This chapter covers two very important types of alkyl halide reactions: nucleophilic substitution reactions and β-elimination reactions. These are among the most common and important reactions in organic chemistry. This chapter also introduces another class of reactive intermediate: carbenes.

If you read Sec. 8.9B, you understand that alkyl halides rarely occur in biological systems. If you are a life-science or premedical student, you might wonder why you should bother learning about the chemistry of compounds that you are not likely to encounter in biology. The reason is that much of our quantitative data and current understanding of reactivity comes from studies on alkyl halides. Moreover, the chemistry of alkyl halides demonstrates in a straightforward way the types of reactivity and mechanism that we’ll encounter in more complex molecules, including those that occur in biological systems. Think of a musical theme and variations: alkyl halide chemistry provides the theme, and the chemistry of alcohols, ethers, and amines will provide the variations. In other words, alkyl halides provide simple models from which we understand the chemistry of other compound classes. These same considerations are equally valid for the chemistry major; furthermore, alkyl halides are important starting materials used in a wide variety of reactions.

9.1 AN OVERVIEW OF NUCLEOPHILIC SUBSTITUTION AND β-ELIMINATION REACTIONS

A. Nucleophilic Substitution Reactions

When a methyl halide or a primary alkyl halide reacts with a Lewis base, such as sodium ethoxide, a reaction occurs in which the Lewis base replaces the halogen, which is expelled as halide ion.

\[
\text{Na}^+ \text{CH}_3\text{CH}_2\text{O}^- + \text{Br}^-\text{CH}_2\text{CH}_3 \rightarrow \text{CH}_3\text{CH}_2\text{O}^-\text{CH}_2\text{CH}_3 + \text{Na}^+ \text{Br}^- \quad (9.1)
\]

sodium ethoxide \hspace{1cm} ethyl bromide \hspace{1cm} diethyl ether \hspace{1cm} sodium bromide
This is an example of a very general type of reaction, called a **nucleophilic substitution reaction**, or **nucleophilic displacement reaction**. In the simplest type of nucleophilic substitution reaction, a Lewis base, acting as a *nucleophile*, donates an electron pair to an *electrophile* to displace a *leaving group*.

\[
\text{Na}^+ \text{CH}_3\text{CH}_2\overset{-}{\text{O}} \rightarrow \text{CH}_3\text{CH}_2\overset{-}{\text{O}} \text{CH}_2\text{CH}_3 + \text{Na}^+ \overset{+}{\text{Br}}^- \quad (9.2)
\]

(You should review these terms in Sec. 3.4B if necessary.) In this chapter, the electrophile will typically be a carbon and the leaving group will typically be a halide ion. As you've already seen, however, there are many examples of nucleophilic substitution reactions that involve other electrophiles and leaving groups.

Although many nucleophiles are anions, others are uncharged. The following equation contains an example of an uncharged nucleophile. In addition, it illustrates an *intramolecular substitution reaction*—a reaction in which the nucleophile and the leaving group are part of the same molecule. In this case, the nucleophilic substitution reaction causes a ring to form.

\[
\text{(CH}_3)_2\overset{\text{N}}{\text{CH}_2} \rightarrow \text{(CH}_3)_2\overset{\text{N}}{\text{CH}_2} \quad (9.3)
\]

Nucleophilic substitution reactions can involve many different nucleophiles, a few of which are listed in Table 9.1. Notice from this table that nucleophilic substitution reactions can be used to transform alkyl halides into a wide variety of other functional groups. We'll discuss nucleophilic substitution reactions in more detail in Secs. 9.4 and 9.6.

**PROBLEM**

9.1 What is the expected nucleophilic substitution product when
(a) methyl iodide reacts with Na⁺ CH₃CH₂CH₂CH₂S⁻?
(b) ethyl iodide reacts with ammonia?

**B. β-Elimination Reactions**

When a tertiary alkyl halide reacts with a Brønsted base such as sodium ethoxide, a very different type of reaction is observed.

\[
\text{Na}^+ \text{C}_2\text{H}_5\overset{-}{\text{O}}^- + \overset{\text{Br}}{\text{H}}\text{CH}_2\overset{\text{C}}{\text{H}}\text{CH}_3 \rightarrow \text{C}_2\text{H}_5\overset{\text{O}}{\text{H}} + \overset{\text{C}}{\text{H}}\text{CH} = \text{C} \overset{\text{CH}_3}{\text{CH}}_3 + \text{Na}^+ \overset{\text{Br}}{\text{Br}}^- \quad (9.4)
\]

*tert*-butyl bromide

2-methylpropene (isobutylene)
**TABLE 9.1 Some Nucleophilic Substitution Reactions**

<table>
<thead>
<tr>
<th>R → X⁻ + Nucleophile (name)</th>
<th>→</th>
<th>X⁻⁻ + Product (name)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R → X⁻⁻ + Y⁻⁻ (another halide)</td>
<td>→</td>
<td>X⁻⁻⁻ + R → Y⁻⁻ (another alkyl halide)</td>
</tr>
<tr>
<td>+ −C≡N⁻⁻⁻ (cyano)</td>
<td>→</td>
<td>+ R → C≡N⁻⁻⁻ (nitrile)</td>
</tr>
<tr>
<td>+ −OH⁻⁻⁻ (hydroxide)</td>
<td>→</td>
<td>+ R → OH⁻⁻⁻ (alcohol)</td>
</tr>
<tr>
<td>+ −OR⁻⁻⁻ (alkoxide)</td>
<td>→</td>
<td>+ R → O⁻⁻⁻⁻ (ether)</td>
</tr>
<tr>
<td>+ −NF⁻ (azide = :N=N=N⁻)</td>
<td>→</td>
<td>+ R → NF⁻ (alkyl azide)</td>
</tr>
<tr>
<td>+ −S⁻⁻⁻⁻ (alkanethiolate)</td>
<td>→</td>
<td>+ R → S⁻⁻⁻⁻ (thioether or sulfide)</td>
</tr>
<tr>
<td>+ −NR⁻⁻⁻⁻ (amine)</td>
<td>→</td>
<td>R → NR⁻⁻⁻⁻ (alkylammonium salt)</td>
</tr>
<tr>
<td>+ −OH₂⁻⁻⁻⁻ (water)</td>
<td>→</td>
<td>R → OH⁻⁻⁻⁻⁻ (alcohol)</td>
</tr>
<tr>
<td>+ −O⁻⁻⁻⁻ (alcohol)</td>
<td>→</td>
<td>R → O⁻⁻⁻⁻⁻ (ether)</td>
</tr>
</tbody>
</table>

This is an example of an elimination reaction: a reaction in which two or more groups (in this case H and Br) are lost from within the same molecule. We’ll discuss the mechanism of this reaction in Sec. 9.5A.

In an alkyl halide, the carbon bearing the halogen is often referred to as the α-carbon, and the adjacent carbons are referred to as the β-carbons. Notice in Eq. 9.4 that the halide is lost from the α-carbon and a proton from a β-carbon.

![Diagram](image)

An elimination that involves loss of two groups from adjacent carbons is called a β-elimination. This is the most common type of elimination reaction in organic chemistry. Notice that a β-elimination reaction is conceptually the reverse of an addition to an alkene.

Strong bases promote the β-elimination reactions of alkyl halides. Among the most frequently used bases are alkoxides, such as sodium ethoxide (Na⁻⁻⁻⁻⁺ C₂H₅O⁻⁻⁻⁻⁻) and potassium tert-butoxide (K⁺ (CH₃)₃C—O⁻⁻⁻⁻⁻). Often the conjugate-acid alcohols of these bases are used as solvents. For example, just as −OH is used as a solution in its conjugate acid water, sodium ethoxide is frequently used as a solution in ethanol, and potassium tert-butoxide in tert-butyl alcohol.

If the reacting alkyl halide has more than one type of β-hydrogen atom, then more than one β-elimination reaction are possible. When these different reactions occur at comparable rates, more than one alkene product are formed, as in the following example.
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C. Competition between Nucleophilic Substitution and \( \beta \)-Elimination Reactions

In the presence of a strong Lewis base such as ethoxide, the nucleophilic substitution reaction is a typical one for primary alkyl halides, and a \( \beta \)-elimination reaction is observed for tertiary alkyl halides. What about secondary alkyl halides? A typical secondary alkyl halide under the same conditions undergoes both reactions. In other words, some molecules of the alkyl halide undergo substitution, while others undergo elimination. This means that the two reactions occur at comparable rates—in other words, the reactions are in competition. In fact, nucleophilic substitution and base-promoted \( \beta \)-elimination reactions are in competition for all alkyl halides with \( \beta \)-hydrogens, even primary and tertiary halides. It happens that in the presence of a strong Bronsted base, nucleophilic substitution is a faster reaction (it “wins the competition”) for many primary alkyl halides, and in most cases \( \beta \)-elimination is a faster reaction for tertiary halides; that is why substitution predominates in the former case and elimination in the latter. However, under some conditions, the results of the competition can be changed. For example, we can sometimes find conditions under which some primary alkyl halides give mostly elimination products.

In the following sections, we’ll focus first on nucleophilic substitution reactions, then on \( \beta \)-elimination reactions. We’ll discuss the factors that govern the reactivities of alkyl halides in each of these reaction types. Although each type of reaction is considered in isolation, keep in mind that substitutions and eliminations are always in competition.

**PROBLEM**

9.2 What product(s) are expected in the ethoxide-promoted \( \beta \)-elimination reaction of each of the following compounds?

(a) 2-bromo-2,3-dimethylbutane  (b) 1-chloro-1-methylcyclohexane

\[
\begin{align*}
H_3C\text{CH} \quad\text{Br} \quad+\quad \text{Na}^+ \quad\text{C}_2\text{H}_5O^- & \quad\rightarrow\quad \text{C}_2\text{H}_3\text{OH} \\
\text{H}_2\text{C} \equiv \text{C} \quad\text{CH}_3 & \quad+\quad \text{HC} \quad\text{CH}_3 \\
\text{from loss of a hydrogen (a)} & \quad+\quad \text{from loss of a hydrogen (b)}
\end{align*}
\]

\[
\begin{align*}
\text{H}_3\text{C} \quad\text{CH} \quad\text{CH}_3 & \quad+\quad \text{C}_2\text{H}_5\text{O}^- \quad\rightarrow\quad \text{C}_2\text{H}_3\text{OH} \\
\text{H}_3\text{C} \quad\text{CH} \quad\text{CH}_3 & \quad+\quad \text{H}_2\text{C} \equiv \text{CH} \quad\text{CH}_3 \\
\text{isopropyl bromide} & \quad+\quad \text{ethyl isopropyl ether} \\
\text{ethoxide} & \quad\quad\text{propene} \\
\text{substitution product (about 50%)} & \quad\quad\text{elimination product (about 50%)}
\end{align*}
\]

**PROBLEM**

9.3 What substitution and elimination products (if any) might be obtained when each of the following alkyl halides is treated with sodium methoxide in methanol?

(a) 2-bromobutane  (b) methyl iodide  
(c) trans-1-bromo-3-methylcyclohexane  (d) (bromomethyl)cyclopentane