Objectives

After completing this section, you should be able to

1. determine whether a given reaction should be classified as an oxidation or a reduction.

2. write an equation to represent the reduction of an aldehyde or ketone using sodium borohydride or lithium aluminum hydride.
   a. discuss the relative advantages and disadvantages of using sodium borohydride or lithium aluminum hydride to reduce aldehydes or ketones to alcohols.
   b. identify the product formed from the reduction of a given aldehyde or ketone.
   c. identify the aldehyde or ketone that should be used to produce a given alcohol in a reduction reaction.
   d. identify the best reagent to carry out the reduction of a given aldehyde or ketone.

3. write an equation to represent the reduction of an ester or a carboxylic acid to an alcohol.
   a. identify the product formed from the reduction of a given ester or carboxylic acid.
   b. identify the esters or carboxylic acids that could be reduced to form a given alcohol.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- (organic) oxidation
- (organic) reduction

Study Notes

In your course in first-year general chemistry, you probably discussed oxidation-reduction reactions in terms of the transfer of electrons and changes in oxidation numbers (oxidation states). In organic chemistry, it is often more convenient to regard reduction as the gain of hydrogen or loss of oxygen, and oxidation as the gain of oxygen or the loss of hydrogen. There is no contradiction in using these various definitions. For example, when hydrogen is added across the double bond of ethene to reduce it to ethane, the oxidation number of the doubly bonded carbon atoms decreases from −II to −III. Similarly, when 2-propanol

\[
\text{OH} \quad \text{(2-propanol)}
\]

is oxidized to acetone

\[
\text{O} \quad \text{(acetone)}
\]

hydrogen is removed from the compound and the oxidation number of the central carbon atom increases from 0 to +II. If necessary, review the concept of oxidation number.
Reduction of Aldehydes and Ketones

The most common sources of the hydride Nucleophile are lithium aluminum hydride (LiAlH₄) and sodium borohydride (NaBH₄). Note! The hydride anion is not present during this reaction; rather, these reagents serve as a source of hydride due to the presence of a polar metal-hydrogen bond. Because aluminum is less electronegative than boron, the Al-H bond in LiAlH₄ is more polar, thereby, making LiAlH₄ a stronger reducing agent.

Addition of a hydride anion (H⁻) to an aldehyde or ketone gives an alkoxide anion, which on protonation yields the corresponding alcohol. Aldehydes produce 1º-alcohols and ketones produce 2º-alcohols.

In metal hydrides reductions the resulting alkoxide salts are insoluble and need to be hydrolyzed (with care) before the alcohol product can be isolated. In the sodium borohydride reduction the methanol solvent system achieves this hydrolysis automatically. In the lithium aluminum hydride reduction water is usually added in a second step. The lithium, sodium, boron and aluminum end up as soluble inorganic salts at the end of either reaction. Note! LiAlH₄ and NaBH₄ are both capable of reducing aldehydes and ketones to the corresponding alcohol.

Example 17.4.1
Mechanism

This mechanism is for a LiAlH$_4$ reduction. The mechanism for a NaBH$_4$ reduction is the same except methanol is the proton source used in the second step.

1) Nucleophilic attack by the hydride anion

\[ \text{R} - \text{C} = \text{O} \rightarrow \text{R} - \text{C} - \text{H} + \text{Li}^+ + \text{AlH}_3 \]

2) The alkoxide is protonated

\[ \text{R} - \text{C} - \text{H} \rightarrow \text{R} - \text{C} - \text{OH} + \text{LiOH} \]

Biological Reduction

Addition to a carbonyl by a semi-anionic hydride, such as NaBH$_4$, results in conversion of the carbonyl compound to an alcohol. The hydride from the BH$_4^-$ anion acts as a nucleophile, adding H$^+$ to the carbonyl carbon. A proton source can then protonate the oxygen of the resulting alkoxide ion, forming an alcohol.
Formally, that process is referred to as a reduction. Reduction generally means a reaction in which electrons are added to a compound; the compound that gains electrons is said to be reduced. Because hydride can be thought of as a proton plus two electrons, we can think of conversion of a ketone or an aldehyde to an alcohol as a two-electron reduction. An aldehyde plus two electrons and two protons becomes an alcohol.

Aldehydes, ketones and alcohols are very common features in biological molecules. Converting between these compounds is a frequent event in many biological pathways. However, semi-anionic compounds like sodium borohydride don't exist in the cell. Instead, a number of biological hydride donors play a similar role.

NADH is a common biological reducing agent. NADH is an acronym for nicotinamide adenine dinucleotide hydride. Instead of an anionic donor that provides a hydride to a carbonyl, NADH is actually a neutral donor. It supplies a hydride to the carbonyl under very specific circumstances. In doing so, it forms a cation, NAD⁺. However, NAD⁺ is stabilized by the fact that its nicotinamide ring is aromatic; it was not aromatic in NADH.

Reduction of Carboxylic Acids and Esters

Carboxylic acids can be converted to 1⁰ alcohols using Lithium aluminum hydride (LiAlH₄). Note that NaBH₄ is not strong enough to convert carboxylic acids or esters to alcohols. An aldehyde is produced as an intermediate during this reaction, but it cannot be isolated because it is more reactive than the original carboxylic acid.
Esters can be converted to $1^\circ$ alcohols using LiAlH$_4$, while sodium borohydride ($\text{NaBH}_4$) is not a strong enough reducing agent to perform this reaction.

$$\text{Ester} \xrightarrow{1) \text{LiAlH}_4} \text{CH}_2\text{-OH} + \text{HO-}R'$$

**Exercises**

**Questions**

**Q17.4.1**

Give the aldehyde, ketone, or carboxylic acid (there can be multiple answers) that could be reduced to form the following alcohols.

(a)

\[\text{OH}\]

(b)

\[\text{OH}\]

(c)

\[\text{OH}\]

(d)
Q17.4.2

Given the following alcohol, draw the structure from which it could be derived using only NaBH₄

(a)

(b)

(c)

(d)
Solutions
S17.4.1

(a) 

(b) 

(c) or 

(d) or 
Note, NaBH₄ is only a strong enough reducing agent to reduce ketones and aldehydes.

(a)

\[
\text{CH}_3\text{CHCH}_2\text{CH} = \text{O}
\]

(b)

\[
\text{O} = \text{C} = \text{O}
\]

(c)

\[
\text{O} = \text{C} = \text{O}
\]

(d)

\[
\text{O} = \text{C} = \text{O} \quad \text{OH}
\]
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