A Preview of Carbonyl Compounds

مروری بر ترکیبات کربونیل دار

Dr M. Mehrdad
University of Guilan, Department of Chemistry, Rasht, Iran
m-mehrdad@guilan.ac.ir

Based on McMurry’s Organic Chemistry, 7th edition
Carbonyl compounds are everywhere.

Most biological molecules contain carbonyl groups, as do most pharmaceutical agents and many of the synthetic chemicals that touch our everyday lives.
# I - Kinds of Carbonyl Compounds

<table>
<thead>
<tr>
<th>Name</th>
<th>General formula</th>
<th>Name ending</th>
<th>Name</th>
<th>General formula</th>
<th>Name ending</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldehyde</td>
<td>( \text{RCH} )</td>
<td>-al</td>
<td>Ester</td>
<td>( \text{RCO}R' )</td>
<td>-oate</td>
</tr>
<tr>
<td>Ketone</td>
<td>( \text{RCC}R' )</td>
<td>-one</td>
<td>Lactone (cyclic ester)</td>
<td>( \text{COC} )</td>
<td>None</td>
</tr>
<tr>
<td>Carboxylic acid</td>
<td>( \text{RCO}H )</td>
<td>-oic acid</td>
<td>Thioester</td>
<td>( \text{RCO}S )</td>
<td>-thioate</td>
</tr>
<tr>
<td>Acid halide</td>
<td>( \text{RCX} )</td>
<td>-yl or -oyl halide</td>
<td>Amide</td>
<td>( \text{RCN} )</td>
<td>-amide</td>
</tr>
<tr>
<td>Acid anhydride</td>
<td>( \text{RCON} )</td>
<td>-oic anhydride</td>
<td>Lactam (cyclic amide)</td>
<td>( \text{COCN} )</td>
<td>None</td>
</tr>
<tr>
<td>Acyl phosphate</td>
<td>( \text{RCON} )</td>
<td>-yl phosphate</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The $-R'$ and $-H$ in these compounds can't act as leaving groups in nucleophilic substitution reactions.

The $-OH$, $-X$, $-OR'$, $-SR$, $-NH_2$, $-OCOR'$, and $-OPO_3^{2-}$ in these compounds can act as leaving groups in nucleophilic substitution reactions.
II - Nature of the Carbonyl Group

Carbonyl group

Alkene
- The carbonyl carbon atom carries a partial positive charge, is an electrophilic (Lewis acidic) site, and reacts with nucleophiles.

- Conversely, the carbonyl oxygen atom carries a partial negative charge, is a nucleophilic (Lewis basic) site, and reacts with electrophiles.

### Bond Length and Activation Energy

<table>
<thead>
<tr>
<th>Bond</th>
<th>Length (pm)</th>
<th>Activation Energy (kJ/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C=O</td>
<td>122</td>
<td>732</td>
</tr>
<tr>
<td>C=O</td>
<td>143</td>
<td>385</td>
</tr>
<tr>
<td>C-C</td>
<td>154</td>
<td>376</td>
</tr>
<tr>
<td>C=O</td>
<td>134</td>
<td>728</td>
</tr>
<tr>
<td>C-C</td>
<td>154</td>
<td>376</td>
</tr>
</tbody>
</table>

*FIGURE 1 Structure of acetaldehyde.*
III - General Reactions of Carbonyl Compounds

- nucleophilic addition
- nucleophilic acyl substitution
- alpha substitution
- Carbonyl condensation
Nucleophilic Addition Reactions of Aldehydes and Ketones (Chapter 19)

A carbonyl compound ($sp^2$-hybridized carbon) + A nucleophile ($Nu^-$) $\rightleftharpoons$ A tetrahedral intermediate ($sp^3$-hybridized carbon)
FIGURE 2 The addition reaction of an aldehyde or a ketone with a nucleophile. Depending on the nucleophile, either an alcohol or a compound with a C=Nu double bond is formed.
Formation of an Alcohol

**Reduction**

Ketone/aldehyde $\rightarrow$ Tetrahedral intermediate $\rightarrow$ Alcohol

**Grignard reaction**

Ketone/aldehyde $\rightarrow$ Tetrahedral intermediate $\rightarrow$ Alcohol
Formation of \( \text{C}=\text{Nu} \)

The second mode of nucleophilic addition, which often occurs with amine nucleophiles, involves elimination of oxygen and formation of a \( \text{C}=\text{Nu} \) double bond. For example, aldehydes and ketones react with primary amines, \( \text{RNH}_2 \), to form \textit{imines}, \( \text{R}_2\text{C}=\text{NR}' \).

**MECHANISM**

Formation of an imine, \( \text{R}_2\text{C}=\text{NR}' \), by reaction of an amine with an aldehyde or a ketone.

1. Addition to the ketone or aldehyde carbonyl group by the neutral amine nucleophile gives a dipolar tetrahedral intermediate.

2. Transfer of a proton from nitrogen to oxygen then yields an amino alcohol intermediate.

3. Dehydration of the amino alcohol intermediate gives neutral imine and water as final products.
Nucleophilic Acyl Substitution Reactions of Carboxylic Acid Derivatives (Chapter 21)

Carboxylic acid derivative

Tetrahedral intermediate

\[ Y = \text{–OR (ester), –Cl (acid chloride), –NH}_2 \text{ (amide), or –OCOR (acid anhydride)} \]
Nucleophilic acyl substitution of an acid chloride with an alkoxide ion yields an ester.

1. Nucleophilic addition of alkoxide ion to an acid chloride yields a tetrahedral intermediate.

2. An electron pair from oxygen expels chloride ion and yields the substitution product, an ester.
Alpha-Substitution Reactions (Chapter 22)

A carbonyl compound

An enolate ion

An enol

An α-substituted carbonyl compound

α position
A carbonyl compound

An enolate ion

A carbonyl compound

An enolate ion

$S_N^2$ reaction
Carbonyl Condensation Reactions (Chapter 23)

Two acetaldehydes

Aldol

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{C} \quad \text{H} & + & & \text{H}_3\text{C} & \quad \text{C} \quad \text{H} \\
& & & \xrightarrow{\text{NaOH}} & & \quad \text{H}_3\text{C} \\
\end{align*}
\]
A carbonyl condensation reaction between two molecules of acetaldehyde yields a hydroxy aldehyde product.

1. Base abstracts an acidic alpha hydrogen from one acetaldehyde molecule, yielding a resonance-stabilized enolate ion.

2. The enolate ion adds as a nucleophile to the carbonyl group of a second acetaldehyde, producing a tetrahedral alkoxide ion.

3. The tetrahedral intermediate is protonated by solvent to yield the neutral aldol product and regenerate the base catalyst.