Objectives

After completing this section, you should be able to

1. describe in detail the methods for preparing aldehydes discussed in earlier units (i.e., the oxidation of primary alcohols and the cleavage of alkenes).
2. write an equation to describe the reduction of an ester to an aldehyde.
   a. identify the product formed when a given ester is reduced with diisobutylaluminum hydride.
   b. identify the reagents and conditions used in the reduction of an ester to an aldehyde.
   c. identify the disadvantages of using diisobutylaluminum hydride to reduce an ester to an aldehyde.
3. describe in detail the methods for preparing ketones discussed in earlier units (i.e., the oxidation of secondary alcohols, the ozonolysis of alkenes, Friedel-Crafts acylation, and the hydration of terminal alkynes).
   a. write an equation to illustrate the formation of a ketone through the reaction of an acid chloride with a dialkylcopper lithium reagent.
   b. identify the ketone produced from the reaction of a given acid chloride with a specified dialkylcopper lithium reagent.
   c. identify the acid chloride, the dialkylcopper lithium reagent, or both, needed to prepare a specific ketone.

Study Notes

You may wish to review the sections in which we discuss the oxidation of alcohols (17.7) and the cleavage of alkenes (8.8). A third method of preparing aldehydes is to reduce a carboxylic acid derivative; for example, to reduce an ester with diisobutylaluminum hydride (DIBAL-H).

There are essentially five methods of preparing ketones in the laboratory. Four of them have been discussed in earlier sections:

1. the oxidation of a secondary alcohol—Section 17.7.
2. the ozonolysis of an alkene—Section 8.8.
3. Friedel-Crafts acylation—Section 16.3.
4. the hydration of a terminal alkyne—Section 9.4.

The “new” method we introduce in this section involves the reaction of an acid chloride with a diorganocopper reagent. The latter substances were discussed in Section 10.7, which you might now wish to review.

Aldehydes and ketones can be prepared using a wide variety of reactions. Although these reactions are discussed in greater detail in other sections, they are listed here as a summary and to help with planning multistep synthetic pathways. Please use the appropriate links to see more details about the reactions.
Oxidation of 1\textsuperscript{o} alcohols with PCC to form aldehydes

\[
\begin{array}{c}
\text{H}_2 \quad \text{C} \quad \text{O} \\
\text{R} \quad \text{C} \quad \text{OH} \quad \text{PCC} \quad \rightarrow \quad \text{R} \quad \text{C} \quad \text{H}
\end{array}
\]

1\textsuperscript{o} Alcohol

Hydration of an alkyne to form aldehydes

Anti-Markovnikov addition of a hydroxyl group to an alkyne forms an aldehyde. The addition of a hydroxyl group to an alkyne causes tautomerization which subsequently forms a carbonyl.

\[
\begin{array}{c}
\text{R} \quad \text{C} \equiv \text{C} \quad \text{H} \\
\text{Alkyne} \\
1) \quad \text{Diisobutylborane} \\
2) \quad \text{H}_2\text{O} \quad \text{NaOH}
\end{array}
\]

Reduction of an ester, acid chloride or nitrile to form aldehydes

\[
\begin{array}{c}
\text{O} \quad \text{C} \quad \text{O} \quad \text{R} \quad \text{R}' \\
\text{Ester} \\
1) \quad \text{DIBAL-H} \\
2) \quad \text{H}_2\text{O}
\end{array}
\]

\[
\begin{array}{c}
\text{O} \quad \text{C} \quad \text{Cl} \quad \text{R} \quad \text{R}' \\
\text{Acid Chloride} \\
1) \quad \text{LiAlH(O-\text{t-Bu})}_2 \\
2) \quad \text{H}_2\text{O}
\end{array}
\]

\[
\begin{array}{c}
\text{R} \quad \text{C} \equiv \text{N} \\
\text{Nitrile} \\
1) \quad \text{DIBAL-H} \\
2) \quad \text{H}_2\text{O}
\end{array}
\]
Oxidation of $2^\circ$ alcohols to form ketones

Typically uses Jones reagent ($\text{CrO}_3$ in $\text{H}_2\text{SO}_4$) but many other reagents can be used

\[
\begin{array}{c}
\text{H} \\
\text{R} \\
\text{C} \\
\text{OH} \\
\text{R'} \\
\text{C} \\
\text{R'} \\
\text{H}_2\text{SO}_4 \\
\end{array}
\xrightarrow{\text{CrO}_3}
\begin{array}{c}
\text{C} \\
\text{R} \\
\text{R'} \\
\end{array}
\]

$2^\circ$ Alcohol

Hydration of an alkyne to form ketones

The addition of a hydroxyl group to an alkyne causes tautomerization which subsequently forms a carbonyl. Markovnikov addition of a hydroxyl group to an alkyne forms a ketone.

\[
\begin{array}{c}
\text{R} \\
\text{C} \\
\text{C} \\
\text{H} \\
\text{H}_2\text{SO}_4 \\
\text{Hg}^{\text{II}} \\
\end{array}
\xrightarrow{\text{H}_2\text{O}}
\begin{array}{c}
\text{R} \\
\text{C} \\
\text{C} \\
\text{H} \\
\text{H}_2\text{SO}_4 \\
\text{Hg}^{\text{II}} \\
\end{array}
\xrightarrow{\text{H}_2\text{O}}
\begin{array}{c}
\text{R} \\
\text{C} \\
\text{CH}_3 \\
\end{array}
\]

Friedel-Crafts acylation to form a ketone

\[
\begin{array}{c}
\text{Cl} \\
\text{R} \\
\text{C} \\
\text{O} \\
\text{C} \\
\text{Cl} \\
\text{AlCl}_3 \\
\end{array}
\xrightarrow{\text{C}}
\begin{array}{c}
\text{R} \\
\text{C} \\
\text{R} \\
\end{array}
\]

Acid Chloride

Reaction of Grignard reagents with nitriles to form ketones

\[
\begin{array}{c}
\text{R} \\
\text{C} \\
\text{N} \\
\text{Nitrile} \\
\text{R'} \\
\text{1) R'MgBr} \\
\text{2) H}_2\text{O} \\
\end{array}
\xrightarrow{1) R'MgBr}
\begin{array}{c}
\text{R} \\
\text{C} \\
\text{R'} \\
\end{array}
\xrightarrow{2) H}_2\text{O}
\begin{array}{c}
\text{R} \\
\text{C} \\
\text{R'} \\
\end{array}
\]
Alkenes can be cleaved using ozone ($O_3$) to form aldehydes and/or ketones:

$$\text{Alkene} \xrightarrow{1) O_3} \text{Aldehyde} + \text{Ketone}$$

This is an example of an Ozonolysis reaction.

Organocuprate reagents convert acid chlorides to ketones:

$$\text{Acid Chloride} \xrightarrow{R^2CuLi} \text{Ketone} + R'Cu$$

Example 1:

$$\text{Acid Chloride} \xrightarrow{(CH_3CH_2)_2CuLi} \text{Ketone}$$

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