Skills to Develop

1. Give two major types of reactions of alcohols.
2. Describe the result of the oxidation of a primary alcohol.
3. Describe the result of the oxidation of a secondary alcohol.

Chemical reactions in alcohols occur mainly at the functional group, but some involve hydrogen atoms attached to the OH-bearing carbon atom or to an adjacent carbon atom. Of the three major kinds of alcohol reactions, which are summarized in Figure \(\PageIndex{1}\), two—dehydration and oxidation—are considered here. The third reaction type—**esterification**—is covered elsewhere.

**Table \(\PageIndex{1}\): Reactions of Alcohols. Oxidation and dehydration of alcohols are considered here.**

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Dehydration of Alcohols

As noted in Figure \(\PageIndex{1}\), an alcohol undergoes dehydration in the presence of a catalyst to form an alkene and water. The reaction removes the OH group from the alcohol carbon atom and a hydrogen atom from an adjacent carbon atom in the same molecule:

\[
\begin{align*}
\text{Ethanol} & \quad \xrightarrow{\text{conc} \ H_2SO_4, \ 180^\circ C} \quad \text{Ethylene} + \text{HOH} \\
\end{align*}
\]

Under the proper conditions, it is possible for the dehydration to occur between two alcohol molecules. The entire OH group of one molecule and only the hydrogen atom of the OH group of the second molecule are removed. The two ethyl groups attached to an oxygen atom form an ether molecule.

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{OH} + \text{HOCH}_2\text{CH}_3 & \quad \xrightarrow{\text{conc} \ H_2SO_4, \ 140^\circ C, \ \text{excess ethanol}} \quad \text{CH}_3\text{CH}_2\text{O} \quad \text{CH}_2\text{CH}_3 + \text{H}_2\text{O} \\
\end{align*}
\]

**(Ethers are discussed in elsewhere)** Thus, depending on conditions, one can prepare either alkenes or ethers by the dehydration of alcohols.

**Note**
Both dehydration and hydration reactions occur continuously in cellular metabolism, with enzymes serving as catalysts and at a temperature of about 37°C. The following reaction occurs in the "Embden–Meyerhof" pathway:

\[
\begin{align*}
\text{2-Phosphoglycerate} & \quad \text{enzyme} \quad \text{Phosphoenolpyruvate} \\
\text{H} & \quad \text{C} & \quad \text{C} & \quad \text{COO}^- & \quad \rightarrow & \quad \text{H} & \quad \text{C} & \quad \text{C} & \quad \text{COO}^- & \quad + & \quad \text{HOH}
\end{align*}
\]

Although the participating compounds are complex, the reaction is the same: elimination of water from the starting material. The idea is that if you know the chemistry of a particular functional group, you know the chemistry of hundreds of different compounds.

**Oxidation of Alcohols**

Primary and secondary alcohols are readily oxidized. We saw earlier how methanol and ethanol are oxidized by liver enzymes to form aldehydes. Because a variety of oxidizing agents can bring about oxidation, we can indicate an oxidizing agent without specifying a particular one by writing an equation with the symbol [O] above the arrow. For example, we write the oxidation of ethanol—a primary alcohol—to form acetaldehyde—an aldehyde—as follows:

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{OH} & \quad \overset{[O]}{\rightarrow} & \quad \text{CH}_3\text{CHO} \\
\text{Ethanol} & \quad \text{(a primary alcohol)} & \quad & \quad \text{Acetaldehyde} & \quad \text{(an aldehyde)}
\end{align*}
\]

We shall see that aldehydes are even more easily oxidized than alcohols and yield carboxylic acids. Secondary alcohols are oxidized to ketones. The oxidation of isopropyl alcohol by potassium dichromate (K$_2$Cr$_2$O$_7$) gives acetone, the simplest ketone:

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}_3 & \quad \overset{\text{K}_2\text{Cr}_2\text{O}_7/\text{H}^+}{\rightarrow} & \quad \text{CH}_3\text{C} & \quad \text{C} & \quad \text{CH}_3 \\
\text{Isopropyl alcohol} & \quad \text{(a secondary alcohol)} & \quad & \quad \text{Acetone} & \quad \text{(a ketone)}
\end{align*}
\]

Unlike aldehydes, ketones are relatively resistant to further oxidation, so no special precautions are required to isolate them as they form. Note that in oxidation of both primary (RCH$_2$OH) and secondary (R$_2$CHOH) alcohols, two hydrogen atoms are removed from the alcohol molecule, one from the OH group and other from the carbon atom that bears the OH group.

**Note**

These reactions can also be carried out in the laboratory with chemical oxidizing agents. One such oxidizing agent is potassium dichromate. The balanced equation (showing only the species involved in the reaction) in this case is as follows:

\[
8\text{H}^+ + \text{Cr}_2\text{O}_7^{2-} + 3\text{CH}_3\text{CH}_2\text{OH} \quad \rightarrow \quad 3\text{CH}_3\text{CHO} + 2\text{Cr}^{3+} + 7\text{H}_2\text{O}
\]
Alcohol oxidation is important in living organisms. Enzyme-controlled oxidation reactions provide the energy cells need to do useful work. One step in the metabolism of carbohydrates involves the oxidation of the secondary alcohol group in isocitric acid to a ketone group:

\[
\begin{array}{c}
\text{Isocitrate} \\
\text{Oxalosuccinate}
\end{array}
\]

The overall type of reaction is the same as that in the conversion of isopropyl alcohol to acetone.

Tertiary alcohols (\(R_3\text{COH}\)) are resistant to oxidation because the carbon atom that carries the \(\text{OH}\) group does not have a hydrogen atom attached but is instead bonded to other carbon atoms. The oxidation reactions we have described involve the formation of a carbon-to-oxygen double bond. Thus, the carbon atom bearing the \(\text{OH}\) group must be able to release one of its attached atoms to form the double bond. The carbon-to-hydrogen bonding is easily broken under oxidative conditions, but carbon-to-carbon bonds are not. Therefore tertiary alcohols are not easily oxidized.

Example \(\PageIndex{1}\)

Write an equation for the oxidation of each alcohol. Use \([\text{O}]\) above the arrow to indicate an oxidizing agent. If no reaction occurs, write “no reaction” after the arrow.

1. \(\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}\)

2. \(\text{CH}_3\text{CHCH}_2\text{CH}_2\text{CH}_3\)

3. \(\text{CH}_3\text{CHCH}_2\text{CH}_2\text{CH}_3\)

SOLUTION

The first step is to recognize the class of each alcohol as primary, secondary, or tertiary.

1. This alcohol has the \(\text{OH}\) group on a carbon atom that is attached to only one other carbon atom, so it is a primary alcohol. Oxidation forms first an aldehyde and further oxidation forms a carboxylic acid.

2. This alcohol has the \(\text{OH}\) group on a carbon atom that is attached to three other carbon atoms, so it is a tertiary alcohol. No reaction occurs.
3. This alcohol has the OH group on a carbon atom that is attached to two other carbon atoms, so it is a secondary alcohol; oxidation gives a ketone.

\[
\text{CH}_3\text{CHCH}_2\text{CH}_2\text{OH} \xrightarrow{\text{oxidation}} \text{CH}_3\text{CHCH}_2\text{CH}_2\text{CH}_2\text{O} \
\]

Exercise \( \PageIndex{1} \)

Write an equation for the oxidation of each alcohol. Use [O] above the arrow to indicate an oxidizing agent. If no reaction occurs, write "no reaction" after the arrow.

1. 

\[
\text{CH}_3\text{CHCH}_2\text{CH}_2\text{OH} \xrightarrow{\text{oxidation}} \text{no reaction} \
\]

2. 

\[
\text{CH}_2\text{CHCH}_2\text{OH} \xrightarrow{\text{oxidation}} \text{no reaction} \
\]

3. 

\[
\text{CH}_3\text{CHCH}_2\text{CH}_2\text{OH} \xrightarrow{\text{oxidation}} \text{no reaction} \
\]

Reactions of Alcohols with Hydrogen Halides (HX)

When alcohols react with a hydrogen halide, a substitution occurs, producing an alkyl halide and water:

Figure

- The order of reactivity of alcohols is \( 3^\circ > 2^\circ > 1^\circ \) methyl.
- The order of reactivity of the hydrogen halides is HI > HBr > HCl (HF is generally unreactive).
The reaction is acid catalyzed. Alcohols react with the strongly acidic hydrogen halides HCl, HBr, and HI, but they do not react with nonacidic NaCl, NaBr, or NaI. Primary and secondary alcohols can be converted to alkyl chlorides and bromides by allowing them to react with a mixture of a sodium halide and sulfuric acid:

Secondary, tertiary, allylic, and benzylic alcohols appear to react by a mechanism that involves the formation of a carbocation in an \( S_{N1} \) reaction with the protonated alcohol acting as the substrate. The \( S_{N1} \) mechanism is illustrated by the reaction tert-butyl alcohol and aqueous hydrochloric acid \((H_3O^+, Cl^-)\). The first two steps in this \( S_{n1} \) substitution mechanism are protonation of the alcohol to form an oxonium ion. Although the oxonium ion is formed by protonation of the alcohol, it can also be viewed as a Lewis acid-base complex between the cation \((R^+)\) and \((H_2O)\). Protonation of the alcohol converts a poor leaving group \((OH^-)\) to a good leaving group \((H_2O^-)\), which makes the dissociation step of the \( S_{N1} \) mechanism more favorable.

In step 3, the carbocation reacts with a nucleophile (a halide ion) to complete the substitution.

When we convert an alcohol to an alkyl halide, we perform the reaction in the presence of acid and in the presence of halide ions and not at elevated temperatures. Halide ions are good nucleophiles (they are much stronger nucleophiles than water), and because halide ions are present in a high concentration, most of the carbocations react with an electron pair of a halide ion to form a more stable species, the alkyl halide product. The overall result is an \( S_{n1} \) reaction.

Not all acid-catalyzed conversions of alcohols to alkyl halides proceed through the formation of carbocations. Primary alcohols and methanol react to form alkyl halides under acidic conditions by an \( S_{N2} \) mechanism. In these reactions, the function of the acid is to produce a protonated alcohol. The halide ion then displaces a molecule of water (a good leaving group) from carbon; this produces an alkyl halide:
Again, acid is required. Although halide ions (particularly iodide and bromide ions) are strong nucleophiles, they are not strong enough to carry out substitution reactions with alcohols themselves. Direct displacement of the hydroxyl group does not occur because the leaving group would have to be a strongly basic hydroxide ion:

We can see now why the reactions of alcohols with hydrogen halides are acid-promoted.

Acid protonates the alcohol hydroxyl group, making it a good leaving group. However, other strong Lewis acids can be used instead of hydrohalic acids. Because the chloride ion is a weaker nucleophile than bromide or iodide ions, hydrogen chloride does not react with primary or secondary alcohols unless zinc chloride or a similar Lewis acid is added to the reaction mixture as well. Zinc chloride, a good Lewis acid, forms a complex with the alcohol through association with an unshared pair of electrons on the oxygen atom. This enhances the hydroxyl's leaving group potential sufficiently so that chloride can displace it.

As we might expect, many reactions of alcohols with hydrogen halides, particularly those in which carbocations are formed, are accompanied by rearrangements. The general rule is that if rearrangement CAN OCCUR (to form more stable or equally stable cations), it will! In these reactions, mixtures of products can be formed.