

Ketones and Aldehydes

Reading: Wade chapter 18, sections 18-1- 18-21

Study Problems: 18-43, 18-44, 18-50, 18-51, 18-52, 18-59, 18-60, 18-62, 18-64, 18-72.

Key Concepts and Skills:

- Interpret the IR, NMR, and UV spectra of aldehydes and ketones
- Write equations for the syntheses of aldehydes and ketones from alcohols, alkenes, alkynes, carboxylic acids, nitriles, acid chlorides, dithianes, and aromatic compounds.
- Propose effective single- and multistep syntheses of aldehydes and ketones.
- Predict the products of reactions of ketones and aldehydes with the following reagents: hydride reducing agents, Wolff-Kishner reagents, Grignard and organolithium reagents, phosphorus ylides, water, HCN, ammonia and primary amines, alcohols, oxidizing agents, hydroxylamine and hydrazine derivatives.
- Use retrosynthetic analysis to propose effective multistep syntheses using ketones and aldehydes as intermediates and protecting the carbonyl group if necessary.

Lecture Topics:

I. Structure of Ketones and Aldehydes

Both Ketones and Aldehydes contain the carbonyl (C=O) group. Ketones have two alkyl groups attached to the carbonyl; aldehydes have only one alkyl group attached to the carbonyl:

Structure:

The carbonyl double bond is shorter, stronger, and more polarized than C=C.

In terms of dipole moment, the carbonyl has an unequal sharing of electron density between the O and C atoms: the pi electrons (less tightly held) are pulled toward Oxygen:

Acetone's dipole moment is 2.9 D, stronger than that of chloromethane ($\text{H}_3\text{C}-\text{Cl}$, 1.9D) and dimethyl ether (CH_3OCH_3 , 1.3D)

II. Review the nomenclature of Ketones and Aldehydes in Text

III. Physical Properties of Aldehydes and Ketones

Dipole-dipole interactions are the main intermolecular force holding ketones and aldehydes in the liquid phase. The dipole-dipole interaction is strong because of the high dipole moment attributable to the carbonyl group, giving ketones and aldehydes higher boiling points than hydrocarbons. However, the dipole-dipole interaction is weaker than hydrogen-bonding interactions, and thus ketones and aldehydes have lower boiling points than alcohols. Nevertheless, aldehydes and ketones are able to engage alcohols and water in hydrogen bonding via the carbonyl oxygen lone-pairs, resulting in the solubility of polar substances like alcohols and water in lower aldehydes and ketones.

IV. Spectroscopy: Review

IR: the carbonyl ($\text{C}=\text{O}$) stretch of aldehydes and ketones is at 1710cm^{-1} . Conjugation lowers this stretching frequency to 1685cm^{-1} . The C-H stretch of aldehydes is at 2710cm^{-1} .

^1H NMR:

^{13}C NMR:

UV spectroscopy: two types of transitions are observed in the UV spectra of ketones and aldehydes. The $\pi \rightarrow \pi^*$ transition is a strong absorption, but is observed in ordinary UV spectra (covering the range 200-400nm) only for conjugated ketones and aldehydes, where the $\pi \rightarrow \pi^*$ energy gap is sufficiently small. The $n \rightarrow \pi^*$ transition is much weaker than the $\pi \rightarrow \pi^*$ transition, and it corresponds to the promotion of a non-bonding electron to π^* . Unconjugated ketones and aldehydes have this transition between 280 and 300 nm; conjugated ketones have this transition between 315 and 330 nm.

V. Preparation of Ketones and Aldehydes

Review:

A. From Alcohols:

B. Ozonolysis of Alkenes

C. Friedel-Crafts Alkylation

D. Hydration of Alkynes

E. Alternative Syntheses of Ketones and Aldehydes

Dithiane alkylation: S_N2 Alkylation of dithiane anions with alkyl halides leads to aldehydes and ketones. Hydrolysis of the intermediate substituted dithianes to the corresponding carbonyl compounds occurs with acidic mercury (II) solutions.

Preparation of Aldehydes and Ketones from Carboxylic Acid Derivatives
Reduction of carboxylic acids:

Grignard Addition to Nitriles:

Reduction Methods:

$\text{LiAlH}(\text{OtBu})_3$ is a milder reducing agent than LiAlH_4 and will reduce acid chlorides selectively to aldehydes without reducing aldehydes further to alcohols

Gilman reagents, R_2CuLi , react with acid chlorides to form ketones; no further addition to the ketone carbonyl is observed (forming tertiary alcohols)

Reactions of Aldehydes and Ketones

1. **Nucleophilic addition reactions:** nucleophile approaches electrophilic carbon atom and dumps electron density into π^* orbital, causing the pi bond of the carbonyl to break and pushing the pi electrons onto oxygen.

Irreversible additions to carbonyls: Strong Nucleophiles

1. **Grignard and organolithium addition:** Highly basic grignard and organolithium reagents add to carbonyl irreversibly to give alcohols; aldehydes give 2° alcohols and ketones give 3° alcohols; formaldehyde gives a 1° alcohol:

2. **Hydride reduction:** NaBH_4 and LiAlH_4 are reducing agents which provide hydride as the nucleophile. Aldehydes are reduced to 1° alcohols, ketones to 2° alcohols:

3. **Wittig reaction:** A ketone or aldehyde reacts with a phosphorous ylide to produce an alkene. This is one of the most useful ways of preparing alkenes. The phosphorous ylide is generated by a two-step process: Triphenyl phosphine reacts with an alkyl halide in $\text{S}_{\text{N}}2$ fashion to generate a phosphonium salt, and then a strong base (like butyllithium) deprotonates the carbon next to the positively charged phosphorous to generate the ylide, which is an internal salt. Note that the major resonance form of the ylide is the zwitterion and not the form containing the double bond (which contains a very weak pi bond due to poor P-C p-orbital overlap).

Addition of the ylide to a carbonyl yields a betaine intermediate, which rapidly becomes an oxaphosphetane. Elimination of phosphine oxide provides the alkene, with the driving force being creation of the strong phosphorous-oxygen double bond.