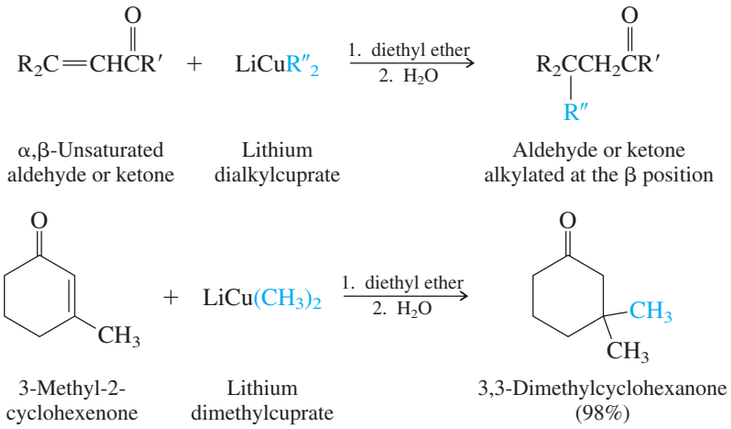
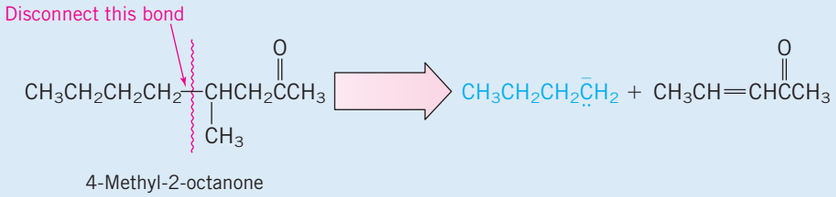


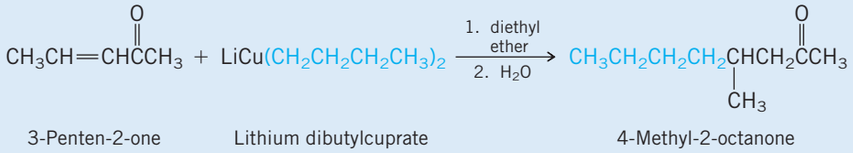
PROBLEM 18.21

Outline two ways in which 4-methyl-2-octanone can be prepared by conjugate addition of an organocuprate to an α,β-unsaturated ketone.

Sample Solution Mentally disconnect one of the bonds to the β carbon so as to identify the group that comes from the lithium dialkylcuprate.



According to this disconnection, the butyl group is derived from lithium dibutylcuprate. A suitable preparation is



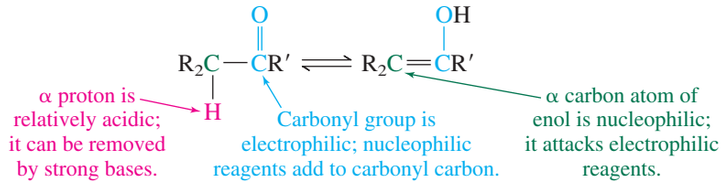
Now see if you can identify the second possibility.

Like other carbon–carbon bond-forming reactions, organocuprate addition to enones is a powerful tool in organic synthesis.

18.15 SUMMARY

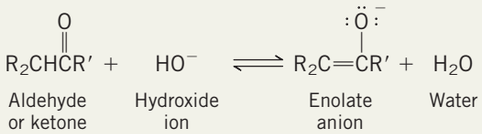
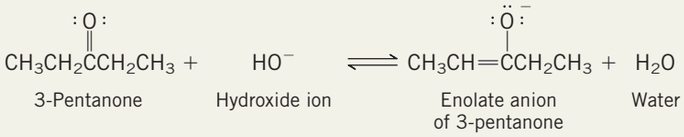
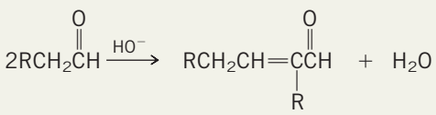
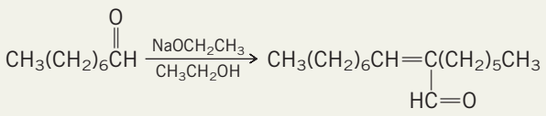
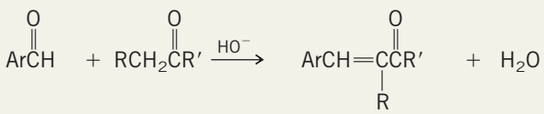
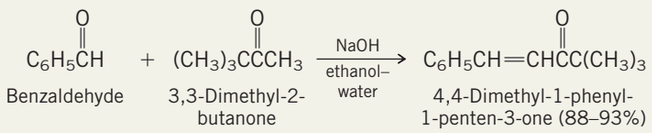
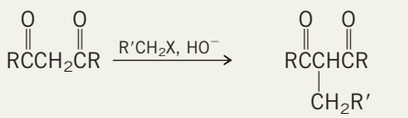
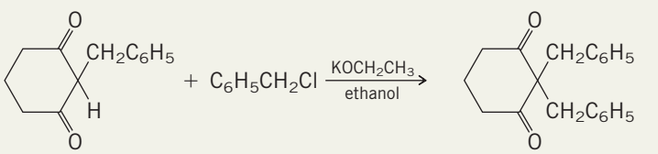
Sections 18.1–18.14

Because aldehydes and ketones exist in equilibrium with their corresponding enol isomers, they can express a variety of different kinds of chemical reactivity.



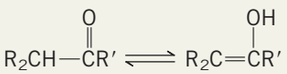
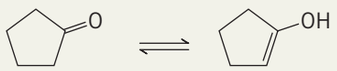
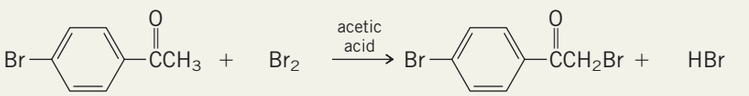
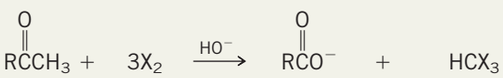
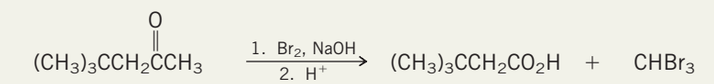
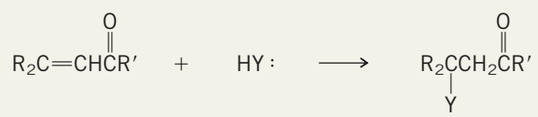
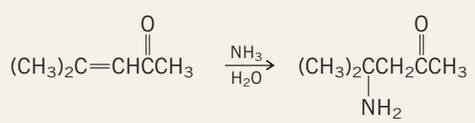
Reactions that proceed via enol or enolate intermediates are summarized in Table 18.2.

TABLE 18.2 Reactions of Aldehydes and Ketones That Involve Enol or Enolate Ion Intermediates

Reaction (section) and comments	General equation and typical example
Enolate ion formation (Section 18.1) An α hydrogen of an aldehyde or a ketone is more acidic than most other protons bound to carbon. Aldehydes and ketones are weak acids, with pK_a's in the 16 to 20 range. Their enhanced acidity is due to the electron-withdrawing effect of the carbonyl group and the resonance stabilization of the enolate anion.	 Aldehyde or ketone; Hydroxide ion; Enolate anion; Water  3-Pentanone; Hydroxide ion; Enolate anion of 3-pentanone; Water
Aldol condensation (Section 18.2) A reaction of great synthetic value for carbon–carbon bond formation. Nucleophilic addition of an enolate ion to a carbonyl group, followed by dehydration of the β-hydroxy aldehyde, yields an α,β-unsaturated aldehyde.	 Aldehyde; α,β-Unsaturated aldehyde; Water  Octanal; 2-Hexyl-2-decenal (79%)
Claisen–Schmidt reaction (Section 18.3) A mixed aldol condensation in which an aromatic aldehyde reacts with an enolizable aldehyde or ketone.	 Aromatic aldehyde; Aldehyde or ketone; α,β-Unsaturated carbonyl compound; Water  Benzaldehyde; 3,3-Dimethyl-2-butanone; 4,4-Dimethyl-1-phenyl-1-penten-3-one (88–93%)
α Alkylation of aldehydes and ketones (Section 18.4) Alkylation of simple aldehydes and ketones via their enolates is difficult. β-Diketones can be converted quantitatively to their enolate anions, which react efficiently with primary alkyl halides.	 β-Diketone; α-Alkyl-β-diketone  2-Benzyl-1,3-cyclohexanedione; Benzyl chloride; 2,2-Dibenzyl-1,3-cyclohexanedione (69%)

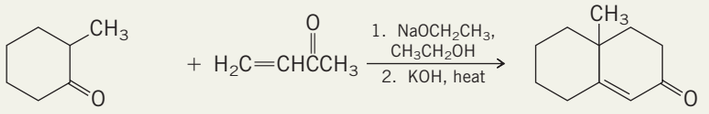
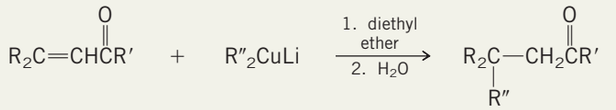
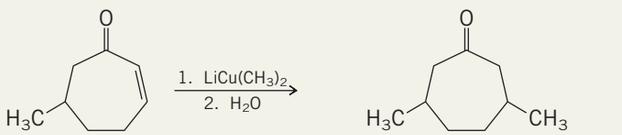
—Continued

TABLE 18.2 Reactions of Aldehydes and Ketones That Involve Enol or Enolate Ion Intermediates *(Continued)*

Reaction (section) and comments	General equation and typical example
Enolization (Sections 18.5–18.6) Aldehydes and ketones having at least one α hydrogen exist in equilibrium with their enol forms. The rate at which equilibrium is achieved is increased by acidic or basic catalysts. The enol content of simple aldehydes and ketones is quite small; β-diketones, however, are extensively enolized.	 Aldehyde or ketone — Enol  $K = 1 \times 10^{-8}$ Cyclopentanone — Cyclopenten-1-ol
α Halogenation (Sections 18.7 and 18.8) Halogens react with aldehydes and ketones by substitution; an α hydrogen is replaced by a halogen. Reaction occurs by electrophilic attack of the halogen on the carbon–carbon double bond of the enol form of the aldehyde or ketone. An acid catalyst increases the rate of enolization, which is the rate-determining step.	 Aldehyde or ketone — Halogen — α-Halo aldehyde or ketone — Hydrogen halide  *p*-Bromoacetophenone — Bromine — *p*-Bromophenacyl bromide (69–72%) — Hydrogen bromide
Haloform reaction (Section 18.9) Methyl ketones are cleaved on reaction with excess halogen in the presence of base. The products are a trihalomethane (haloform) and a carboxylate salt.	 Methyl ketone — Halogen — Carboxylate ion — Trihalomethane (haloform)  4,4-Dimethyl-2-pentanone — 3,3-Dimethylbutanoic acid (89%) — Bromoform
Conjugate addition to α,β-unsaturated carbonyl compounds (Sections 18.11–18.14) The β-carbon atom of an α,β-unsaturated carbonyl compound is electrophilic; nucleophiles, especially weakly basic ones, yield the products of conjugate addition to α,β-unsaturated aldeydes and ketones.	 α,β-Unsaturated aldehyde or ketone — Nucleophile — Product of conjugate addition  4-Methyl-3-penten-2-one — 4-Amino-4-methyl-2-pentanone (63–70%)

—Continued

TABLE 18.2 Reactions of Aldehydes and Ketones That Involve Enol or Enolate Ion Intermediates *(Continued)*

Reaction (section) and comments	General equation and typical example
Robinson annulation (Section 18.13) A combination of conjugate addition of an enolate anion to an α,β-unsaturated ketone with subsequent intramolecular aldol condensation.	 2-Methylcyclohexanone; Methyl vinyl ketone; 6-Methylbicyclo[4.4.0]-1-decen-3-one (46%)
Conjugate addition of organocopper compounds (Section 18.14) The principal synthetic application of lithium dialkylcuprate reagents is their reaction with α,β-unsaturated carbonyl compounds. Alkylation of the β carbon occurs.	 α,β-Unsaturated aldehyde or ketone; Lithium dialkylcuprate; β-Alkyl aldehyde or ketone  6-Methylcyclohept-2-enone; 3,6-Dimethylcycloheptanone (85%)

PROBLEMS

18.22 (a) Write structural formulas for all the noncyclic aldehydes and ketones of molecular formula C_4H_6O.

(b) Are any of these compounds stereoisomers?

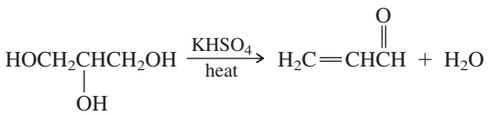
(c) Are any of these compounds chiral?

(d) Which of these are α,β-unsaturated aldehydes or α,β-unsaturated ketones?

(e) Which of these can be prepared by a simple (i.e., not mixed) aldol condensation?

18.23 The main flavor component of the hazelnut is (2*E*,5*S*)-5-methyl-2-hepten-4-one. Write a structural formula showing its stereochemistry.

18.24 The simplest α,β-unsaturated aldehyde *acrolein* is prepared by heating glycerol with an acid catalyst. Suggest a mechanism for this reaction.



18.25 In each of the following pairs of compounds, choose the one that has the greater enol content, and write the structure of its enol form: