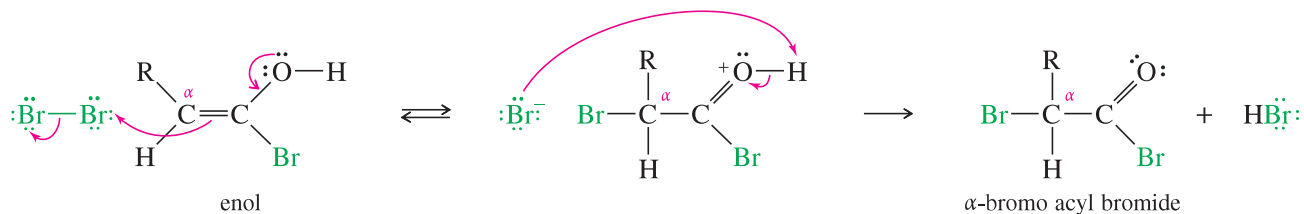
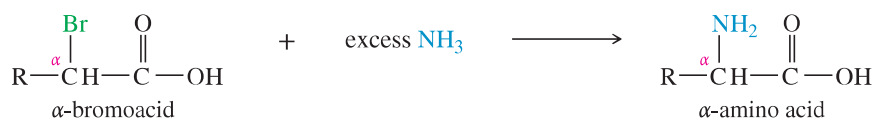


The enol is nucleophilic, attacking bromine to give the  $\alpha$ -brominated acyl bromide.



If a derivative of the  $\alpha$ -bromoacid is desired, the  $\alpha$ -bromo acyl bromide serves as an activated intermediate (similar to an acid chloride) for the synthesis of an ester, amide, or other derivative. If the  $\alpha$ -bromoacid itself is needed, a water hydrolysis completes the synthesis.

One of the common uses for  $\alpha$ -bromoacids is to convert them to  $\alpha$ -amino acids. Often, simply treating them with a large excess of ammonia gives the  $\alpha$ -amino acid directly.



### PROBLEM 22-17

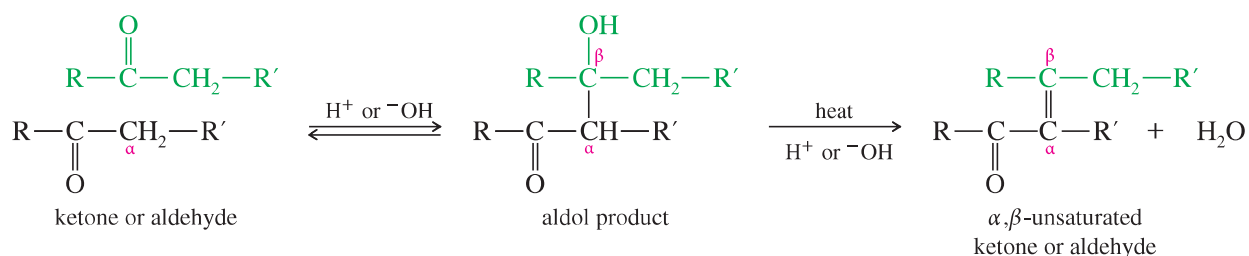
Show the products of the reactions of these carboxylic acids with  $\text{PBr}_3/\text{Br}_2$  before and after hydrolysis.

- (a) pentanoic acid    (b) phenylacetic acid    (c) succinic acid    (d) oxalic acid

## 22-7 The Aldol Condensation of Ketones and Aldehydes

**Condensations** are some of the most important enolate reactions of carbonyl compounds. Condensations combine two or more molecules, often with the loss of a small molecule such as water or an alcohol. Under basic conditions, the **aldol condensation** involves the nucleophilic addition of an enolate ion to another carbonyl group. The product, a  $\beta$ -hydroxy ketone or aldehyde, is called an **aldol** because it contains both an *aldehyde* group and the hydroxy group of an *alcohol*. The aldol product may dehydrate to an  $\alpha,\beta$ -unsaturated carbonyl compound.

### The aldol condensation



### 22-7A Base-Catalyzed Aldol Condensations

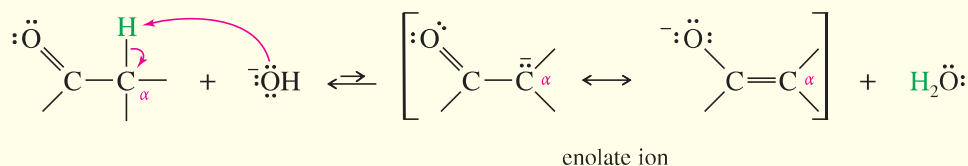
Under basic conditions, the aldol condensation occurs by a nucleophilic addition of the enolate ion (a strong nucleophile) to a carbonyl group. Protonation gives the aldol product.



## KEY MECHANISM 22-9 Base-Catalyzed Aldol Condensation

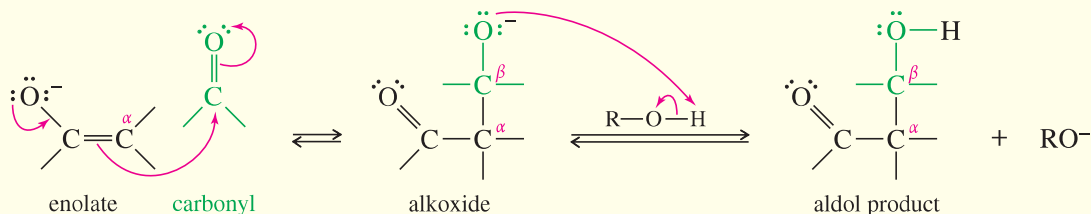
The base-catalyzed aldol involves the nucleophilic addition of an enolate ion to a carbonyl group.

**Step 1:** A base removes an  $\alpha$  proton to form an enolate ion.



**Step 2:** The enolate ion adds to the carbonyl group.

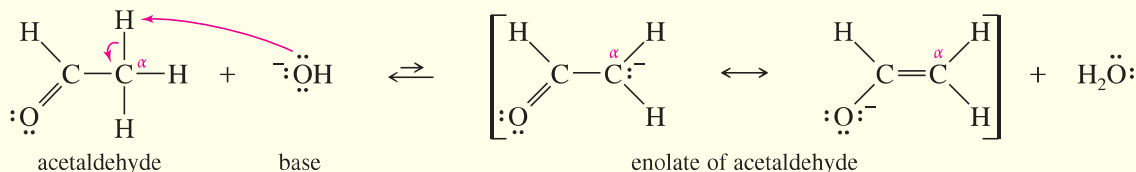
**Step 3:** Protonation of the alkoxide gives the aldol product.



**EXAMPLE:** Aldol condensation of acetaldehyde.

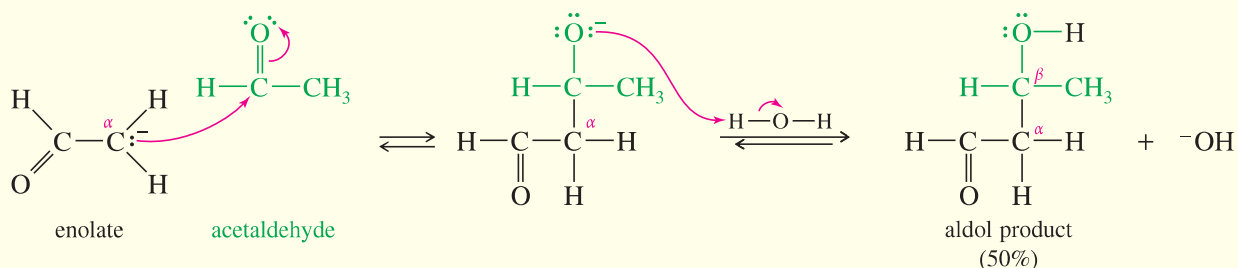
The enolate ion of acetaldehyde attacks the carbonyl group of another acetaldehyde molecule. Protonation gives the aldol product.

**Step 1:** A base removes an  $\alpha$  proton to form an enolate ion.



**Step 2:** The enolate ion adds to the carbonyl group.

**Step 3:** Protonation of the alkoxide gives the aldol product.



The aldol condensation is reversible, establishing an equilibrium between reactants and products. For acetaldehyde, conversion to the aldol product is about 50%. Ketones also undergo aldol condensation, but equilibrium concentrations of the products are generally small. Aldol condensations are sometimes accomplished by clever experimental methods. For example, Figure 22-2 shows how a good yield of the acetone aldol product (“diacetone alcohol”) is obtained, even though the equilibrium concentration of the product is only about 1%. Acetone is boiled so it condenses into a chamber containing an insoluble basic catalyst. The reaction can take place only in the catalyst chamber. When the solution returns to the boiling flask, it contains about 1% diacetone alcohol. Diacetone alcohol is less volatile than acetone, remaining in the boiling flask while acetone boils and condenses (refluxes) in contact with the catalyst. After several hours, nearly all the acetone is converted to diacetone alcohol.

### Application: Biochemistry

Aldolases are enzymes that form aldol products, most commonly in the metabolism of carbohydrates or sugars. In contrast to the chemical reaction, aldolases generate just one product stereospecifically. Hence, they are sometimes used in organic synthesis for key transformations.

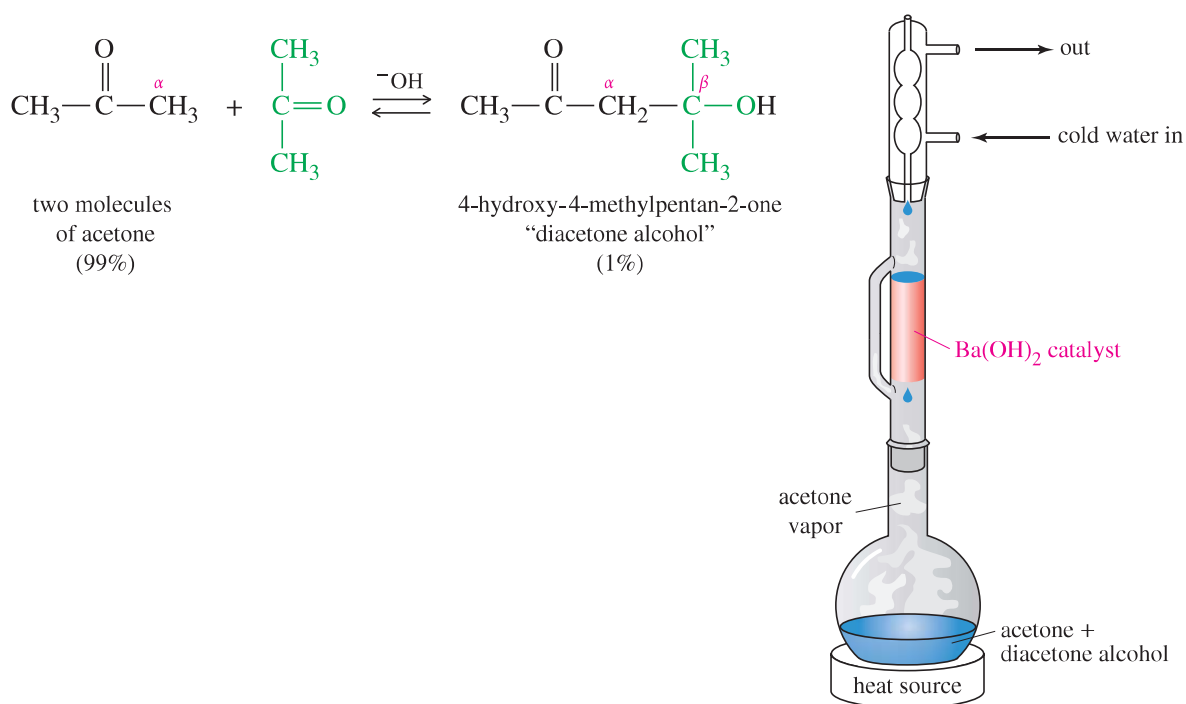


FIGURE 22-2

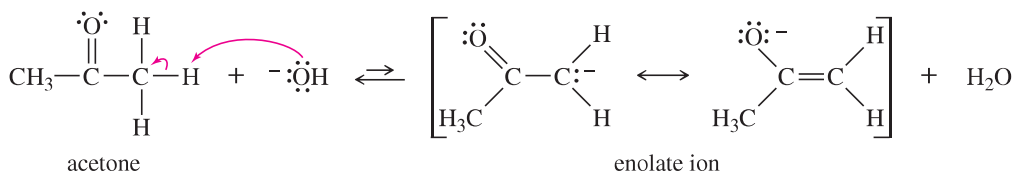
Driving an aldol condensation to completion. The aldol condensation of acetone gives only 1% product at equilibrium, yet a clever technique gives a good yield. Acetone refluxes onto a basic catalyst such as  $\text{Ba}(\text{OH})_2$ . The nonvolatile diacetone alcohol does not reflux, so its equilibrium concentration gradually increases until nearly all the acetone is converted to diacetone alcohol.

## SOLVED PROBLEM 22-3

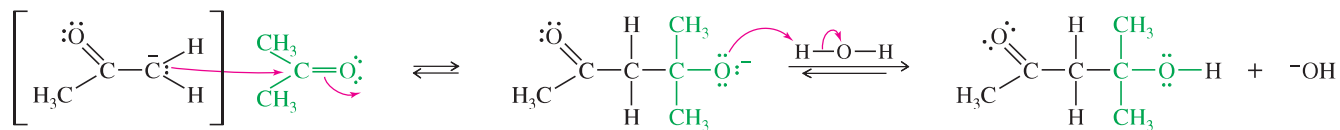
Propose a mechanism for the base-catalyzed aldol condensation of acetone (Figure 22-2).

## SOLUTION

The first step is formation of the enolate to serve as a nucleophile.



The second step is a nucleophilic attack by the enolate on another molecule of acetone. Protonation gives the aldol product.



## PROBLEM 22-18

Propose a mechanism for the aldol condensation of cyclohexanone. Do you expect the equilibrium to favor the reactant or the product?

## PROBLEM 22-19

Give the expected products for the aldol condensations of

- (a) propanal.      (b) phenylacetaldehyde.      (c) pentan-3-one.