The general description "organohalogen" refers to compounds with covalent carbon–halogen bonding. Substances such as bromomethane, \( \text{CH}_3\text{Br} \), and chloroethene, \( \text{CH}_2=\text{CHCl} \), are examples of organohalogen compounds, whereas others such as methylammonium chloride, \( \text{CH}_3\text{NH}_3\text{Cl} \), which have no carbon–halogen bonds, are not. We are concerned in this chapter only with compounds that have covalent carbon–halogen bonds.

There is wide diversity in the nature of organohalogen compounds but, of necessity, we have restricted this chapter to alkyl, cycloalkyl, alkenyl, alkynyl, and aryl halides. Some of the chemistry of the carbon–halogen bonds already will be familiar to you because it involves the addition, substitution, and elimination reactions discussed in previous chapters. To some extent, we will amplify these reactions and consider nucleophilic substitution by what are called the addition-elimination and elimination-addition mechanisms. Subsequently, we will discuss the formation of carbon–metal bonds from carbon–halogen bonds. The latter type of reaction is of special value because compounds that have carbon–metal bonds are potent reagents for the formation of carbon–carbon bonds, as we will show later in this chapter.

Although large numbers of organohalogenes are known, very few of them occur naturally. Thyroid hormones (e.g., thyroxine) that contain iodine
are exceptions; other organohalogens are found as mold metabolites (such as griseofulvin) and in marine organisms:

\[
\text{ thyroxine }
\]

Almost all of the organohalogen compounds in use today are synthetic in origin. You may wonder why, if nature doesn't choose to make them, man elects to do so. The main interest to us here is that they are very useful intermediates for the synthesis of a wide range of other compounds. However, vast quantities of synthetic halogen compounds, particularly polyhalogen compounds, are used as pesticides, cleaning solvents, anaesthetics, aerosol propellants, refrigerants, polymers, and so on. The wisdom of this massive use of materials that are foreign to our natural environment gradually is being reevaluated as the long-term detrimental effects of many of these chemicals become known. For example, many of the chlorinated hydrocarbons such as DDT, Chlordane, and Lindane, which have been used very widely as insecticides, now are at least partially banned because of concern for their long-term effects on nontarget species, including man.
Sometimes the long-term effects are quite unexpected and difficult to predict. For example, millions of kilograms of CF₂C₁₂, which is used as a propellant, have been released into the atmosphere from aerosol cans. This compound appears to be wholly free of direct adverse physiological effects. However, as the substance diffuses into the upper atmosphere, it is slowly decomposed by sunlight to produce chlorine atoms. Serious danger then is possible because chlorine atoms are known to catalyze the decomposition of ozone, and it is the ozone layer in the upper atmosphere that absorbs most of the sun’s ultraviolet radiation that is strongly harmful to life.

14-1 PHYSICAL PROPERTIES

The physical properties of haloalkanes are much as one might expect. Volatility decreases: (a) with increasing molecular weight along a homologous series, (b) with increasing atomic number of the halogen, and (c) with the structure of the alkyl group in the order such that tertiary < secondary < primary for isomeric halides. These trends are apparent from the physical properties listed in Table 14-1, which includes data for simple halogen derivatives of alkanes, alkenes, alkynes, and arenes.

The boiling points of many halogen compounds are similar to hydrocarbons of the same molecular weight, but there are some conspicuous exceptions. Iodomethane, for example, has about the same molecular weight as decane (MW 142), but the boiling point of iodomethane is 132° lower than that of decane. Likewise, fluorocarbons (e.g., tetrafluoromethane, CF₄, MW 88, bp -129°) are far more volatile than hydrocarbons of similar weights (e.g., hexane, C₆H₁₄, MW 86, bp 69°).

In general, halogen compounds are insoluble in water but are readily soluble in organic solvents and, with the exception of some fluoro and monochloro compounds, they are more dense than water. Aryl halides are fairly pleasant smelling liquids, but arylmethyl (benzylic) halides of structure ArCH₂X are irritating to the eyes, skin, and nasal passages. Toxicity varies, but the chlorinated hydrocarbons such as CCl₄ ("carbon tet") and CHCl₂—CHCl₂ are quite toxic and should be used with care.
# Table 14-1
Physical Properties of Organic Halides

<table>
<thead>
<tr>
<th>Name</th>
<th>Formula</th>
<th>MW</th>
<th>$\text{Mp, } ^\circ\text{C}$</th>
<th>$\text{Bp, } ^\circ\text{C}$</th>
<th>Density, $\alpha_x^{20}, \text{g ml}^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alkyl halides</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fluomethane</td>
<td>$\text{CH}_3\text{F}$</td>
<td>34</td>
<td>$-142$</td>
<td>$-78$</td>
<td>–</td>
</tr>
<tr>
<td>chloromethane</td>
<td>$\text{CH}_3\text{Cl}$</td>
<td>50.5</td>
<td>$-97$</td>
<td>$-24$</td>
<td>–</td>
</tr>
<tr>
<td>bromomethane</td>
<td>$\text{CH}_3\text{Br}$</td>
<td>95</td>
<td>$-94$</td>
<td>4.5</td>
<td>$1.730^{0/4}$</td>
</tr>
<tr>
<td>iodomethane</td>
<td>$\text{CH}_3\text{I}$</td>
<td>142</td>
<td>$-67$</td>
<td>42.8</td>
<td>2.28</td>
</tr>
<tr>
<td>tetrafluoromethane</td>
<td>$\text{CF}_4$</td>
<td>88</td>
<td>$-184$</td>
<td>$-129$</td>
<td>–</td>
</tr>
<tr>
<td>tetrachloromethane</td>
<td>$\text{CCl}_4$</td>
<td>154</td>
<td>$-23$</td>
<td>76.7</td>
<td>1.594</td>
</tr>
<tr>
<td>chloroethane</td>
<td>$\text{CH}_2\text{CH}_2\text{Cl}$</td>
<td>64.5</td>
<td>$-138$</td>
<td>12.3</td>
<td>$0.9214^{0/4}$</td>
</tr>
<tr>
<td>1-chloropropane</td>
<td>$\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$</td>
<td>78.5</td>
<td>$-122$</td>
<td>47</td>
<td>$0.890^{20/20}$</td>
</tr>
<tr>
<td>1-chlorobutane</td>
<td>$\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$</td>
<td>92.5</td>
<td>$-123$</td>
<td>78.5</td>
<td>0.886</td>
</tr>
<tr>
<td>2-chlorobutane</td>
<td>$\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$</td>
<td>92.5</td>
<td>$-131$</td>
<td>68</td>
<td>0.871</td>
</tr>
<tr>
<td>2-chloro-2-methyl-propane</td>
<td>$(\text{CH}_3)_2\text{C}—\text{Cl}$</td>
<td>92.5</td>
<td>$-27$</td>
<td>51</td>
<td>$0.847^{15/4}$</td>
</tr>
<tr>
<td><strong>Alkenyl halides</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fluoroethene</td>
<td>$\text{CH}_2\equiv\text{CHF}$</td>
<td>46</td>
<td>$-161$</td>
<td>$-72$</td>
<td>–</td>
</tr>
<tr>
<td>chloroethene</td>
<td>$\text{CH}_2\equiv\text{CHCl}$</td>
<td>62.5</td>
<td>$-160$</td>
<td>$-14$</td>
<td>0.911</td>
</tr>
<tr>
<td>1,1-dichloroethene</td>
<td>$\text{CH}_2\equiv\text{CCl}_2$</td>
<td>97</td>
<td>$-123$</td>
<td>31.7</td>
<td>1.213</td>
</tr>
<tr>
<td>tetrafluoroethene</td>
<td>$\text{CF}_2\equiv\text{CF}_2$</td>
<td>100</td>
<td>$-131$</td>
<td>$-76$</td>
<td>1.519</td>
</tr>
<tr>
<td>tetrachloroethene</td>
<td>$\text{CCl}_2\equiv\text{CCl}_2$</td>
<td>165.8</td>
<td>$-22$</td>
<td>121</td>
<td>1.623</td>
</tr>
<tr>
<td><strong>Alkynyl halides</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fluoroethyne</td>
<td>$\text{HC}≡\text{CF}$</td>
<td>44</td>
<td>$&gt;-196$</td>
<td>$-104$</td>
<td>–</td>
</tr>
<tr>
<td>chloroethyne</td>
<td>$\text{HC}≡\text{CCl}$</td>
<td>60.5</td>
<td>$-126$</td>
<td>$-32$</td>
<td>–</td>
</tr>
<tr>
<td>bromoethyne</td>
<td>$\text{HC}≡\text{CBr}$</td>
<td>105</td>
<td>–</td>
<td>4.7</td>
<td>–</td>
</tr>
<tr>
<td>iodoethyne</td>
<td>$\text{HC}≡\text{CI}$</td>
<td>152</td>
<td>–</td>
<td>32</td>
<td>–</td>
</tr>
<tr>
<td><strong>Aryl halides</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fluorobenzene</td>
<td>$\text{C}_6\text{H}_5\text{F}$</td>
<td>96.0</td>
<td>$-42$</td>
<td>85</td>
<td>1.024</td>
</tr>
<tr>
<td>chlorobenzene</td>
<td>$\text{C}_6\text{H}_5\text{Cl}$</td>
<td>112.5</td>
<td>$-45$</td>
<td>132</td>
<td>1.107</td>
</tr>
<tr>
<td>bromobenzene</td>
<td>$\text{C}_6\text{H}_5\text{Br}$</td>
<td>157</td>
<td>$-31$</td>
<td>156</td>
<td>1.495</td>
</tr>
<tr>
<td>iodoobenzene</td>
<td>$\text{C}_6\text{H}_5\text{I}$</td>
<td>204</td>
<td>$-31$</td>
<td>189</td>
<td>1.832</td>
</tr>
</tbody>
</table>

![2-chloromethylbenzene](image1)

$\text{CH}_3\equiv\text{CCl}$

$\text{CH}_3\equiv\text{CCl}$

$\text{CH}_3\equiv\text{CCl}$
14-2 SPECTROSCOPIC PROPERTIES

Organohalogen compounds give rise to strong absorptions in the infrared arising from stretching vibrations of the carbon–halogen bond. The frequency of absorption decreases as the mass of the halogen increases. For monohaloalkanes the absorptions useful for identification are those of C—F at 1100–1000 cm⁻¹ and C—Cl at 850–550 cm⁻¹. The C—Br and C—I absorptions are below 690 cm⁻¹ and therefore are out of range of most commercial spectrophotometers. Because these bands are in the fingerprint region or far infrared, it is difficult to infer the presence of halogen in a molecule solely from its infrared spectrum.

Apart from fluorine, the magnetic properties of halogen nuclei do not complicate proton or ¹³C nuclear magnetic resonance spectra of organohalogen compounds. But fluorine (¹⁹F) has a spin of 1/2 and causes spin-spin splitting of the resonances of neighboring magnetic nuclei (¹³C, ¹H, and other ¹⁹F nuclei). Proton chemical shifts are influenced strongly by the presence of halogen, which serves to deshield neighboring protons by electronegativity effects (see Section 9-10E).

The mass spectra of chlorine- and bromine-containing compounds clearly show the abundance ratios of the stable isotopes ³⁵Cl:³⁷Cl = 3:1 and ⁷⁹Br:⁸¹Br = 1:1 in the molecular ions and those ionic fragments which contain halogens (see Section 9-11).

Exercise 14-1 Deduce the structures of the two compounds whose nmr and infrared spectra are shown in Figure 14-1 (p. 540). Assign as many of the infrared bands as you can and analyze the nmr spectra in terms of chemical shifts and spin-spin splittings.

14-3 ALKYL HALIDES

The important chemistry of alkyl halides, RX, includes the nucleophilic (Sₐ) displacement and elimination (E) reactions discussed in Chapter 8. Recall that tertiary alkyl halides normally are reactive in ionization (Sₐ1) reactions, whereas primary halides, and to a lesser extent secondary halides, are reactive in Sₐ2 reactions, which occur by a concerted mechanism with inversion of configuration (Sections 8-4 to 8-7).

Elimination competes with substitution in many Sₐ reactions and can become the major pathway at high temperatures or in the presence of strong base. Elimination (E₂), unlike displacement (Sₐ2), is insensitive to steric hindrance in the alkyl halide. In fact, the E₂ reactivity of alkyl halides is tert RX > sec RX > prim RX, which is opposite to their Sₐ2 reactivity.
Figure 14-1 Infrared and proton nmr spectra of substance $C_4H_7Br$ and substance $C_5H_8Br_2$ (see Exercise 14-1). Nmr spectra are at 60 MHz with reference to TMS at 0.0.
Several useful reactions for the synthesis of alkyl halides that we already have encountered are summarized below with references to the sections that supply more detail:

$$\text{RH} + \text{Cl}_2 \xrightarrow{hv} \text{RCl} + \text{HCl}$$  \hspace{1cm} (Section 4-5)

$$\text{RCH}=\text{CH}_2 + \text{HCl} \rightarrow \text{RCHCH}_3 + \text{Cl}$$  \hspace{1cm} (Section 10-4)

$$\text{RCH}=\text{CH}_2 + \text{HBr} \xrightarrow{hv \text{ or peroxides}} \text{RCH}_2\text{CH}_2\text{Br}$$  \hspace{1cm} (Section 10-7)

$$\text{ROH} + \text{HBr} \rightarrow \text{RBr} + \text{H}_2\text{O}$$  \hspace{1cm} (Section 8-7D)

A summary of these and some other reactions for the synthesis of organohalogen compounds is given in Table 14-5 at the end of the chapter (pp. 587–589).

---

**Exercise 14-2**

a. Methyl iodide can be prepared from potassium iodide and dimethyl sulfate. Why is dimethyl sulfate preferable to methanol in reaction with potassium iodide?

b. 1-Bromobutane can be prepared from 1-butanol and sodium bromide in concentrated sulfuric acid. What is the function of the sulfuric acid?

c. Some people like to put salt in their beer. Assess the possibility of CH₃CH₂Cl poisoning from the reaction of NaCl with the ethanol in beer. Give your reasoning.

d. Both isopropyl bromide and tert-butyl bromide react with sodium ethoxide in ethanol. Which bromide would give the most alkene? Which bromide would give the most alkene on solvolysis in 60% aqueous ethanol? Of the two reagents, sodium ethoxide in ethanol or 60% aqueous ethanol, which would give the most alkene with each bromide? Give your reasoning.

---

**14-3A Allylic (2-Propenyl) Halides**

Halogen compounds in which the carbon-halogen bond is adjacent to a double bond, as in $\text{C}≡\text{C}―\text{C}―\text{X}$ are known as **allylic halides**. The simplest example is 3-chloropropene, $\text{CH}_2≡\text{CHCH}_2\text{Cl}$, which is made on a large scale by the radical chlorination of propene at 400°C:

$$\text{CH}_2≡\text{CH}―\text{CH}_3 + \text{Cl}_2 \xrightarrow{400^\circ} \text{CH}_2≡\text{CH}―\text{CH}_2―\text{Cl} + \text{HCl}$$

Most of the 3-chloropropene prepared in this manner is converted to other important compounds. For example, addition of hypochlorous acid
gives a mixture of dichloropropanols, which on treatment with base gives a substance known commercially as "epichlorohydrin":

\[
\begin{align*}
\text{CH}_2\text{=CHCH}_2\text{Cl} & \xrightarrow{\text{HOCl}} \text{HOCH}_2\text{CHCH}_2\text{Cl} + \text{ClCH}_2\text{CHCH}_2\text{Cl} \\
\text{CH}_2\text{=CHCH}_2\text{Cl} & \xrightarrow{\text{Ca(OH)}_2} \text{chloromethyloxacyclopropane (chloromethyloxirane, "epichlorohydrin")}
\end{align*}
\]

The ring closure reaction with Ca(OH)$_2$ is an internal $S_{N}2$ reaction. Hydroxide ion converts the alcohol to an alkoxide ion that acts as a nucleophile in displacing the neighboring chlorine:

\[
\begin{align*}
\text{ClCH}_2\text{CHCH}_2\text{Cl} & \xrightarrow{\text{HO}^-} \text{ClCH}_2\text{CHCH}_2\text{Cl} \\
\text{ClCH}_2\text{CH}^-\text{CH}_2\text{Cl} & \xrightarrow{\text{H}^+} \text{ClCH}_2\text{CHCH}_2\text{Cl}
\end{align*}
\]

A general method for preparing allylic halides is by addition of hydrogen halides to conjugated dienes. This reaction usually produces a mixture of 1,2- and 1,4-addition products (see Section 13-2):

\[
\begin{align*}
\text{CH}_2\text{=CH}^-\text{CH}^-\text{CH}_2 + \text{HCl} & \rightarrow \\
\text{Cl} & \downarrow \\
\text{CH}_3\text{=CH}^-\text{CH}=\text{CH}_2 + \text{CH}_3\text{CH}=\text{CH}^-\text{CH}_2\text{Cl}
\end{align*}
\]

A second general method involves the bromination of alkenes with N-bromosuccinimide (the Wohl–Ziegler reaction). A radical-chain reaction takes place between N-bromosuccinimide (NBS) and alkenes, which com-
monly is initiated by light, peroxides, or other catalysts, and yields allylic bromides:

\[
\begin{align*}
\text{CH}_2\text{C}=\text{C} \text{H}_3 + & \quad \text{N} \quad - \text{Br} \quad \overset{h\nu \text{ or peroxides}}{\rightarrow} \quad \text{CH}_2\text{C}=\text{C} \text{H}_2\text{Br} + & \quad \text{N} \quad - \text{H} \\
\text{N-bromosuccinimide} & \quad 3\text{-bromopropene} & \quad \text{succinimide}
\end{align*}
\]

This reaction, like the chlorination of propene, is highly selective in that the so-called allylic C—H is attacked preferentially.

From bond energies (Table 4-6) we know that the weakest C—H bonds of propene are to the allylic hydrogens, \(\text{H}_2\text{C}=\text{C} \text{HCH}_2\text{—H}\). Therefore, in the first step of radical-chain chlorination of propene, an allylic hydrogen is removed by a chlorine atom (Equation 14-1). The allylic C—H bonds are weaker than the alkenic C—H bonds because of the extra stabilization of the radical obtained on hydrogen abstraction (Equation 14-1). Two equivalent valence-bond structures (1a and 1b) can be written for the 2-propenyl radical; the electron delocalization enhances the stability of the radical (see Section 6-5C):

\[
\begin{align*}
\text{CH}_2\text{C}=\text{C} \text{H} \quad \text{CH} \quad \text{H} + & \quad \text{Cl} \cdot \quad - \text{HCl} \\
\text{[CH}_2\text{C}=\text{C} \quad \text{H} \quad \text{CH} \quad \text{H} \quad \text{CH} \quad = \text{C} \text{H}_2] & \quad \sim \quad \text{[CH}_2\text{C}=\text{C} \quad \text{H} \quad \text{CH} \quad = \text{C} \text{H}_2] \\
\text{1a} & \quad \text{1b} & \quad 1
\end{align*}
\]

In the second step of the chain reaction (Equation 14-2) the propenyl radical can form a carbon–halogen bond at either end by abstracting a halogen atom from the halogenating agent:

\[
\begin{align*}
\text{CH}_2\text{C}=\text{C} \quad \text{H} \quad \text{CH} \quad \text{Cl} + & \quad \text{Cl} \cdot \\
\text{[CH}_2\text{C}=\text{C} \quad \text{H} \quad \text{CH} \quad = \text{C} \text{H}_2] & \quad \sim \quad \text{[CH}_2\text{C}=\text{C} \quad \text{H} \quad \text{CH} \quad = \text{C} \text{H}_2] \\
\text{1a} & \quad \text{1b} & \quad 1 \\
\text{Cl}_2 & \quad \text{Cl}_2
\end{align*}
\]

\[
\begin{align*}
\text{CH}_2\text{C}=\text{C} \quad \text{H} \quad \text{CH} \quad \text{Cl} + & \quad \text{Cl} \cdot \\
\text{Cl} \text{CH}_2\text{C}=\text{C} \quad \text{H} \quad \text{CH} \quad = \text{C} \text{H}_2 + & \quad \text{Cl} \cdot \\
\end{align*}
\]

The Cl· atom produced now can participate in Reaction 14-1, thereby continuing the chain. With propene the intermediate radical gives the same product, 2-propenyl chloride, irrespective of whether a chlorine atom is transferred.
Exercise 14-3 The reaction of N-bromosuccinimide (NBS) with alkenes to produce allylic bromides is thought to involve molecular bromine produced by the reaction

\[
\text{N-Br} + \text{HBr} \rightarrow \text{N-H} + \text{Br}_2
\]

Show the propagation steps that probably are involved in the radical-chain bromination of cyclohexene with NBS, assuming that bromine atoms are produced from NBS in the initiation steps. What by-products would you anticipate?

Exercise 14-4 Give a reasonable method for the synthesis of the following compounds from organic compounds not containing a halogen. Indicate the structures of any major by-products expected.

a. \[
\begin{array}{c}
\text{CH} = \text{CHCH}_2\text{Cl} \\
\end{array}
\]

d. \[
\begin{array}{c}
\text{CH}_3\text{CH} = \text{CH} - \text{CH} = \text{CH}_3 \\
\end{array}
\]

b. \[
\begin{array}{c}
\text{HC} = \text{CCH}_2\text{Br} \\
\end{array}
\]

e. \[
\begin{array}{c}
(\text{CH}_2 = \text{CH})_2\text{CHCl} \\
\end{array}
\]

c. \[
\begin{array}{c}
\text{Cl} \\
\end{array}
\]

14-3B \( S_N \) Reactions of Allylic Halides

The carbon–halogen bonds of allylic halides are especially reactive in both \( S_N1 \) and \( S_N2 \) reactions (Table 14-6). The reasons for the enhanced \( S_N1 \) reactivity have been discussed previously (Section 8-7B). For example, the ease
with which 1-chloro-2-butene ionizes compared to 1-chlorobutane is attributed to the stability of the 2-butenyl cation, which is stabilized by electron delocalization. The positive charge is distributed between C1 and C3, and the nucleophile (water) attacks at both positions to give mixtures of products. The same results are obtained if one starts with 3-chloro-1-butene because the same cation is formed:

CH$_3$CH═CH—CH$_2$—Cl

1-chloro-2-butene

\[ \begin{align*}
\text{CH}_3\text{CH}═\text{CH}—\text{CH}_2\text{OH} + \text{CH}_3\text{CH}═\text{CH}—\text{CH}_2 \\
\text{2-buten-1-ol} + \text{3-buten-2-ol}
\end{align*} \]

Exercise 14-5 In the presence of only traces of ionizing agents, either pure 1-chloro-2-butene or 3-chloro-1-butene is converted slowly to a 50–50 equilibrium mixture of the two chlorides. Explain.

The high reactivity of allylic halides in $S_n$ reactions indicates some special stabilization of the transition state ascribable to resonance involving the adjacent $\pi$ bond. We can express this in terms of the valence-bond structures, 2a–2c, for the transition state of the reaction of iodide ion with 3-chloropropene (Section 8-7A). The extra stabilization over the corresponding transition state for the reaction of iodide with a saturated chloride (e.g., CH$_3$CH$_2$CH$_2$Cl + I$^-$ \[\rightarrow\] CH$_3$CH$_2$CH$_2$I + Cl$^-$) arises from the contribution of 2c. An alternative atomic-orbital picture of the transition state is shown in Figure 14-2.
14 Organohalogen and Organometallic Compounds

14-3C Benzylic (Phenylmethyl) Halides

Reactivities comparable to allylic halides are found in the nucleophilic displacement reactions of benzylic halides by $S_N1$ and $S_N2$ mechanisms (Table 14-6). The ability of the benzylic halides to undergo $S_N1$ reactions clearly is related to the stability of the resulting benzylic cations, the electrons of which are extensively delocalized. Thus, for phenylmethyl chloride,

When the halogen substituent is located two or more carbons from the aryl group as in 2-phenylethyl bromide, $C_6H_5CH_2CH_2Br$, the pronounced activating effect evident in benzylic halides disappears, and the reactivity of the halides is essentially that of a primary alkyl halide (e.g., $CH_3CH_2CH_2Br$).

Benzylic halides can be prepared by the same radical-halogenating agents that give allylic halides from alkenes. These include Cl₂, Br₂, N-bromosuccinimide (Section 14-3A), $SO_2Cl_2$, and tert-butyl hypochlorite (see Exercise 4-18):

\[
\begin{align*}
\text{Ph-CH}_2\text{Cl} & \rightarrow \text{Ph-CH}_3 + \text{Cl}^- \\
\text{CH}_3 \text{C-H} + \text{Br}_2 & \xrightarrow{h\nu} \text{CH}_3 \text{C-Br} + \text{HBr}
\end{align*}
\]
The benzylic C–H bond is weaker and more reactive than primary alkane C–H bonds because of the stabilization of benzylic radicals (see Table 4-6 and Exercises 6-11 and 14-6).

**Exercise 14-6**  
**a.** Write the initiation and propagation steps involved in the radical bromination of methylbenzene (toluene) with bromine. Write the low-energy valence-bond structures of the intermediate phenylmethyl radical.  
**b.** Calculate $\Delta H^0$ for the following reactions of the radical, using the C–Br bond strength of $C_6H_5CH_2Br$ (55 kcal), and any other necessary bond energies. Assume that stabilization arising from electron delocalization is 38 kcal for a phenyl group (Section 6-5A) and 5 kcal for the triene structure 3.

![Radical Bromination Reaction](image)

What can you conclude from these calculations about the stability of 3 and the likelihood of its formation in this kind of bromination?

**Exercise 14-7** Explain the following observations.  
**a.** 1,2-Propadiene gives 3-chloropropyne on radical chlorination with either $Cl_2$ or tert-butyl hypochlorite.  
**b.** 1-Chloro-2-propanone could be regarded as a kind of allylic chloride, but it is very unreactive under $S_{n1}$ conditions although it is highly reactive in $S_{n2}$ reactions.  
**c.** The enantiomers of 3-chloro-1-butene racemize somewhat more rapidly than they give solvolysis products, under conditions that favor $S_{n1}$ reactions when a good ionizing but weakly nucleophilic solvent is used.

**Exercise 14-8** Would you expect the behavior of 3-chloropropyne to more nearly resemble 1-chloropropane or 3-chloropropene in nucleophilic displacement reactions? Give your reasoning.
The most readily available alkenyl halide is chloroethene (vinyl chloride), which can be prepared by a number of routes:

\[
\begin{align*}
CH≡CH &+ HCl & CH₂=CH₂ &+ Cl₂ \\
&100-200° & HgCl₂ & 400° \\
&\text{chloroethene} & OH⁻ & E₂ \\
&CH₂=CH₂ & CH₃-CHCl₂ \\
&Cl & Cl \\
&\uparrow CuCl₂, 250-315° \\
&CH₂=CH₂ &+ HCl &+ O₂
\end{align*}
\]

The most economical commercial preparation is high-temperature chlorination of ethene. A useful modification of this process uses hydrogen chloride in place of chlorine. An oxidizing agent is required to raise the oxidation state of chlorine in HCl to that of Cl₂; molecular oxygen is used for this purpose along with cupric salts as catalysts.

General methods of preparation for alkenyl and alkynyl halides are listed in Table 14-5. By the alkynyl halides we mean 1-halo-alkynes. One interesting method by which they may be prepared employs 1-alkynes with hypohalites:

\[
C₆H₅C≡CH + NaOBr \rightarrow C₆H₅C≡CBr + NaOH
\]

bromophenylethyne (87%)

This kind of reaction does not proceed with either alkanes or alkenes.

14-4A Uses of Alkenyl Halides

Chloroethene is produced in vast quantities for the production of polymers (polyvinyl chloride) and copolymers:

\[
n(\text{CH}_₂=\text{CHCl}) \rightarrow \left(\text{CH}_₂-\text{CH} \right)_n
\]
These polymers commonly are described as PVC plastics or less specifically as "vinyl." They are materials that may be either flexible or rigid according to what they are mixed with, and they are used in the manufacture of many familiar articles such as plastic curtains, rainwear, floor tile, synthetic leather goods, upholstery, table mats, phonograph records, insulation, plastic pipes, tubing, and packaging materials.

Recently, it has been found that persons working in plants that manufacture and use chloroethene have an unusually high incidence of an unusual type of liver cancer. As a result, strict safety regulations and pollution standards have been set for plants where chloroethene is made or used. The once widespread use of chloroethene as a propellant for aerosol cans has been curtailed. Polyvinyl chloride itself seems to be quite safe, but there are possible problems with its incorporation into interior building materials, clothing, and upholstery because heat, such as fire, causes polyvinyl chloride to decompose, thereby producing hydrogen chloride as one decomposition product. In closed areas the toxicity of hydrogen chloride gas may be as serious a hazard as the fire itself. Other polymers may give off similarly toxic products on strong heating.

14-4B Chemical Properties

The outstanding chemical characteristic of alkenyl halides is their general inertness in $S_N1$ and $S_N2$ reactions. Thus chloroethene fails to react with silver nitrate in ethanol (i.e., low $S_N1$ reactivity), fails to react with potassium iodide in acetone (i.e., low $S_N2$ reactivity), and only reacts slowly with sodium hydroxide to give ethyne (low E2 reactivity). The haloalkynes, such as $RC≡C−Cl$, are similarly unreactive.

It is not surprising that $≡C−X$ and $≡C−X$ bonds are hard to break heterolytically. In general, $C−X$ bonds are strong in alkenyl halides (cf. Table 4-6) and this property tends to make them less reactive than alkyl halides. Furthermore, double- and triple-bonded carbons are more strongly electron-attracting than saturated ($sp^3$) carbons, which is the reason why 1-alkynes and alkenes are stronger acids (Section 11-8) than alkanes. Consequently it is easier to break a $≡C−H$ bond in the sense $C:≡H$ than as $≡C:≡H$. It also will be more difficult to ionize a carbon-halogen bond to $C:≡X$ if the carbon is unsaturated. Therefore ethenyl and ethynyl cations, such as $CH_2≡CH$ and $HC≡C$, are difficult to generate from the corresponding halides. Superior leaving groups are required, such as trifluoromethanesulfonate, $−OSO_2CF_3$ (see Section 8-7C):

$$H\begin{array}{c}\text{S}\end{array}−CF_3\quad →\quad H\quad C\begin{array}{c}\text{S}\end{array}−H + O\quad S\begin{array}{c}\text{S}\end{array}−CF_3$$

ethenyl cation
The reason for the lack of $S_N2$ reactivity in ethenyl or ethynyl halides may be that the attacking nucleophile is unable to react by the concerted inversion mechanism that invariably is observed with alkyl halides:

Nevertheless, substitution of the halogen does occur under some circumstances. In such cases, the nucleophile first adds to the multiple bond, and in a subsequent step the halogen leaves as halide ion. This is an "addition-elimination" mechanism, of which we will have more examples later:

$$
\text{C}_6\text{H}_5\text{C} ≡ \text{C} ≡ \text{Cl} + \text{Nu} \xrightarrow{\text{addition}} \text{C}_6\text{H}_5\text{C} ≡ \text{C} ≡ \text{Cl} + \text{Nu} \xrightarrow{\text{elimination}} \text{C}_6\text{H}_5\text{C} ≡ \text{C} ≡ \text{Nu}
$$

**Exercise 14-9** Arrange the following halides in order of expected *increasing reactivity* towards (a) sodium iodide in acetone and (b) silver nitrate in ethanol. Indicate your reasoning.

$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{Cl}, \text{C}_6\text{H}_5\text{C} ≡ \text{C} ≡ \text{Cl}, \text{C}_6\text{H}_5\text{C} ≡ \text{CC}_2\text{H}_5\text{Cl}, \text{C}_6\text{H}_5\text{CH} ≡ \text{CHCl}$

**Exercise 14-10** Write a reasonable mechanism for the formation of phenylethanoic acid on heating phenylbromoethyne with potassium hydroxide in aqueous alcohol:

$$
\text{C}_6\text{H}_5\text{C} ≡ \text{CBr} \xrightarrow{\text{KOH, H}_2\text{O}} \text{C}_6\text{H}_5\text{OH} \xrightarrow{\text{H}^+} \text{C}_6\text{H}_5\text{CH}_2\text{CO}_2\text{H}
$$

**14-5 CYCLOALKYL HALIDES**

The cycloalkyl halides, except for cyclopropyl halides, have physical and chemical properties that are similar to those of the open-chain secondary halides and can be prepared by the same types of reactions (Table 14-5). All the cycloalkyl halides undergo $S_N2$ reactions rather slowly and, with nucleophiles that are reasonably basic ($\overset{\circ}{\text{OH}}, \overset{\circ}{\text{OC}}_2\text{H}_5, \overset{\circ}{\text{C}} ≡ \text{N}$, etc.), E2 reactions
can be expected to predominate (Table 14-6). The rate of carbocation formation leading to $S_N1$ and $E1$ reactions is sensitive to ring size but, except for the small-ring halides, the carbocation reactions are normal in most other respects.

The cyclopropyl halides are exceptional in that their behavior is much more like alkenyl halides than like secondary alkyl halides. Thus cyclopropyl chloride undergoes $S_N1$ and $S_N2$ reactions much less rapidly than isopropyl or cyclohexyl chlorides. A relationship between the reactivity of cyclopropyl chloride and chloroethene is not surprising in view of the general similarity between cyclopropane rings and double bonds (Section 12-5). This similarity extends to cyclopropylmethyl derivatives as well. Cyclopropylmethyl chloride is reactive in both $S_N1$ and $S_N2$ reactions in much the same way as 3-chloropropene:

\[
\begin{align*}
&\text{CH}_2\text{CHCHCl} \quad \text{cyclopropylmethyl chloride} \quad \text{similar high } S_N \text{ reactivities} \\
&\text{CH}_2\text{CHCHCl} \quad \text{3-chloropropene}
\end{align*}
\]

\[
\begin{align*}
&\text{CH}_2\text{CHCl} \quad \text{cyclopropyl chloride} \quad \text{similar low } S_N \text{ reactivities} \\
&\text{CH}_2\text{CHCl} \quad \text{chloroethene}
\end{align*}
\]

### 14-6 ARYL HALIDES

Aryl halides have a halogen directly bonded to a carbon of an aromatic ring. Examples are bromobenzene, fluorobenzene, and 2,4-dichloromethylbenzene:

\[
\begin{align*}
&\text{Br} \quad \text{bromobenzene} \\
&\text{F} \quad \text{fluorobenzene} \\
&\text{CH}_3\text{Cl} \quad \text{2,4-dichloromethylbenzene (2,4-dichlorotoluene)}
\end{align*}
\]

Some of the methods by which alkyl halides are prepared do not work for aryl halides because it is difficult to form C–halogen bonds at aromatic ring carbons by nucleophilic displacement reactions. The most common ways
of forming $\text{C}_\text{aryl}-\text{halogen}$ bonds are by substitution of $\text{C}_\text{aryl}—\text{H}$ by electrophilic halogenating agents (e.g., $\text{Br}_2$ or $\text{Cl}_2$),

$$\begin{align*}
\text{H} \\
\text{Cl} \\
\text{NO}_2 \\
\text{NO}_2
\end{align*}
\xrightarrow{\text{Br}_2, \text{FeBr}_3} 
\begin{align*}
\text{Br} \\
\text{C}_\text{aryl} \\
\text{C}_\text{aryl} \\
\text{NO}_2
\end{align*}
\xrightarrow{\text{HBr}}
$$

and by replacement of $\text{C}—\text{NH}_2$ by $\text{C}—\text{halogen}$. These reactions are listed in Table 14-5 and will be discussed in more detail in Chapters 22 and 23.

**14-6A Nucleophilic Aromatic Displacement Reactions**

The carbon–halogen bonds of aryl halides are like those of alkenyl halides in being much stronger than those of alkyl halides (see Table 4-6). *The simple aryl halides generally are resistant to attack by nucleophiles in either $S_{\text{N}}1$ or $S_{\text{N}}2$ reactions* (Table 14-6). However, this low reactivity can be changed dramatically by changes in the reaction conditions and the structure of the aryl halide. In fact, nucleophilic displacement becomes quite rapid (a) when the aryl halide is activated by substitution with strongly electron-attracting groups such as $\text{NO}_2$, and (b) when very strongly basic nucleophilic reagents are used.

**14-6B Addition-Elimination Mechanism of Nucleophilic Substitution**

Although the simple aryl halides are inert to the usual nucleophilic reagents, considerable activation is produced by strongly electron-attracting substituents provided these are located in either the ortho or para positions, or both. For example, the displacement of chloride ion from $1$-chloro-$2,4$-dinitrobenzene by dimethylamine occurs readily in ethanol solution at room temperature. Under the same conditions chlorobenzene completely fails to react; thus the activating influence of the two nitro groups amounts to a factor of at least $10^8$.
A related reaction is that of 2,4-dinitrofluorobenzene with the amino groups of peptides and proteins, and this reaction provides a means for analysis of the N-terminal amino acids in polypeptide chains. (See Section 25-7B.)

In general, the reactions of activated aryl halides closely resemble the 
\[ \text{S}_2 \text{N}^2 \] displacement reactions of aliphatic halides. The same nucleophilic reagents are effective (e.g., \( \text{CH}_3\text{O}^\ominus \), \( \text{HO}^\ominus \), and \( \text{RNH}_2 \)); the reactions are second order overall (first order in halide and first order in nucleophile); and for a given halide the more nucleophilic the attacking reagent, the faster the reaction. However, there must be more than a subtle difference in mechanism because an aryl halide is unable to pass through the same type of transition state as an alkyl halide in \[ \text{S}_2 \text{N}^2 \] displacements.

The generally accepted mechanism of nucleophilic aromatic substitution of aryl halides carrying activating groups involves two steps that are closely analogous to those briefly described in Section 14-4 for alkenyl and alkynyl halides. The first step involves attack of the nucleophile \( Y^\ominus \) at the carbon bearing the halogen substituent to form an intermediate carbanion 4 (Equation 14-3). The aromatic system is destroyed on forming the anion, and the carbon at the reaction site changes from planar (\( sp^2 \) bonds) to tetrahedral (\( sp^3 \) bonds).

\text{Step 1: addition}

\[
\begin{align*}
\text{CH}_3\text{N} & \quad \text{CH}_3 \\
\text{NO}_2 & \quad \text{NO}_2 \\
\text{+ (CH}_\text{3})_2\text{NH}_2\text{Cl} & \quad \text{4} \\
n & \quad n \\
\end{align*}
\]

In the second step, loss of an anion, \( X^\ominus \) or \( Y^\ominus \), regenerates an aromatic system, and, if \( X^\ominus \) is lost, the overall reaction is nucleophilic displacement of \( X \) by \( Y \) (Equation 14-4).

\text{Step 2: elimination}

\[
\begin{align*}
\text{X} & \quad \text{Y} \\
\text{Y} & \quad \text{X}^\ominus \\
\text{4} & \quad \text{Y} \\
\end{align*}
\]
In the case of a neutral nucleophilic reagent, Y or HY, the reaction sequence would be the same except for the necessary adjustments in the charge of the intermediate:

![Chemical structure](image)

Why is this reaction pathway generally unfavorable for the simple aryl halides? The answer is that the intermediate 4, which we can express as a hybrid of the valence-bond structures 4a–4c, is too high in energy to be formed at any practical rate. Not only has 4 lost the aromatic stabilization of the benzene ring, but its formation results in transfer of negative charge to the ring carbons, which themselves are not very electronegative:

![Chemical structures](image)

However, when strongly electron-attracting groups are located on the ring at the ortho-para positions, the intermediate anion is stabilized by delocalization of electrons from the ring carbons to more favorable locations on the substituent groups. As an example, consider the displacement of bromine by OCH₃ in the reaction of 4-bromonitrobenzene and methoxide ion:

![Chemical structure](image)

The anionic intermediate formed by addition of methoxide ion to the aryl halide can be described by the valence-bond structures 5a–5d. Of these struc-
tures 5d is especially important because in it the charge is transferred from the ring carbons to the oxygen of the nitro substituent:

\[
\begin{align*}
\text{Br} & \quad \text{OCH}_3 \\
\text{N}^+ & \quad \text{O}^- \\
\text{O} & \quad \text{N}^- \\
\end{align*}
\]

\[5a\]

\[
\begin{align*}
\text{Br} & \quad \text{OCH}_3 \\
\text{N}^+ & \quad \text{O}^- \\
\text{O} & \quad \text{N}^- \\
\end{align*}
\]

\[5b\]

\[
\begin{align*}
\text{Br} & \quad \text{OCH}_3 \\
\text{N}^+ & \quad \text{O}^- \\
\text{O} & \quad \text{N}^- \\
\end{align*}
\]

\[5c\]

\[
\begin{align*}
\text{Br} & \quad \text{OCH}_3 \\
\text{N}^+ & \quad \text{O}^- \\
\text{O} & \quad \text{N}^- \\
\end{align*}
\]

\[5d\]

Substituents in the meta positions have much less effect on the reactivity of an aryl halide because delocalization of electrons to the substituent is not possible. No formulas can be written analogous to 5c and 5d in which the negative charges are both on atoms next to positive nitrogen, C—N—O and O—N—O,

\[
\begin{align*}
\text{CH}_3 & \quad \text{O} \\
\text{Br} & \quad \text{N}^+ \\
\text{O} & \quad \text{N}^- \\
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3 & \quad \text{O} \\
\text{Br} & \quad \text{N}^+ \\
\text{O} & \quad \text{N}^- \\
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3 & \quad \text{O} \\
\text{Br} & \quad \text{N}^+ \\
\text{O} & \quad \text{N}^- \\
\end{align*}
\]

In a few instances, stable compounds resembling the postulated reaction intermediate have been isolated. One classic example is the complex 7 (isolated by J. Meisenheimer), which is the product of the reaction of either the methyl aryl ether 6 with potassium ethoxide, or the ethyl aryl ether 8 and potassium methoxide:
Exercise 14-11 a. Write resonance structures analogous to structures 5a through 5d to show the activating effect of $-\text{C}=\text{N}$ and $-\text{SO}_2\text{R}$ groups in nucleophilic substitution of the corresponding 4-substituted chlorobenzenes.

b. How would you expect the introduction of methyl groups ortho to the activating group to affect the reactivity of 4-bromonitrobenzene and 4-bromocyanobenzene toward ethoxide ion? (Investigate the geometry of the anion intermediate.)

Exercise 14-12 Would you expect 4-bromonitrobenzene or (4-bromophenyl)-trimethylammonium chloride to be more reactive in bimolecular replacement of bromine by ethoxide ion? Why?

Exercise 14-13* Would you expect 4-chloromethoxybenzene and 4-chlorotrifluoromethylbenzene to be more, or less, reactive than chlorobenzene toward methoxide ion? Explain.

Exercise 14-14* Whereas the order of reactivity of alkyl halides toward a given nucleophile is $I > Br > Cl > F$, the reverse order of reactivity frequently is observed with aryl halides ($F > Cl = Br = I$). What does this signify regarding the relative rates of the addition and elimination steps (Equations 14-3 and 14-4) in this kind of aromatic substitution?

Exercise 14-15 The reactions of several 1-substituted 2,4-dinitrobenzenes with piperidine (azacyclohexane), Equation 14-5, proceed at nearly the same rate, independent of the nature of $X$. Rationalize this observation in terms of a mechanism of nucleophilic aromatic substitution.

$$\begin{array}{c}
\text{X} \\
\text{NO}_2 \\
\text{NO}_2 \\
\text{C}_6\text{H}_5 \text{NH} \\
\text{CH}_3\text{OH} \\
\text{NO}_2 \\
\text{NO}_2 \\
\text{X}^- \\
\end{array}$$

$X = \text{C}_6\text{H}_5\text{S}, \text{Br}, \text{Cl}, \text{C}_6\text{H}_5\text{SO}_2, \text{p-NO}_2\text{C}_6\text{H}_4\text{O}, \text{I}$

Exercise 14-16* The reaction of 1-fluoro-2,4-dinitrobenzene with dimethylamine is catalyzed by weak bases. How may this observation be explained? (Consider possible intermediates, rate-determining steps, etc.)
Exercise 14-17 Write the products of the following reactions:

a. \[
\text{F} \quad \text{NO}_2 \quad + \quad \text{NaSCH}_3 \quad \rightarrow
\]

b. \[
\text{Cl} \quad \text{NO}_2 \quad + \quad \text{(CH}_3)_2\text{NH} \quad \rightarrow
\]

c. \[
\text{Cl} \quad \text{Cl} \quad + \quad \text{NaOCH}_3 \quad \rightarrow
\text{Cl} \quad \text{C} \equiv \text{N} \quad \text{(one mole)}
\]

14-6C Elimination-Addition Mechanism of Nucleophilic Aromatic Substitution. Arynes

The reactivities of aryl halides, such as the halobenzenes, are exceedingly low toward nucleophilic reagents that normally effect displacements with alkyl halides and activated aryl halides. Substitutions do occur under forcing conditions of either high temperatures or very strong bases. For example, chlorobenzene reacts with sodium hydroxide solution at temperatures around 340° and this reaction was once an important commercial process for the production of benzenol (phenol):

\[
\text{Cl} \quad \text{+ NaOH} \quad \text{H}_2\text{O} \quad \text{340°} \quad \rightarrow \quad \text{OH} \quad \text{+ NaCl}
\]

In addition, aryl chlorides, bromides, and iodides can be converted to arenes \( \text{ArNH}_2 \) by the conjugate bases of amines. In fact, the reaction of potassium amide with bromobenzene is extremely rapid, even at temperatures as low as \(-33°\), with liquid ammonia as solvent:

\[
\text{Br} \quad \quad \text{+ KNH}_2 \quad \text{NH}_3(l) \quad \text{-33°} \quad \rightarrow \quad \text{NH}_2 \quad \text{+ KBr}
\]
However, displacement reactions of this type differ from the previously discussed displacements of activated aryl halides in that rearrangement often occurs. That is, the entering group does not always occupy the same position on the ring as that vacated by the halogen substituent. For example, the hydrolysis of 4-chloromethylbenzene at 340° gives an equimolar mixture of 3- and 4-methylbenzenols:

\[
\begin{align*}
\text{CH}_3 & \quad \text{NaOH(aq)} \quad \text{340°} \\
\text{Cl} & \quad \text{CH}_3 \\
\text{OH} & \quad \text{50%} \\
& \quad \text{50%}
\end{align*}
\]

Even more striking is the exclusive formation of 3-methoxybenzenamine in the amination of 2-chloromethoxybenzene. Notice that this result is a violation of the principle of least structural change (Section 1-1H):

\[
\begin{align*}
\text{OCH}_3 & \quad \text{NaNH}_2, \text{NH}_3(l) \quad \text{33°} \\
\text{Cl} & \quad \text{OCH}_3 \\
& \quad \text{3-methoxybenzenamine}
\end{align*}
\]

The mechanism of this type of reaction has been studied extensively, and much evidence has accumulated in support of a stepwise process, which proceeds first by base-catalyzed elimination of hydrogen halide (HX) from the aryl halide—as illustrated below for the amination of bromobenzene:

**Elimination**

\[
\begin{align*}
\text{Br} & \quad \text{H} \quad \text{NH}_2 \quad \text{NH}_3 \\
\text{Br} & \quad \text{benzyne} \\
\text{9}
\end{align*}
\]

The product of the elimination reaction is a highly reactive intermediate 9 called benzyne, or dehydrobenzene, which differs from benzene in having two less hydrogens and an extra bond between two ortho carbons. Benzyne reacts rapidly with any available nucleophile, in this case the solvent, ammonia, to give an addition product:

**Addition**

\[
\begin{align*}
\text{9} & \quad + \text{NH}_3 \quad \text{NH}_3 \\
& \quad \text{benzenamine (aniline)}
\end{align*}
\]
The rearrangements in these reactions result from the attack of the nucleophile at one or the other of the carbons of the extra bond in the intermediate. With benzyne the symmetry is such that no rearrangement would be detected. With substituted benzynes isomeric products may result. Thus 4-methylbenzyne, \(10\), from the reaction of hydroxide ion with 4-chloro-1-methylbenzene gives both 3- and 4-methylbenzenols:

\[
\begin{align*}
\text{Cl} & \quad \text{OH} \quad 340^\circ \\
\text{CH}_3 & \quad \text{H}_2\text{O} \\
\text{CH}_3 & \quad \text{CH}_3 \\
\end{align*}
\]

In the foregoing benzyne reactions the base that produces the benzyne in the elimination step is derived from the nucleophile that adds in the addition step. This need not always be so, depending on the reaction conditions. In fact, the synthetic utility of aryne reactions depends in large part on the success with which the aryne can be generated by one reagent but captured by another. One such method will be discussed in Section 14-10C and involves organometallic compounds derived from aryl halides. Another method is to generate the aryne by thermal decomposition of a 1,2-disubstituted arene compound such as \(11\), in which both substituents are leaving groups—one leaving with an electron pair, the other leaving without:

\[
\text{11} \quad \text{heat} \quad \text{9} + \text{N}_2 + \text{CO}_2
\]

When \(11\) decomposes in the presence of an added nucleophile, the benzyne intermediate is trapped by the nucleophile as it is formed. Or, if a conjugated diene is present, benzyne will react with it by a \([4 + 2]\) cycloaddition. In the absence of other compounds with which it can react, benzyne will undergo \([2 + 2]\) cycloaddition to itself:

\[
\text{CH}_3\text{OH} \quad \text{CH}_3\text{OH}
\]

biphenylene
Exercise 14-18 Two valence-bond structures are possible for benzyne:

\[ \text{H} - \text{C} - \text{H} \leftrightarrow \text{H} - \text{C} = \text{H} \]

How do these differ from the Kekulé structures usually written for benzene? Devise an atomic-orbital model for benzyne.

Exercise 14-19 The intervention of benzyne in the amination of chlorobenzene, bromobenzene, and iodobenzene with sodium amide in liquid ammonia originally was demonstrated by J. D. Roberts using \(^{14}\text{C}\)-labeled halobenzenes. Show explicitly how the use of a chlorobenzene-\(^{14}\text{C}\) label could differentiate between amination by \textit{addition-elimination} (Section 14-6B) versus amination by \textit{elimination-addition} (benzyne mechanism).

Exercise 14-20 In the hydrolysis of chlorobenzene-\(^{14}\text{C}\) with \(4M\) aqueous sodium hydroxide at \(34^\circ\), the products are 58% benzenol-\(^{14}\text{C}\) and 42% benzenol-\(^{2}\text{C}\). Calculate the percentage of reaction proceeding (a) by an elimination-addition mechanism, and (b) by direct nucleophilic displacement. Would you expect the amount of direct displacement to increase, or decrease, if the reaction were carried out (a) at \(240^\circ\) and (b) with lower concentrations of sodium hydroxide? Give your reasoning.

Exercise 14-21 Explain the following observations:

\(\text{a.}\) 2,6-Dimethylchlorobenzene does not react with potassium amide in liquid ammonia at \(-33^\circ\).

\(\text{b.}\) Fluorobenzene, labeled with deuterium in the 2- and 6-positions, undergoes rapid exchange of deuterium for hydrogen in the presence of potassium amide in liquid ammonia, but does not form benzenamine (aniline).

Exercise 14-22* Bromobenzene reacts rapidly with potassium tert-butoxide in \((\text{CH}_3)_2\text{SO}\) (methylsulfinylmethane, dimethyl sulfoxide, DMSO) to give tert-butyl phenyl ether:

\[ \text{Br} + \text{KOC(CH}_3)_3 \rightarrow \text{OC(CH}_3)_3 + \text{KBr} \]

A comparable reaction does not take place in tert-butyl alcohol as solvent (see Section 8-7F). Suggest a mechanism for the reaction and explain why DMSO is a better solvent for the reaction than tert-butyl alcohol. What products would you expect to be formed using 4-bromo-1-methylbenzene in place of bromobenzene?
14-6D Uses for Aryl Halogen Compounds

As with most organic halides, aryl halides most often are synthetic intermediates for the production of other useful substances. For example, chlorobenzene is the starting aryl halide for the synthesis of DDT; it also is a source of benzenol (phenol, Section 14-6C) which, in turn, has many uses (Section 26-1).

Several aromatic chloro compounds are used extensively as insecticides, herbicides, fungicides, and bactericides. They also have acquired much notoriety because in some instances their indiscriminant usage has led to serious problems. For example, hexachlorophene is an external bactericide that until recently was used in cosmetic preparations such as soaps, deodorants, and so on. Its use has been discontinued because of compelling evidence that it can be absorbed through the skin in amounts that are dangerous, if not lethal, for infants and small children.

Other pesticides, notably DDT (p. 536) and the herbicides 2,4-D and 2,4,5-T have been partially banned for different reasons (Exercise 14-23).

Exercise 14-23* Both 2,4-D and 2,4,5-T are herbicides that have been used for weed control and as defoliating agents in jungle warfare. Apart from the arguments for or against the use of chemicals for such purposes, there have been reports of serious dermatitis among the industrial workers who produce these substances.

The cause finally was traced to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), which is produced as an impurity in the manufacture of 2,4,5-T.
This substance (TCDD) is very toxic. In addition to the dermatitis it produces, it is a potent teratogen (induces birth abnormalities). The lethal dose is less than $10^{-6}$ g for guinea pigs. Its presence in 2,4,5-T can be eliminated, but the conditions by which it is formed are pertinent to our present discussion.

The production of 2,4,5-T involves the substitution of one chlorine of 1,2,4,5-tetrachlorobenzene with hydroxide ion to give 12. This is followed by a second displacement reaction, this time on chloroethanoate by the sodium salt of 12:

If the temperature of the first step exceeds $160^\circ$, then two molecules of 12 react in a double nucleophilic displacement to give TCDD.

**a.** Write reasonable mechanisms for the steps by which two molecules of 12 are converted to TCDD.

**b.** Would you expect TCDD to be formed in the preparation of 2,4-D from 1,2,4-trichlorobenzene? Explain.

---

**14-7 POLYHALOGENATED ALKANES AND ALKENES**

**14-7A Useful Compounds**

Polychlorination of methane yields the di-, tri-, and tetrachloromethanes cheaply and efficiently:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Formula</th>
<th>CAS Number</th>
<th>Molecular Mass</th>
<th>Boiling Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dichloromethane</td>
<td>CH₂Cl₂</td>
<td>75-09-2</td>
<td>74.96</td>
<td>40°C</td>
</tr>
<tr>
<td>Trichloromethane</td>
<td>CHCl₃</td>
<td>75-01-8</td>
<td>133.57</td>
<td>61°C</td>
</tr>
<tr>
<td>Tetrachloromethane</td>
<td>CCl₄</td>
<td>75-00-0</td>
<td>202.98</td>
<td>77°C</td>
</tr>
</tbody>
</table>

These substances have excellent solvent properties for nonpolar and slightly polar substances. Chloroform once was used widely as an inhalation anesthetic. However, it has a deleterious effect on the heart and is oxidized slowly by atmospheric oxygen to highly toxic carbonyl dichloride (phosgene, COCl₂). Commercial chloroform contains about 1% ethanol, which destroys any COCl₂ formed by oxidation.
Carbon tetrachloride commonly was employed as a cleaning solvent, although its considerable toxicity entails considerable hazard when used indiscriminately. It has been used as a fire-extinguishing fluid for petroleum fires, but its toxicity and tendency to form still more toxic carbonyl dichloride makes it undesirable for confined areas. The common laboratory practice of removing traces of water from solvents with metallic sodium should not be applied to halogenated compounds; carbon tetrachloride–sodium mixtures are shock sensitive and can detonate.

Trichloroethene ("Tri-Clene", bp 87°) is a widely used dry-cleaning solvent. It can be prepared from either ethene or ethyne:

\[
\text{HC} \equiv \text{CH} + 2\text{Cl}_2 \rightarrow \text{CHCl}_2 \equiv \text{CHCl}_2 \xrightarrow{\text{Ca(OH)}_2} \text{Cl} \quad \text{Cl} \quad \text{H} \quad \text{H} \\
\text{CH}_2 \equiv \text{CH}_2 + 3\text{Cl}_2 \xrightarrow{300^\circ} \text{Cl} \quad \text{Cl} \quad \text{Cl} \quad \text{Cl} \quad \text{H}_2 \text{O} \\
\]

Compared with monohaloalkanes, polyhalogen compounds have quite different reactivities and behavior toward nucleophiles and bases. Thus dichloromethane reacts with hydroxide ion by an \( \text{S}_2 \) mechanism much less readily than methyl chloride. The chloromethanol formed then undergoes a rapid \( \text{E}_2 \) elimination to give methanal (formaldehyde), a substance that exists in water largely as dihydroxymethane:

\[
\begin{align*}
\text{CH}_2\text{Cl}_2 & \overset{\text{S}_2}{\underset{\text{H}_2\text{O}}{\rightarrow}} \left[ \begin{array}{c}
\text{O} \\
\text{H}
\end{array} \right] \\
\text{H}_2\text{C} \equiv \text{O} & \overset{\text{E}_2}{\rightarrow} \text{CH}_2 \text{OH}
\end{align*}
\]

Trichloromethane (chloroform) reacts quite differently with base than does chloromethane or dichloromethane—as will be described in the following section.

14-7B \( \alpha \) Elimination. Carbenes

Trihalomethanes, such as trichloromethane (chloroform), are quite reactive toward strong base. The base, such as hydroxide, removes the hydrogen of \( \text{HCCl}_3 \) as a proton much more rapidly than it attacks the carbon in the \( \text{S}_2 \) manner. The carbanion so formed, \( \text{Cl}_3\text{C}^\text{−} \), is unstable and loses chloride ion to form a highly reactive neutral intermediate, \( \text{Cl}_2\text{CCl} \), called dichlorocarbene:

\[
\begin{align*}
\text{Cl}_3\text{C}^\text{−} \overset{\text{OH}}{\underset{\text{OH}}{\rightleftharpoons}} & \text{Cl}_3\text{C}^\oplus + \text{H}_2\text{O} \\
\text{Cl}_3\text{C}^\oplus & \overset{\text{slow}}{\rightarrow} \text{Cl}_2\text{CCl} + \text{Cl}^\ominus 
\end{align*}
\]
This intermediate has only six valence electrons around carbon and therefore is strongly electrophilic. In aqueous solution it reacts rapidly to form carbon monoxide and methanoate (formate) ion:

\[
: \text{CCl}_2 \xrightarrow{\text{H}_2\text{O}, \text{fast}} \text{CO} + 2\text{Cl}^-
\]

\[
: \text{OH}^- \xrightarrow{} \text{HC} + 2\text{Cl}^-
\]

The formation of :CCl₂ from HCCl₃ by the reactions of Equation 14-6 results in the elimination of HCl—the leaving groups, H and Cl, both originating from the same carbon atom. Such reactions are not uncommon and are called α eliminations or 1,1 eliminations to distinguish them from E1 and E2 reactions, which are β eliminations or 1,2 eliminations. Still other possibilities are reactions such as γ or 1,3 eliminations, but these take on the character of internal Sₕ₂ reactions and will not be considered in detail here.

\[
\alpha \text{ elimination: } \begin{aligned} \text{H} \\ \text{C} \end{aligned} \xrightarrow{\alpha} \begin{aligned} \text{C}: + [\text{HX}] \\ \text{X} \end{aligned}
\]

\[
\beta \text{ elimination: } \begin{aligned} \text{H} \\ \text{C} \end{aligned} \xrightarrow{\beta} \begin{aligned} \text{C} &=& \text{C} + [\text{HX}] \\ \text{X} \end{aligned}
\]

\[
\gamma \text{ elimination: } \begin{aligned} \text{H} \\ \text{C} \end{aligned} \xrightarrow{\gamma} \begin{aligned} \text{C} &=& \text{C} + [\text{HX}] \\ \text{X} \end{aligned}
\]

The product of α elimination is a neutral species that resembles a carbocation in having only six carbon valence electrons. The simplest carbene is :CH₂, methylene. Carbenes are highly reactive, so much so that they cannot be isolated. Their involvement in reactions usually has to be inferred from the nature of the products or the reaction kinetics. The characteristic carbene reactions involve forming an electron-pair bond to the carbene carbon by reacting with σ bonds, π bonds, or unshared pairs (n). Some of these reactions are illustrated here for methylene (:CH₂).

Life with carbenes is substantially complicated by the fact that there are two different forms (singlet and triplet) of :CH₂ and presumably of all other carbenes. The two forms of :CH₂ differ considerably in their reactivity. One is the singlet, which has its unshared electrons paired, while the other is the triplet with the same electrons unpaired. For :CH₂, the singlet form is the less stable and more reactive, whereas with :CCl₂, the triplet is the less stable and more reactive.
with $\sigma$ bonds (insertion):

\[ \begin{array}{c}
\text{C} : X + : \text{CH}_2 \\
\rightarrow \text{C} : \text{CH}_2 : X
\end{array} \] (most likely with singlet :\text{CH}_2)\textsuperscript{1}

with $\pi$ bonds ([2 + 1] cycloaddition):

\[ \begin{array}{c}
\text{C} = \text{C} + : \text{CH}_2 \\
\rightarrow \text{C} - \text{C} - \text{CH}_2
\end{array} \]

with unshared pairs (dimerization, addition):

\[ \begin{align*}
\text{H}_2\text{C} : + : \text{CH}_2 & \rightarrow \text{H}_2\text{C}=\text{CH}_2 \\
\text{H}_2\text{C} : + : \text{N}=\text{N} & \rightarrow \text{H}_2\text{C}=\text{N}=\text{N} \\
\text{H}_2\text{C} : + : \text{C}=\text{O} & \rightarrow \text{H}_2\text{C}=\text{C}=\text{O}
\end{align*} \]

Carbenes are much more reactive toward carbon–carbon double bonds than toward single bonds. Without doubt the most useful feature of $\alpha$ elimination is that it provides a practical route to cyclopropanes and cyclopropenes by [2 + 1] cycloaddition of carbenes to double or triple bonds. These additions are stereospecific suprafacial additions if they involve singlet carbenes, but can give mixtures with triplet carbenes:

\[ \begin{array}{c}
\text{C} \text{C} \text{C} \\
\rightarrow \text{C} \text{C} \text{C}
\end{array} \]

\[ \begin{array}{c}
\text{C} \text{C} \text{C} \\
\text{H} \text{H} \text{H} \\
\rightarrow \text{C} \text{C} \text{C} \text{C} \text{C} \text{C}
\end{array} \]

\[ \begin{array}{c}
\text{CH}_2=\text{CH} : \\
\rightarrow \text{HC} = \text{CH}
\end{array} \] (an intramolecular addition)

Carbene precursors are compounds that have or acquire good leaving groups (e.g., halide ions). Thus, halogen compounds frequently are carbene sources. Trihalomethanes are the oldest known sources of dihalocarbenes; but there are other methods for generating carbenes, and some of these are listed for reference in Table 14-2 (see also Section 14-10C). There is a question as to whether a “free” carbene actually is formed in some of these reactions, particularly those involving metals, but for our purposes we will classify them as routes to carbenes or carbenelike species.
### Table 14-2

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Comments</th>
</tr>
</thead>
</table>
| 1. **Trihalomethanes and strong base**  
Br₃CH + Br⁻OC(CH₃)₃ → Br₂C⁺ + Br⁻ + HOC(CH₃)₃ | Gives dihalocarbenes; to trap the carbene with an alkene, an aprotic solvent is preferred. |
| 2. **Haloalkanes and alkyllithiums**  
Br₂C⁺ + CH₂Li → [Br₂C⁻Li⁺] + CH₂Br | Tetraphalomethanes give dihalocarbenes. (See Section 14-10C.) |
|  | Br₂C⁺ + LiBr |
|  | RCH₂Cl + C₄H₉Li → [RCH₂Cl⁻Li⁺] + C₄H₁₀ |
|  | RCH₂⁺ + LiCl |
| 3. **Diodomethane and zinc (Simmons-Smith Reaction)**  
CH₂I₂ + Zn → [IZnCH₂I]⁻ | Appears to generate a singlet :CH₂⁺ metal complex; zinc must be activated with copper. |
|  | CH₂I⁺ + ZnI₂ |
| 4. **Dissociation of trihaloacetates**  
Cl₃C⁻O⁻O⁻ → heat [Cl₂C⁺]⁻ + CO₂ | Salt is heated in aprotic solvent (e.g., 1,2-dimethoxyethane). |
|  | Cl₂C⁺ + Cl⁻ |
| 5. **Dissociation of trihalomethylmercury compounds**  
C₆H₅HgCCl₃Br → Cl₂C⁺ + C₆H₅HgBr | Widely applicable to formation of alkyl, aryl, keto, and carboalkoxy carbenes. |
| 6. **Dissociation of diazoalkanes**  
H₂C⁺⁺N⁺⁺N⁺⁺ → hν or heat H₂C⁺ + N₂ |  |
| 7. **Dissociation of ketenes**  
H₂C⁺⁺C⁺⁺O⁺⁺ → hν H₂C⁺ + CO |  |

*These reactions normally produce singlet carbenes. However, the singlet CH₂⁺ formed in Reactions 6 and 7 may undergo some interconversion to the more stable triplet form, especially if an otherwise inert material is present that can facilitate the singlet–triplet transformation.*
Many carbenes, like carbocations, rearrange to more stable structures by the migration of a neighboring group to the electron-deficient carbon. Thus phenylmethylcarbene rearranges to ethenylbenzene (styrene):

\[
\begin{align*}
\text{C}_6\text{H}_5\text{H} & \rightarrow \text{C}_6\text{H}_5\text{CH}_2 \rightarrow \text{C}_6\text{H}_5\text{CH} = \text{CH}_2 \\
\text{phenylmethylcarbene} & \quad \text{ethenylbenzene}
\end{align*}
\]

**Exercise 14-24** What products would you expect from the reaction of bromoform, CHBr₃, with potassium tert-butoxide in tert-butyl alcohol in the presence of (a) *trans*-2-butene and (b) *cis*-2-butene?

**Exercise 14-25** Devise atomic-orbital models of the singlet and triplet forms of :CH₂. Of these one has a much greater H—C—H angle than the other. Deduce whether the triplet or the singlet form should have the wider H—C—H angle. (Remember the Pauli principle, Section 6-1.)

14-7C Fluorochloromethanes

Replacement of either one or two of the chlorines of carbon tetrachloride by fluorine can be achieved readily with antimony trifluoride containing some antimony pentachloride. The reaction stops after two chlorines have been replaced. The antimony trifluoride can be regenerated continuously from the antimony chloride by addition of anhydrous hydrogen fluoride:

\[
\begin{align*}
\text{SbCl}_3\text{CCl}_4 + \text{SbF}_3 & \rightarrow \text{SbCl}_3 + 3\text{CFCl}_3 \\
\text{bp} & \ 25^\circ \\
\text{SbCl}_3\text{CCl}_4 + 2\text{SbF}_3 & \rightarrow 3\text{CF}_2\text{Cl}_2 + 2\text{SbCl}_3 \\
\text{bp} & \ -30^\circ
\end{align*}
\]

Both products are useful as refrigerants, particularly for household refrigerators and air-conditioning units, under the trade name Freon. Difluorodichloromethane (Freon 12) also is employed as a propellant in aerosol bombs, shaving-cream dispensers, and other such containers. It is nontoxic, odorless, nonflammable, and will not react with hot concentrated mineral acids or metallic sodium. This lack of reactivity is generally characteristic of the difluoromethylene group, provided the fluorines are not located on an unsaturated carbon. Attachment of a fluorine atom to a carbon atom bonded to one or more chlorine atoms tends greatly to reduce the reactivity of the chlorines toward almost all types of reagents. Possible environmental problems associated with these substances were discussed in the introduction to this chapter.
14-7D Fluorocarbons

During World War II, plastics and lubricating compounds of unusual chemical and thermal stability were required for many applications, in particular for pumping apparatus used to separate $^{235}\text{U}$ from $^{238}\text{U}$ by diffusion of corrosive uranium hexafluoride through porous barriers. It was natural to consider the use of substances made only of carbon and fluorine (fluorocarbons) for such purposes, and considerable effort was spent on methods of preparing compounds such as $(-\text{CF}_2)_n$. Today, many such substances are in common use. These often are called "perfluoro-" compounds, which indicates that all available hydrogens of the parent compound are replaced by fluorine. Thus perfluorocyclohexane is $(\text{CF}_2)_6$. A widely used perfluorocarbon is the plastic material $(-\text{CF}_2)_n$, which is produced in quantity by radical polymerization of tetrafluoroethene:

$$n(\text{CF}_2=\text{CF}_2) \xrightarrow{R} (-\text{CF}_2=\text{CF}_2)_n$$

The product ("Teflon") is a solid, chemically inert substance that is stable to around 300°C. It makes excellent electrical insulation and gasket materials. It also has self-lubricating properties, which are exploited in the preparation of low-adhesion surfaces (such as "nonstick" fry pans) and light-duty bearings.

Tetrafluoroethene can be made on a commercial scale by the following method:

$$3\text{CHCl}_3 + 2\text{SbF}_5 \xrightarrow{\text{SbCl}_5} 3\text{CHClF}_2 + 2\text{SbCl}_3$$

$$2\text{CHClF}_2 \xrightarrow{700-900°, 90\% \text{ yield}} \text{CF}_2=\text{CF}_2 + 2\text{HCl}$$

The latter reaction involves difluorocarbene ($:\text{CF}_2$):

$$\text{CHClF}_2 \rightarrow :\text{CF}_2 + \text{HCl}$$

$$2 :\text{CF}_2 \rightarrow \text{CF}_2=\text{CF}_2$$

In the presence of peroxides, tetrafluoroethene polymerizes to the long-chain polymer. If peroxides are excluded, $[2 + 2]$ cycloaddition occurs in high yield to give octafluorocyclobutane (see Section 13-3D):

$$2\text{CF}_2=\text{CF}_2 \rightarrow \begin{array}{c} \text{CF}_2=\text{CF}_2 \\ \text{CF}_2=\text{CF}_2 \end{array}$$

Similar cycloaddition reactions occur with chlorotrifluoroethene and 1,1-dichloro-2,2-difluoroethene.

Radical polymerization of chlorotrifluoroethene gives a useful polymer (Kel-F) that is similar to Teflon.

An excellent elastomer of high chemical resistance (Viton) can be made by copolymerizing hexafluoropropene with 1,1-difluoroethene. The product is stable to 300°C and is not attacked by hot concentrated nitric acid. Although expensive, it is unrivaled among elastomers for chemical durability under extreme conditions.
14-7E Properties of Fluorocarbons

The fluorocarbons have extraordinarily low boiling points relative to the hydrocarbons of comparable molecular weight. As seen in Figure 14-3, their boiling points are nearly the same or even lower than those of the alkanes or cycloalkanes with the same number of carbons. Thus octafluorocyclobutane boils 17° lower than cyclobutane, despite an almost fourfold greater molecular weight!

\[
\begin{align*}
\text{CH}_2=\text{CH}_2 & \quad \text{CF}_2=\text{CF}_2 \\
\text{CH}_2=\text{CH}_2 & \quad \
\text{bp} +12° & \quad \text{bp} -5° \\
\text{MW} = 56 & \quad \text{MW} = 200
\end{align*}
\]

Fluorocarbons are very insoluble in most polar solvents and are only slightly soluble in alkanes in the kerosene range. The higher-molecular-weight fluorocarbons are not even miscible in all proportions with their lower-molecular-weight homologs.

The physiological properties of organofluorine compounds vary widely. Dichlorodifluoromethane and the saturated fluorocarbons appear to be completely nontoxic. In contrast, perfluoro-2-methylpropene is exceedingly toxic, more so than the war gas, carbonyl dichloride (COCl₂). Sodium fluoroethanoate (CH₂FCO₂Na) and 2-fluoroethanol are toxic fluorine derivatives of oxygen-containing organic substances. The fluoroethanoate salt is sold commercially as a rodenticide. Interestingly, sodium trifluoroethanoate is nontoxic.

Fluorocarbon derivatives have another interesting and potentially useful property. They dissolve large quantities of oxygen. This fact, combined with their nontoxicity, has led to their use as blood replacements in heart surgery on experimental animals. Mice can live totally immersed in oxygen-saturated liquid fluorocarbons.

Figure 14-3 Boiling points of straight-chain fluorocarbons (CₙF₂ₙ₊₂) and hydrocarbons (CₙH₂ₙ₊₂)
One of the more important reactions of organohalogen compounds is the formation of organometallic compounds by replacement of the halogen by a metal atom. Carbon is positive in carbon–halogen bonds and becomes negative in carbon–metal bonds, and therefore carbon is considered to be reduced in formation of an organometallic compound (see Section 11-1):

\[
\begin{align*}
\text{C}^{\delta+} : \text{Halogen} & \rightarrow \text{C}^{\delta-} \text{Metal} \\
\end{align*}
\]

This transformation is of value because it makes an electrophilic carbon into a nucleophilic carbon. Organometallic compounds are a convenient source of nucleophilic carbon. A typical example of their utility is the way they achieve addition of nucleophilic carbon to carbonyl groups with formation of carbon–carbon bonds:

\[
\begin{align*}
\text{C}^{\delta-} \text{Metal} + \text{C}=\text{O} & \rightarrow \text{C}:\text{C}^{\delta+} \text{O}^{\delta-} \text{Metal} \\
\end{align*}
\]

In this chapter we will restrict our discussion of organometallic compounds to the alkyl and aryl compounds of magnesium and lithium, and the sodium and potassium salts of 1-alkynes. These substances normally are derived directly or indirectly from organohalogen compounds and are used very widely in organic synthesis. Organometallic compounds of transition metals and of boron are discussed in Chapters 11 and 31.

How carbon–metal bonds are formed depends on the metal that is used. Conditions that are suitable for one metal may be wholly unsuited for another. Some organometallic compounds react very sluggishly even toward acids, whereas others react avidly with water, oxygen, carbon dioxide, and almost all solvents but the alkanes themselves. Reactivity increases with increasing polarity of the carbon-metal bond, which is determined by the electropositivity of the metal. Strongly electropositive metals, such as sodium and potassium, form largely ionic bonds to carbon, as we have mentioned in the case of alkynide salts, \( \text{RC} \equiv \text{C}^{\delta+} \text{Na}^{\delta-} \) (Section 11-8). Estimates of the ionic character of various carbon–metal bonds are given in Table 14-3, and it will be seen that organosodium and organopotassium compounds have the most ionic bonds
and they are, in fact, among the most reactive organometallic compounds known. Many organosodium and organopotassium compounds burn spontaneously when exposed to air and react violently with water and carbon dioxide. As might be expected from their saltlike character, they are non-volatile and do not dissolve readily in nonpolar solvents. In contrast, the more covalent, less ionic, organometallic compounds, such as \((\text{CH}_3)_2\text{Hg}\), are far less reactive; they are stable in air, quite volatile, and dissolve in nonpolar solvents.

All of these compounds must be handled with great care because some are dangerously reactive and others are very toxic. They seldom are isolated from the solutions in which they are prepared but are used immediately in other reactions.

### Table 14-3

<table>
<thead>
<tr>
<th>C–K</th>
<th>51</th>
<th>C–Mg</th>
<th>35</th>
<th>C–Sn</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>C–Na</td>
<td>47</td>
<td>C–Al</td>
<td>22</td>
<td>C–Pb</td>
<td>12</td>
</tr>
<tr>
<td>C–Li</td>
<td>43</td>
<td>C–Zn</td>
<td>18</td>
<td>C–Hg</td>
<td>9</td>
</tr>
<tr>
<td>C–Ca</td>
<td>43</td>
<td>C–Cd</td>
<td>15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 14-3 Percent Ionic Character of Carbon–Metal Bonds


---

14-10 Preparation of Organometallic Compounds. Metals with Organic Halides

14-10A Metals with Organic Halides

The reaction of a metal with an organic halide is a convenient method for preparation of organometallic compounds of reasonably active metals such as lithium, magnesium, and zinc. Ethers, particularly diethyl ether and oxacyclopentane (tetrahydrofuran), provide inert, slightly polar media in which organometallic compounds usually are soluble. Care is necessary to exclude moisture, oxygen, and carbon dioxide, which would react with the organometallic compound. This can be accomplished by using an inert atmosphere of nitrogen or helium.

\[
\text{CH}_3\text{Br} + 2\text{Li} \xrightarrow{(\text{CH}_3\text{CH}_2)_2\text{O}} \text{CH}_3\text{Li} + \text{LiBr} \quad \text{methylolithium}
\]

\[
\text{CH}_3\text{CH}_2\text{Br} + \text{Mg} \xrightarrow{(\text{CH}_3\text{CH}_2)_2\text{O}} \text{CH}_3\text{CH}_2\text{MgBr} \quad \text{ethylmagnesium bromide}
\]

The reactivity order of the halides is I > Br > Cl >> F. Whereas magnesium and lithium react well with chlorides, bromides, and iodides, zinc is satisfactory
only with bromides and iodides. Mercury only reacts when amalgamated with sodium. Sodium and potassium present special problems because of the high reactivity of alkylsodium and alkylpotassium compounds toward ether and organic halides. Alkane solvents usually are necessary.

Alkenyl, alkynyl, and aryl halides, like alkyl halides, can be converted to the corresponding magnesium and lithium compounds. However, the reaction conditions, such as choice of solvent, can be critical. Bromoethene, for instance, can be converted to ethenylmagnesium bromide in good yield if the solvent is oxacyclopentane [tetrahydrofuran, \((\text{CH}_2)_4\text{O}\)]:

\[
\text{CH}_2\text{═CH—Br} + \text{Mg} \rightarrow \text{CH}_2\text{═CH—MgBr}
\]

The more reactive allylic and benzylic halides present a problem—not so much in forming the organometallic derivative as in keeping it from reacting further with the starting halide. An often unwanted side reaction in the preparation of organometallic compounds is a displacement reaction, probably of the \(S_n2\) type:

\[
\text{CH}_2\text{═CH—CH}:+ \text{R} \rightarrow \text{CH}_2\text{═CH—CH—R} + \text{MgCl}
\]

This problem can be lessened greatly by using a large excess of magnesium and dilute solutions of the allylic halide to minimize the coupling reaction.

The same difficulty also occurs in the preparation of alkylsodium compounds. The starting halide \(RX\) couples with \(RNa\) (to give \(R—R\) and \(NaX\)) or is converted to an alkene. These reactions appear to involve radical intermediates undergoing combination and disproportionation (Section 10-8C):

\[
\text{CH}_3\text{CH}_2::\text{Br} + \text{Na} \rightarrow \text{CH}_3\text{CH}_2:: + \text{Br} + \text{Na}^+
\]

\[
\text{CH}_3\text{CH}_2:: + \text{Na} \rightarrow \text{CH}_3\text{CH}_2\text{Na}
\]

\[
2\text{CH}_3\text{CH}_2:: \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3 \rightarrow \text{CH}_2\text{═CH}_2 + \text{CH}_3\text{CH}_3
\]

In the absence of metallic sodium, ethylsodium probably still reacts with ethyl bromide by a radical reaction rather than \(S_n2\) or E2. This happens because \(\text{CH}_3\text{CH}_2::\) tends to lose an electron easily and can act like metallic sodium to donate an electron to \(\text{CH}_3\text{CH}_2\text{Br}\) to form an ethyl radical and itself become an ethyl radical:

\[
\text{CH}_3\text{CH}_2:: + \text{CH}_3\text{CH}_2::\text{Br} \rightarrow 2\text{CH}_3\text{CH}_2:: + \text{Br}^-
\]
Reactions between the resulting radicals then produce butane, ethane, and ethene.

The point at which one can expect $S_{N}2$ and $E_{2}$ reactions to go faster than radical formation as the structures of the halides and the nature of the metal are changed is not yet clearly defined. However, it is becoming increasingly evident that there are substitution reactions of "unactivated" aryl halides that proceed without rearrangement by way of radical intermediates. The key step in these reactions is donation of an electron to one of the unfilled $\pi$ orbitals of the ring and subsequent ejection of a halide ion:

$$\text{Cl} \cdot + e^{-} \rightarrow \left[ \text{Cl} \cdot \right]^{-} \rightarrow \text{Cl}^{-} + \text{Cl}$$

Such a mechanism probably is involved in the formation of organometallic compounds from aryl halides and metals.

**Exercise 14-26** Write the structures of the products of the following equations:

- a. $C_{8}H_{8}CH_{2}CH_{2}MgBr + (CH_{3})_{2}SO_{4}$
- b. $C_{2}H_{5}MgBr + CH_{3}C≡C-CH_{2}Br$
- c. $CH_{2}≡CH-CH_{2}Li + CH_{2}≡CH-CH_{2}Cl$
- d. $CH_{3}CH_{2}CH_{2}MgBr + ClCH_{2}OCH_{3}$
- e. $C_{4}H_{8}Na + C_{4}H_{8}Br$

**14-10B Some Other Preparations of Organometallic Compounds**

Brief descriptions follow of less general but very useful methods of forming organometallic compounds (also see Table 14-7). In each of these preparations the solvent must be inert to all of the organometallic compounds involved.

**Halogen-metal exchange**

$$RBr + R'Li \leftrightarrow RLi + R'Br$$

The equilibrium in these reactions favors formation of the organometallic compound with the metal attached to the more electronegative $R$ group. The method is mainly used in the preparation of organolithium compounds derived...
from unreactive halides such as aryl, ethenyl, or ethynyl halides. These halides do not always react readily with lithium metal, but may react well with butyllithium:

\[
\text{Br}
\begin{array}{c}
\text{Cl} \\
+ \\
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Li} \\
\longrightarrow
\end{array}
\text{Li}
\begin{array}{c}
\text{Cl} \\
+ \\
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Br}
\end{array}
\]

Displacement of one metal by another

\[
\text{R}_2\text{Hg} + 2\text{Na} \rightleftharpoons 2\text{RNa} + \text{Hg}
\]

Here the equilibrium is such that the R group favors attachment to the more electropositive metal.

Organometallic compounds with metallic halides

\[
\text{RMgCl} + \text{HgCl}_2 \rightleftharpoons \text{RHgCl} + \text{MgCl}_2
\]

\[
\text{RLi} + \text{CuI} \rightleftharpoons \text{RCu} + \text{LiI}
\]

The equilibrium favors the products with R connected to the less electropositive metal so the reaction tends to form a less reactive organometallic compound from a more reactive one.

Organometallic compounds from acidic hydrocarbons

Some organometallic compounds are prepared best by the reaction of a strong base or an alkyl metal derivative with an acidic hydrocarbon, such as an alkyne:

\[
\text{CH}_3\text{C}==\text{CH} + \text{NaNH}_2 \longrightarrow \text{CH}_3\text{C}==\text{CNa} + \text{NH}_3 \quad \text{(Section 11-8)}
\]

\[
\text{CH}_3\text{C}==\text{C}:\text{H} + \text{CH}_3\text{MgBr} \longrightarrow \text{CH}_3\text{C}==\text{C}==\text{MgBr} + \text{CH}_4
\]

An especially important example is that of 1,3-cyclopentadiene, which is acidic because its conjugate base (cyclopentadienide anion) is greatly stabilized by electron delocalization. The anion is formed easily from the hydrocarbon and methylolithium:
Diorganometallic compounds cannot be prepared from dihalides if the halogens are separated by three C-C bonds or less because elimination or other reactions usually predominate. With active metals and 1,1-, 1,2-, or 1,3-dihalides, the following reactions normally occur:

\[
\begin{align*}
\text{CH}_2\text{I}_2 + \text{Zn} & \xrightarrow{\text{Cu}} \left[ \begin{array}{c} \text{ZnI} \\ \text{CH}_2 \\ I \end{array} \right] \xrightarrow{\text{ZnI}_2} \text{CH}_2 \\
\text{BrCH}_2-\text{CH}_2-\text{Br} + \text{Mg} & \rightarrow \text{CH}_2=\text{CH}_2 + \text{MgBr}_2 \\
\text{BrCH}_2-\text{CH}_2-\text{CH}_2\text{Br} + \text{Mg} & \rightarrow \left[ \begin{array}{c} \text{CH}_2 \\ \text{CH}_2 \end{array} \right] + \text{MgBr}_2
\end{align*}
\]

When the halogens are at least four carbons apart a diorganometallic compound can be formed:

\[
\text{BrCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Br} + 2\text{Mg} \rightarrow \text{BrMgCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{MgBr} \quad \text{(mostly)}
\]

Carbenes, \( \text{R}_2\text{C} \) (Section 14-7B) are produced by \( \alpha \) eliminations from polyhalogen compounds with organometallic reagents. The first step is halogen-metal exchange and this is followed by elimination of metal halide:

\[
\begin{align*}
\text{CBr}_4 + \text{CH}_3\text{Li} & \rightarrow \text{Br}_2\text{C} + \text{CH}_3\text{Br} & \text{(halogen-metal exchange)} \\
\text{Br}_2\text{C} & + \text{LiBr} \rightarrow \text{Br}_2\text{C}: + \text{LiBr} & \text{(metal-halide elimination)}
\end{align*}
\]

Elimination reactions of this type can be useful in synthesis for the formation of carbon–carbon bonds. For example, if dibromocarbene is generated in the presence of an alkene, it will react by cycloaddition to give a cyclopropane derivative:

\[
\begin{array}{c}
\text{CBr}_2 \\
\text{Br}
\end{array} \quad + \quad \text{CBr}_2 \quad \rightarrow \quad \begin{array}{c}
\text{Br} \\
\text{Br}
\end{array}
\]

A related example is the generation of benzyne from 1-bromo-2-fluorobenzene with magnesium in oxacyclopentane (tetrahydrofuran). If the temperature is kept around 0°, 2-fluorophenylmagnesium bromide is formed. At higher temperatures, magnesium halide is eliminated and benzyne results:

\[
\begin{array}{c}
\text{Br} \\
\text{Br}
\end{array} \quad + \quad \text{MgFBr} \quad \rightarrow \quad \begin{array}{c}
\text{Br} \\
\text{Br}
\end{array}
\]
If a diene is present, the benzyne will react with it by a [4 + 2] cycloaddition as in the following example:

\[
\text{Exercise 14-27}^* \text{ Show the steps involved in the formation of 2,3-pentadiene from } \text{cis}-2\text{-butene (1 mole), carbon tetrabromide (1 mole), and methyllithium (2 moles). (See Section 14-7B for pertinent reactions.)}
\]

\[
\text{Exercise 14-28}^* \text{ Show how the following transformations might be achieved. Define the reaction conditions as closely as possible. More than one step may be required.}
\]

\[
a. \text{C}_6\text{H}_5\text{CH}=\text{CH}_2 \rightarrow \text{C}_6\text{H}_5\text{C}=\text{CCl}_2
\]

\[
b. \text{Fluorobenzene} + \text{Cyclohexane} \rightarrow \text{Product}
\]

\[
c. \text{C}_6\text{H}_5\text{CHBrCCHBrC}_6\text{H}_5 \rightarrow \text{H}_3\text{C}_6\text{C}=\text{CC}_6\text{H}_5
\]

14-11 ORGANO MAGNESIUM COMPOUNDS

For many years the most important organometallic compounds for synthetic purposes have been the organomagnesium halides, or Grignard reagents. They are named after Victor Grignard, who discovered them and developed their use as synthetic reagents, for which he received a Nobel Prize in 1912. As already mentioned, these substances customarily are prepared in dry ether solution from magnesium turnings and an organic halide:

\[
\text{CH}_3\text{I} + \text{Mg} \xrightarrow{\text{ether}} \text{CH}_3\text{MgI} \quad 95\% \text{ yield}
\]
Chlorides often react sluggishly and, in addition, may give an unwelcome precipitate of magnesium chloride, which, unlike magnesium bromide and iodide, is only very slightly soluble in ether. Organomagnesium fluorides eluded preparation until quite recently.

Although we usually write the structure of a Grignard reagent as RMgX, in which X is a halogen, the structure of the reagent in ether solution is more complex. There is a rapidly established equilibrium between the organomagnesium halide (RMgX) and the corresponding dialkylmagnesium (RMgR):

$$2\text{RMgX} \rightleftharpoons \text{R}_2\text{Mg} + \text{MgX}_2$$

Both of these species, RMgX and R₂Mg, are reactive, and in ether solvents are solvated by coordination of the ether oxygen to magnesium. They further associate as dimers or higher polymers in solution. Although it is an oversimplification to regard a Grignard reagent as RMgX, most of the reactions can be rationalized easily by this simple structure.

### 14-12 ORGANOMAGNESIUM AND ORGANOLITHIUM COMPOUNDS IN SYNTHESIS

#### 14-12A Additions to Carbonyl Groups.

**Synthesis of Alcohols**

The most important synthetic use of Grignard reagents and organolithium reagents is to form new carbon–carbon bonds by addition to polar multiple bonds, particularly carbonyl bonds. An example is the addition of methylmagnesium iodide to methanal:

$$\text{CH}_3\text{MgI} + \text{H}_2\text{C}=\text{O} \rightarrow \text{CH}_3\text{CH}_2\text{O} - \text{MgI} \xrightarrow{\text{H}_2\text{O}} \text{CH}_3\text{CH}_2\text{OH}$$

The yields of addition products in reactions of this kind are generally high. The adducts have metal–oxygen bonds that can be broken readily by acid hydrolysis to give the organic product. Grignard reagents seldom add to carbon–carbon multiple bonds (however, see Section 14-12D).

With suitable variations of the carbonyl compound, a wide range of compounds can be built up from substances containing fewer carbon atoms per molecule. The products formed when several types of carbonyl compounds
react with Grignard reagents are listed in Table 14-4. The sequence of reactions starting with an organic halide, RX, amounts to the addition of R—H across a carbonyl bond.2

\[
RX + Mg \rightarrow RMgX
\]

\[
\begin{align*}
\text{C} &= \text{O} \quad \text{RX} \quad \text{RMgX} \\
\text{RMgX} + H^+ &\rightarrow \text{R} - \text{C} - \text{OMgX} \\
\text{R} - \text{C} - \text{OMgX} &\rightarrow \text{R} - \text{C} - \text{OH}
\end{align*}
\]

*Primary alcohols* can be prepared by the addition of RMgX or RLi to methanal, CH₂=O,

\[
\begin{align*}
\text{C}_5\text{H}_{11}\text{C} &= \text{CH} + \text{C}_2\text{H}_5\text{MgCl} &\rightarrow & \text{C}_5\text{H}_{11}\text{C} &= \text{CMgCl} \\
\text{1-heptyne} &\rightarrow & \text{1. H}_2\text{C} &= \text{C} = \text{O} \\
&\rightarrow & \text{2. H}^+, \text{H}_2\text{O} &\rightarrow & \text{C}_5\text{H}_{11}\text{C} &= \text{CCH}_2\text{OH}
\end{align*}
\]

2-octyn-1-ol (82%)

Alcohols of formula RCH₂CH₂OH can be prepared by addition of RMgX to oxacyclopropane (oxirane):

\[
\begin{align*}
\text{C}_6\text{H}_5\text{Br} + \text{Mg} &\rightarrow \text{C}_6\text{H}_5\text{MgBr} \\
\text{C}_6\text{H}_5\text{MgBr} + \text{CH}_2\text{CH}_2\text{CH}_2\text{OH} &\rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{OH}
\end{align*}
\]

2-phenylethanol (70%)

It is not possible to add RH to \(\text{C} = \text{O}\) directly because \(\Delta G^0\) generally is somewhat unfavorable \([+5 \text{ kcal for CH}_4 + (\text{CH}_3)_2\text{C} = \text{O} \rightarrow (\text{CH}_3)_2\text{COH}]\). How we get around this unfavorable equilibrium in practice provides an interesting example of how energy can be (and is) squandered to achieve some particular desired result; for example, the reaction \(\text{CH}_3\text{CH}_3 + \text{CH}_3\text{CHO} \rightarrow \text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)\text{OH}\) has \(\Delta H^0 = -12\) kcal but \(\Delta G^0 = +0.5\) kcal. A possible sequence is

\[
\begin{align*}
\text{CH}_3\text{CH}_3 + \text{Br}_2 &\rightarrow \text{CH}_3\text{CH}_2\text{Br} + \text{HBr} &\Delta H^0 = -10 \text{ kcal} \\
\text{CH}_3\text{CH}_2\text{Br} + 2\text{Li} &\rightarrow \text{CH}_3\text{CH}_2\text{Li} + \text{LiBr} &\Delta H^0 = -76 \text{ kcal} \\
\text{CH}_3\text{CH}_2\text{Li} + \text{CH}_3\text{CH} &= \text{O} \rightarrow \text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)\text{OLi} \\
\text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)\text{OLi} + \text{H}_2\text{O} &\rightarrow \text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)\text{OH} + \text{LiOH} \quad (aq) \\
\end{align*}
\]

The overall result is the expenditure of \(10 + 76 + 71 = 157\) kcal to achieve a reaction that itself has \(\Delta H^0 = -12\) kcal, but an unfavorable \(\Delta G^0\). (Li is used in this example rather than Mg because the heat of formation of \(\text{C}_2\text{H}_5\text{MgBr}\) is not available.)
Table 14-4
Products from the Reaction of Grignard Reagents (RMgX) with Carbonyl Compounds

<table>
<thead>
<tr>
<th>Reactant</th>
<th>Product</th>
<th>Hydrolysis product</th>
<th>Customary yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>methanal (formaldehyde)</td>
<td>RCH₂OMgX</td>
<td>prim-alcohol, RCH₂OH</td>
<td>good</td>
</tr>
<tr>
<td>other aldehydes</td>
<td>R′C=OOMgX</td>
<td>sec-alcohol, R′CH₂OH</td>
<td>good</td>
</tr>
<tr>
<td>ketone</td>
<td>R′R″C=OOMgX</td>
<td>tert-alcohol, R′R″C=OH</td>
<td>good to poor</td>
</tr>
<tr>
<td>carbon dioxide</td>
<td>CO₂OC₁₂MgX</td>
<td>carboxylic acid, RCO₂H</td>
<td>good</td>
</tr>
<tr>
<td>carboxylic ester</td>
<td>R′R″C=OOC₁₂MgX</td>
<td>tert-alcohol, R′R″C=OH</td>
<td>good to poor</td>
</tr>
<tr>
<td>acid chloride</td>
<td>R=OOC₁₂MgX</td>
<td>tert-alcohol, R=OOC₁₂H</td>
<td>good to poor</td>
</tr>
<tr>
<td>N,N-dimethylcarboxamide</td>
<td>RCH₂OMgX</td>
<td>ketone, R′=N(CH₃)₂OC₁₂</td>
<td>good to poor</td>
</tr>
</tbody>
</table>
Secondary alcohols are obtained from aldehydes, whereas ketones give tertiary alcohols:

\[
\text{CH}_3\text{I} \xrightarrow{\text{Mg}} \text{CH}_3\text{MgI} \quad 1. \quad \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CHO} \quad \text{2.} \quad \text{NH}_4\text{Cl, H}_2\text{O} \quad \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CHCH}_3 \quad \text{OH} \\
\text{2-hexanol (66\%)}
\]

Hydrolysis of the intermediate R—OMgX compound is achieved best with aqueous ammonium chloride solution. Addition of water gives an unpleasant mess of \(\text{Mg(OH)}_2\), whereas addition of strong acids such as HCl or H\(_2\)SO\(_4\) can lead to side reactions of dehydration and so on, especially with tertiary alcohols (Section 8-9C):

\[
\text{ROMgX} + \text{NH}_4\text{Cl} \quad \xrightarrow{\text{H}_2\text{O}} \quad \text{ROH} + \text{MgCl} + \text{NH}_3
\]

Tertiary alcohols also are obtained from both acyl halides, RCOCl, and esters, RCO\(_2\)R, by the addition of two moles of Grignard reagent. The first mole of RMgX adds to the carbonyl bond to give the adducts 13 or 14:

\[
\text{CH}_3\equiv\text{C} + \text{RMgX} \longrightarrow \text{CH}_3\equiv\text{CCl} \\
\text{ester} \quad \text{OMgX} \quad \text{acid chloride}
\]

\[
\text{CH}_3\equiv\text{C} + \text{RMgX} \longrightarrow \text{CH}_3\equiv\text{COC}_2\text{H}_5 \\
\text{ester} \quad \text{OMgX}
\]

However, these first-formed adducts are unstable and decompose to a ketone, \(\text{CH}_3\text{COR}\), and magnesium salts, MgXCl or MgXOC\(_2\)H\(_5\). The ketone usually
cannot be isolated, but reacts rapidly with more RMgX ultimately to give a tertiary alcohol:

\[
\begin{align*}
\text{CH}_3\text{C}^\text{Cl} \quad &\xrightarrow{\text{O}^\text{-}\text{MgX}} \quad \text{CH}_3\text{C}^\text{O} \quad + \text{MgXCl (or MgOC}_2\text{H}_5) \\
\text{or} \quad &\xrightarrow{1. \text{RMgX}} \quad \text{2. H}^+, \text{H}_2\text{O} \\
\text{CH}_3\text{C}^\text{OC}_2\text{H}_5 \quad &\xrightarrow{\text{O}^\text{-}\text{MgX}} \quad \text{CH}_3\text{C}^\text{OH} \\
\end{align*}
\]

Exercise 14-29 Addition of Grignard reagents, RMgX, to diethyl carbonate, O=\(\text{C} \quad \text{(OC}_2\text{H}_5)_2\), gives tertiary alcohols, \(\text{R}_3\text{COH}\), on hydrolysis. Write the steps involved in this reaction.

Exercise 14-30 Write structures for the products of the following reactions involving Grignard reagents. Show the structures of both the intermediate substances and the substances obtained after hydrolysis with \(\text{NH}_4\text{Cl}\) solution. Unless otherwise specified, assume that sufficient Grignard reagent is used to effect those addition reactions that occur readily at room temperature.

\begin{align*}
a. \quad \text{C}_6\text{H}_5\text{MgBr} + \text{C}_6\text{H}_5\text{CHO} \\
b. \quad \text{CH}_3\text{MgI} + \text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5 \\
c. \quad \text{CH}_3\text{CH}_2\text{MgBr} + \text{ClCO}_2\text{C}_2\text{H}_5 \\
d. \quad \text{C}_6\text{H}_5\text{MgBr} + (\text{CH}_3\text{O})_2\text{C}^\equiv\text{O} \\
e. \quad \text{[Diagram] C}^\equiv\text{Cl} + \text{CH}_3\text{MgCl} \\
\end{align*}

Exercise 14-31 Show how each of the following substances could be prepared from the indicated organic halide and any other appropriate organic compounds:

\begin{align*}
a. \quad \text{[Diagram] CH}_2\text{OH} \quad \text{from} \quad \text{[Diagram] Cl} \\
b. \quad \text{CH}_2^\equiv\text{CHC}(\text{CH}_3)_2\text{OH} \quad \text{from} \quad \text{CH}_3\text{I} \\
c. \quad \text{C}_6\text{H}_5\text{C}^\equiv\text{CCH}_2\text{OH} \quad \text{from} \quad \text{C}_2\text{H}_5\text{Cl} \\
d. \quad \text{CH}_3\text{CH}_2\text{CH(OH)CH}_3 \quad \text{from} \quad \text{C}_2\text{H}_5\text{Cl} \\
\end{align*}

**Organolithium compounds** behave very much like Grignard reagents, but with increased reactivity. They offer advantages over the magnesium compounds when the R group or the carbonyl compound is highly branched. For instance, isopropyllithium adds in good yield to 2,4-dimethyl-3-pentanone,
whereas isopropylmagnesium bromide fails completely to give the normal addition product:

\[
\begin{align*}
\text{CH}_3 & \quad \text{O} \quad \text{CH}_3 \\
\text{CH} & \quad \text{C} \quad \text{CH} \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CHMgBr} \\
\end{align*}
\]

Failure of Grignard reagents to add in the normal way generally is because reactions by alternative paths occur more rapidly. If the Grignard reagent has a hydrogen on the carbon adjacent to the point of attachment of \(-\text{MgX}\) (i.e., a \(\beta\) hydrogen), then reduction can occur, with the effect of adding \(\text{H}_2\) to the carbonyl group.

**Side reactions—reduction**

\[
\begin{align*}
\text{R}_2\text{C} & \quad \text{O} \quad \text{MgX} \\
\text{H} & \quad \text{C} \quad \text{C} \quad \text{C} \\
\text{H} & \quad \text{MgX} \\
\end{align*}
\]

Furthermore, if the carbonyl compound has a hydrogen located on the carbon next to the carbonyl group, the Grignard reagent can behave as a base and remove this hydrogen as a proton. The result is that the compound becomes an enolate salt and \(\text{RMgX}\) becomes \(\text{RH}\).

**Side reactions—enolization**

\[
\begin{align*}
\text{C} & \quad \text{O} \quad \text{MgX} \\
\text{H} & \quad \text{R} \\
\text{C} & \quad \text{C} \\
\end{align*}
\]

Apparently, the complicating side reactions observed with \(\text{RMgX}\) are not nearly as important with \(\text{RLi}\). The reasons for this difference are not well understood.
Exercise 14-32 Write structures for the addition, enolization, and reduction products possible for the following reactions:

a. \( CH_3COC_2H_5 + (CH_3)_2CMgX \)

b. \( C_6H_5COC_2H_5 + CH_3CH_2MgX \)

c. \( C_6H_5CH=CHCO_2C_2H_5 + C_6H_5MgX \)

14-12B Synthesis of Carboxylic Acids

The reaction of carbon dioxide with Grignard reagents initially gives a magnesium salt of a carboxylic acid, \( RCO_2MgX \):

\[
\begin{align*}
\text{Mg}^+ & \quad \text{ether} \\
\text{RCO}_2^- & \quad \text{RMgX} \\
\text{X} & \quad \text{RCO}_2MgX \\
\end{align*}
\]

This salt, which has a carbonyl group, in principle could add a second RMgX. However, further addition is usually slow, and for most practical purposes the reaction stops at this stage. If the reaction can go further, the worst way to run it is by bubbling \( CO_2 \) into the Grignard solution. This exposes the first-formed \( RCO_2MgX \) to excess RMgX and may lead to further addition reactions. The easy way to avoid this problem is to pour the RMgX solution onto powdered Dry Ice (solid CO). Hydrolysis of the product (here a stronger acid than \( NH_4Cl \) is required) generates the carboxylic acid, \( RCO_2H \):

\[
\begin{align*}
\text{RX} & \quad \text{Mg}^+ \\
\text{ether} & \quad \text{RMgX} \\
\text{CO}_2 & \quad \text{RCO}_2^- \\
\text{H}^+ & \quad \text{RCO}_2H \\
\end{align*}
\]

14-12C Synthesis of Ketones

Although organomagnesium compounds are not sufficiently reactive to add to carboxylate anions, alkyllithium compounds add quite well. A useful synthesis of methyl ketones involves the addition of methyllithium to the lithium salt of a carboxylic acid:

1. Lithium benzoate + \( CH_3Li \) → Lithium phenylethanol
2. Phenylethanol + \( H_2O \) → Phenylacetone
Other methods begin with acid chlorides or esters and attempt to add only one mole of RMgX:

\[
\begin{align*}
\text{O} & \quad \text{RMgX} \quad \text{OMgX} \quad \text{O} \\
\text{CH}_3 - C - Cl & \quad \rightarrow \quad \text{CH}_3 - C - Cl & \quad \rightarrow \quad \text{CH}_3 - C - R \\
\text{O} & \quad \text{R} & \quad \text{Cl}
\end{align*}
\]

The disadvantage of using Grignard reagents for this purpose is that they add very rapidly to the ketone as it is formed. There are two ways in which this disadvantage can be minimized. First, one can add the Grignard solution to an excess of acid chloride solution (the so-called “inverse addition” procedure) to keep the concentration of RMgX in the reaction mixture low, and hope that the reaction will stop at the ketone stage. However, this device seldom works very well with acid chlorides. Better results can be obtained with RMgX and R'CON(CH₃)₂ (see Exercise 14-63). The second method is to use a less reactive organometallic compound—one that will react with RCOCl but not with R₂C=O. One easy way to do this is to add cadmium chloride to the Grignard solution, whereby an organocadmium compound, R₂Cd, is formed (cf. Section 14-10B, Method 3). In the presence of magnesium halides, R₂Cd reacts moderately rapidly with acid chlorides, but only slowly with ketones. The addition therefore can be arrested at the ketone stage:

\[
2\text{RMgCl} + \text{CdCl}_2 \rightarrow \text{R}_2\text{Cd} + 2\text{MgCl}_2
\]

Alkylcopper compounds, R—Cu, also are selective reagents that react with acid chlorides to give ketones, but do not add to esters, acids, aldehydes, or ketones. The R—Cu compounds can be prepared from CuI and the alkyl-lithium. With an excess of the alkyl-lithium, the alkylcopper is converted to R₂CuLi:

\[
\begin{align*}
\text{CH}_3\text{Li} + \text{CuI} & \rightarrow \text{CH}_3\text{Cu} & \text{CH}_3\text{Li} & \rightarrow (\text{CH}_3)_2\text{CuLi} \\
\text{Cl} & \quad \text{C} & \quad \text{O} & \quad \text{Cl} \\
\text{Cl} & \quad \text{O} & \quad \text{ether} & \quad \text{ether}
\end{align*}
\]

**Exercise 14-33**  Grignard reagents, such as CH₃MgI, often add to the triple bond of nitriles, RC≡N, to give adducts that, on hydrolysis, yield ketones, RCOCH₃. Show the possible steps involved.
Exercise 14-34 Show the products expected from the following combinations of reagents. Write the structures of the initial adducts and also the products they give on acid hydrolysis:

a. $(\text{CH}_3)_2\text{CMgCl} + \text{CO}_2$

b. $\text{CO}_2\text{H} + 2\text{CH}_3\text{Li}$

c. $\text{C}_6\text{H}_5\text{C} - \text{Cl} + \text{CD}_3\text{MgCl} + \text{CdCl}_2$

d. $\text{CH}_3\text{C} - \text{Cl} + \text{CD}_3\text{Li} + \text{CuI}$

Exercise 14-35 Show how the following compounds could be synthesized by reasonable reactions from the indicated compound and any other needed reagents.

a. $\text{C} - \text{CH}_3$ from chlorocyclohexane

b. $\text{C}_6\text{H}_5\text{C} - \text{CO}_2\text{H}$ from phenylethyne

c. $\text{ClC} \equiv \text{CCO}_2\text{H}$ from ethyne

14-12D 1,4 Additions to Unsaturated Carbonyl Compounds

A conjugated alkenone, $\text{C} = \text{C} - \text{C} = \text{O}$, can react with an organometallic reagent by a normal 1,2 addition across the carbonyl group, or by 1,4 addition to the conjugated system.

1,4 addition

On hydrolysis, the 1,4 adduct first yields the corresponding enol, but this is normally unstable and rearranges rapidly to the ketone. The final product therefore corresponds to addition of $\text{R} - \text{H}$ across the carbon-carbon double bond:
Organomagnesium and organolithium compounds can add both 1,2 and 1,4 to alkenones, and the relative importance of each mode of addition depends on the structure of the reactants. This sort of dual behavior can be a nuisance in synthetic work because it leads to separation problems and low yields. Organocopper compounds are a great help in this situation because they show a very high selectivity for 1,4 addition and add to unsaturated ketones in excellent yield:

![Chemical reaction diagram]

**Exercise 14-36** Predict the products expected from the reactions of the following compounds:

- **a.** \( \text{CH}_2\text{=CH-C-C-CH}_3 + \text{C}_2\text{H}_5\text{MgBr} \)
- **b.** \( \text{CH}_2\text{=CH-C-O-C-CH}_2 \) + \( \text{C}_2\text{H}_5\text{MgBr} \)
- **c.** \( \text{CH}_2\text{=CH-C-O-C-CH}_3 + \text{C}_6\text{H}_5\text{Cu} \)
- **d.** \( \text{CH}_2\text{=CH-C-O-C-CH}_2 \) + \( \text{C}_2\text{H}_5\text{MgBr} + \text{CuI} \)

**Exercise 14-37** Would you expect the overall energy change (after hydrolysis) to be more favorable for 1,2 or 1,4 addition of a Grignard reagent to \( \text{CH}_2\text{=CH-C-OCH}_3 \)? Give your reasoning.

---

### 14-12E Oxygen, Sulfur, and Halogens

Grignard reagents react with oxygen, sulfur, and halogens to form substances containing C-O, C-S, and C-X bonds, respectively:

\[
\begin{align*}
\text{RMgX} + \text{O}_2 & \rightarrow \text{R-O-O-MgX} & \text{RMgX} + \text{H}_2\text{O} & \rightarrow 2\text{ROH} \\
\text{RMgX} + \frac{1}{2}\text{S}_8 & \rightarrow \text{RSMgX} & \text{H}_2\text{O}, \text{H}^+ & \rightarrow \text{RSH} \\
\text{RMgX} + \text{I}_2 & \rightarrow \text{RI} + \text{MgX}_1
\end{align*}
\]
These reactions are not often important for synthesis because the products, ROH, RSH, and RX, can be obtained more conveniently and directly from alkyl halides by $S_N1$ and $S_N2$ displacement reactions, as described in Chapter 8. However, when both $S_N1$ and $S_N2$ reactions are slow or otherwise impractical, as for neopentyl derivatives, the Grignard reactions can be very useful:

\[
\begin{align*}
\text{CH}_3 - \text{C} - \text{CH}_2\text{Cl} & \xrightarrow{\text{Mg}} \text{CH}_3 - \text{C} - \text{CH}_2\text{MgCl} & \xrightarrow{\text{I}_2} \text{CH}_3 - \text{C} - \text{CH}_2\text{I} \\
\text{neopentyl chloride} & & \text{neopentyl iodide}
\end{align*}
\]

Also, oxygenation of a Grignard reagent at low temperatures provides an excellent method for the synthesis of hydroperoxides:

\[
\text{RMgX} + \text{O}_2 \xrightarrow{-70^\circ} \text{ROOMgX} \xrightarrow{\text{H}^+} \text{ROOH}
\]

To prevent formation of excessive amounts of the alcohol, inverse addition is desirable (i.e., a solution of Grignard reagent is added to ether through which oxygen is bubbled rather than bubbling oxygen through a solution of the Grignard reagent).

### Table 14-5
Methods of Preparation of Organic Halides

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alkyl halides</strong></td>
<td></td>
</tr>
<tr>
<td>1. Alcohols and hydrogen halides</td>
<td>Reactivity: tertiary $&gt;$ secondary $&gt;$ primary; chlorides require ZnCl$_2$ as catalyst (Section 15-5A); rearrangement is common when the displacement is $S_N1$ type.</td>
</tr>
<tr>
<td>ROH + HBr $\xrightarrow{}$ RBr + H$_2$O</td>
<td></td>
</tr>
<tr>
<td>ROH + HCl $\xrightarrow{\text{ZnCl}_2}$ RCl + H$_2$O</td>
<td></td>
</tr>
<tr>
<td>2. Alcohols and phosphorus halides</td>
<td>Best with primary ROH; pyridine (azabenzene, a weak nitrogen base) acts to keep the acidity low, which may reduce side reactions such as rearrangement.</td>
</tr>
<tr>
<td>3ROH + PBr$_3$ $\xrightarrow{\text{pyridine}}$ 3RBr + H$_3$PO$_4$</td>
<td>As in Method 2. (See Section 15-5A.)</td>
</tr>
<tr>
<td>3. Alcohols and thionyl chloride</td>
<td>Radical-chain reaction (Sections 4-4 and 4-5); Br$_2$ is more selective than Cl$_2$; used for preparation of 2-propenyl and arylmethyl halides; other reagents include SO$_2$Cl$_2$ (Section 4-5B), tert-butyl hypochlorite and N-bromosuccinimide (Section 14-3A).</td>
</tr>
<tr>
<td>ROH + SOCl$_2$ $\xrightarrow{\text{pyridine}}$ RCl + SO$_2$ + HCl</td>
<td></td>
</tr>
<tr>
<td>4. Halogenation of hydrocarbons</td>
<td></td>
</tr>
<tr>
<td>RH + X$_2$ $\xrightarrow{hv}$ RX + HX</td>
<td></td>
</tr>
</tbody>
</table>
Table 14-5 (continued)
Methods of Preparation of Organic Halides

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>5. <strong>Addition of hydrogen halides to alkenes</strong></td>
<td></td>
</tr>
<tr>
<td>RCH=CH₂ + HX → RCH⁻CH₃</td>
<td></td>
</tr>
<tr>
<td>HBr, peroxides → RCH₂CH₂Br</td>
<td></td>
</tr>
<tr>
<td>See Sections 10-4 and 10-7.</td>
<td></td>
</tr>
<tr>
<td>6. <strong>Addition of halogens to alkenes</strong></td>
<td></td>
</tr>
<tr>
<td>RCH=CH₂ + X₂ → RCHXCH₂X</td>
<td></td>
</tr>
<tr>
<td>Gives 1,2-dihalides (Section 10-3A).</td>
<td></td>
</tr>
<tr>
<td>7. <strong>Inorganic halides and carbonyl compounds</strong></td>
<td></td>
</tr>
<tr>
<td>( \text{R}_c\text{C}=\text{O} \xrightarrow{\text{PCl}_3} \text{R}_c\text{Cl}_2 )</td>
<td></td>
</tr>
<tr>
<td>( \text{MoF}_5 \xrightarrow{\text{R}_c\text{F}_2} )</td>
<td></td>
</tr>
<tr>
<td>Gives 1,1-dihalides (Section 16-4D).</td>
<td></td>
</tr>
<tr>
<td>8. <strong>Organometallic compounds and halogens</strong></td>
<td></td>
</tr>
<tr>
<td>RMgX + X₂ → RX + MgX₂</td>
<td></td>
</tr>
<tr>
<td>RHgX + X₂ → RX + HgX₂</td>
<td></td>
</tr>
<tr>
<td>Of limited use because the RX compound is usually the source of the organometallic reagent (however, see Section 14-12E).</td>
<td></td>
</tr>
<tr>
<td>9. <strong>Chloromethylation of arenes</strong></td>
<td></td>
</tr>
<tr>
<td>( \text{ArH} + \text{CH}_3\text{O} + \text{HCl} \xrightarrow{(-\text{H}_2\text{O})} \text{ArCH}_2\text{Cl} )</td>
<td></td>
</tr>
<tr>
<td>Electrophilic substitution of ArH; gives benzylic (arylmethyl) chlorides (see Section 26-4A, Exercise 22-21).</td>
<td></td>
</tr>
</tbody>
</table>

**Alkenyl halides**

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>10. <strong>Addition of halogens and hydrogen halides to alkenyes</strong></td>
<td></td>
</tr>
<tr>
<td>RC≡CH + HX → RCX≡CH₂ + RCH≡CHX</td>
<td></td>
</tr>
<tr>
<td>May require mercury catalyst (Section 10-5).</td>
<td></td>
</tr>
<tr>
<td>11. <strong>Elimination of hydrogen halides from dihalides</strong></td>
<td></td>
</tr>
<tr>
<td>RCHXCH₂X \xrightarrow{\text{base}} \text{RCH≡CHX} + \text{RCX≡CH}_2</td>
<td></td>
</tr>
<tr>
<td>E2 (see Section 8-8).</td>
<td></td>
</tr>
</tbody>
</table>

**1-Alkynyl halides**

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>12. <strong>Halogenation of alkynide salts</strong></td>
<td></td>
</tr>
<tr>
<td>RC≡CNa + X₂ → RC≡CX</td>
<td></td>
</tr>
<tr>
<td>As in Method 8.</td>
<td></td>
</tr>
<tr>
<td>13. <strong>Halogenation of 1-alkynes with hypohalites</strong></td>
<td></td>
</tr>
<tr>
<td>RC≡CH + HOX → RC≡CX</td>
<td></td>
</tr>
<tr>
<td>Very useful (Section 14-4).</td>
<td></td>
</tr>
</tbody>
</table>
**Table 14-5 (continued)**

Methods of Preparation of Organic Halides

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>14. Elimination of hydrogen halides</strong></td>
<td>As in Method 11.</td>
</tr>
<tr>
<td>[ \text{RCH} = \text{CX}_2 \xrightarrow{\text{base}} \text{RC} \equiv \text{CX} ]</td>
<td></td>
</tr>
<tr>
<td><strong>15. Chloroethynylation of electrophilic carbon</strong></td>
<td>See Sections 14-10B and 11-8C.</td>
</tr>
<tr>
<td>[ \text{CIC} \equiv \text{CH} \xrightarrow{\text{NaNH}_2} \text{CIC} \equiv \text{CNa} \xrightarrow{\text{RX}} \text{CIC} \equiv \text{CR} ]</td>
<td></td>
</tr>
</tbody>
</table>

**Aryl halides**

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>16. Halogenation of arenes</strong></td>
<td>Electrophilic substitution of ArH; may require a catalyst ([\text{Fe}(II) \text{ or } I_2]); used for Cl(_2) and Br(_2) (see Section 22-4D).</td>
</tr>
<tr>
<td>[ \text{ArH} + \text{X}_2 \rightarrow \text{ArX} + \text{HX} ]</td>
<td></td>
</tr>
<tr>
<td><strong>17. From aromatic amines</strong></td>
<td>Amine is converted to diazonium salt ((\text{ArN}_2\text{O})), which is replaced by halide ion; a copper catalyst is required (see Section 23-10B).</td>
</tr>
<tr>
<td>[ \text{ArNH}_2 \xrightarrow{\text{HONO}} \text{ArN}_2 \xrightarrow{\text{Cu(I)/Cu(II)}} \text{X} \rightarrow \text{ArX} ]</td>
<td></td>
</tr>
</tbody>
</table>

**Table 14-6**

Reactivities of Organohalogen Compounds in Displacement and Elimination Reactions

<table>
<thead>
<tr>
<th>Organic halide</th>
<th>(S_n2)</th>
<th>Reactivity (E_2)</th>
<th>(S_n1, E_1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>\text{prim-alkyl, RCH}_2\text{X}</td>
<td>good</td>
<td>fair</td>
<td>very poor</td>
</tr>
<tr>
<td>\text{sec-alkyl, R}_2\text{CHX}</td>
<td>fair</td>
<td>fair</td>
<td>fair</td>
</tr>
<tr>
<td>\text{tert-alkyl, R}_3\text{CX}</td>
<td>poor</td>
<td>good</td>
<td>good</td>
</tr>
<tr>
<td>\text{allylic, RCH} \equiv \text{CHCH}_2\text{X}</td>
<td>good</td>
<td>—</td>
<td>good</td>
</tr>
<tr>
<td>\text{benzylic, } \includegraphics[width=1cm]{benzene} \equiv \text{CH}_2\text{X}</td>
<td>good</td>
<td>—</td>
<td>good</td>
</tr>
<tr>
<td>\text{alkenyl, RCH} \equiv \text{CHX}</td>
<td>poor</td>
<td>fair</td>
<td>poor</td>
</tr>
<tr>
<td>\text{alkynyl, R} \equiv \text{CX}</td>
<td>poor</td>
<td>—</td>
<td>poor</td>
</tr>
<tr>
<td>\text{aryl, } \includegraphics[width=1cm]{phenyl} \equiv \text{X}</td>
<td>very poor</td>
<td>—</td>
<td>poor</td>
</tr>
</tbody>
</table>
### Table 14-7
Methods of Preparation of Organometallic Compounds

<table>
<thead>
<tr>
<th>Method</th>
<th>Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Organohalogen compounds with metals:</td>
<td>( RX + Mg \xrightarrow{\text{ether}} RMgX )</td>
</tr>
<tr>
<td>solvent is diethyl ether or oxacyclopentane (tetrahydrofuran); inert</td>
<td>atmosphere desirable to keep out moisture and air; mostly used for</td>
</tr>
<tr>
<td>magnesium and lithium</td>
<td></td>
</tr>
<tr>
<td>2. Halogen–metal exchange:</td>
<td>( RX + R'Li \rightarrow RLi + R'X )</td>
</tr>
<tr>
<td>used when Method 1 fails because the halide is unreactive</td>
<td></td>
</tr>
<tr>
<td>3. Metal–metal exchange:</td>
<td>( RLi + CuI \rightarrow RCu + LiI )</td>
</tr>
<tr>
<td>replacement of one metal by a less electropositive metal</td>
<td></td>
</tr>
<tr>
<td>4. Metal–metal exchange:</td>
<td>( R_2Mg + 2Li \rightarrow 2RLi + Mg )</td>
</tr>
<tr>
<td>replacement of one metal by a more electropositive metal</td>
<td></td>
</tr>
<tr>
<td>5. Replacement of acidic hydrogen</td>
<td>( RC=CH + \text{NaNH}_2 \xrightarrow{\text{NH}_3} RC=CNa )</td>
</tr>
<tr>
<td>( RC=CH + RMgX \rightarrow RC=CMgX + RH )</td>
<td></td>
</tr>
</tbody>
</table>

### Additional Reading


Supplementary Exercises

14-38 What products do you expect from the following reactions? Give your reasoning. Show the structures of the intermediate compounds in sequences of the type $\longrightarrow \longrightarrow$.

a. $\text{C}_6\text{H}_5\text{C}=\text{CH} \xrightarrow{\text{NaNH}_2, \text{NH}_3} \text{CH}_2\text{CH}_3$

b. $\text{CH}_2=\text{CH} \xrightarrow{\text{ICl, heat}}$

c. $\text{CH}_2=\text{CH}_2 + \text{Br}_2 \xrightarrow{\text{sunlight}}$

d. $\text{CH}_3\text{CH}_2\text{OH} + \text{Kl} + \text{H}_3\text{PO}_4 \xrightarrow{\text{reflux}}$

e. $\text{CH}_3\text{C}-\text{CH}_2\text{CH}_3 \xrightarrow{48\% \text{HBr}}$

14-39 In the reaction of 14-38e, when the aqueous acid is mixed with 2-methyl-2-butanol, the mixture is initially homogeneous, but it soon separates into two phases. Explain why two phases appear. On separation of the phases using a separatory funnel, which layer (upper or lower) would contain the organic product? If you were unsure, how could you quickly find out?

14-40 Suppose one could hydrolyze pure cis-1-chloro-2-butene exclusively by (a) the $\text{S}_\text{N}1$ mechanism or (b) the $\text{S}_\text{N}2$ mechanism. Would you expect the 2-butenol formed in each case to be the cis isomer, the trans isomer, or a mixture? Explain.

14-41 The intermediate carbocation formed by $\text{S}_\text{N}1$ reactions of either 3-chloro-3-methyl-1-butene or 4-chloro-2-methyl-2-butene reacts with water to give a mixture of 2-methyl-3-buten-2-ol and 3-methyl-2-buten-1-ol. Which alcohol would you expect to predominate under conditions of equilibrium control? On the basis of steric hindrance, charge distribution in the cation, and so on, which alcohol should be favored under conditions of kinetic control? (Review Sections 6-5C, 10-4A, and 11-3.) Give your reasoning.
14-42 Explain why 2-chloropyridine is more reactive than 3-chloropyridine in nucleophilic substitution reactions.

\[
\begin{align*}
\text{2-chloropyridine} & & \text{3-chloropyridine} \\
\end{align*}
\]

14-43 Explain why 2-chloropyridine reacts with potassium amide (KNH₂) in liquid ammonia solution at \(-33^\circ\) to give 2-aminopyridine, whereas 3-chloropyridine under the same conditions gives a mixture of 65% 4-aminopyridine and 35% 3-aminopyridine.

14-44 Write a structural formula for a compound that fits each of the following descriptions:

a. an aryl halogen compound that reacts with sodium iodide in acetone but not with aqueous silver nitrate solution
b. an organic fluoro compound that is more reactive in displacement reactions than the corresponding iodo compound
c. an aryl bromide that cannot undergo substitution by the elimination-addition (benzyne) mechanism
d. the monobromomononitronaphthalene expected to be least reactive toward ethoxide ion in ethanol

14-45 Explain why the substitution reactions of the following halonaphthalenes give about the same ratio of 1-and 2-naphthyl products independently of the halogen substituent and the nucleophilic reagent. Show the steps involved.
14-46 For each of the following pairs of compounds describe a chemical test, preferably a test-tube reaction, that will distinguish between the two compounds. Write a structural formula for each compound and equations for the reactions involved.

a. chlorobenzene and phenylmethyl chloride
b. 4-nitrochlorobenzene and 3-nitrochlorobenzene
c. \( \text{Cl} \begin{array}{c} \text{C} \\ \text{C} \\ \text{CH}_3 \end{array} \) and \( \text{Cl} \begin{array}{c} \text{C} \\ \text{C} \\ \text{CH}_2\text{Cl} \end{array} \)
d. \( \text{CH}_3\text{C} \equiv \text{C} \equiv \text{Br} \) and \( \text{BrCH}_2\text{C} \equiv \text{CH} \)

14-47 Show how benzyne can be formed from the following reagents:

a. fluorobenzene and phenyllithium
b. \( \text{C}_6\text{H}_5\text{N}^{+}(\text{CH}_3)_3 \) + \( \text{KNH}_2 \)
c. 1,2-dibromobenzene + butyllithium

14-48 Indicate the steps involved in each of the following transformations:

a. \( \text{C}_6\text{H}_5\text{Br} + \text{C}_6\text{H}_5\text{C} \equiv \text{CH} \xrightarrow{2\text{KNH}_2(\text{excess}), \text{NH}_3(\text{i}), -33^\circ} \text{C}_6\text{H}_5\text{C} \equiv \text{CC}_6\text{H}_5 \)

The reaction does not occur unless more than one mole of \( \text{KNH}_2 \) per mole of \( \text{C}_6\text{H}_5\text{Br} \) is used.

b. \( \text{C}_6\text{H}_5\text{Cl} \xrightarrow{\text{C}_6\text{H}_5\text{Li} \text{(excess)} \text{ether}} \text{C}_6\text{H}_5\text{N} \begin{array}{c} \text{H} \\ \text{O} \\ \text{N} \end{array} \begin{array}{c} \text{H} \\ \text{CH}_3 \end{array} \)

c. \( \text{C}_6\text{H}_5\text{CO}_2^2 \) + \( \text{C}_6\text{H}_5\text{C} \equiv \text{O} \rightarrow \text{C}_6\text{H}_5\text{C} \equiv \text{C}_6\text{H}_5 \)

14-49 Predict the products of the following reactions:

a. \( \text{BrC}_6\text{H}_{\text{F}} \) + \( \text{C}_6\text{H}_5\text{O} \xrightarrow{1\text{-butyllithium}\text{ether}} \)}
14-50 Nucleophilic displacement of the halogen of 3,5-dimethyl-4-nitrobromobenzene is much slower than with the corresponding compound lacking the methyl groups. Give a reasonable explanation of this observation. (Construction of molecular models will help.)

14-51 Methylmagnesium halides have been employed as analytical reagents for the determination of the number of acidic hydrogens in a molecule (the Zerewitinoff determination). The method involves measuring the amount of methane produced from a given weight of compound (such as RH, with an acidic hydrogen) by the following reaction:

\[
\text{Excess methylmagnesium iodide and } 0.1776 \text{ g of Compound A (formula } \text{C}_4\text{H}_{10}\text{O}_3\text{) react to give 84.1 ml of methane collected over mercury at 740 mm and 25°. How many acidic hydrogens does Compound A possess per molecule? Suggest a possible structure on the basis that spectral data indicate (a) there is no } \text{C=O} \text{ group in the molecule and (b) A is achiral.}
\]

14-52 From the nature of the carbon-metal bonds in organometallic compounds, predict the products of the following reactions. Give your reasoning.

a. \( \text{CH}_3\text{MgCl} + \text{ICl} \)

b. \( \text{C}_6\text{H}_5\text{Li} + \text{CH}_3\text{OH} \)

c. \( \text{CH}_3\text{Li} + \text{HC≡CH} \)

d. \( \text{C}_6\text{H}_5\text{Li} + \text{Cul} \)

14-53 a. Show the steps and reaction intermediates by which the product is formed in the following reaction sequence:

b. Draw structures for the products in each step of the following sequence:

\[
\text{C}_2\text{H}_5\text{Cl} \xrightarrow{\text{Mg, ether}} \text{C}_2\text{H}_5\text{C≡CH} \xrightarrow{\text{CO}_2} \text{CH}_3\text{Li} \xrightarrow{\text{H}^+, \text{H}_2\text{O}}
\]

14-54 The following experimental observations have been reported:

1. tert-Butyl chloride was added to lithium metal in dry ether at 35°. A vigorous reaction ensued with evolution of hydrocarbon gases. After all the lithium metal was
consumed, the mixture was poured onto Dry Ice. The only acidic product that could be isolated (small yield) was 4,4-dimethylpentanoic acid.

2. tert-Butyl chloride was added to lithium metal in dry ether at $-40^\circ$. After all the lithium had reacted, the mixture was carbonated and gave a good yield of 2,2-dimethylpropanoic acid.

3. tert-Butyl chloride was added to lithium metal in dry ether at $-40^\circ$. After all the lithium was consumed, ethene was bubbled through the mixture at $-40^\circ$ until no further reaction occurred. Carbonation of this mixture gave a good yield of 4,4-dimethylpentanoic acid.

a. Give a reasonably detailed analysis of the results obtained and show as best you can the mechanisms involved in each reaction.
b. Would similar behavior be expected with methyl chloride? Explain.
c. Would you expect that a substantial amount of 6,6-dimethylheptanoic acid would be found in Observation 3? Explain.

14-55 Predict the products of each of the following Grignard reactions before and after hydrolysis. Give reasoning or analogies for each.

a. $\text{CH}_3\text{MgI} + \text{HCO}_2\text{C}_2\text{H}_5 \rightarrow$
b. $\text{CH}_3\text{CH}_2\text{CH}($MgBr$)$CH$_3_ + 2,4$-dimethyl-3-pentanone $\rightarrow$
c. $\text{CH}_3\text{CH}_2\text{MgBr} + \text{CS}_2 \rightarrow$
d. $\text{CH}_3\text{CH}_2\text{MgBr} + \text{NH}_3 \rightarrow$

e. (\[
\begin{array}{c}
\text{CH}_3 \\
\text{CH}_3 \\
\text{CH}_3 \\
\end{array}
\]
)\text{COH} from $\text{CH}_3\text{Br}$

14-56 Show how each of the following substances can be synthesized from the indicated starting materials by a route that involves organometallic substances in at least one step:

a. (\[
\begin{array}{c}
\text{CH}_3 \\
\text{CH}_3 \\
\text{CH}_3 \\
\end{array}
\]
)\text{D} from (\[
\begin{array}{c}
\text{CH}_3 \\
\text{CH}_3 \\
\text{CH}_3 \\
\end{array}
\]
)$\text{CCl}$
b. $\text{CH}_3\text{C}=$\text{CO}_2\text{H}$ from $\text{CH}\equiv\text{CH}$
c. $\text{CH}_3\equiv\text{C}=$\text{CH}_2$I$ from (\[
\begin{array}{c}
\text{CH}_3 \\
\text{CH}_3 \end{array}
\]
)$\text{C}$
d. $\text{CH}_3\equiv\text{C}=$\text{CH}($\text{CH}_3$)$_2$ (three ways)

e. (\[
\begin{array}{c}
\text{CH}_3 \\
\text{CH}_3 \\
\text{CH}_3 \\
\end{array}
\]
)\text{COH} from $\text{CH}_3\text{Br}$
f. $\text{CH}_3\equiv\text{C}=$\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ from (\[
\begin{array}{c}
\text{CH}_3 \\
\text{CH}_3 \\
\text{CH}_3 \\
\end{array}
\]
)$\text{CCl}_2\text{Cl}$
g. 1,5-hexadiene from propene

e. (\[
\begin{array}{c}
\text{CH}_3 \\
\text{CH}_3 \\
\text{CH}_3 \\
\end{array}
\]
)\text{COH} from $\text{CH}_3\text{Br}$

14-57 Predict the products of each of the following reactions both before and after hydrolysis:

a. $\text{O}$\text{Cl} + (\[
\begin{array}{c}
\text{CH}_3 \\
\text{CH}_3 \\
\text{CH}_3 \\
\end{array}
\]
)$\text{Cd}$ \rightarrow$

b. $\text{C}_6\text{H}_5$\text{C}=$\text{NN}$\text{H}$ \rightarrow 1$. (\[
\begin{array}{c}
\text{C}_6\text{H}_5\text{Li} \\
\text{ether} \\
\end{array}
\]
)$\rightarrow 2$. $\text{CO}_2$
c. HC≡CCH₂Br → 1. Mg-ether → 2. HC≡CCH₂Br

d. (CH₃)₃CBr → 1. Mg-ether → 2. O₂, -70°C

BrCH₂CH₂Br

BrCH₂CH₂Br

Na

e. CH₂Cl₂ + 1-butyllithium ether

14-58 Each of the following equations represents a “possible” but not actually feasible Grignard synthesis. Consider each equation and determine why it will not proceed satisfactorily as written. Give your reasoning and show what the actual product will be.

a. (CH₃)₂CMgBr + [(CH₃)₂CH]₂CΞO → (CH₃)₃C[(CH₃)₂CH]₂COH

b. (CH₃)₃CCH₂MgBr + [(CH₃)₂CH]₂CΞO → (CH₃)₃CCH₂[(CH₃)₂CH]₂COH

c. CH₃MgI + CH₃(CH₂)₂COCl → CH₃(CH₂)₂COCH₃

d. CH₃MgI + CH₃CH≡N→CH₃ → CH₃CH₂N(CH₃)₂

e. BrCH₂CH₂O₂CC₂H₅ → (C₂H₅)₂O Grignard reagent → CH₂O → HOCH₂CH₂CH₂O₂CC₂H₅

f. CH₂=CHCH₂MgCl + C₂H₅Br → CH₂=CH(CH₂)₂CH₃

14-59 What products would you expect to predominate in the following reactions:

a. C₆H₅MgBr + CH₃O → CH₃

b. CH₃MgBr + (CH₃)₃CC(C₃H₃)

c. CH₃MgBr + CH₃

14-60 Suggest possible reactions by which the following compounds could be prepared from ethyne and any other necessary compounds:

a. ClC≡C(CH₂)₄C≡CCl

b. C≡CCl

c. CH₃←C←C₂H₆

b. OH

b. C≡CCl

d. CH₂≡CHCH₂C≡CCH₃
14-61* The rate of addition of dimethylmagnesium to excess diphenylmethanone (benzophenone) in diethyl ether initially is cleanly second order, that is, first order in ketone and first order in (CH₂)₂Mg. As the reaction proceeds, the rate no longer follows a strictly second-order rate overall. Suggest how the apparent specific rate could change as the reaction proceeds.

14-62* An interesting isomer of benzene is "benzvalene" (tricyclo[2.1.0.0^5,6]-2-hexene). This substance, which like prismane (Section 12-10) can decompose with explosive violence, has been synthesized by T. Katz from lithium cyclopentadienide, dichloromethane, and methyllithium:

\[
\begin{align*}
\text{Li} & \quad + \quad \text{CH₂Cl₂} + \text{CH₃Li} \quad \rightarrow \quad \text{0} + 2\text{LiCl} + \text{CH₄}
\end{align*}
\]

"benzvalene"

Write a mechanism for this reaction that you can support by analogy with other reactions discussed in this chapter or by reasonable mechanistic arguments.

14-63 Table 14-4 shows that the addition of RMgX to R'CON(CH₃)₂ gives RCOR', although addition of RMgX to R'CO₂CH₃ and R'COCI lead to R'R₂COH. Assuming that similar mechanistic steps are involved throughout, why might R'CON(CH₃)₂ give a different product than R'CO₂CH₃ or R'COCI? Show your reasoning.

14-64 The formation of alcohols with organometallic compounds by the Grignard synthesis can be used to achieve the reaction RH + C=O to give R−C−OH, which generally has an unfavorable equilibrium constant. If you were looking for an industrial synthesis of 2-butanol by a reaction that would have a favorable equilibrium constant, which of the following might be better candidates than CH₃CH₃ + CH₃CH=O → CH₃CH₂CH(CH₃)OH. Give your reasoning.

a. CH₂=CH₂ + CH₂CH₂OH
b. CH₃CH₃ + CH₂CH₂OH
c. CH₃CH₂CH₂CH₃ + 1/2O₂
d. CH₃CH₂CH−CH₂ + H₂
e. CH₃CH₂CH=CH₂ + H₂O

14-65 Compound X, of formula C₃H₉Br₃, with methyllithium formed bromocyclopropane and 3-bromopropene. The nmr spectrum of X showed a one-proton triplet at 5.9 ppm, a two-proton triplet at 3.55 ppm, and a complex resonance centered at 2.5 ppm downfield from TMS. What is the structure of X? Account for the products observed in its reaction with methyllithium.
There have been many proposals for the occurrence of a so-called $S_\text{N}2'$ mechanism that would produce a concerted substitution with rearrangement for allylic halides. One possible example is

\[
\text{ClCH}_2\underset{\text{CH}}{\text{CH}}\underset{\text{CH}}{\text{CH}}\text{CH}_3 + \text{O}_2\text{CCH}_3 \rightarrow \text{CH}_2=\text{CH}\underset{\text{CH}}{\text{CH}}\underset{\text{O}_2\text{CCH}_3}{\text{O}}
\]

Consider whether this mechanism is operating for the particular example from the following experimental results. Give your reasoning.

1. Silver ethanoate in ethanoic acid with 1-chloro-2-butene gives 65% 2-butenyl ethanoate and 35% 1-methyl-2-propenyl ethanoate.

2. Ethanoate ion (1M) in ethanoic acid with 1-chloro-2-butene gives a mixture of about 85% 2-butenyl ethanoate and 15% 1-methyl-2-propenyl ethanoate. About 36% of the overall reaction product results from a process that is zero order in ethanoate ion, whereas 64% comes from a process that is first order in ethanoate ion.

3. Ethanoate ion in 2-propanone reacts with 1-chloro-2-butene to give only 2-butenyl ethanoate, and with 3-chloro-1-butene to give only 1-methyl-2-propenyl ethanoate.

(This exercise involves many of the ideas developed in Chapter 8 and you may wish to review Sections 8-4A, 8-4B, and 8-7, especially 8-7F.)