10.6 OXIDATION OF ALCOHOLS

A. Oxidation to Aldehydes and Ketones

Primary and secondary alcohols can be oxidized by reagents containing Cr(VI)—that is, chromium in the +6 oxidation state—to give certain types of carbonyl compounds (compounds that contain the carbonyl group, C=O). For example, secondary alcohols are oxidized to ketones:

\[
\text{2-octanol} \xrightarrow{\text{Na}_2\text{Cr}_2\text{O}_7, \text{aqueous } \text{H}_2\text{SO}_4} \text{2-octanone} \quad \text{(94\% yield)}
\]

(10.35)

Several forms of Cr(VI) can be used to convert secondary alcohols into ketones. Three of these are chromate (CrO}_4^{2-}), dichromate (Cr_2O}_7^{2-}), and chromic anhydride or chromium trioxide (CrO}_3). The first two reagents are customarily used under strongly acidic conditions; the last is often used in pyridine. In all cases, the chromium is reduced to a form of Cr(III) such as Cr^{3+}.

Primary alcohols react with Cr(VI) reagents to give aldehydes. However, if water is present, the reaction cannot be stopped at the aldehyde stage because aldehydes are further oxidized to carboxylic acids:

\[
\text{2-methyl-1-butanol} \xrightarrow{\text{K}_2\text{Cr}_2\text{O}_7, \text{aqueous } \text{H}_2\text{SO}_4} \text{2-methylbutanal} \xrightarrow{\text{K}_2\text{Cr}_2\text{O}_7, \text{aqueous } \text{H}_2\text{SO}_4} \text{2-methylbutanoic acid} \quad \text{(92\% yield)}
\]

(10.37)

For this reason, anhydrous preparations of Cr(VI) are generally used for the laboratory preparation of aldehydes from primary alcohols. One commonly used reagent of this type is a complex of pyridine, HCl, and chromium trioxide called pyridinium chlorochromate, which goes by the acronym “PCC.” This reagent is typically used in methylene chloride solvent.

\[
\text{1-decanol} \xrightarrow{\text{CrO}_3, \text{pyridine}} \text{decanal} \quad \text{(92\% yield)}
\]

(10.38)

Water promotes the transformation of aldehydes into carboxylic acids because, in water, aldehydes are in equilibrium with hydrates formed by addition of water across the C=O double bond.
Aldehyde hydrates are really alcohols and therefore can be oxidized just like secondary alcohols. Because of the absence of water in anhydrous reagents such as PCC, a 1,1-diol does not form, and the reaction stops at the aldehyde.

Tertiary alcohols are not oxidized under the usual conditions. For oxidation of alcohols at the \(\alpha\)-carbon to occur, the \(\alpha\)-carbon atom must bear one or more hydrogen atoms.

The mechanism of alcohol oxidation by Cr(VI) involves several steps that have close analogies to other reactions. Consider, for example, the oxidation of isopropyl alcohol to the ketone acetone by chromic acid (\(\text{H}_2\text{CrO}_4\)). The first steps of the reaction involve an acid-catalyzed displacement of water from chromic acid by the alcohol to form a chromate ester. (This ester is analogous to ester derivatives of other strong acids; Sec. 10.3C.)

After protonation of the chromate ester (Eq. 10.40b), it decomposes in a \(\beta\)-elimination reaction (Eq. 10.40c).

This last step is essentially an E2 reaction. Because Cr(VI) is particularly electronegative, especially when protonated, the chromium readily accepts an electron pair and is thus reduced. The reaction is so rapid that the Brønsted base in the reaction can be very weak; in fact, water is the base in Eq. 10.40c. In the resulting \(\text{H}_2\text{CrO}_3\) by-product, chromium is in a +4 oxidation state. The ultimate by-product is \(\text{Cr}^{3+}\) because, in subsequent reactions, Cr(IV) and Cr(VI) react to give two equivalents of a Cr(V) species, which then oxidizes an additional molecule of alcohol by a similar mechanism.

\[
\text{Cr(IV)} + \text{Cr(VI)} \longrightarrow 2 \text{Cr(V)} \quad (10.41a)
\]

\[
\text{Cr(V)} + (\text{CH}_3)_2\text{CH} \longrightarrow \text{OH} \longrightarrow \text{Cr(III)} + (\text{CH}_3)_2\text{C} \longrightarrow + 2 \text{H}^+ \quad (10.41b)
\]
10.6 OXIDATION OF ALCOHOLS

B. Oxidation to Carboxylic Acids

As noted in the previous section (Eq. 10.37), primary alcohols can be oxidized to carboxylic acids using aqueous solutions of Cr(VI), such as aqueous potassium dichromate ($K_2Cr_2O_7$) in acid. Another useful reagent for oxidizing primary alcohols to carboxylic acids is potassium permanganate ($KMnO_4$) in basic solution:

As shown in this equation, the immediate product of the permanganate oxidation is the conjugate base of the carboxylic acid because the reaction is run in alkaline solution. Isolation of the carboxylic acid itself requires addition of a strong acid such as $HCl$ or $H_2SO_4$ in a second step.

The manganese in $KMnO_4$ is in the Mn(VII) oxidation state; in the oxidation of alcohols, it is reduced to Mn(IV), a common form of Mn(IV). Because $KMnO_4$ reacts with alkene double bonds (Sec. 11.5A), Cr(VI) is required for the oxidation of alcohols that contain double or triple bonds (see Eq. 10.36).

Potassium permanganate is not used for the oxidation of secondary alcohols to ketones because many ketones react further with the alkaline permanganate reagent.

PROBLEMS

10.26 Give the product expected when each of the following alcohols reacts with pyridinium chlorochromate (PCC).

(a) \( \text{CH}_2\text{CH}_2\text{OH} \)

(b) HO—\( \text{CH}_2\text{CH}_2\text{OH} \)
10.27 From which alcohol and by what method would each of the following compounds best be prepared by an oxidation?

(a) \((\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{CO}_2\text{H}\)

(b) \(\text{CH}_3\text{CH}_2\text{CCH}_2\text{CH}_3\)

(c) \((\text{CH}_3)_2\text{CCH}_2\text{CH}_2\text{CH}_2\text{OH}\)

(d) \(\text{CH}==\text{O}\)

10.7 BIOLOGICAL OXIDATION OF ETHANOL

Oxidation and reduction reactions are very important in living systems. A typical biological oxidation is the conversion of ethanol into acetaldehyde, the principal reaction by which ethanol is removed from the bloodstream.

\[
\text{CH}_3\text{CH}_2\text{OH} \xrightarrow{\text{biological oxidation}} \text{CH}_3\text{CH==O} \quad (10.43)
\]

The reaction is carried out in the liver and is catalyzed by an enzyme called alcohol dehydrogenase. (Recall from Sec. 4.9C that enzymes are biological catalysts.) The oxidizing agent is not the enzyme, but a large molecule called *nicotinamide adenine dinucleotide*, abbreviated NAD<sup>+</sup>; the structure of NAD<sup>+</sup> and a convenient abbreviated structure for it are shown in Fig. 10.1. When

![Figure 10.1 Abbreviated and full structures of NAD<sup>+</sup>. The colored portion of the full structure is abbreviated as an R-group.](image-url)