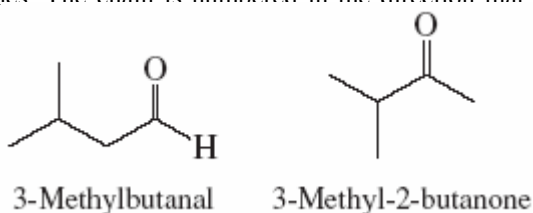


Aldehydes and Ketones: Nucleophilic Addition to the Carbonyl Group

SUMMARY

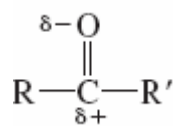
The chemistry of the carbonyl group is probably the single most important aspect of organic chemical reactivity. Classes of compounds that contain the carbonyl group include many derived from carboxylic acids (acyl chlorides, acid anhydrides, esters, and amides) as well as the two related classes discussed in this chapter: *aldehydes* and *ketones*.

Section 17.1 The substitutive IUPAC names of aldehydes and ketones are developed by identifying the longest continuous chain that contains the carbonyl group and replacing the final *-e* of the corresponding alkane by *-al* for aldehydes and *-one* for ketones. The chain is numbered in the direction that gives the lowest locant to the carbon of the carbonyl group.



Ketones may also be named using functional class IUPAC nomenclature by citing the two groups attached to the carbonyl in alphabetical order followed by the word *ketone*. Thus, 3-methyl-2-butanone (substitutive) becomes isopropyl methyl ketone (functional class).

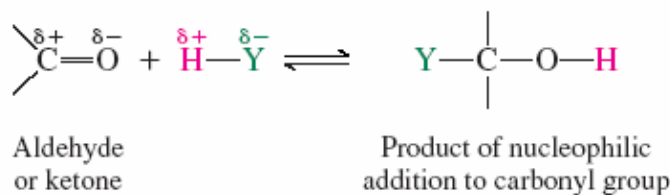
Section 17.2 The carbonyl carbon is sp^2 -hybridized, and it and the atoms attached to it are coplanar. Aldehydes and ketones are polar molecules. Nucleophiles attack CPO at carbon (positively polarized) and electrophiles, especially protons, attack oxygen (negatively polarized).



Section 17.3 Aldehydes and ketones have higher boiling points than hydrocarbons, but have lower boiling points than alcohols.

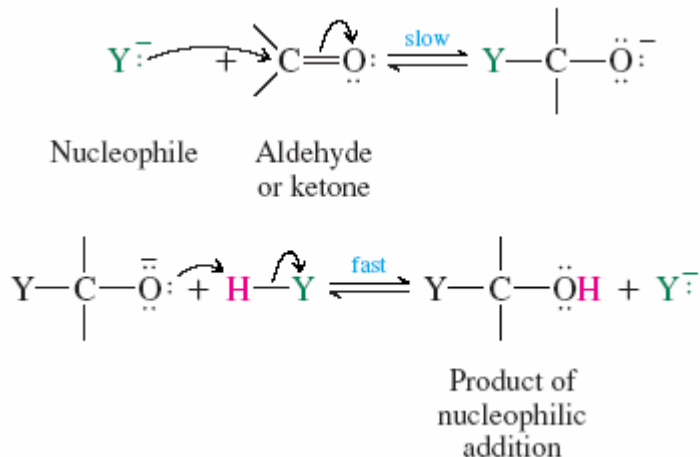
Section 17.4 The numerous reactions that yield aldehydes and ketones discussed in earlier chapters and reviewed in Table 17.1 are sufficient for most syntheses.

Sections 17.5–17.13 The characteristic reactions of aldehydes and ketones involve *nucleophilic addition* to the carbonyl group and are summarized in Table 17.5. Reagents of the type HY react according to the general equation

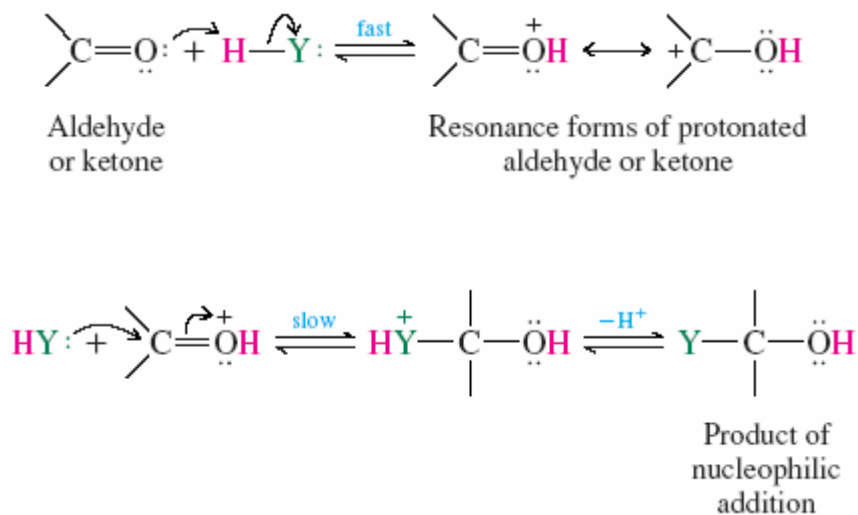


Aldehydes undergo nucleophilic addition more readily and have more favorable equilibrium constants for addition than do ketones.

The step in which the nucleophile attacks the carbonyl carbon is rate-determining in both base-catalyzed and acid-catalyzed nucleophilic addition. In the base-catalyzed mechanism this is the first step.



Under conditions of acid catalysis, the nucleophilic addition step follows protonation of the carbonyl oxygen. Protonation increases the carbocation character of a carbonyl group and makes it more electrophilic.



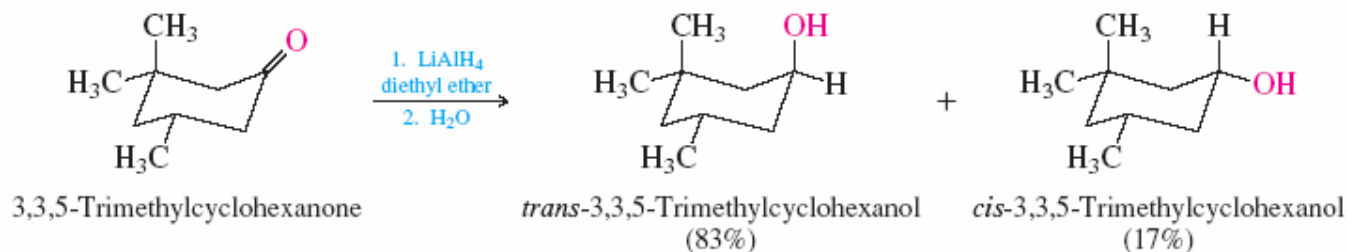
Often the product of nucleophilic addition is not isolated but is an intermediate leading to the ultimate product. Most of the reactions in Table 17.5 are of this type.

TABLE 17.5

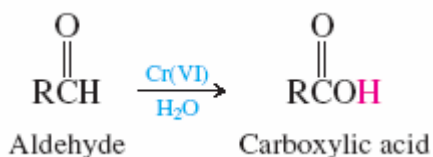
Nucleophilic Addition to Aldehydes and Ketones

Reaction (section) and comments	General equation and typical example
Hydration (Section 17.6) Can be either acid- or base-catalyzed. Equilibrium constant is normally unfavorable for hydration of ketones unless R, R', or both are strongly electron-withdrawing.	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}' + \text{H}_2\text{O} \rightleftharpoons \text{R}-\overset{\text{OH}}{\underset{\text{OH}}{\text{C}}}-\text{R}'$ <p>Aldehyde or ketone Water Geminal diol</p>
	$\text{ClCH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_3 \xrightleftharpoons{\text{H}_2\text{O}} \text{ClCH}_2-\overset{\text{OH}}{\underset{\text{OH}}{\text{C}}}-\text{CH}_3$ <p>Chloroacetone (90% at equilibrium) Chloroacetone hydrate (10% at equilibrium)</p>
Cyanohydrin formation (Section 17.7) Reaction is catalyzed by cyanide ion. Cyanohydrins are useful synthetic intermediates; cyano group can be hydrolyzed to $-\text{CO}_2\text{H}$ or reduced to $-\text{CH}_2\text{NH}_2$.	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}' + \text{HCN} \rightleftharpoons \text{R}-\overset{\text{OH}}{\underset{\text{CN}}{\text{C}}}-\text{R}'$ <p>Aldehyde or ketone Hydrogen cyanide Cyanohydrin</p>
	$\text{CH}_3\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2\text{CH}_3 \xrightarrow[\text{H}^+]{\text{KCN}} \text{CH}_3\text{CH}_2-\overset{\text{OH}}{\underset{\text{CN}}{\text{C}}}-\text{CH}_2\text{CH}_3$ <p>3-Pentanone 3-Pentanone cyanohydrin (75%)</p>
Reaction with secondary amines (Section 17.11) Isolated product is an enamine. Carbinolamine intermediate cannot dehydrate to a stable imine.	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_2\text{R}' + \text{R}''_2\text{NH} \rightleftharpoons \text{R}-\overset{\text{R}''\text{NR}''}{\text{C}}=\text{CHR}' + \text{H}_2\text{O}$ <p>Aldehyde or ketone Secondary amine Enamine Water</p>
	$\text{Cyclohexanone} + \text{Morpholine} \xrightarrow[\text{heat}]{\text{benzene}} \text{1-Morpholinocyclohexene} + \text{H}_2\text{O}$ <p>Cyclohexanone Morpholine 1-Morpholinocyclohexene (85%)</p>
The Wittig reaction (Sections 17.12–17.13) Reaction of a phosphorus ylide with aldehydes and ketones leads to the formation of an alkene. A versatile method for the regiospecific preparation of alkenes.	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}' + (\text{C}_6\text{H}_5)_3\text{P}^+-\overset{\ominus}{\text{C}}(\text{A})(\text{B}) \longrightarrow \text{R}-\overset{\text{A}}{\text{C}}=\overset{\text{B}}{\text{C}}-\text{R}' + (\text{C}_6\text{H}_5)_3\text{P}^+-\text{O}^-$ <p>Aldehyde or ketone Wittig reagent (an ylide) Alkene Triphenylphosphine oxide</p>
	$\text{CH}_3-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_3 + (\text{C}_6\text{H}_5)_3\text{P}^+-\overset{\ominus}{\text{C}}\text{HCH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \xrightarrow{\text{DMSO}} (\text{CH}_3)_2\text{C}=\text{CHCH}_2\text{CH}_2\text{CH}_2\text{CH}_3 + (\text{C}_6\text{H}_5)_3\text{P}^+-\text{O}^-$ <p>Acetone 1-Pentylidenetriphenylphosphorane 2-Methyl-2-heptene (56%) Triphenylphosphine oxide</p>

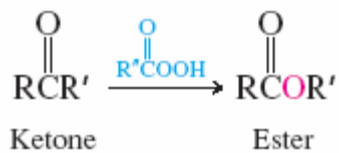
Section 17.14 Nucleophilic addition to the carbonyl group is *stereoselective*. When one direction of approach to the carbonyl group is less hindered than the other, the nucleophile normally attacks at the less hindered face.



Section 17.15 Aldehydes are easily oxidized to carboxylic acids.



Section 17.16 The oxidation of ketones with peroxy acids is called the *Baeyer–Villiger oxidation* and is a useful method for preparing esters.



Section 17.17 A strong peak near 1700 cm^{-1} in the IR spectrum is characteristic of compounds that contain a C=O group. The ^1H and ^{13}C NMR spectra of aldehydes and ketones are affected by the deshielding of a C=O group. The proton of an HO-C=O group appears in the δ 8–10 range. The carbon of a C=O group is at δ 190–210.