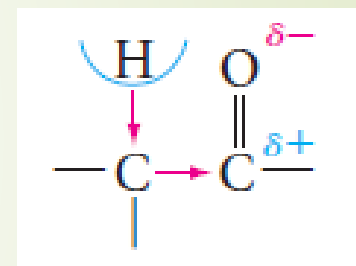


Acidity of α -Hydrogens; the Enolate Anion

- The α -hydrogen in a carbonyl compound is more acidic than a normal hydrogen bonded to a carbon atom.

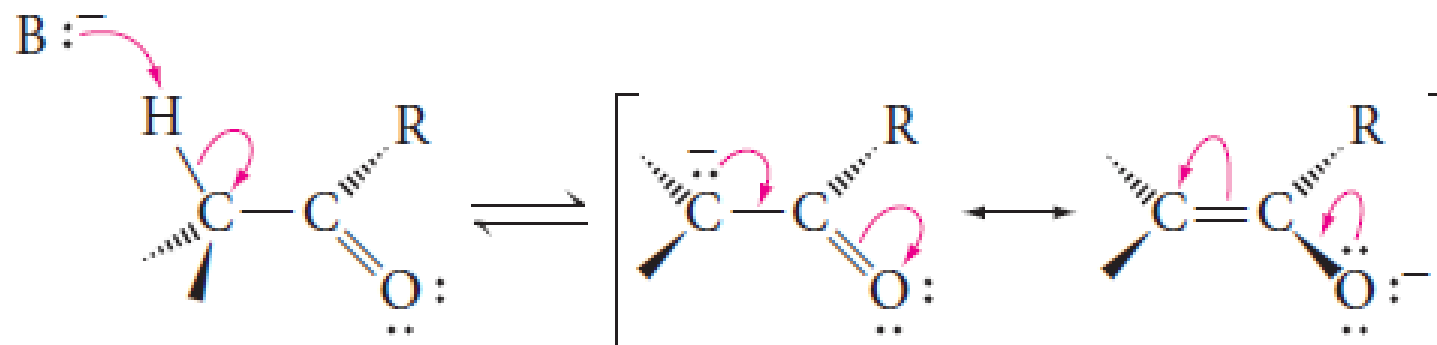
There are two reasons.

First, the carbonyl carbon carries a partial positive charge. Bonding electrons are displaced toward the carbonyl carbon and away from the α -hydrogen (shown by the red arrows below), making it easy for a base to remove the α -hydrogen as a proton.



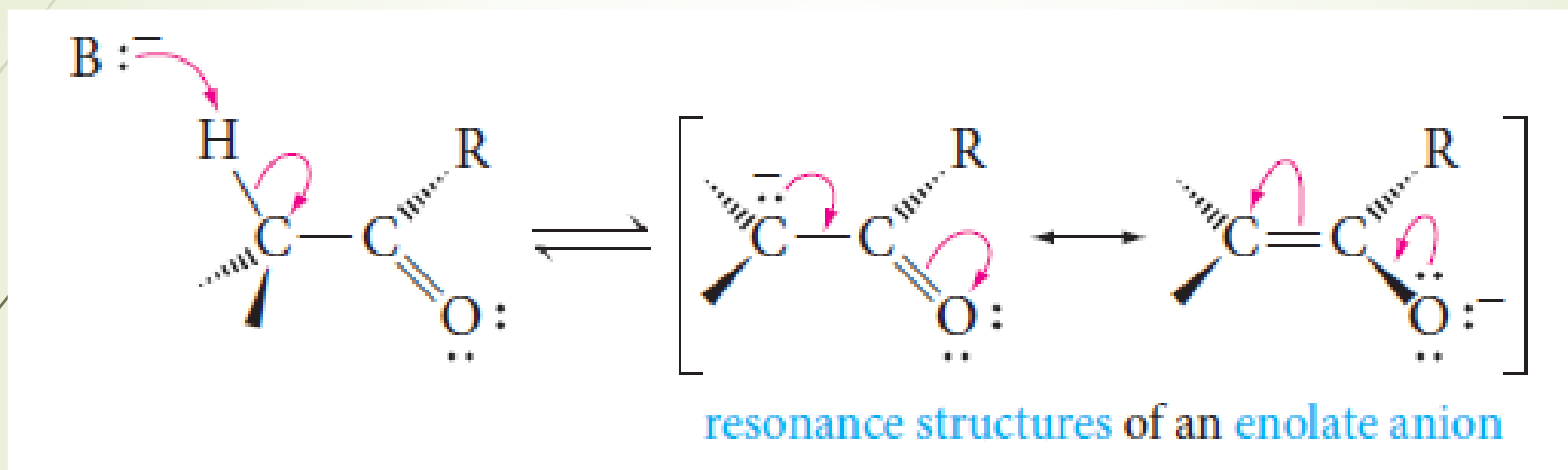
1

Second, the resulting anion is stabilized by resonance.



resonance structures of an enolate anion

Acidity of Alpha Hydrogens; the Enolate Anion



2

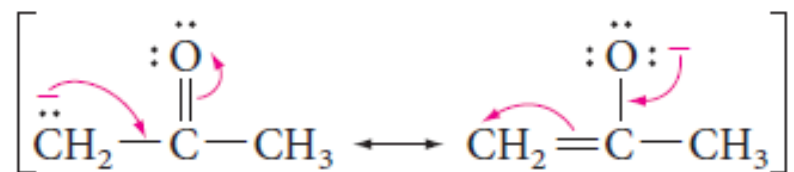
The anion is called an **enolate anion**. Its negative charge is distributed between the α -carbon and the carbonyl oxygen atom.

An **enolate anion** is formed by removal of the α -hydrogen of a ketone or aldehyde.

EXAMPLE

Draw the formula for the enolate anion of acetone.

Solution



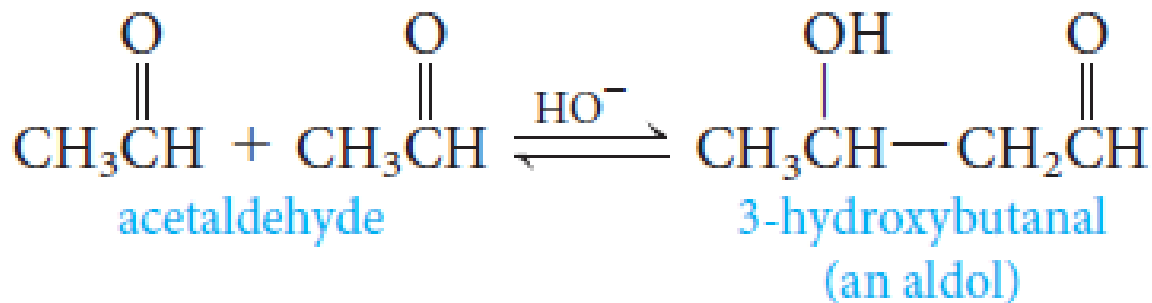
3

PROBLEM

Draw the resonance contributors to the enolate anion of a. propanal
b. cyclopentanone

The Aldol Condensation

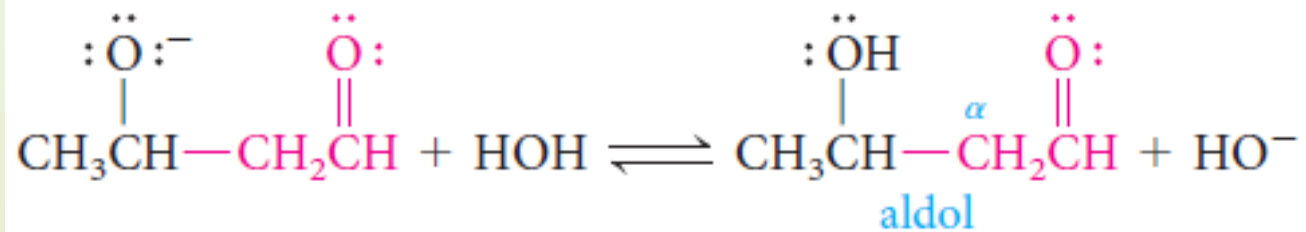
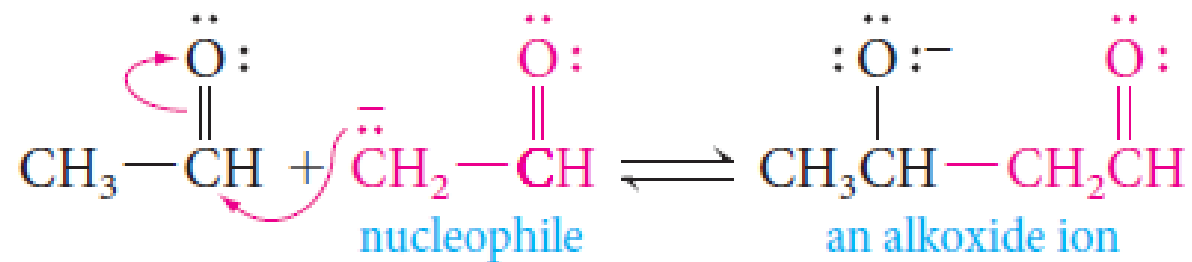
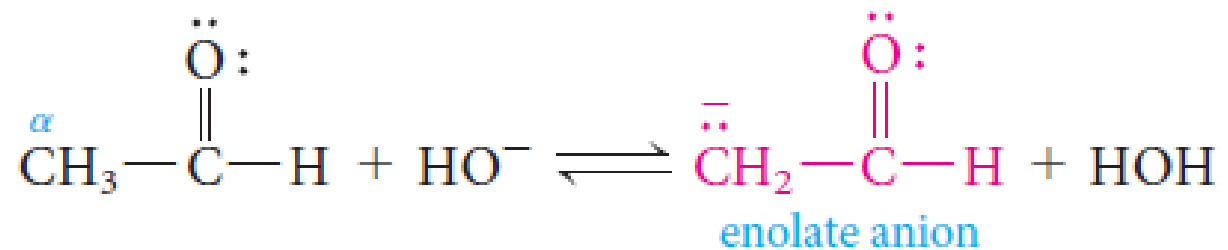
Enolate anions may act as carbon nucleophiles. They add reversibly to the carbonyl group of another aldehyde or ketone molecule in a reaction called the **aldol condensation**, an extremely useful carbon–carbon bond-forming reaction.



The product is called an **aldol** (so named because the product is both an *aldehyde* and an *alcohol*).

The Aldol Condensation

Mechanism



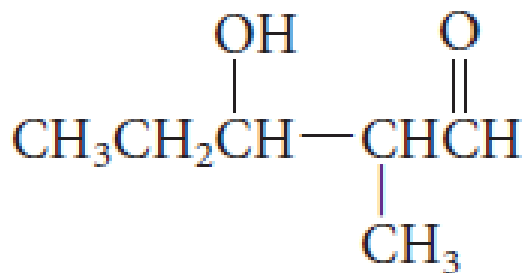
An aldol is a
3-hydroxyaldehyde
or 3-hydroxyketone.

The Aldol Condensation

EXAMPLE

Give the structure of the aldol that is obtained by treating propanal ($\text{CH}_3\text{CH}_2\text{CH}=\text{O}$) with base.

Solution



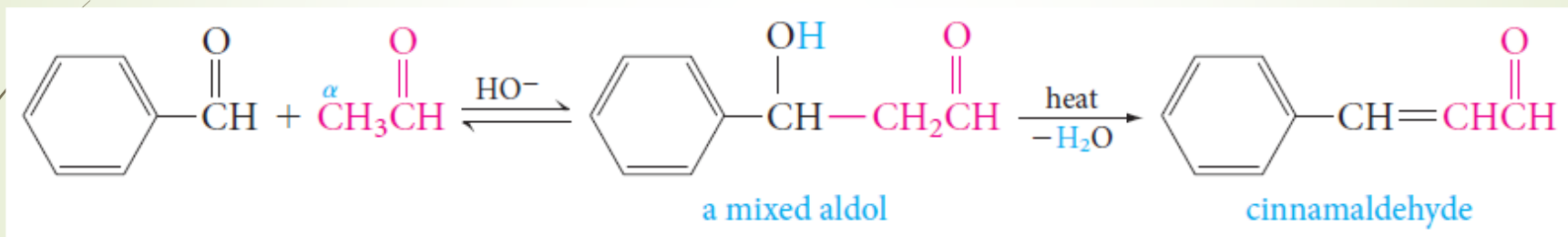
6

PROBLEM

Write out the steps in the mechanism for formation of the product in the above Example

The Mixed Aldol Condensation

Consider, for example, the reaction between acetaldehyde and benzaldehyde, when treated with base. Only acetaldehyde can form an enolate anion (benzaldehyde has no α -hydrogen). If the enolate ion of acetaldehyde adds to the benzaldehyde carbonyl group, a mixed aldol condensation occurs.



7

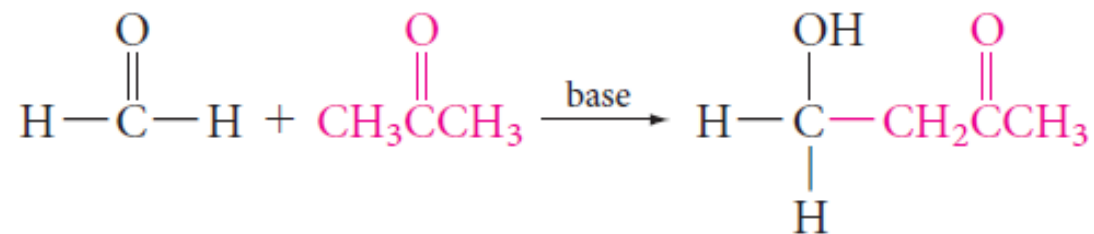
In this particular example, the resulting mixed aldol eliminates water on heating to give cinnamaldehyde

The Mixed Aldol Condensation

EXAMPLE

Write the structure of the mixed aldol obtained from acetone and formaldehyde.

Solution Of the two reactants, only acetone has α -hydrogens.



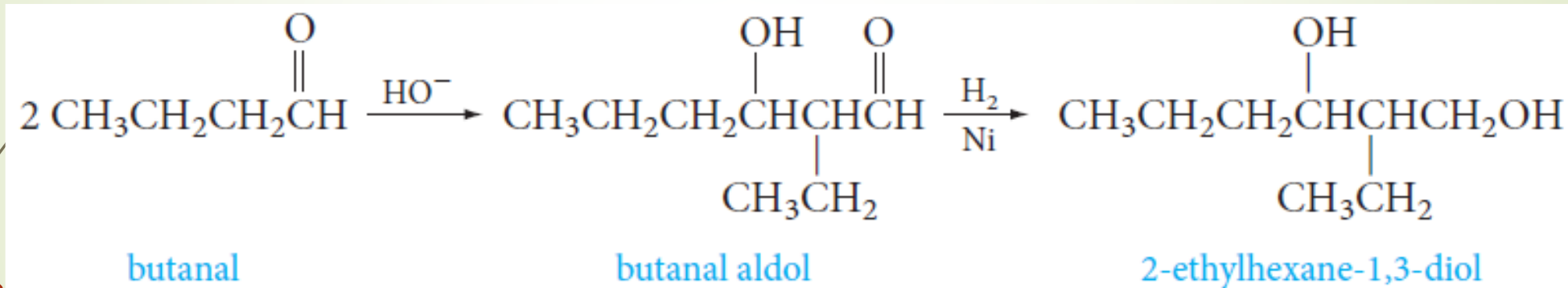
8

PROBLEM: Write the steps of the mechanism for the above reaction.

PROBLEM: Write the structure of the mixed aldol obtained from propanal and benzaldehyde. What structure is obtained from dehydration of this mixed aldol?

Commercial Syntheses via the Aldol Condensation

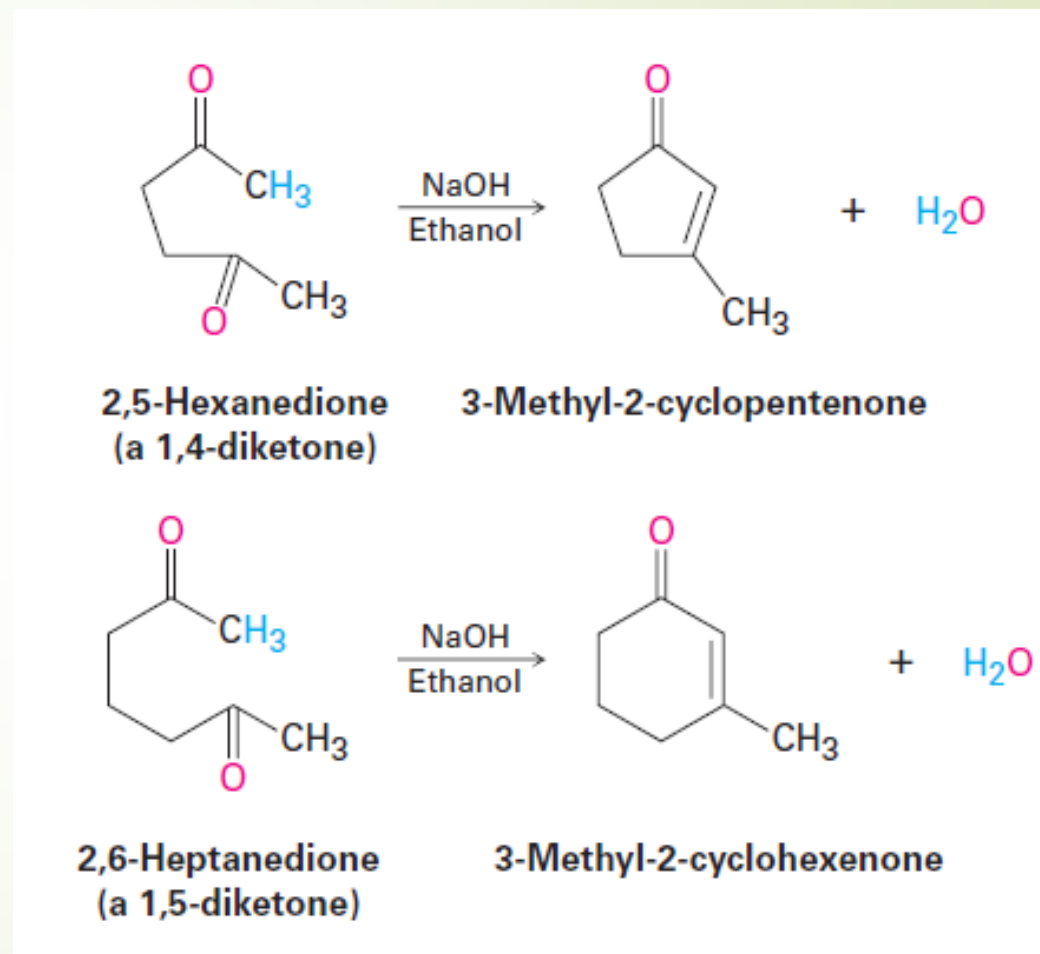
Butanal is the starting material for the synthesis of the mosquito repellent (2-ethylhexane-1,3-diol). The first step is an aldol condensation, and the second step is reduction of the aldehyde group to a primary alcohol.



PROBLEM : 2-Ethylhexanol, used commercially in the manufacture of plasticizers and synthetic lubricants, is synthesized from butanal via its aldol product. Devise a route to it.

Intramolecular Aldol Reactions

When *dicarbonyl* compounds are treated with base, however, an Intramolecular Aldol reaction can occur, leading to the formation of a cyclic product



Intramolecular Aldol Reactions

Intramolecular aldol reaction of 2,5-hexanedione yields 3-methyl-2-cyclopentenone rather than the alternative cyclopropene.

The relatively strain-free cyclopentenone product is considerably more stable than the highly strained cyclopropene alternative

