Chapter 20: Aldehydes and Ketones

Nomenclature of Aldehydes and Ketones

- for both aldehydes and ketones, the parent chain is the longest continuous carbon chain that contains the carbon of the carbonyl group
- numbering (locant) priority is given to the carbonyl carbon
- aldehydes always have the carbonyl group at carbon 1, so a number is not needed
- ketones have the "one" suffix, aldehydes have the "al" suffix

Review of the Synthesis of Aldehydes and Ketones

A. Friedel-Crafts Acylation

B. Oxidation of Alcohols (most common method)

Problems: 5
Review of Reactions of Aldehydes and Ketones

A. Oxidation of Aldehydes

\[
\text{OH} \xrightarrow{\text{PCC}} \text{H} \xrightarrow{\text{KMnO}_4} \text{OH}
\]

- aldehydes may be oxidized using KMnO\(_4\) or Jones reagent to the carboxylic acid
- since aldehydes are usually synthesized via oxidation of 1° alcohols, the synthesis of carboxylic acids is usually accomplished via direct oxidation of 1° alcohols with the strong oxidizing agents
- ketones CANNOT be oxidized further

B. Reduction of Aldehydes and Ketones

\[
\text{O} \xrightarrow{\text{Zn(Hg), HCl}} \text{OH}
\]

- Clemmensen or Wolff-Kishner reduction of aldehydes and ketones leads to reduction of the carbonyl group to a CH\(_2\) group

\[
\text{OH} \xrightarrow{\text{H}_2, \text{Pt}^\circ} \text{H}
\]

- hydrogenation of ketones forms 2° alcohols (the opposite reaction of the oxidation process)
- hydrogenation of aldehydes forms 1° alcohols

Problems: 6

General Reactivity of Aldehydes and Ketones

- both aldehydes and ketones have partial positive charge at the carbon of the carbonyl group due to the polar C=O bond
- the partial charge on the aldehyde is greater since it is flanked by a single electron-donating alkyl group
- while both aldehydes and ketones are reactive towards nucleophilic addition, aldehydes are more reactive due to i) the greater partial positive charge and ii) less steric interference
Mode of Attack of Strong Nucleophiles on the Carbonyl Group of Aldehydes and Ketones

*Nucleophiles attack the partially positively charged carbon of the carbonyl group by pushing electrons into the polarized pi bond*

*The pi electrons are forced onto the electronegative oxygen atom*

*These reactions are often followed up by addition of acidic water (HCl, H₂O or H₃O⁺) to protonate the negatively charged oxygen and form a neutral product*

**Addition of Strong Nucleophiles to Aldehydes and Ketones**

**A. Addition of Organometallic Reagents**

\[
\begin{align*}
\text{O} & \quad \text{NaNH}_2 \\
\text{1. CH₃CH₂Li} & \quad \text{2. H}_3\text{O}^+ \\
\text{O} & \quad \text{1. H} \\
\text{2. H}_3\text{O}^+ & \quad \text{CHO} \\
\text{1. CH₃MgBr} & \quad \text{2. H}_3\text{O}^+ \\
\text{O} & \quad \text{1. ?} \\
\text{2. H}_3\text{O}^+ & \quad \text{OH}
\end{align*}
\]

*These types of nucleophilic additions to aldehydes and ketones are critical reactions since they result in the formation of new C-C bonds!*

*These reactions, therefore, provide a way in which to create larger molecules from readily available smaller molecules*

Problems: 7
B. Addition of HCN

1. NaCN
2. $\text{H}_3\text{O}^+$

$\text{HCN}$ catalytic NaCN

- there are two methods for addition of HCN to a carbonyl group. The net result is the same
- the product of addition is referred to as a "cyanohydrin" to reflect the presence of both the cyanide AND hydroxyl groups
- as with the organometallics, this reaction forms a new C-C bond

C. Addition of Hydride (hydride reduction)

- a "hydride" is a hydrogen with an extra electron, giving it a negative charge
- sodium hydride is the simplest form of hydride, but in this form it acts only as a strong base and never as a nucleophile
- $\text{NaBH}_4$ and LiAlH$_4$ are both sources of nucleophilic hydride

Examples

1. $\text{NaBH}_4$
2. $\text{H}_3\text{O}^+$

1. $\text{LiAlH}_4$
2. HCl, H$_2$O

- reduction of aldehydes with either $\text{NaBH}_4$ OR LiAlH$_4$ results in the formation of $1^\circ$ alcohols
- reduction of ketones with either $\text{NaBH}_4$ OR LiAlH$_4$ results in the formation of $2^\circ$ alcohols
Summary of Nucleophilic Addition Reactions of Aldehydes and Ketones

\[
\text{R} - \text{R'}(\text{H}) \xrightarrow{\text{nu}} \text{product}
\]

<table>
<thead>
<tr>
<th>nucleophile</th>
<th>catalyst</th>
<th>type of product</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{H}^-) (hydride, (\text{NaBH}_4) or (\text{LiAlH}_4))</td>
<td>none</td>
<td>(\text{H}_2\text{O}) alcohol (1° from aldehyde, 2° from ketone)</td>
</tr>
<tr>
<td>(\text{R}^-) (Grignard, alkyllithium)</td>
<td>none</td>
<td>alcohol (2° from aldehyde, 3° from ketone)</td>
</tr>
<tr>
<td>(\text{C} \equiv \text{N}) (cyanide)</td>
<td>none</td>
<td>cyanohydrin</td>
</tr>
</tbody>
</table>

D. Addition of Alcohols

- alkoxides are strong nucleophiles but alcohols are poor nucleophiles
- alcohols will not react with aldehydes or ketones in the absence of an acid catalyst
- an acid catalyst protonates a lone pair of the oxygen atom of the carbonyl group
- protonation increases the partial positive charge on the carbon and enhances the reactivity of the carbonyl towards nucleophilic addition
- under acidic conditions, aldehydes and ketones will react with the weaker alcohol nucleophile
- the most common acid catalysts are \(\text{H}_3\text{PO}_4\), \(\text{H}_2\text{SO}_4\), \(\text{HCl}\) or para-toluenesulfonic acid (TsOH)

\[
\text{R} - \text{OH} \xrightarrow{\text{H}^+} \text{R} - \text{R'}(\text{H}) + \text{OH}^-
\]

- reaction of aldehydes or ketones with alcohols under acid catalysis results in the addition of TWO equivalents of the alcohol to the carbonyl group. The product is called a "ketal"
- if a diol such as ethylene glycol is used, both ends of the diol add across the carbonyl group to form a cyclic ketal
- cyclic ketals are the most often utilized type of ketal
Ketals are "ether-like" compounds that behave like ethers, i.e., they are fairly unreactive.

- The ketal formation process can be reversed by addition of water under acidic conditions.
- Ketals act as carbonyl "protecting groups" in that they can be placed on a carbonyl group to keep it from reacting and then removed when desired.

**Glucose, Sorbitol and other Sweeteners**

- Sorbitol
- Glucose
- α-D-glucose (hemiacetal)
- Sucrose (table sugar)
- Sucralose (Splenda™)
- Saccharin (Sweet 'N Low™)
- Stevia (Truvia™)
Addition/Elimination Reactions of Aldehydes and Ketones

A. The Wittig Reaction

**Overall Reaction:**

- the Wittig reaction takes place between an aldehyde or a ketone and a Wittig reagent
- the final product is replacement of the C=O double bond by a C=C double bond

**Reaction Steps**

**Examples**

- (Ph)₃P=CHCH₂CH₃
- (Ph)₃P=CHCHO
B. Imine Formation

**Overall Reaction:**

- when a 1° amine reacts with a ketone or aldehyde, an imine product results
- an acid catalyst [usually TsOH or HCl] is often needed
- the final product is replacement of the C=O double bond by a C=N double bond

**Reaction Steps**

**Examples**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Reaction Steps</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃CH₂NH₂</td>
<td>CH₃CH₂NH₂ + H⁺</td>
</tr>
<tr>
<td>TsOH</td>
<td>CH₃CH₂NH₂ + H⁺</td>
</tr>
</tbody>
</table>

**enzyme**

**trans-retinal**

**enzyme**

**cis-retinal**

**Protein**

**Protein**

**LIGHT**
### Summary of Nucleophilic Addition Reactions of Aldehydes and Ketones

<table>
<thead>
<tr>
<th>nucleophile</th>
<th>catalyst</th>
<th>type of product</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>single addition reactions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{H}^-$ (hydride, NaBH₄ or LiAlH₄)</td>
<td>none</td>
<td>alcohol (1° from aldehyde, 2° from ketone)</td>
</tr>
<tr>
<td>$\text{R}^-$ (Grignard, alkyllithium)</td>
<td>none</td>
<td>alcohol (2° from aldehyde, 3° from ketone)</td>
</tr>
<tr>
<td>$\text{R}^-$ (organocuprate)</td>
<td>none</td>
<td>Michael addition to α,β-unsaturated aldehydes and ketones</td>
</tr>
<tr>
<td>$\text{C≡N}$ (cyanide)</td>
<td>none</td>
<td>cyanohydrin</td>
</tr>
<tr>
<td><strong>double addition reactions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{ROH}$ (alcohols)</td>
<td>$\text{H}^+$</td>
<td>acetal</td>
</tr>
<tr>
<td><strong>addition-elimination reactions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Ph)$_3$P=CR$_2$ (Wittig reagents)</td>
<td>none</td>
<td>alkene</td>
</tr>
<tr>
<td>$\text{R-NH}_2$ (1° amine)</td>
<td>$\text{H}^+$ sometimes</td>
<td>imine</td>
</tr>
</tbody>
</table>