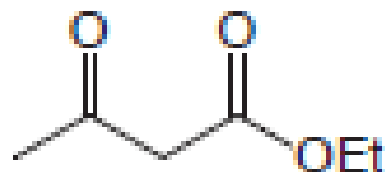


The Acetoacetic Ester Synthesis

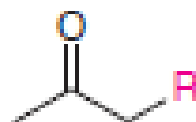
Synthesis of Methyl Ketones



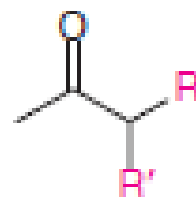
Acetoacetic ester
(ethyl acetoacetate;
ethyl 3-oxobutanoate)

Ethyl acetoacetate is a useful reagent for the preparation of substituted acetones (methyl ketones) of the types shown below.

1



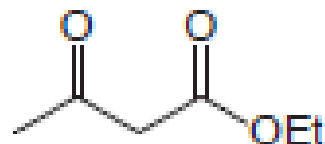
A monosubstituted acetone



A disubstituted acetone

The Acetoacetic Ester Synthesis

Synthesis of Methyl Ketones



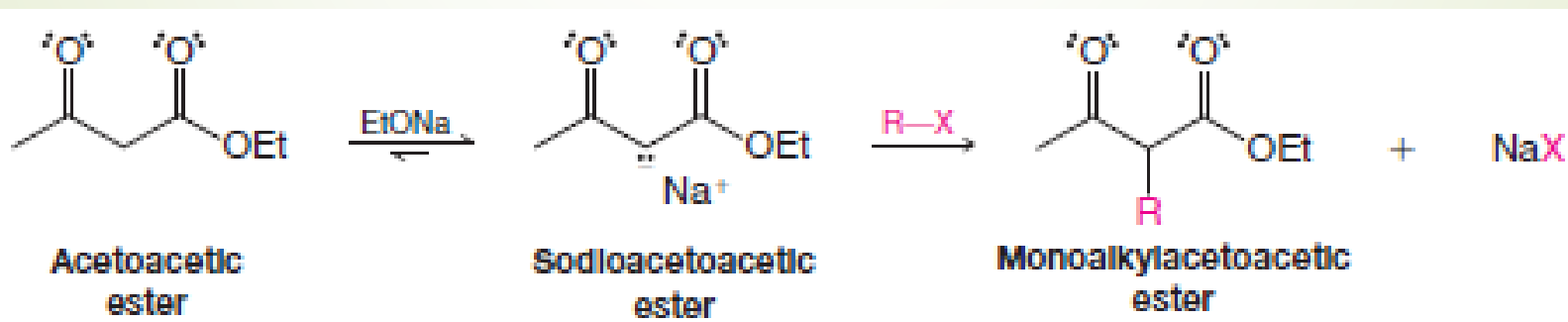
Acetoacetic ester
(ethyl acetoacetate;
ethyl 3-oxobutanoate)

Acetoacetic ester



β -Dicarbonyl compound, can easily be converted to an enolate using sodium ethoxide. We can then alkylate the resulting enolate (called sodioacetoacetic ester) with an alkyl halide.

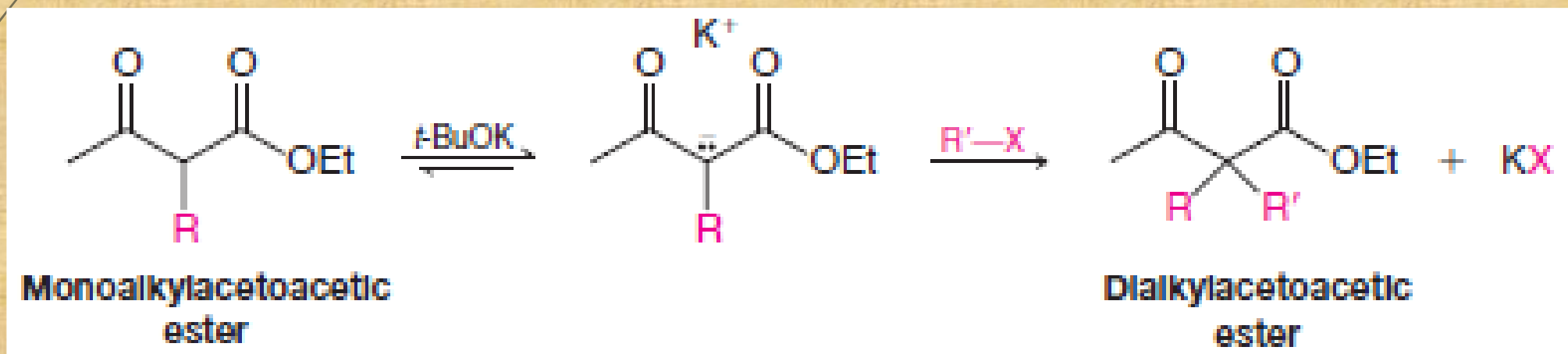
2



The Acetoacetic Ester Synthesis

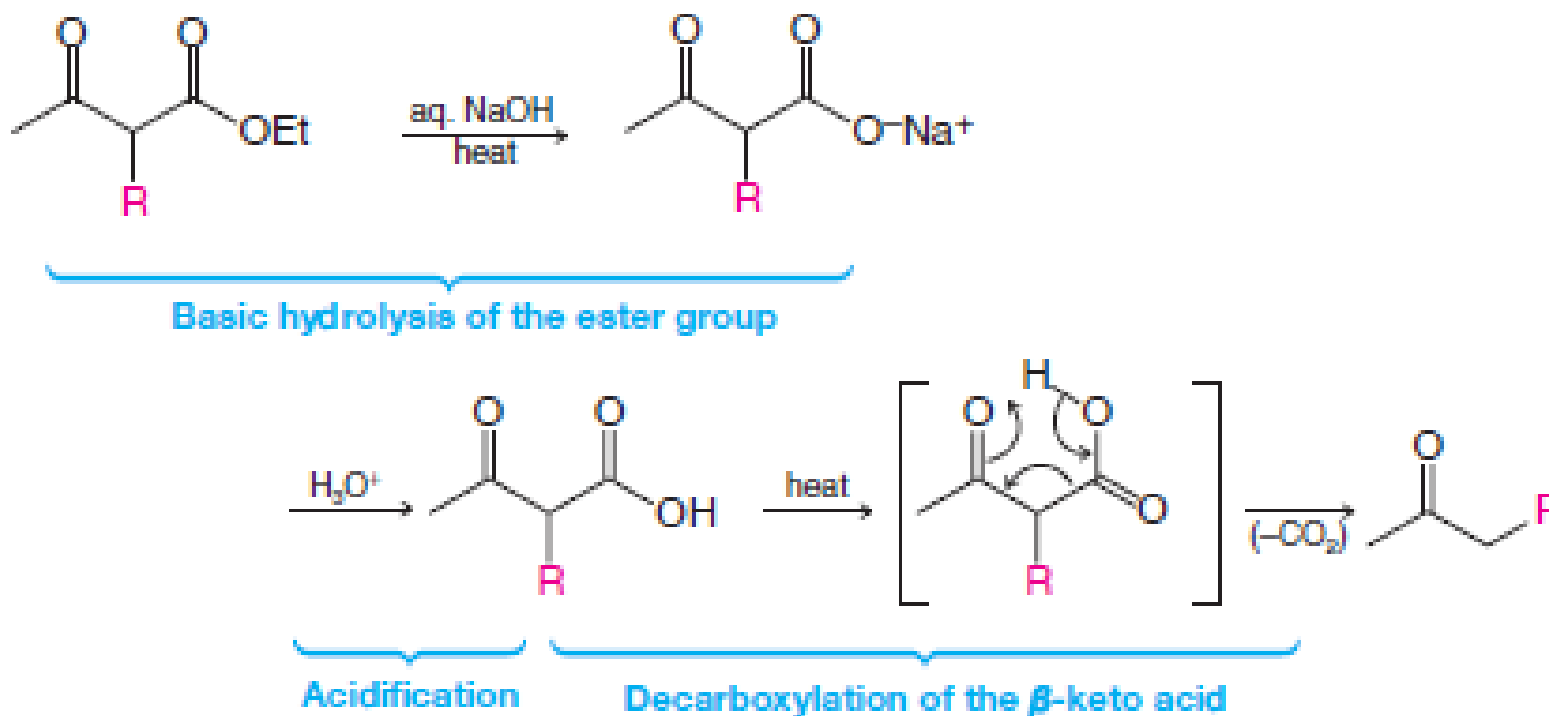
Synthesis of Methyl Ketones

Dialkylation The monoalkylacetoacetic ester shown above still has one appreciably acidic hydrogen, and, if we desire, we can carry out a second alkylation. Because a monoalkylacetoacetic ester is somewhat less acidic than acetoacetic ester itself due to the electron-donating effect of the added alkyl group, it is usually helpful to use a stronger base than ethoxide ion for the second alkylation. Use of potassium *tert*-butoxide is common because it is a stronger base than sodium ethoxide. Potassium *tert*-butoxide, because of its steric bulk, is also not likely to cause transesterification.



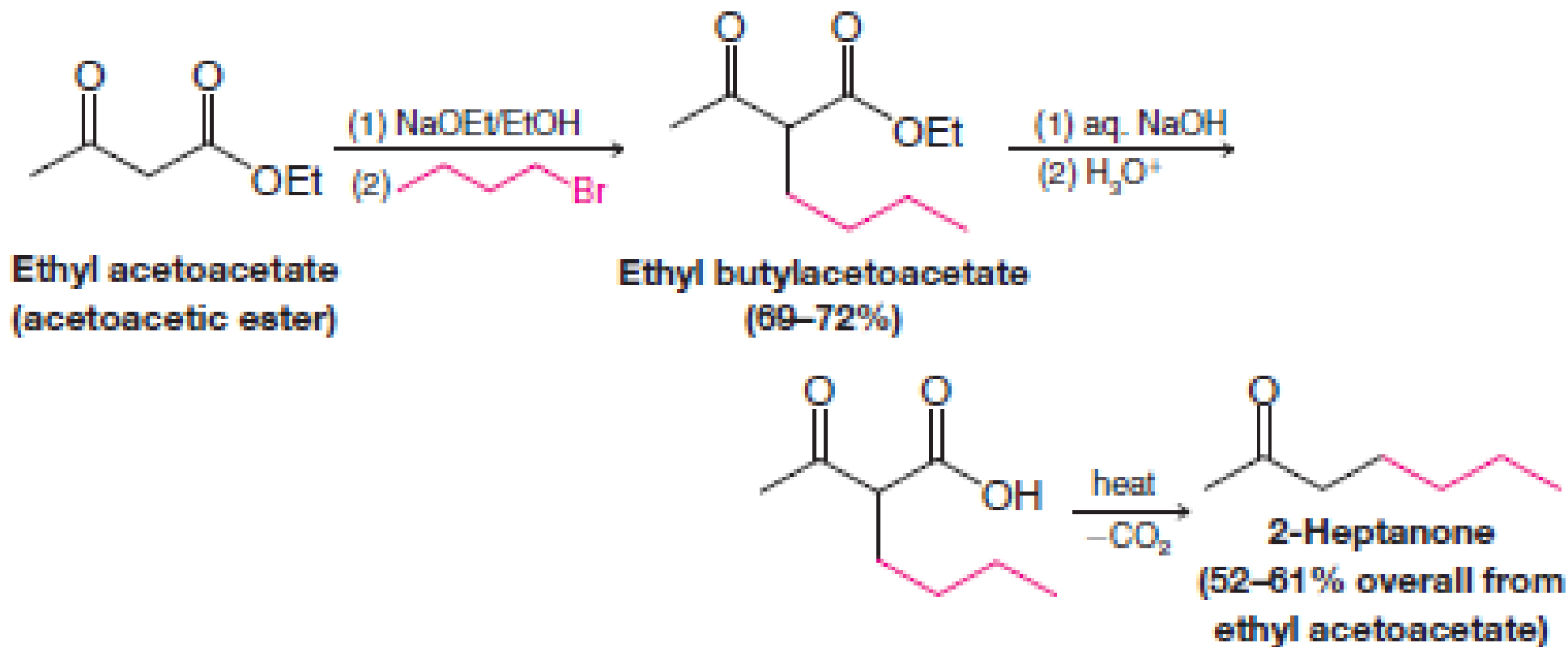
The Acetoacetic Ester Synthesis Synthesis of Methyl Ketones

Substituted Methyl Ketones To synthesize a monosubstituted methyl ketone (monosubstituted acetone), we carry out only one alkylation. Then we hydrolyze the monoalkylacetoacetic ester using aqueous sodium or potassium hydroxide. Subsequent acidification of the mixture gives an alkyl-acetoacetic acid, and heating this β -keto acid to 100°C brings about decarboxylation



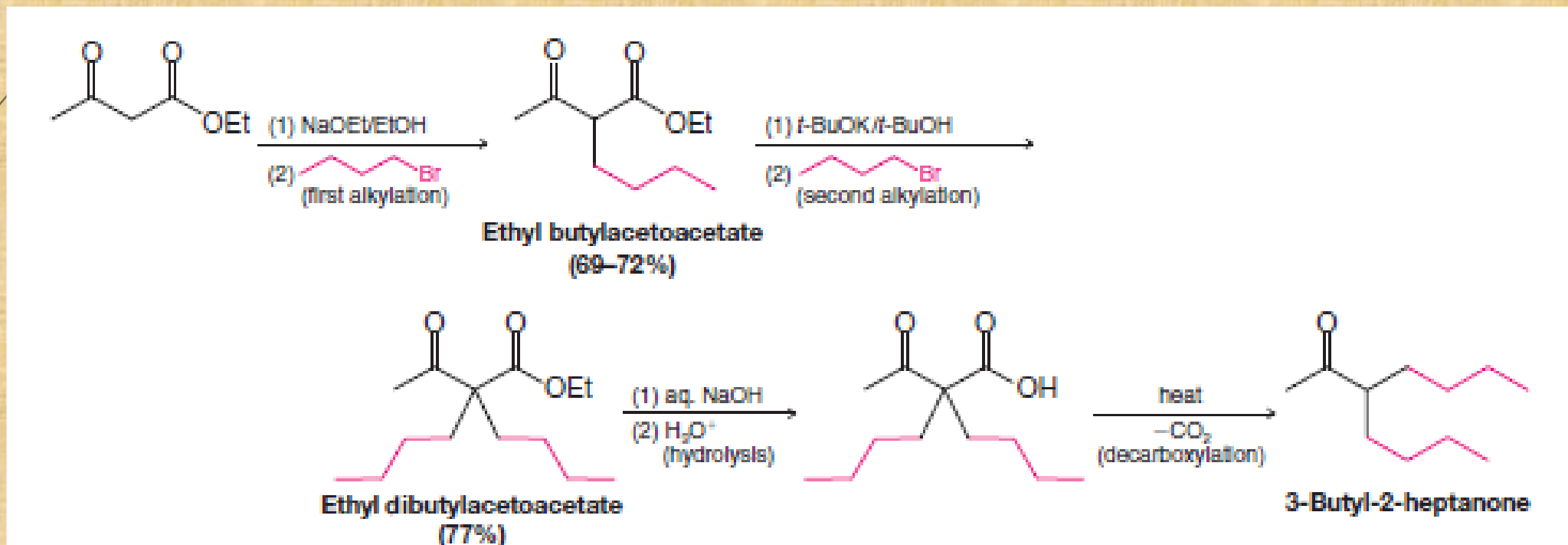
The Acetoacetic Ester Synthesis Synthesis of Methyl Ketones

A specific example is the following synthesis of 2-heptanone:



The Acetoacetic Ester Synthesis Synthesis of Methyl Ketones

If our goal is the preparation of a disubstituted acetone, we carry out two successive alkylations, we hydrolyze the dialkylacetoacetic ester that is produced, and then we decarboxylate the dialkylacetoacetic acid. An example of this procedure is the synthesis of 3-butyl-2-heptanone.



The Acetoacetic Ester Synthesis Synthesis of Methyl Ketones

Practice Problem

Show how you would use the acetoacetic ester synthesis to prepare (a) 3-propyl-2-hexanone and (b) 4-phenyl-2-butanone.

Good Luck