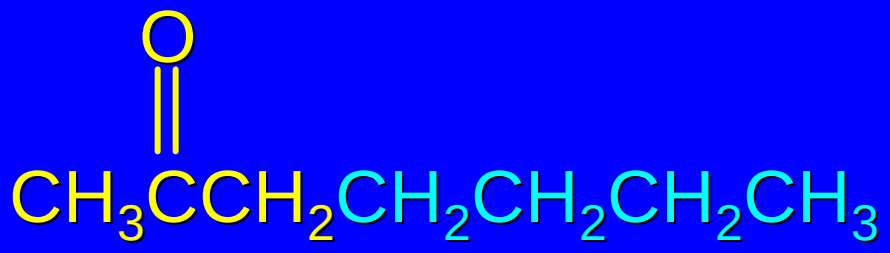


Example


CH3CCH2COCH2CH3
1. NaOCH2CH3
2. CH3CH2CH2CH2Br
CH3CCHCOCH2CH3
CH2CH2CH2CH3

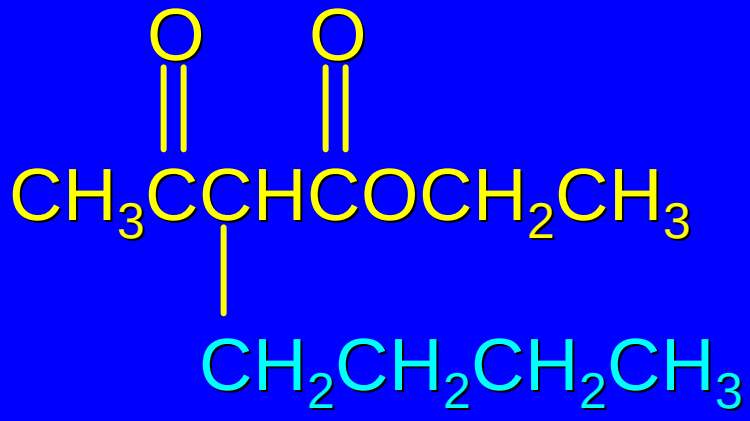
(70%)

Example

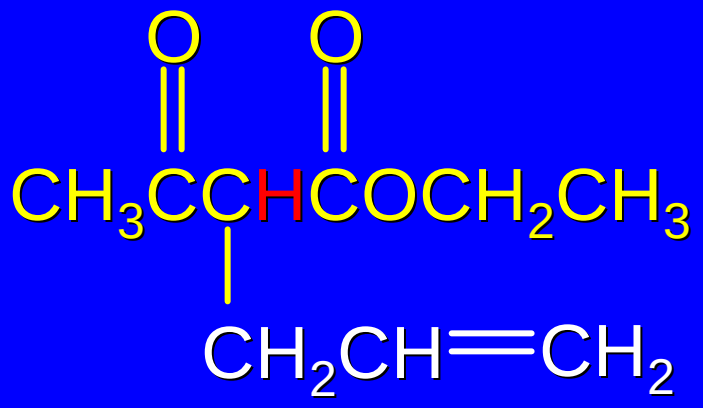


(60%)

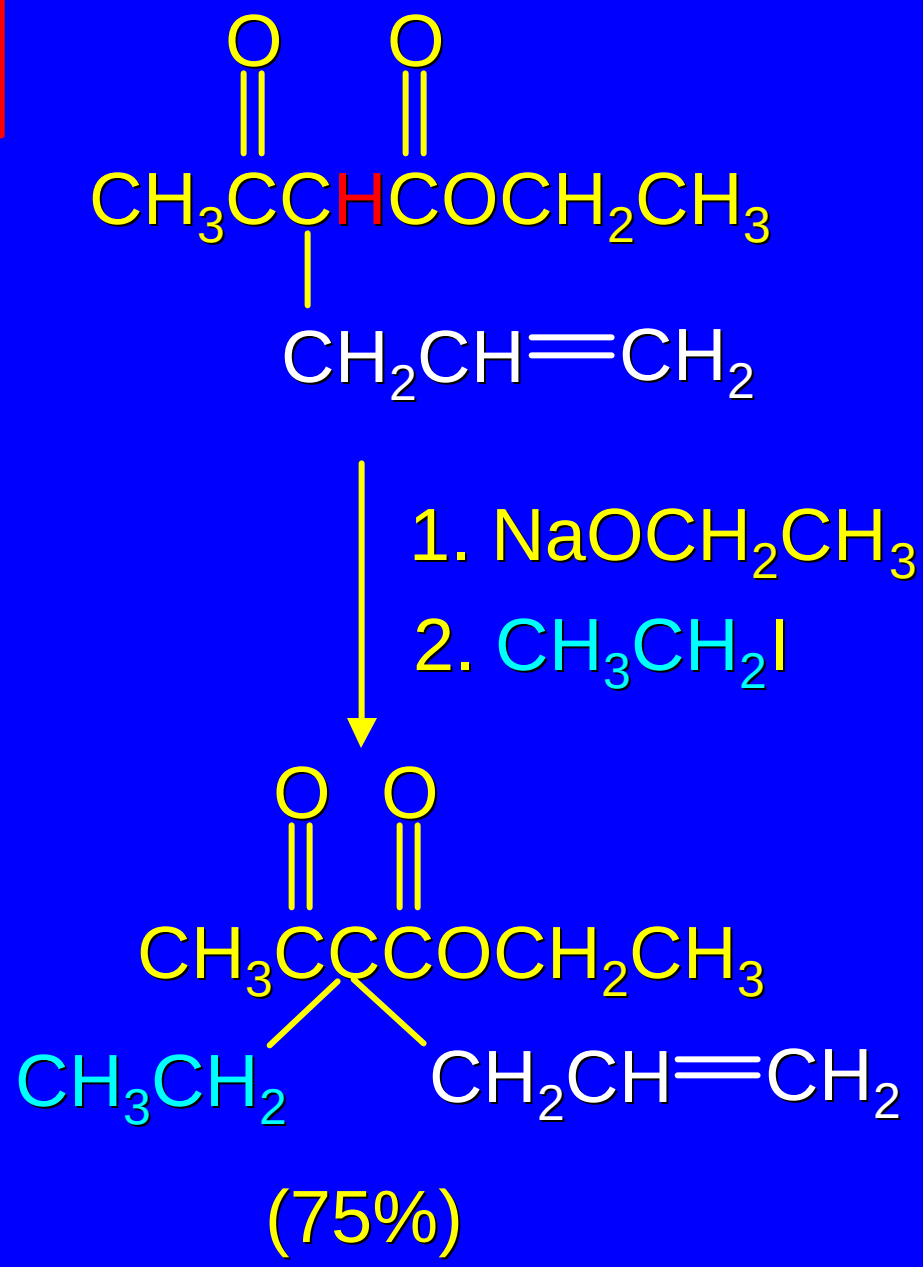
1. $NaOH, H_2O$
2. H^+
3. heat, $-CO_2$



Example:
Dialkylation



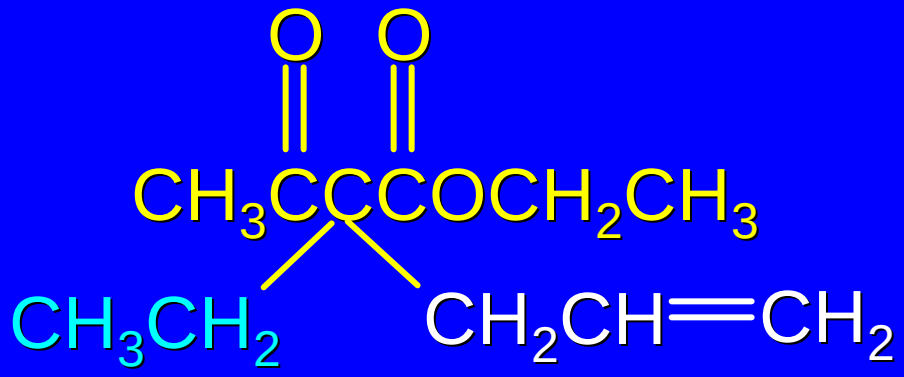
Example:
Dialkylation



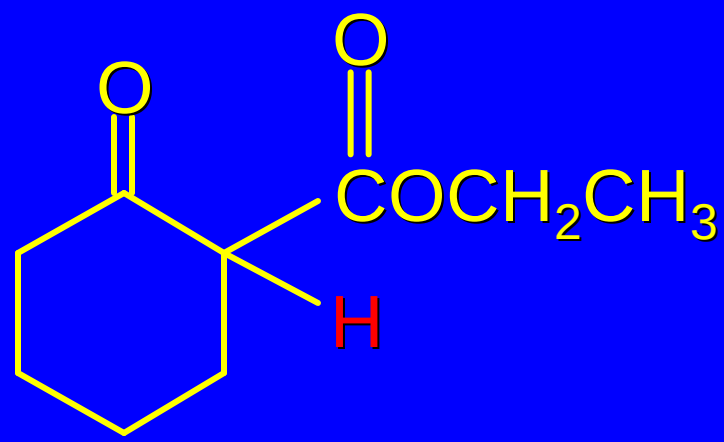
(75%)

Example:
Dialkylation

1. NaOH, H_2O
2. H^+
3. heat, $-CO_2$

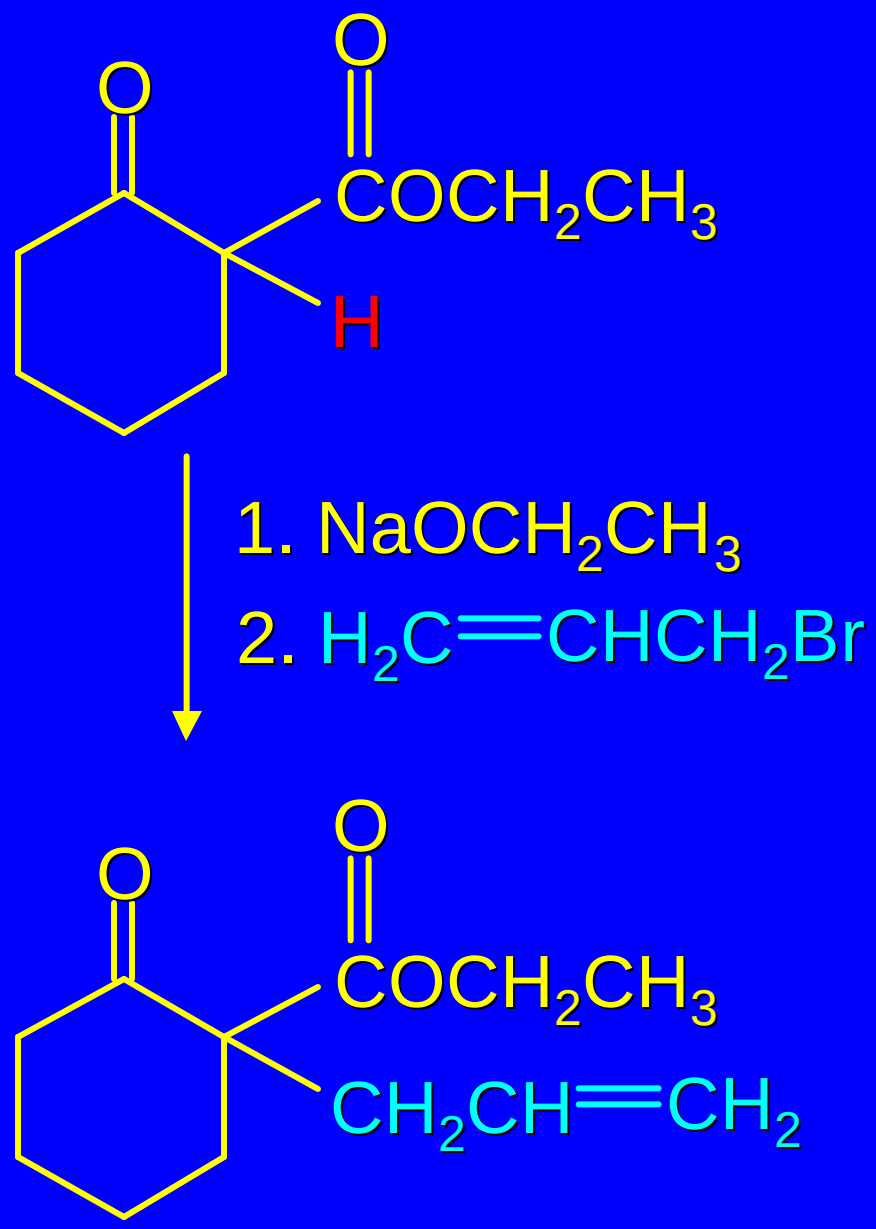


Another Example



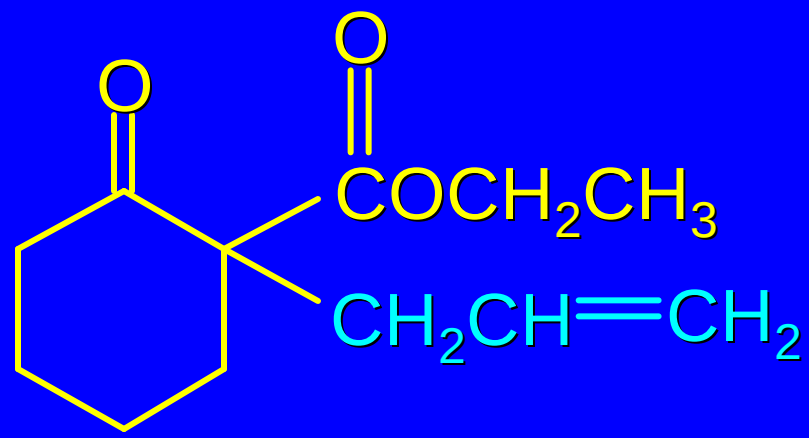
β-Keto esters other than ethyl acetoacetate may be used.

Another Example

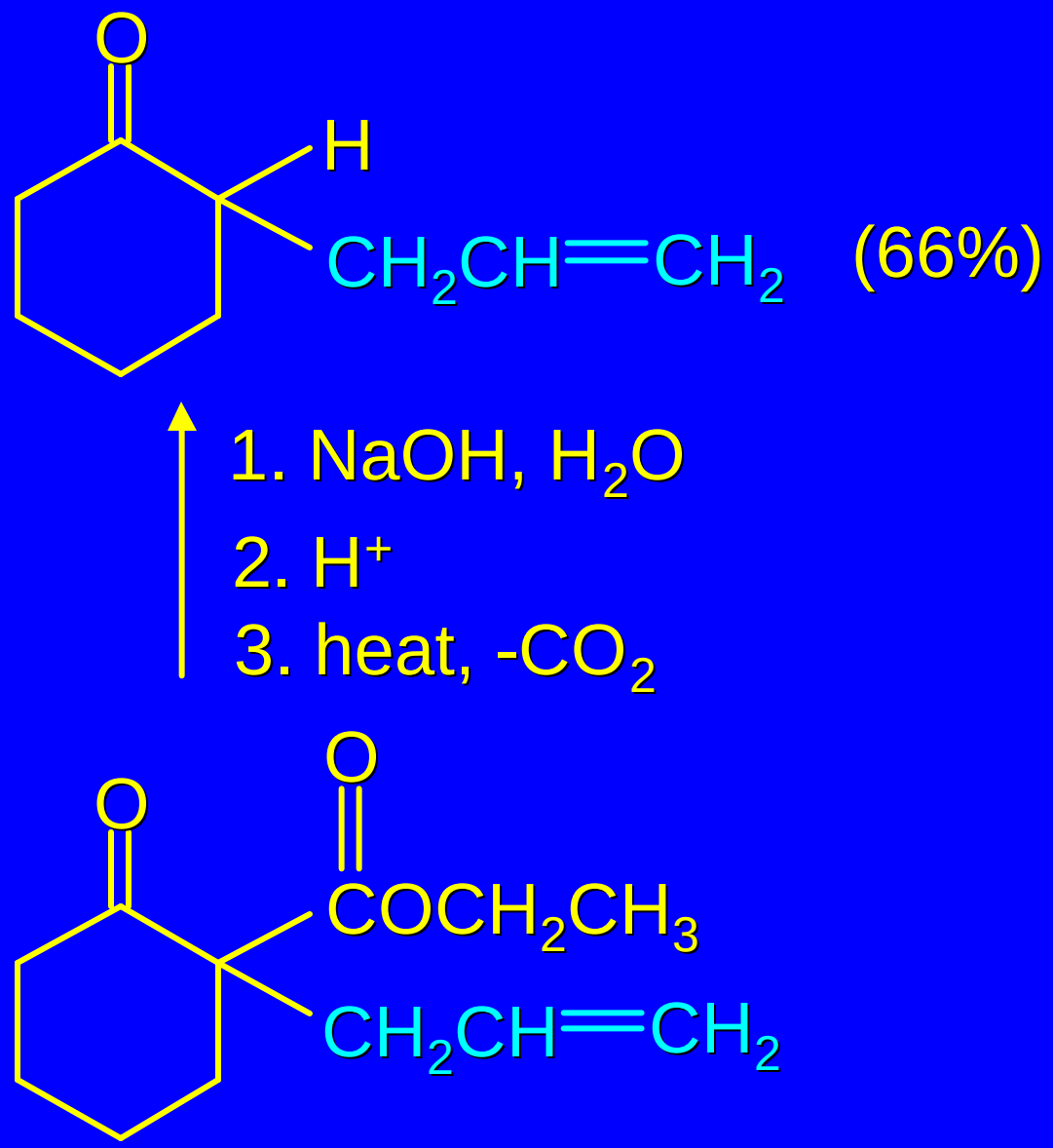


(89%)

Another Example



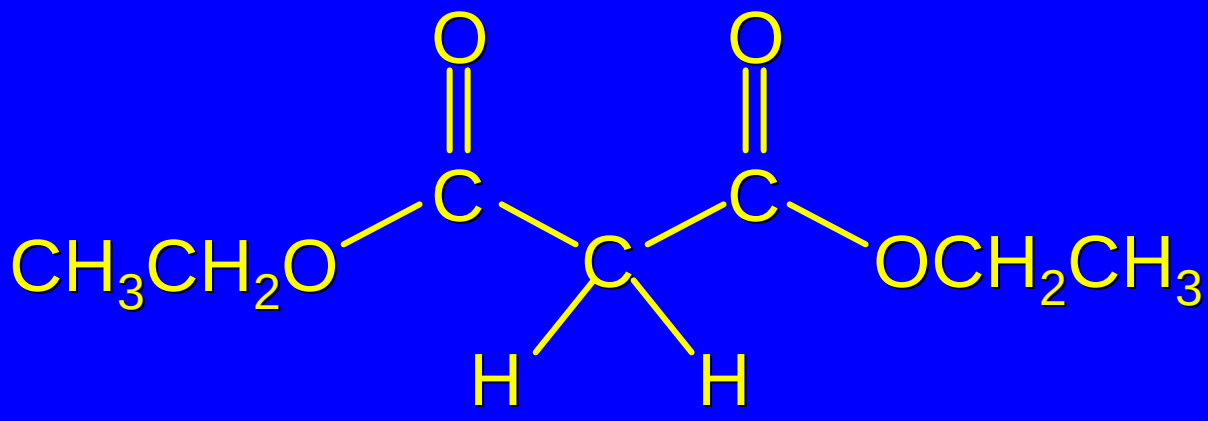
Another Example



21.7

The Malonic Ester Synthesis

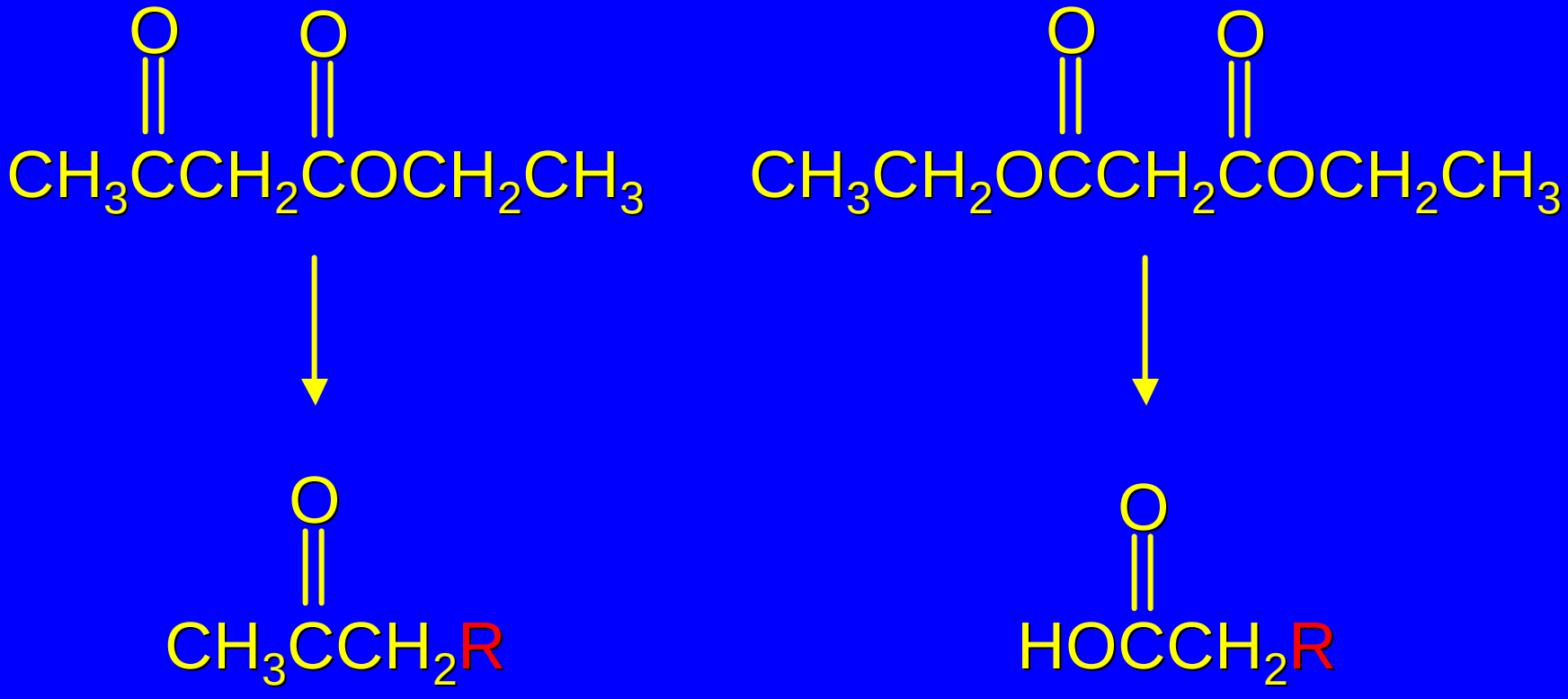
Malonic Ester



Malonic ester is another name for *diethyl malonate*.

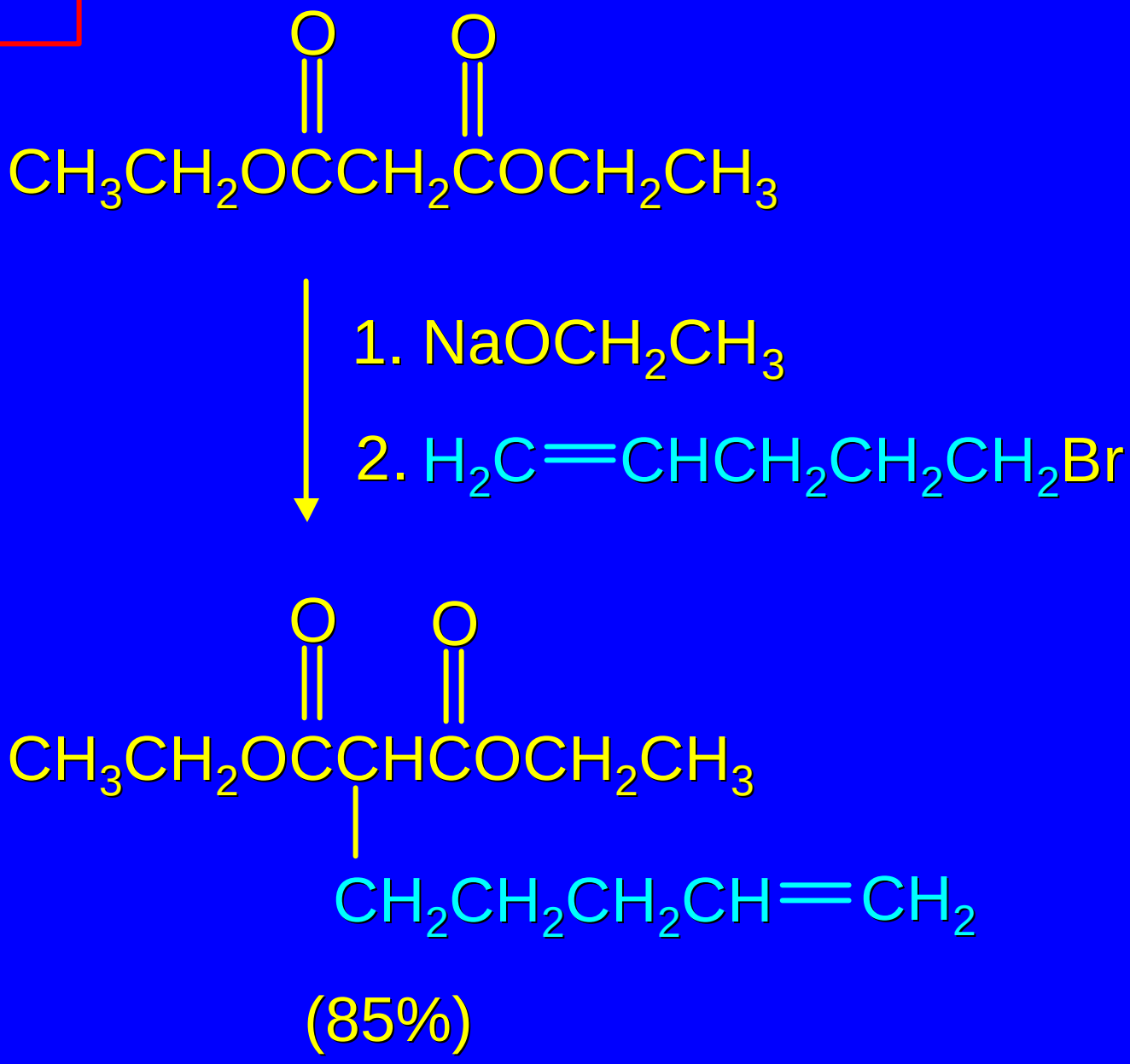
The "malonic ester synthesis" uses diethyl malonate as a reactant for the preparation of carboxylic acids.

An Analogy

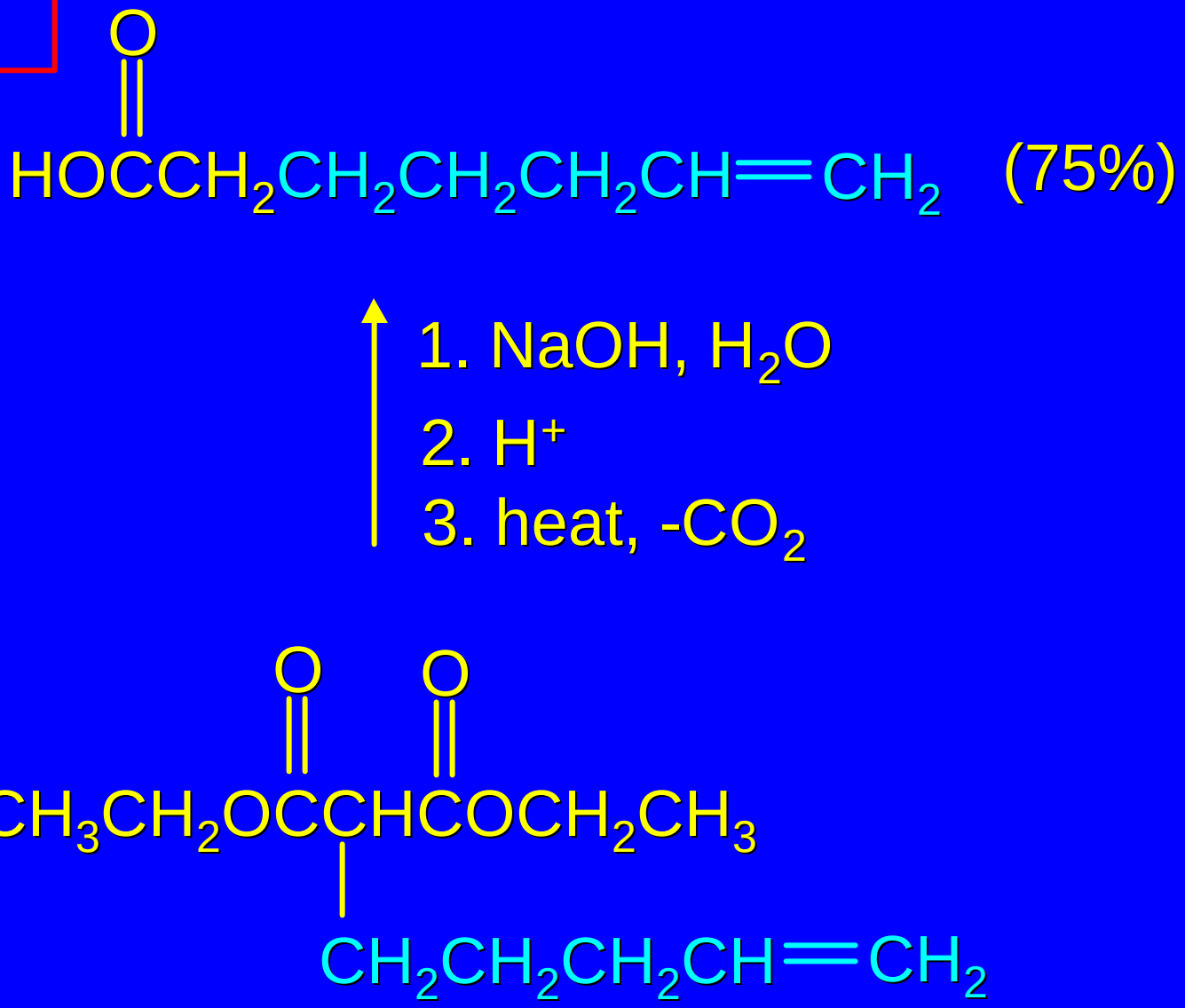


The same procedure by which ethyl acetoacetate is used to prepare ketones converts diethyl malonate to carboxylic acids.

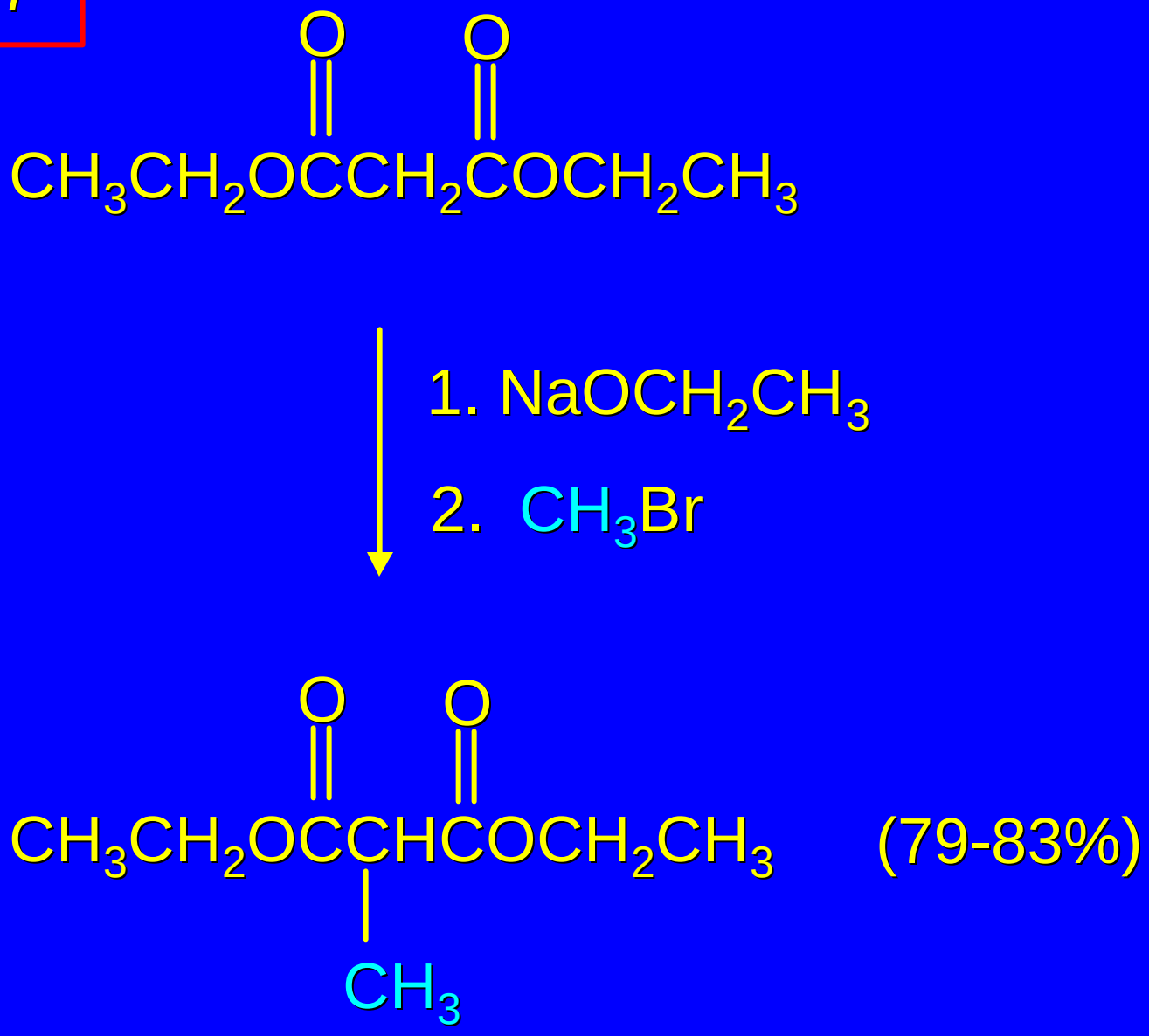
Example


CH3CH2OCCH2COCH2CH3
1. NaOCH2CH3
2. H2C=CHCH2CH2CH2Br
CH3CH2OCCHCOCH2CH3
CH2CH2CH2CH=CH2
(85%)

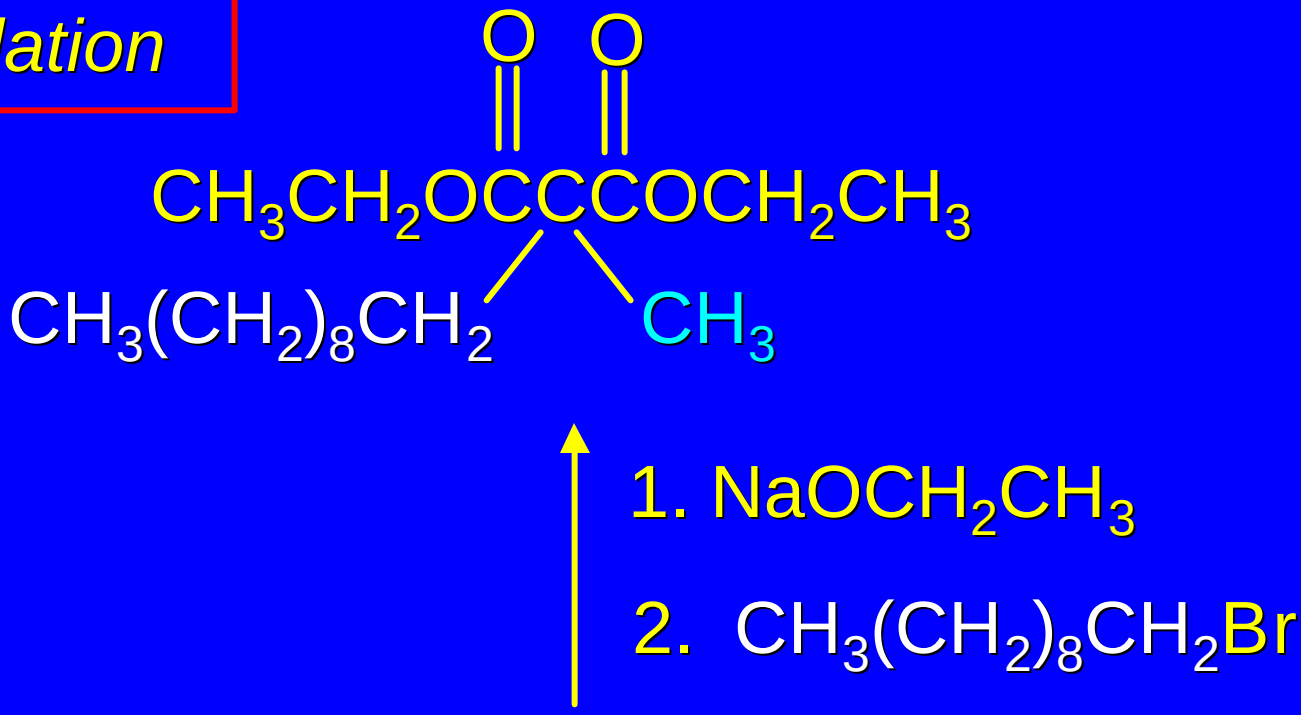
Example

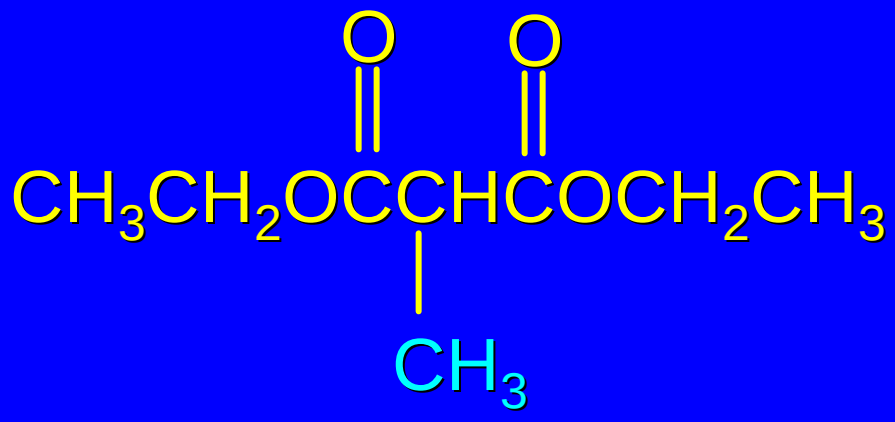

HOCCH2CH2CH2CH2CH=CH2
(75%)
1. NaOH, H2O
2. H+
3. heat, -CO2
CH3CH2OCCHCOCH2CH3
CH2CH2CH2CH=CH2

Dialkylation

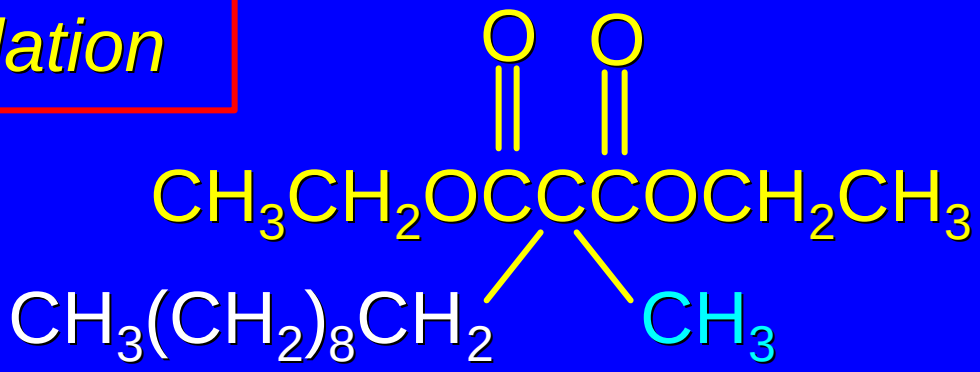


Dialkylation

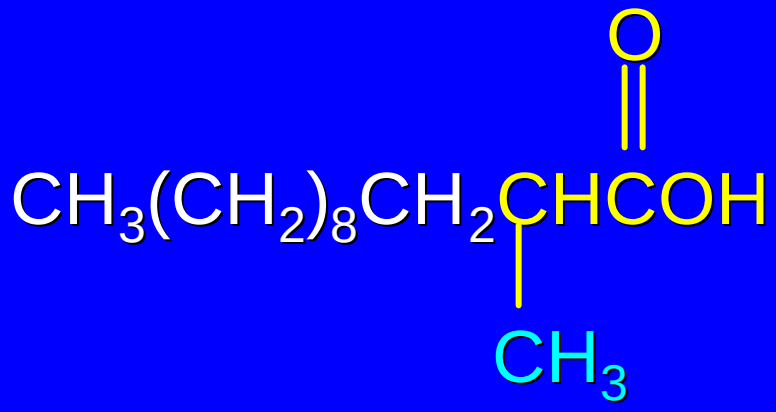




Dialkylation

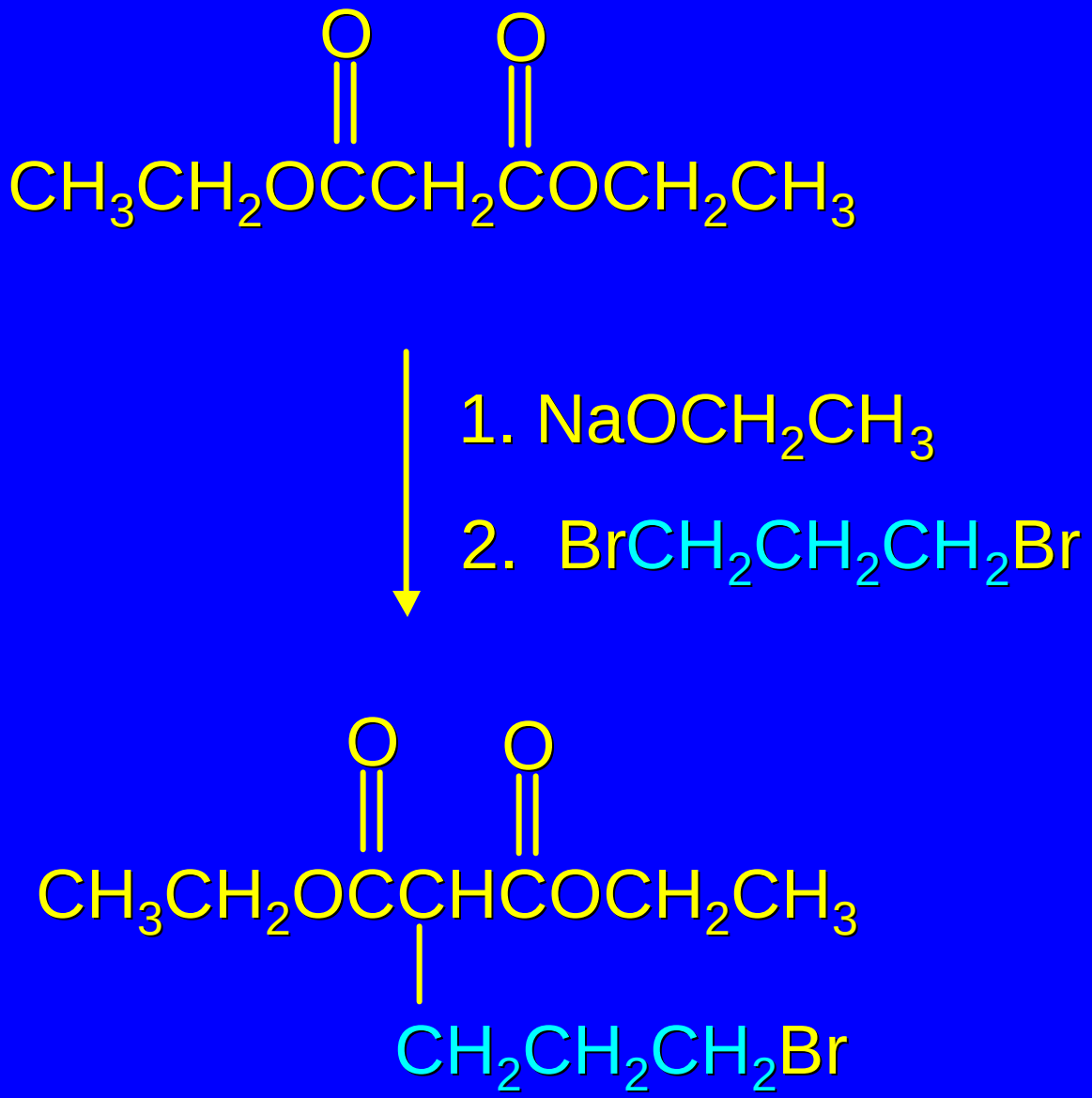


1. NaOH, H_2O
2. H^+
3. heat, $-CO_2$



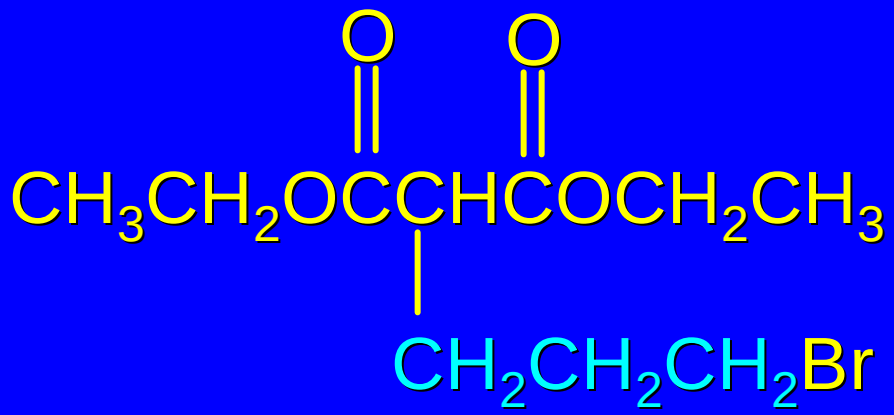
(61-74%)

Another Example

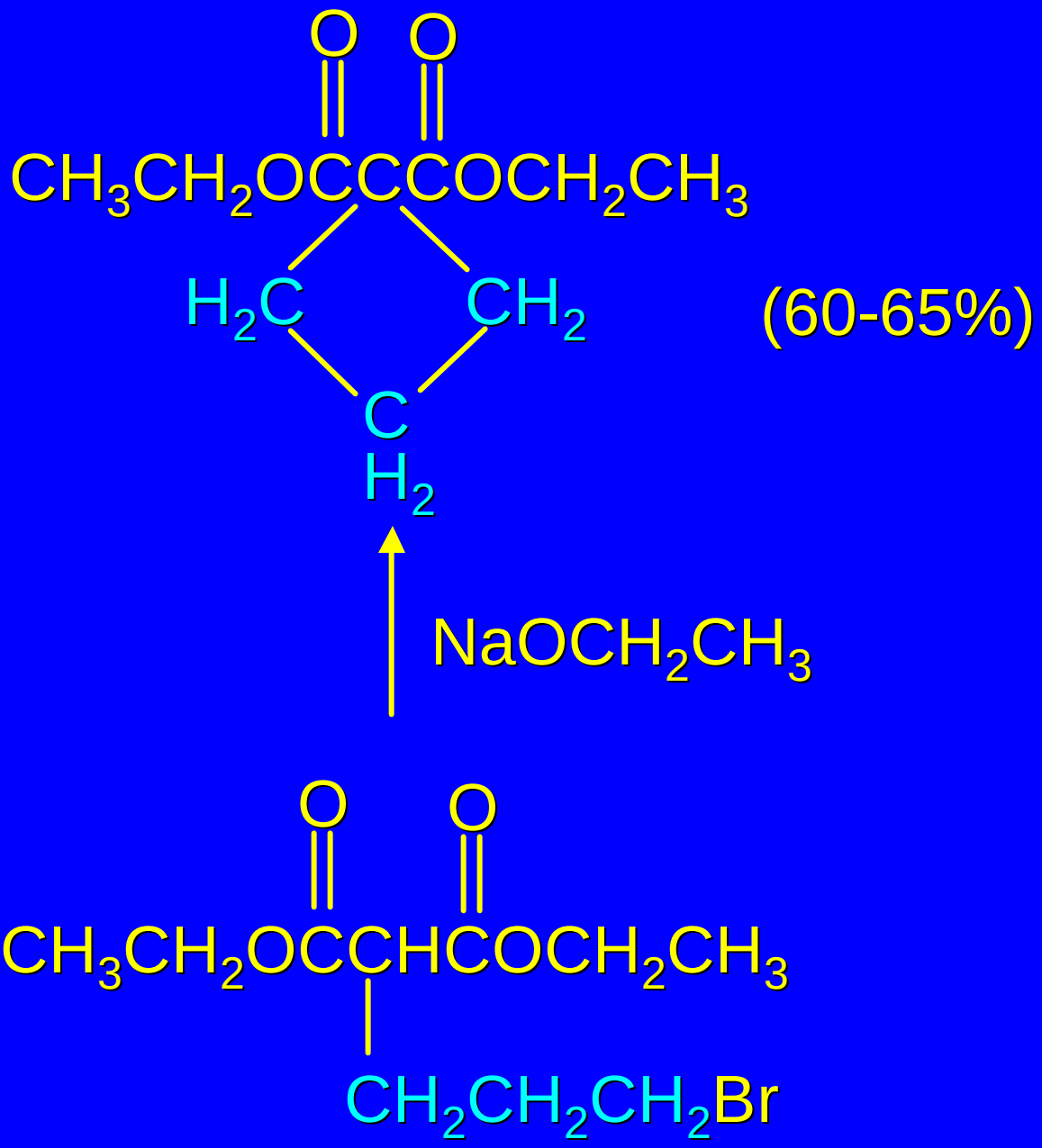


Another Example

This product is not isolated, but cyclizes in the presence of sodium ethoxide.



Another Example



(60-65%)

Another Example