17.5
Reactions of Aldehydes and Ketones:
A Review and a Preview
Already covered in earlier chapters:

- reduction of C=O to CH$_2$
  - Clemmensen reduction
  - Wolff-Kishner reduction
- reduction of C=O to CH$_2$OH
- addition of Grignard and organolithium reagents
17.6
Principles of Nucleophilic Addition to Carbonyl Groups:
Hydration of Aldehydes and Ketones
Hydration of Aldehydes and Ketones
**Substituent Effects on Hydration Equilibria**

Compounds with alkyl groups:
- **Electronic effect**: alkyl groups stabilize the reactants compared to H.
- **Steric effect**: alkyl groups crowd the product.

Chemical equation:

\[
\text{RCR'} + \text{H}_2\text{O} \rightleftharpoons \text{RCCR'}\text{OH}\text{OH} \text{ compared to H}
\]
### Equilibrium Constants for Hydration

<table>
<thead>
<tr>
<th>C=O</th>
<th>Hydrate</th>
<th>K</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₂=O</td>
<td>CH₂(OH)₂</td>
<td>41</td>
<td>99.96</td>
</tr>
<tr>
<td>CH₃CH=O</td>
<td>CH₃CH(OH)₂</td>
<td>0.018</td>
<td>50</td>
</tr>
<tr>
<td>(CH₃)₃CCH=O</td>
<td>(CH₃)₃CCH(OH)₂</td>
<td>0.0041</td>
<td>19</td>
</tr>
<tr>
<td>(CH₃)₂C=O</td>
<td>(CH₃)₂C(OH)₂</td>
<td>0.000025</td>
<td>0.14</td>
</tr>
</tbody>
</table>
When does equilibrium favor hydrate?

when carbonyl group is destabilized

• alkyl groups stabilize C=O
• electron-withdrawing groups destabilize C=O
Substituent Effects on Hydration Equilibria

\[
R = \text{CH}_3: \quad K = 0.000025
\]

\[
R = \text{CF}_3: \quad K = 22,000
\]
Mechanism of Hydration (base)

Step 1:

\[
\text{H} \quad \text{O}^- \quad + \quad \text{C}=\text{O} \quad \rightarrow \quad \text{HO}^-\text{C}=\text{O}^-\text{O}^-
\]
Mechanism of Hydration (base)

Step 2:

\[
\text{HO} - \text{C} - \text{OH} + \text{H} \rightarrow \text{HO} - \text{C} - \text{O} - \text{H} + \text{H}_2\text{O}
\]
*Mechanism of Hydration (acid)*

**Step 1:**

\[
\text{C} = \text{O} : + \text{H} - \text{O} : \text{H} \rightarrow \text{C} = \text{O} + \text{H} - \text{O} : \text{H}
\]
Mechanism of Hydration (acid)

Step 2:

$$\text{Step 2:} \quad \text{H}_2\text{O} + \text{C}≡\text{O} \rightarrow \text{H}_2\text{O}^-\text{C}\text{O}^-$$
Mechanism of Hydration (acid)

Step 3:
17.7 Cyanohydrin Formation
Cyanohydrin Formation

\[ C═O⁻ : + HCN \rightleftharpoons :N\equiv C - C\equiv O\equiv H \]
Cyanohydrin Formation

\[
\begin{array}{c}
\text{Cyanogen} \\
\text{Formaldehyde}
\end{array}
\]
Cyanohydrin Formation
Cyanohydrin Formation

\[
\begin{align*}
\text{Cyanohydrin Formation} \\
\text{(Diagram showing the reaction process)}
\end{align*}
\]
Cyanohydrin Formation

\[ \text{N} \equiv \text{C} \quad \text{C} \quad \text{O} \quad \text{H} \]

\[ \text{H} \quad \text{O} \quad \text{H} \]

\[ \text{N} \equiv \text{C} \quad \text{C} \quad \text{O} \quad \text{H} \]
Example

Cl

| Cl | O | Cl

2,4-Dichlorobenzaldehyde

| Cl | CH | Cl |

NaCN, water

then H$_2$SO$_4$

2,4-Dichlorobenzaldehyde cyanohydrin (100%)
Acetone cyanohydrin is used in the synthesis of methacrylonitrile (see problem 17.6).