**PROBLEM 17.13**
Show the products of these reactions:

![Diagram](image)

**17.7 **FRIEDEL-CRAFTS ALKYLATION

Developed by C. Friedel and J. M. Crafts, the reaction of an alkyl halide with an aromatic compound in the presence of a Lewis acid catalyst, usually AlCl₃, results in the substitution of the alkyl group onto the aromatic ring:

![Equation](image)

In most cases the electrophile is the carbocation that is generated when the halide acts as a leaving group. The role of the aluminum chloride is to complex with the halogen to make it a better leaving group. From the point of view of the alkyl halide, the mechanism is an SN1 reaction with the pi electrons of the aromatic ring acting as the nucleophile (see Figure 17.4).

Although the most common method for generating the electrophile for the alkylation reaction employs an alkyl halide and aluminum trichloride, it can be generated in other ways also. For example, the reaction in the following equation uses the reaction of an alcohol and an acid to produce the carbocation:

![Equation](image)
Alternatively, the carbocation can be generated by protonation of an alkene. This reaction resembles the additions to alkenes discussed in Chapter 11. An example is provided by the following equation:

\[
\text{PhCH}_2\underset{\text{Cl}}{\text{Cl}} \overset{\text{AlCl}_3}{\rightarrow} \text{PhCH}_2\overset{\text{Cl}}{\text{AlCl}_3} \overset{\text{PhCH}_2}{\rightarrow} \text{PhCH}_2^+ + \text{AlCl}_4^-
\]

The carbocation acts as an electrophile and reacts with a pair of pi electrons of the aromatic ring. Or this can be viewed as an \( S_{N}1 \) reaction, with the weakly nucleophilic aromatic ring attacking the carbocation. The remainder of the mechanism is identical to the general mechanism outlined in Figure 17.1.

Several limitations occur with the Friedel-Crafts alkylation reaction. First, the alkyl group that is added to the ring is an activating group. This causes the alkylated product to be more reactive (by a factor of about 2) than the starting aromatic compound. Therefore, a significant amount of product where two or more alkyl groups have been added is commonly formed. The best solution to this problem is to use a large excess of the aromatic compound that is to be alkylated. This can easily be accomplished for compounds that are readily available, such as benzene or toluene, by using them as the solvent for the reaction. Note that the Friedel-Crafts alkylation is the only one of these electrophilic aromatic substitution reactions in which the product is more reactive than the starting material. All of the other reactions put deactivated groups on the ring, so they do not suffer from the problem of multiple substitution.
A second limitation is that aromatic compounds substituted with moderately or strongly deactivating groups cannot be alkylated. The deactivated ring is just too poor a nucleophile to react with the unstable carbocation electrophile before other reactions occur that destroy it.

The final limitation is one that plagues all carbocation reactions: rearrangements. Because the aromatic compound is a weak nucleophile, the carbocation has a lifetime that is longer than is the case in most of the other reactions involving this intermediate, allowing ample time for rearrangements to occur. An example is provided by the following equation:

\[
\begin{align*}
\text{Butylbenzene} & \quad \text{sec-Butylbenzene} \\
34\% & \quad 66\%
\end{align*}
\]

Despite these limitations, alkylation of readily available aromatic compounds, such as benzene and toluene, using carbocations that are not prone to rearrange, is a useful reaction. Intramolecular applications of this reaction have proven to be especially valuable.

**PROBLEM 17.14**
Show all of the steps in the mechanism for the formation of both products in this reaction:

\[
\text{Butylbenzene} + \text{sec-Butylbenzene}
\]

**PROBLEM 17.15**
Show the products of these reactions:

\[
a) \quad \text{OCH}_3 + \text{Cl} \quad \text{AlCl}_3 \quad \text{b) \quad NHCCCH}_3 + \text{CH}_2 \quad \text{H}_2\text{SO}_4
\]
**PROBLEM 17.16**
Show syntheses of these compounds from benzene:

![Images of chemical structures](a) benzene, (b) benzene with Cl, (c) benzene with Cl and AlCl₃, (d) benzene with OH and H₂SO₄, (e) benzene with AlCl₃, (f) benzene with Cl and AlCl₃.

**PRACTICE PROBLEM 17.2**

Explain which of these routes would provide a better method for the preparation of *p*-nitrotoluene:

Route A: 
\[ \text{HNO}_3 \rightarrow \text{H}_2\text{SO}_4 \]

Route B: 
\[ \text{CH}_3\text{Cl} \rightarrow \text{AlCl}_3 \]

**Solution**
Route A works fine. Toluene is readily nitrated, and the methyl group is an ortho/para director. The only problem is that both the desired compound and its *ortho*-isomer are produced and must be separated. (This is a common problem, and we usually assume that the separation can be accomplished, although it is not always easy in the laboratory.) Route B is unsatisfactory because the Friedel-Crafts alkylation reaction does not work with deactivated compounds such as nitrobenzene. Furthermore, even if the alkylation could be made to go, the nitro group is a meta director, so the desired product would not be formed.
Focus On

Synthetic Detergents, BHT, and BHA

A soap is the sodium salt of carboxylic acid attached to a long, nonpolar hydrocarbon chain. When a soap is placed in hard water, the sodium cations exchange with cations such as Ca$^{2+}$ and Mg$^{2+}$. The resulting calcium and magnesium salts are insoluble in water and precipitate to form “soap scum.”

$$2 \text{CH}_3\text{(CH}_2\text{)}_{16}\text{CO}_2^- \text{Na}^+ + \text{Ca}^{2+} \longrightarrow [\text{CH}_3\text{(CH}_2\text{)}_{16}\text{CO}_2^-]_2 \text{Ca}^{2+} + 2 \text{Na}^+$$

Synthetic detergents were invented to alleviate this problem. Rather than use the anion derived from a carboxylic acid with a large nonpolar group, detergents employ the anion derived from a sulfonic acid attached to a large nonpolar group. The calcium and magnesium salts of these sulfonic acids are soluble in water, so detergents do not precipitate in hard water and can still accomplish their cleaning function.

Two of the reactions that are used in the industrial preparation of detergents are electrophilic aromatic substitution reactions. First, a large hydrocarbon group is attached to a benzene ring by a Friedel-Crafts alkylation reaction employing tetrapropene as the source of the carbocation electrophile. The resulting alkylbenzene is then sulfonated by reaction with sulfuric acid. Deprotonation of the sulfonic acid with sodium hydroxide produces the detergent.

The exact structure of the alkyl group on the benzene ring is not important as long as it is large enough to confer the necessary hydrophobic character. Tetrapropene was used in the early versions of detergents because it was readily and cheaply available from the treatment of propene with acid. In this reaction, four propenes combine to form tetrapropene through carbocation intermediates. (In addition to the compound shown in the equation, an isomer with the double bond between carbon 2 and carbon 3 is also formed. If you are interested in the mechanism for this reaction, it is a variation of the cationic polymerization mechanism described later in Section 24.3.)
However, the detergent prepared from tetrapropene caused a problem in sewage treatment plants. The microorganisms that degrade such compounds start from the end of the hydrocarbon chain and seem to have trouble proceeding through tertiary carbons. The presence of several tertiary carbons in the tetrapropene chain slows its biodegradation to the point at which a significant amount passes through a treatment plant unchanged. This causes the resulting effluent and the waterways into which it is discharged to become foamy, an environmentally unacceptable result.

To solve this problem, most modern detergents are prepared from straight-chain alkenes. The resulting linear alkylbenzenesulfonate detergents are more easily degraded, and our rivers are no longer foamy. An example of a typical alkylation is shown in the following equation:

\[
\begin{align*}
4 \text{CH}_3(\text{CH}_2)_6\text{CH} &= \text{CH(\text{CH}_2)_3CH}_3 + \text{H}_3\text{PO}_4 \xrightarrow{205^\circ\text{C} \text{1000 psi}} \text{CH}_3(\text{CH}_2)_6\text{CH(\text{CH}_2)_6CH}_3
\end{align*}
\]

**PROBLEM 17.17**

What isomeric alkyl benzene should also be formed in this reaction?

Butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA) are antioxidants that are added to foods and many other organic materials to inhibit decomposition caused by reactions with oxygen. Perhaps you have seen these compounds listed among the ingredients on your cereal box at breakfast. (The mechanism of operation for these antioxidants is described in Section 21.8.) Both of these compounds are prepared by Friedel-Crafts alkylation reactions. BHT is synthesized by the reaction of \( p \)-methylphenol with 2-methylpropene in the presence of an acid catalyst.

\[
\begin{align*}
\text{OH} &+ 2 \text{CH}_3\text{C} &= \text{CH}_2 \xrightarrow{\text{AlCl}_3 \text{HCl}} \text{OH} \\
\text{CH}_3 & & \\
\text{p-Methylphenol} & & \text{2-Methylpropene} \\
\text{(p-hydroxytoluene)} & & \text{(isobutylene)} \\
& & \text{Butylated hydroxytoluene} \\
& & \text{(BHT)}
\end{align*}
\]

Continued
17.8 **Friedel-Crafts Acylation**

The reaction of an aromatic compound with an acyl chloride in the presence of a Lewis acid (usually AlCl₃) results in the substitution of an acyl group onto the aromatic ring. An example of this reaction, known as the Friedel-Crafts acylation, is provided by the following equation:

$$
\text{Benzene} + \text{Acetyl chloride} \xrightarrow{\text{AlCl₃}} \text{Acetophenone} + \text{HCl (61%)}
$$

The electrophile, an acyl cation, is generated in a manner similar to that outlined in Figure 17.4 for the generation of the carbocation electrophile from an alkyl halide. First the Lewis acid, aluminum trichloride, complexes with the chlorine of the acyl chloride. Then AlCl₃ leaves, generating an acyl cation. The acyl cation is actually more stable than most other carboxations that we have encountered because it has a resonance structure that has the octet rule satisfied for all of the atoms:
Some Additional Useful Reactions

This section presents several additional reactions that are very useful in the synthesis of aromatic compounds because they provide methods to convert substituents that can be attached by electrophilic substitution reactions to other substituents that cannot be attached directly. The mechanisms of these reactions need not concern us here.

The first of these reactions converts a nitro group to an amino group. This reduction can be accomplished using hydrogen and a catalyst or by using acid and a metal (Fe, Sn, or SnCl₂). Examples are provided in the following equations:

\[
\text{PhNO}_2 + \text{H}_2 + \text{Pt} \rightarrow \text{PhNH}_2
\]

(80%)

\[
\text{PhNO}_2 + \text{H}_2\text{SO}_4 \rightarrow \text{PhCO}_2\text{H} + \text{CO}_2
\]

(69%)

\[
\text{PhNO}_2 + \text{H}_2\text{SO}_4 \rightarrow \text{PhNH}_2\text{CO}_2\text{H} + \text{CO}_2
\]

(68%)

First the amino group was converted to a hydroxy group via a diazonium ion (Section 17.10). The benzene ring was reduced with hydrogen and a catalyst to produce cyclohexanol. Oxidation with potassium dichromate (Section 10.14) gave cyclohexanone. The bonds between the carbonyl carbon and both \( \alpha \)-carbons were then cleaved by a series of reactions not covered in this book. The carbon of the carbonyl group was converted to carbon dioxide in this process. One-half of the original radioactivity was found in the carbon dioxide, and the other one-half was found in the other product, 1,5-pentanediame. Additional experiments showed that the \( ^{14}\text{C} \) in the diamine product was located at C-1 or C-5.
This reaction is important because it provides a method to place an amino substituent onto the benzene ring, a substitution that cannot be accomplished directly by electrophilic attack. And, as illustrated in the following example, this opens all of the substitution reactions that can be accomplished through diazonium ion reactions.

Several procedures can be used to convert the carbonyl group of an aldehyde or ketone to a methylene group. One reaction, known as the Clemmensen reduction, employs amalgamated zinc (zinc plus mercury) and hydrochloric acid as the reducing agent. An example is provided by the following equation:

Another reaction that can be used to accomplish the same transformation is the Wolff-Kishner reduction. In this procedure the aldehyde or ketone is heated with hydrazine and potassium hydroxide in a high boiling solvent. An example is provided in the following equation. (The mechanism for the Wolff-Kishner reduction is presented in Section 18.8.) The Clemmensen reduction and the Wolff-Kishner reduction are
complementary because one employs acidic conditions and the other employs basic conditions.

\[
\text{O} \quad \text{NH}_2\text{NH}_2 \quad \Delta
\]

\[
\text{H}_2\text{Pd} \quad \text{OH} \quad \text{OH}
\]

The reduction of the carbonyl group of an aromatic ketone to a methylene group can also be accomplished by catalytic hydrogenation. An example of this method is shown in the following equation. Note that the carbonyl group in this reaction must be attached directly to the aromatic ring. The Clemmensen and Wolff-Kishner reductions do not have this restriction.

These reactions are quite useful in the preparation of aromatic compounds substituted with primary alkyl groups. For example, suppose a synthesis of butylbenzene is required. We might first consider preparing this compound by a Friedel-Crafts alkylation reaction. However, using a primary alkyl halide in this reaction invariably results in carbocation rearrangement. The reaction of benzene with 1-chlorobutane produces a mixture of butylbenzene (34%) and sec-butylbenzene (66%) (see page 692). The low yield of the desired primary product and the difficulty in obtaining it pure from the product mixture make this an unacceptable synthetic route. A much better synthesis can be accomplished in two steps by first preparing 1-phenyl-1-butanone by a Friedel-Crafts acylation reaction using benzene and butanoyl chloride, followed by conversion of the carbonyl group to a methylene group by one of these reduction reactions. As shown in the equation on the preceding page, the Clemmensen reduction accomplishes this transformation in 88% yield.

The final reaction in this section provides a method to prepare aromatic rings bonded to a carboxylic acid group. Because we do not have a direct way to attach this group, this procedure is very useful. The reaction is usually accomplished by oxidation of a methyl group to the carboxylic acid employing hot potassium permanganate in basic solution:
Although methyl groups are most commonly oxidized in these reactions, other alkyl groups can also be employed, as long as the carbon that is bonded to the aromatic ring is not quaternary. Note that the use of aromatic compounds with larger alkyl groups still gives the same product as would be produced from the oxidation of the compound substituted with a methyl group. The extra carbons are lost as carbon dioxide:

\[
\text{PROBLEM 17.27}
\]
Show the products of these reactions:

\[\text{PROBLEM 17.28}
\]
Show syntheses of these compounds from the indicated starting materials:

a) from benzene  b) from \(m\)-chloronitrobenzene