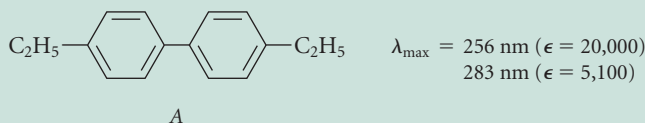


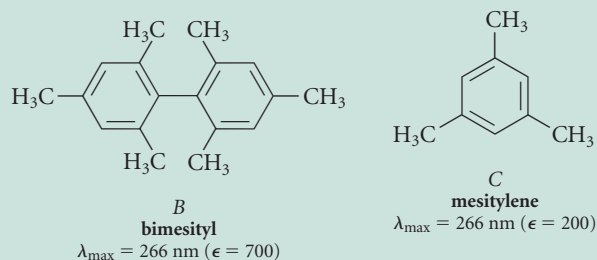
This hybridization allows one of its electron pairs to occupy a  $2p$  orbital, which has the same size, shape, and orientation as the carbon  $2p$  orbitals of the ring. In other words, an oxygen  $2p$  orbital overlaps more effectively with the carbon  $2p$  orbitals of the ring than an oxygen  $sp^3$  orbital would. (We learned about the same effect in resonance-stabilized allylic systems; p. 713). The UV spectrum of anisole is a direct consequence of this overlap.

## PROBLEMS

- 16.10 (a) Explain why compound *A* has a UV spectrum with considerably greater  $\lambda_{\max}$  values and intensities than are observed for ethylbenzene.



- (b) In view of your answer to part (a), explain why the UV spectra of compounds *B* and *C* are virtually identical.



- 16.11 How could you distinguish styrene ( $\text{Ph}-\text{CH}=\text{CH}_2$ ) from ethylbenzene by UV spectroscopy?

## 16.4 ELECTROPHILIC AROMATIC SUBSTITUTION REACTIONS OF BENZENE

The most characteristic reaction of benzene and many of its derivatives is *electrophilic aromatic substitution*. In an **electrophilic aromatic substitution** reaction, a hydrogen of an aromatic ring is substituted by an electrophile—that is, by a Lewis acid. The general pattern of an electrophilic aromatic substitution reaction is as follows, where E is the electrophile:

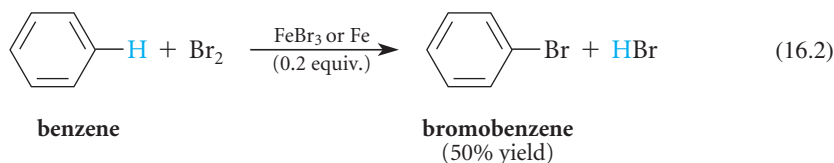


(Note that in this reaction and in others that follow, only one of the six benzene hydrogens is shown explicitly to emphasize that one hydrogen is lost in the reaction.)

All *electrophilic aromatic substitution reactions occur by similar mechanisms*. This section surveys some of the most common electrophilic aromatic substitution reactions and their mechanisms.

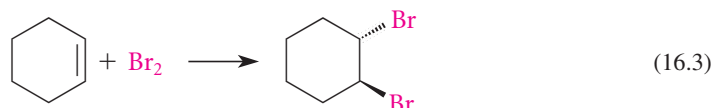
## A. Halogenation of Benzene

When benzene reacts with bromine under harsh conditions—liquid bromine, no solvent, and the Lewis acid  $\text{FeBr}_3$  as a catalyst—a reaction occurs in which *one* bromine is substituted for a ring hydrogen.



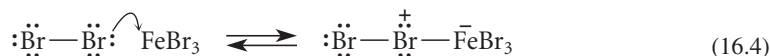
(Because iron reacts with  $\text{Br}_2$  to give  $\text{FeBr}_3$ , iron filings can be used in place of  $\text{FeBr}_3$ .) An analogous chlorination reaction using  $\text{Cl}_2$  and  $\text{FeCl}_3$  gives chlorobenzene.

This reaction of benzene with halogens differs from the reaction of alkenes with halogens in two important ways. First is the type of product obtained. Alkenes react spontaneously with bromine and chlorine, even in dilute solution, to give *addition products*.

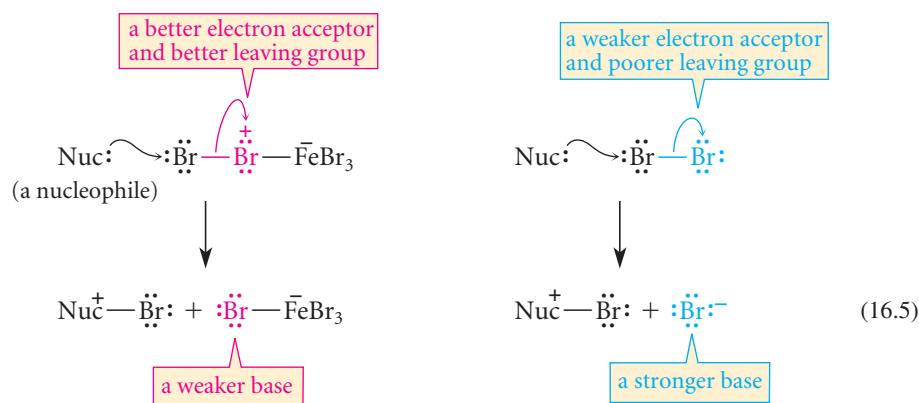


Halogenation of benzene, however, is a *substitution reaction*; a ring hydrogen is *replaced* by a halogen. Second, the reaction conditions for benzene halogenation are *much* more severe than the conditions for addition of halogens to an alkene.

The first step in the mechanism of benzene bromination is the formation of a complex between  $\text{Br}_2$  and the Lewis acid  $\text{FeBr}_3$ .

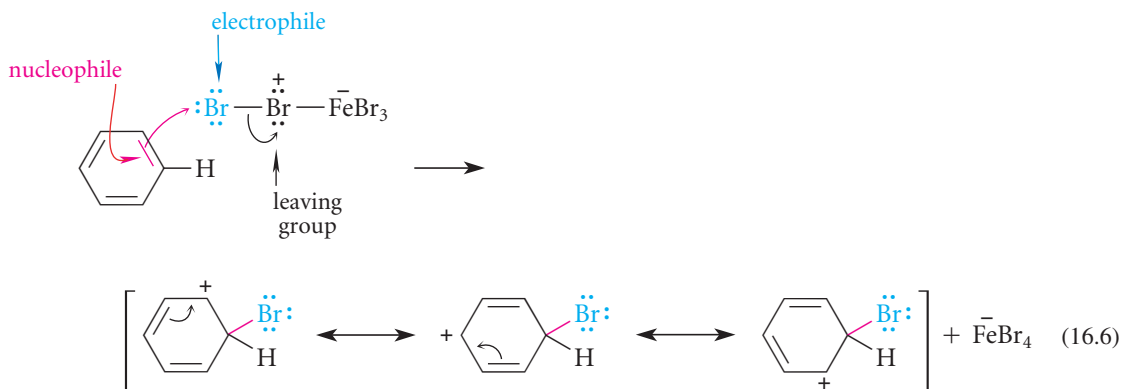


Formation of this complex results in a formal positive charge on one of the bromines. A positively charged bromine is a better electron acceptor, and thus a better leaving group, than a bromine in  $\text{Br}_2$  itself. Another (and equivalent) explanation of the leaving-group effect is that  $\text{FeBr}_4^-$  is a weaker base than  $\text{Br}^-$ . (Remember from Sec. 9.4F that weaker bases are better leaving groups.)  $\text{FeBr}_4^-$  is essentially the product of a Lewis acid–base association reaction of  $\text{Br}^-$  with  $\text{FeBr}_3$ . Therefore, in  $\text{FeBr}_4^-$ , an electron pair on  $\text{Br}^-$  has already been donated to Fe, and is thus less available to act as a base, than a “naked” electron pair on  $\text{Br}^-$  itself.



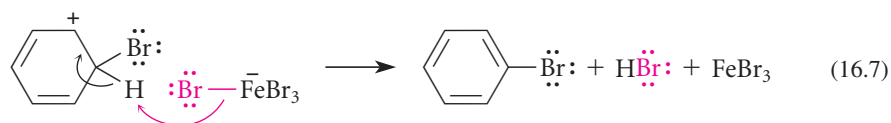
As you learned in Sec. 9.4F,  $-\text{Br}$  is a good leaving group. The fact that a much better leaving group than  $-\text{Br}$  is required for electrophilic aromatic substitution illustrates how unreactive the benzene ring is.

In the second step of the mechanism, this complex reacts with the  $\pi$  electrons of the benzene ring. The  $\pi$  electrons act as a nucleophile, the  $\text{Br}$  as an electrophile, and  $^-\text{FeBr}_4$  as a leaving group.

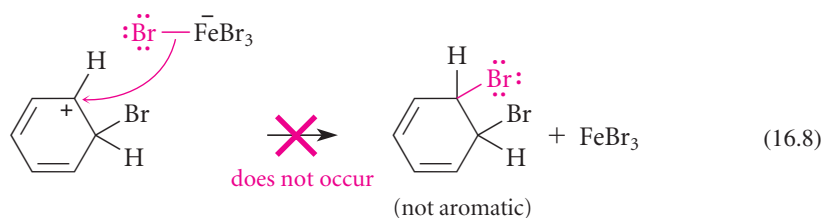


Although this step results in the formation of a resonance-stabilized carbocation, it also disrupts the aromatic stabilization of the benzene ring. Harsh conditions (high reagent concentrations, high temperature, and a strong Lewis acid catalyst) are required for this reaction to proceed at a useful rate because this step does not occur under the much milder conditions used to bring about bromine addition to an alkene.

The reaction is completed when a bromide ion (complexed to  $\text{FeBr}_3$ ) acts as a base to remove the ring proton, regenerate the catalyst  $\text{FeBr}_3$ , and give the products bromobenzene and  $\text{HBr}$ .



Recall that loss of a  $\beta$ -proton is one of the characteristic reactions of carbocations (Sec. 9.6B). Another typical reaction of carbocations—reaction of bromide ion at the electron-deficient carbon itself—doesn't occur because the resulting addition product would not be aromatic:



By losing a  $\beta$ -proton instead (Eq. 16.7), the carbocation can form bromobenzene, a stable aromatic compound.

### PROBLEM

- 16.12 A small amount of a by-product, *p*-dibromobenzene, is also formed in the bromination of benzene shown in Eq. 16.2. Write a curved-arrow mechanism for formation of this compound.

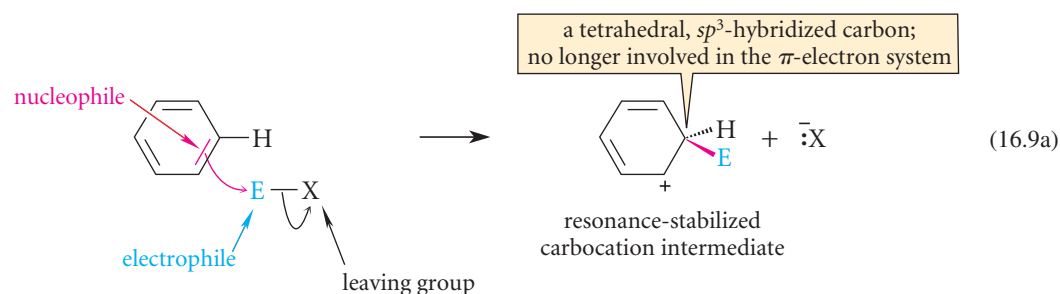
## B. Electrophilic Aromatic Substitution

Halogenation of benzene is one of many **electrophilic aromatic substitution** reactions. The bromination of benzene, for example, is an *aromatic substitution* because a hydrogen of benzene (the aromatic compound that undergoes substitution) is replaced by another group (bromine). The reaction is *electrophilic* because the substituting group reacts as an electrophile, or Lewis acid, with the benzene  $\pi$  electrons. In bromination, the Lewis acid is a bromine in the complex of bromine and the  $\text{FeBr}_3$  catalyst (Eq. 16.6).

We've considered two other types of substitution reactions: *nucleophilic substitution* (the  $\text{S}_{\text{N}}2$  and  $\text{S}_{\text{N}}1$  reactions, Secs. 9.4 and 9.6) and *free-radical substitution* (halogenation of alkanes, Sec. 8.9A). In a nucleophilic substitution reaction, the substituting group acts as a nucleophile, or Lewis base; and in free-radical substitution, free-radical intermediates are involved.

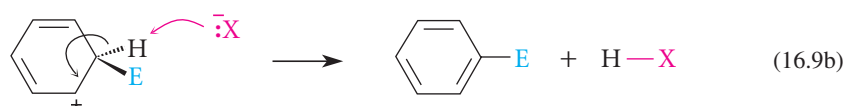
*Electrophilic aromatic substitution is the most typical reaction of benzene and its derivatives.* As you learn about other electrophilic substitution reactions, it will help you to understand them if you can identify in each reaction the following three mechanistic steps:

- Step 1** **Generation of an electrophile.** The electrophile in bromination is the complex of bromine with  $\text{FeBr}_3$ , formed as shown in Eq. 16.4.
- Step 2** **Nucleophilic reaction of the  $\pi$  electrons of the aromatic ring with the electrophile to form a resonance-stabilized carbocation intermediate.**



The electrophile approaches the  $\pi$ -electron cloud of the ring above or below the plane of the molecule. In the carbocation intermediate, the carbon at which the electrophile reacts becomes  $sp^3$ -hybridized and tetrahedral. This step in the bromination mechanism is Eq. 16.6.

- Step 3** **Loss of a proton from the carbocation intermediate to form the substituted aromatic compound.** The proton is lost from the carbon at which substitution occurs. This carbon again becomes part of the aromatic  $\pi$ -electron system.

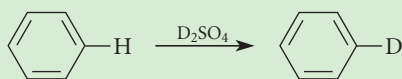


This step in the bromination mechanism is Eq. 16.7.

This sequence is classified as *electrophilic* substitution because we focus on the nature of the group—an electrophile—that reacts with the aromatic ring. However, the mechanism really involves nothing fundamentally new: like both *electrophilic addition* (Sec. 5.1) and *nucleophilic substitution* (Sec. 9.1), the reaction involves the reactions of nucleophiles, electrophiles, and leaving groups.

## Study Problem 16.1

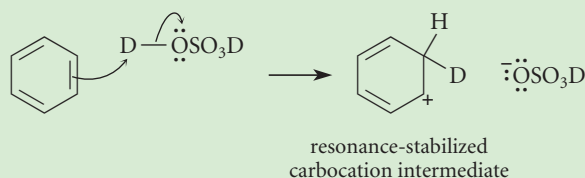
Give a curved-arrow mechanism for the following electrophilic substitution reaction.



**Solution** Construct the mechanism in terms of the three preceding steps.

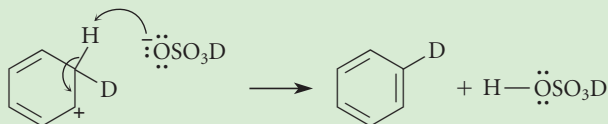
**Step 1** In this reaction, a hydrogen of the benzene ring has been replaced by an isotope  $D$ , which must come from the  $D_2SO_4$ . Because protons (in the form of Brønsted acids) are good electrophiles, the  $D_2SO_4$  itself can serve as the electrophile.

**Step 2** Reaction of the benzene  $\pi$  electrons with the electrophile involves protonation of the benzene ring by the isotopically substituted acid:



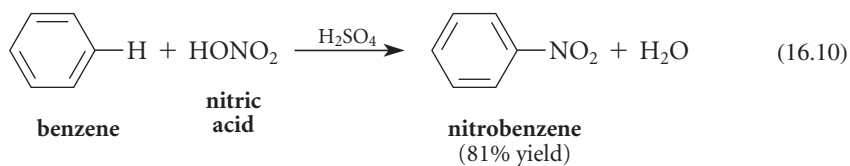
(If you're asking where that "extra" hydrogen in the carbocation came from, don't forget that each carbon of the benzene ring has a single hydrogen that is not shown explicitly in the skeletal structure. One of these is shown in the carbocation because it is involved in the next step.) You should draw the resonance structures of the carbocation intermediate.

**Step 3** Removal of the proton gives the final product:



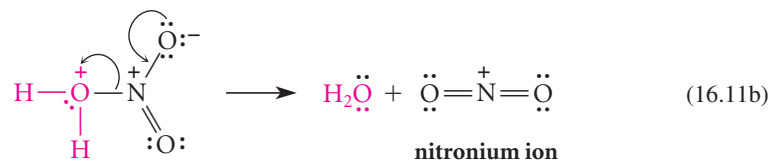
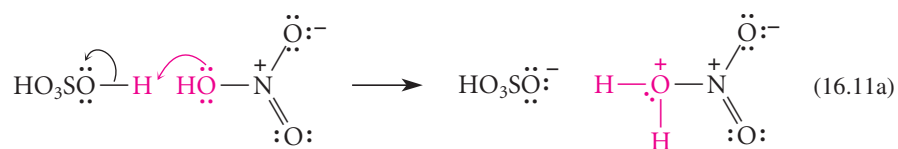
### C. Nitration of Benzene

Benzene reacts with concentrated nitric acid, usually in the presence of a sulfuric acid catalyst, to form nitrobenzene. In this reaction, called *nitration*, the nitro group,  $-\text{NO}_2$ , is introduced into the benzene ring by electrophilic substitution.

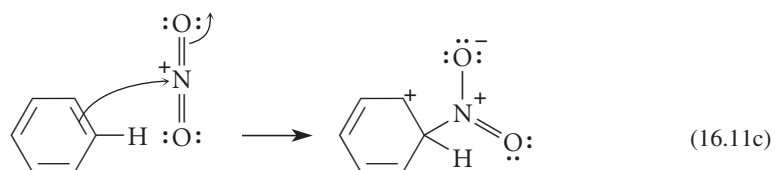


This reaction fits the mechanistic pattern of the electrophilic aromatic substitution reaction outlined in the previous section:

**Step 1** **Generation of the electrophile.** In nitration, the electrophile is  $^+\text{NO}_2$ , the *nitronium ion*. This ion is formed by the acid-catalyzed removal of the elements of water from  $\text{HNO}_3$ .

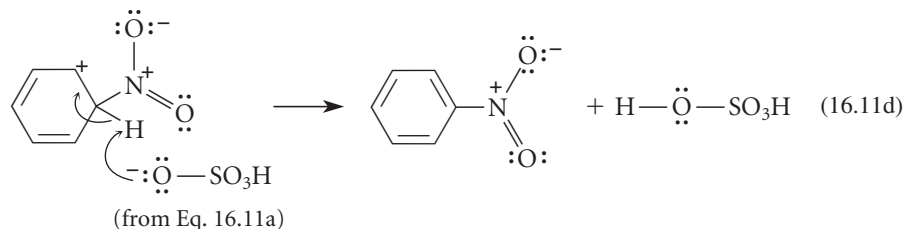


**Step 2** Reaction of the benzene  $\pi$  electrons with the electrophile to form a carbocation intermediate.



(Notice that either of the oxygens can accept the electron pair.)

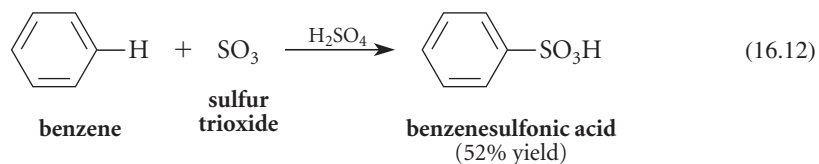
**Step 3** Loss of a proton from the carbocation to give a new aromatic compound.



Nitration is the usual way that nitro groups are introduced into aromatic rings.

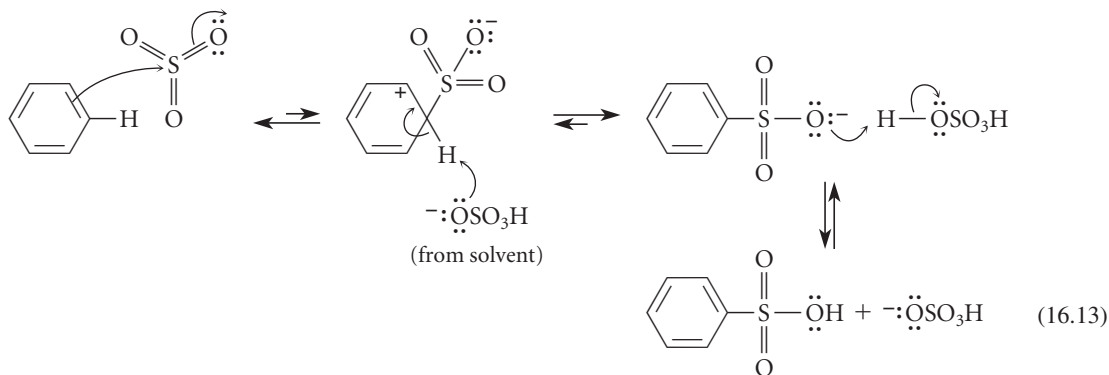
#### D. Sulfonation of Benzene

Another electrophilic substitution reaction of benzene is its conversion into benzenesulfonic acid.



(Sulfonic acids were introduced in Sec. 10.3A as their sulfonate ester derivatives.) This reaction, called *sulfonation*, occurs by two mechanisms that operate simultaneously. Both mechanisms involve sulfur trioxide, a fuming liquid that reacts violently with water to give  $\text{H}_2\text{SO}_4$ . The source of  $\text{SO}_3$  for sulfonation is usually a solution of  $\text{SO}_3$  in concentrated  $\text{H}_2\text{SO}_4$  called *fuming sulfuric acid* or *oleum*. This material is one of the most acidic Brønsted acids available commercially.

In one sulfonation mechanism, the electrophile is neutral sulfur trioxide. When sulfur trioxide reacts with the benzene ring  $\pi$  electrons, an oxygen accepts the electron pair displaced from sulfur.



Sulfonic acids such as benzenesulfonic acid are rather strong acids. (Notice the last equilibrium in Eq. 16.13 and the structural resemblance of benzenesulfonic acid to another strong acid, sulfuric acid.)

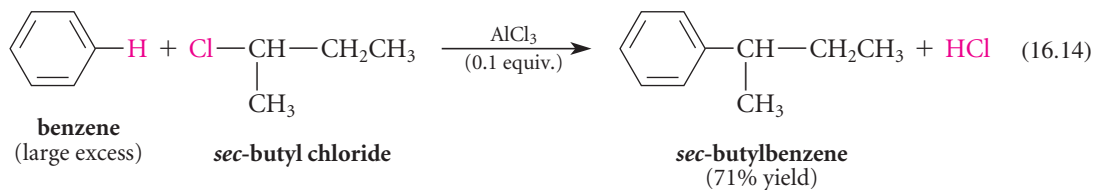
Sulfonation, unlike many electrophilic aromatic substitution reactions, is reversible. The  $-\text{SO}_3\text{H}$  (sulfonic acid) group is replaced by a hydrogen when sulfonic acids are heated with steam (Problem 16.50, p. 782).

### PROBLEMS

- 16.13** A second sulfonation mechanism involves protonated sulfur trioxide as the electrophile. Show the protonation of  $\text{SO}_3$ , and draw a curved-arrow mechanism for the reaction of protonated  $\text{SO}_3$  with benzene to give benzenesulfonic acid.
- 16.14** A compound called *p*-toluenesulfonic acid is formed when toluene is sulfonated at the para position. Draw the structure of this compound, and give the curved-arrow mechanism for its formation.

## E. Friedel–Crafts Alkylation of Benzene

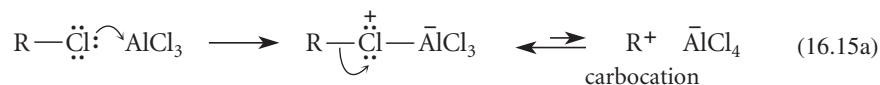
The reaction of an alkyl halide with benzene in the presence of a Lewis acid catalyst gives an alkylbenzene.



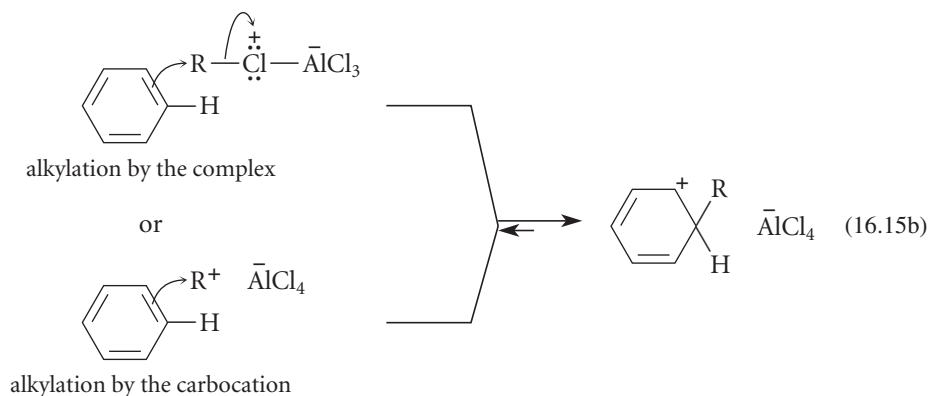
This reaction is an example of a *Friedel–Crafts alkylation*. Recall that an *alkylation* is a reaction that results in the transfer of an alkyl group (Sec. 10.3B). In a **Friedel–Crafts alkylation**, an alkyl group is transferred to an aromatic ring in the presence of an acid catalyst. In the preceding example, the alkyl group comes from an alkyl halide and the catalyst is the Lewis acid aluminum trichloride,  $\text{AlCl}_3$ .

The electrophile in a Friedel–Crafts alkylation is formed by the complexation of the Lewis acid  $\text{AlCl}_3$  with the halogen of an alkyl halide in much the same way that the electrophile in

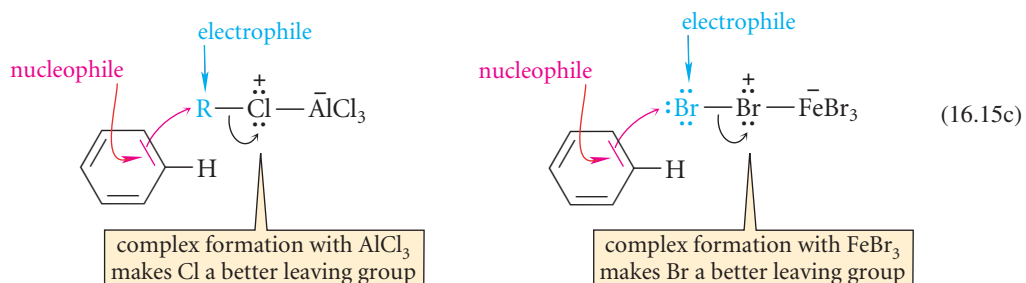
the bromination of benzene is formed by the complexation of  $\text{FeBr}_3$  with  $\text{Br}_2$  (Eq. 16.4, p. 751). If the alkyl halide is secondary or tertiary, this complex can further react to form carbocation intermediates.



Either the alkyl halide–Lewis acid complex, or the carbocation derived from it, can serve as the electrophile in a Friedel–Crafts alkylation.



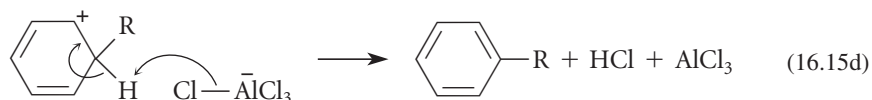
Compare the role of  $\text{AlCl}_3$  in enhancing the effectiveness of the chloride leaving group with the similar role of  $\text{FeBr}_3$  or  $\text{FeCl}_3$  in the bromination (Eq. 16.5, p. 751) or chlorination of benzene:



We've learned three general reactions of carbocations:

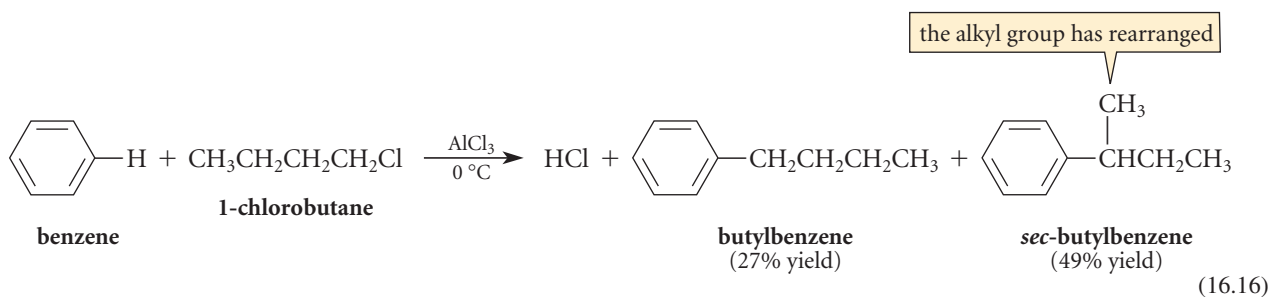
1. reaction with nucleophiles (Secs. 4.7B–D, 9.6B)
2. rearrangement to other carbocations (Sec. 4.7B)
3. loss of a  $\beta$ -proton to give an alkene (Sec. 9.6B) or aromatic ring (Eq. 16.7, Sec. 16.4A)

The reaction of a carbocation with the benzene  $\pi$  electrons is an example of reaction 1.  
Loss of a proton to chloride ion completes the alkylation.

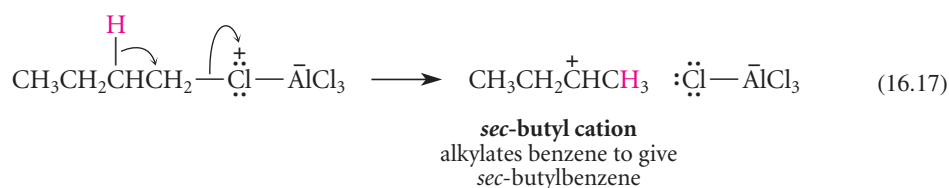


Because some carbocations can rearrange, it is not surprising that rearrangements of alkyl groups are observed in some Friedel–Crafts alkylations:

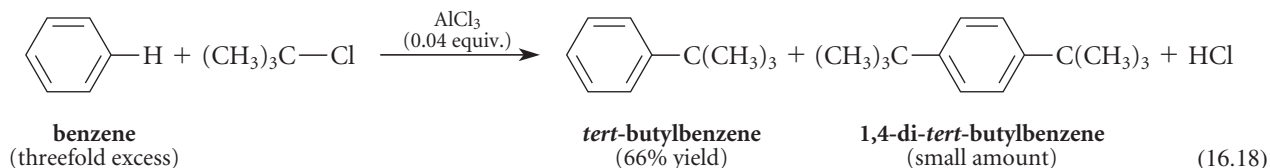




In this example, the alkyl group in the *sec*-butylbenzene product has rearranged. Because primary carbocations are too unstable to be involved as intermediates, it is probably the complex of the alkyl halide and  $\text{AlCl}_3$  that rearranges. This complex has enough carbocation character that it behaves like a carbocation.



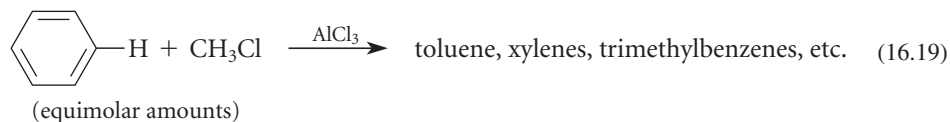
As we might expect, rearrangement in the Friedel–Crafts alkylation is not observed if the carbocation intermediate is not prone to rearrangement.



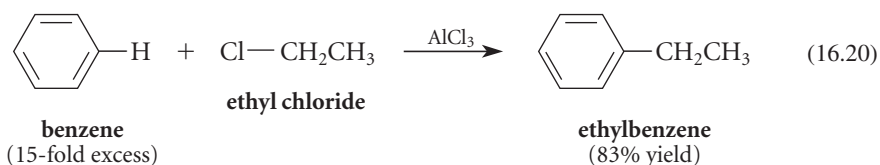
In this example, the alkylating cation is the *tert*-butyl cation; because it is tertiary, this carbocation does not rearrange.

Alkylbenzenes such as butylbenzene (Eq. 16.16) that are derived from rearrangement-prone alkyl halides are generally not prepared by the Friedel–Crafts alkylation, but rather by other methods that we'll consider in Secs. 19.12 and 18.10B.

Another complication in Friedel–Crafts alkylation is that the alkylbenzene products are more reactive than benzene itself (for reasons discussed in Sec. 16.5B). This means that the product can undergo further alkylation, and mixtures of products alkylated to different extents are observed.



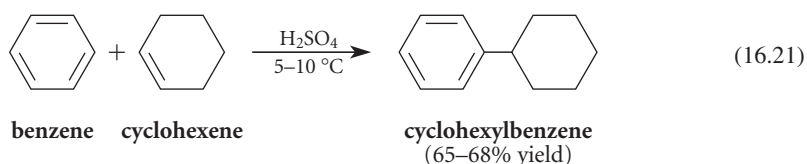
(Notice also the product of double alkylation in Eq. 16.18.) However, a monoalkylation product can be obtained in good yield if a large excess of the aromatic starting material is used. For example, in the following equation the 15-fold molar excess of benzene ensures that a molecule of alkylating agent is much more likely to encounter a molecule of benzene in the reaction mixture than a molecule of the ethylbenzene product.



**STUDY GUIDE LINK 16.2**  
**Different Sources of**  
**the Same Reactive**  
**Intermediate**

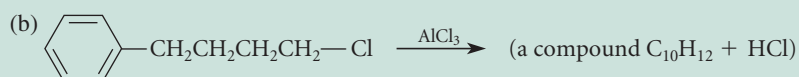
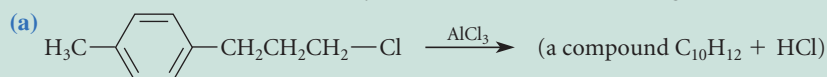
(Notice also the use of excess starting material in Eqs. 16.14 and 16.18.) This strategy is practical only if the starting material is cheap, and if it can be readily separated from the product.

Alkenes and alcohols can also be used as the alkylating agents in Friedel–Crafts alkylation reactions. The carbocation electrophiles in such reactions are generated from alkenes by protonation and from alcohols by dehydration. (Recall that carbocation intermediates are formed in the protonation of alkenes and dehydration of alcohols; Secs. 4.7B, 4.9B, 10.1.)



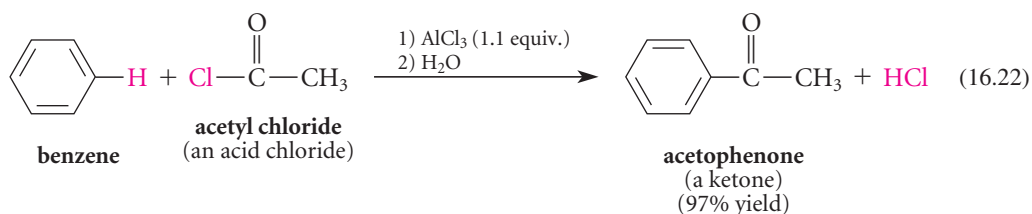
## PROBLEMS

- 16.15** (a) Give a curved-arrow mechanism for the reaction shown in Eq. 16.21.  
 (b) Explain why the same product is formed if cyclohexanol is used instead of cyclohexene in this reaction.
- 16.16** What electrophilic substitution product is formed when 2-methylpropene is added to a large excess of benzene containing HF and the Lewis acid  $\text{BF}_3$ ? By what mechanism is it formed?
- 16.17** Predict the product of the following reaction and give the curved-arrow mechanism for its formation. (*Hint:* Friedel–Crafts alkylations can be used to form rings.)



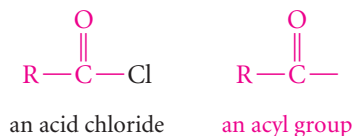
## F. Friedel–Crafts Acylation of Benzene

When benzene reacts with an acid chloride in the presence of a Lewis acid such as aluminum trichloride ( $\text{AlCl}_3$ ), a ketone is formed.

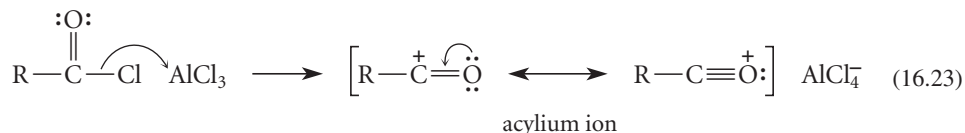


This reaction is an example of a *Friedel–Crafts acylation* (pronounced AY-suh-LAY-shun). In an **acylation reaction**, an *acyl group* is transferred from one group to another. In the

**Friedel–Crafts acylation**, an acyl group, typically derived from an acid chloride, is introduced into an aromatic ring in the presence of a Lewis acid.

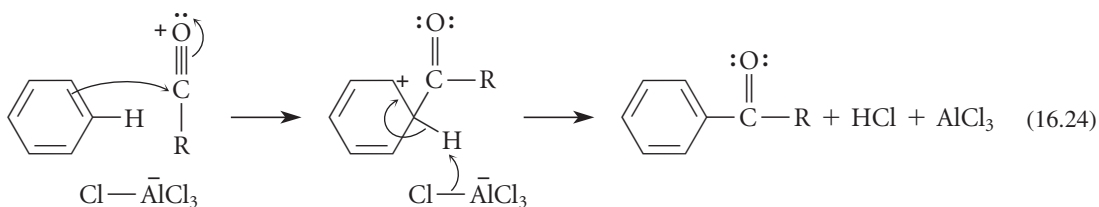


The electrophile in the Friedel–Crafts acylation reaction is a carbocation called an *acylium ion*. This ion is formed when the acid chloride reacts with the Lewis acid  $\text{AlCl}_3$ .

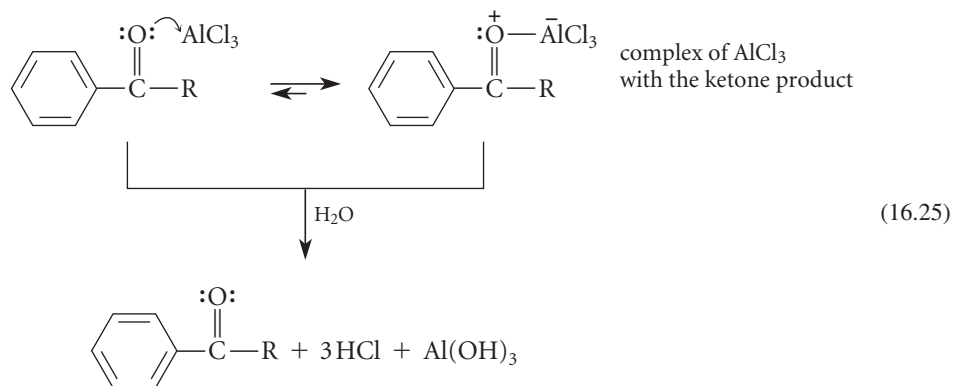


Weaker Lewis acids, such as  $\text{FeCl}_3$  and  $\text{ZnCl}_2$ , can be used to form acylium ions in Friedel–Crafts acylations of aromatic compounds that are more reactive than benzene.

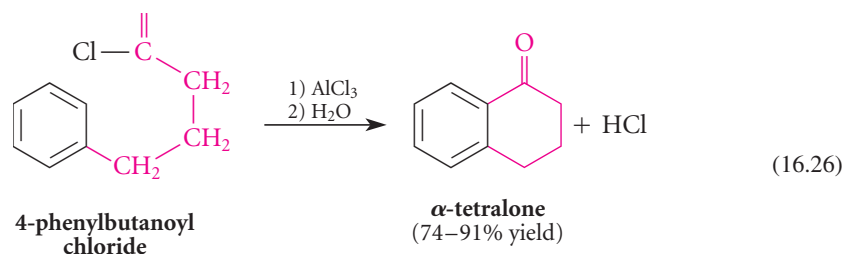
The acylation reaction is completed by the usual steps of electrophilic aromatic substitution (Sec. 16.4B):



As we'll learn in Sec. 19.6, ketones are weakly basic. Because of this basicity, the ketone product of the Friedel–Crafts acylation reacts with the Lewis acid in a Lewis acid–base association to form a complex that is catalytically inactive. This complex is the actual product of the acylation reaction. The formation of this complex has two consequences. First, at least one equivalent of the Lewis acid must be used to ensure its presence throughout the reaction. (Notice, for example, that 1.1 equivalent of  $\text{AlCl}_3$  is used in Eq. 16.22.) This is in contrast to the Friedel–Crafts *alkylation*, in which  $\text{AlCl}_3$  can be used in catalytic amounts. Second, the complex must be destroyed before the ketone product can be isolated. This is usually accomplished by pouring the reaction mixture into ice water.



Both Friedel–Crafts alkylation and acylation reactions can occur *intramolecularly* when the product contains a five- or six-membered ring. (See also Problem 16.17.)



In this reaction, the phenyl ring “bites back” on the acylium ion within the same molecule to form a bicyclic compound. This type of reaction can only occur at an adjacent ortho position because reaction at other positions would produce highly strained products. When five- or six-membered rings are involved, this process is much faster than reaction of the acylium ion with the phenyl ring of another molecule. (Sometimes this reaction can be used to form larger rings as well.) This is another illustration of the *proximity effect*: the kinetic advantage of intramolecular reactions (Sec. 11.7B).

The multiply substituted products observed in Friedel–Crafts *alkylation* (Sec. 16.4E) are not a problem in Friedel–Crafts *acylation* because the ketone products of acylation are much less reactive than the benzene starting material, for reasons discussed in Sec. 16.5B.

The Friedel–Crafts alkylation and acylation reactions are important for two reasons. First, the alkylation reaction is useful for preparing certain alkylbenzenes, and the acylation reaction is an excellent method for the synthesis of aromatic ketones. Second, they provide other ways to form carbon–carbon bonds. Here is an updated list of reactions that form carbon–carbon bonds.

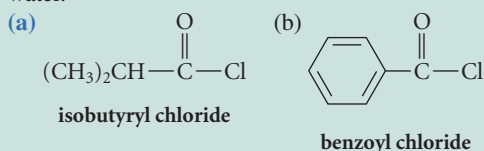
1. addition of carbenes and carbenoids to alkenes (Sec. 9.8)
2. reaction of Grignard reagents with ethylene oxide and lithium organocuprate reagents with epoxides (Sec. 11.4C)
3. reaction of acetylenic anions with alkyl halides or sulfonates (Sec. 14.7B)
4. Diels–Alder reactions (Sec. 15.3)
5. Friedel–Crafts reactions (Secs. 16.4E and 16.4F)

### Charles Friedel and James Mason Crafts

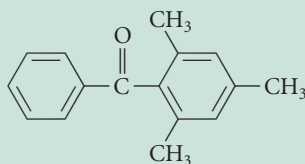
The Friedel–Crafts acylation and alkylation (Sec. 16.4E) reactions are named for their discoverers, the French chemist Charles Friedel (1832–1899) and the American chemist James Mason Crafts (1839–1917). The two men met in Paris while in the laboratory of Charles Adolphe Wurtz (1817–1884), one of the most famous chemists of that time. In 1877, Friedel and Crafts began their collaboration on the reactions that were to bear their names. Friedel subsequently became a very active figure in the development of chemistry in France, and Crafts served for a time as president of the Massachusetts Institute of Technology.

### PROBLEMS

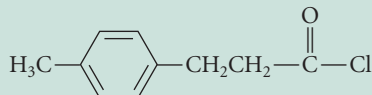
16.18 Give the structure of the product expected from the reaction of each of the following compounds with benzene in the presence of one equivalent of  $\text{AlCl}_3$ , followed by treatment with water.



16.19 Show two different Friedel–Crafts acylation reactions that can be used to prepare the following compound.



16.20 The following compound reacts with  $\text{AlCl}_3$  followed by water to give a ketone *A* with the formula  $\text{C}_{10}\text{H}_{10}\text{O}$ . Give the structure of *A* and a curved-arrow mechanism for its formation.

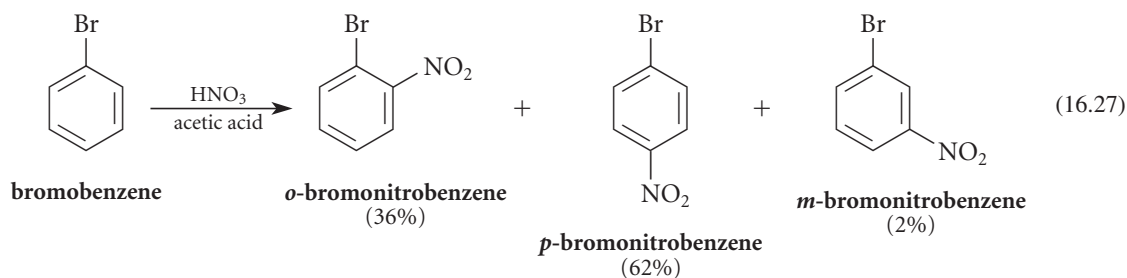


## 16.5

## ELECTROPHILIC AROMATIC SUBSTITUTION REACTIONS OF SUBSTITUTED BENZENES

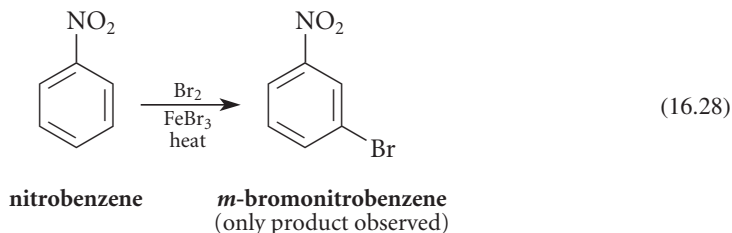
## A. Directing Effects of Substituents

When a monosubstituted benzene undergoes an electrophilic aromatic substitution reaction, three possible disubstitution products might be obtained. For example, nitration of bromobenzene could in principle give *ortho*-, *meta*-, or *para*-bromonitrobenzene. If substitution were totally random, an *ortho*:*meta*:*para* product ratio of 2:2:1 would be expected. (Why?) It is found experimentally that this substitution is *not* random, but is *regioselective*.



Other electrophilic substitution reactions of bromobenzene also give mostly *ortho* and *para* isomers. If a substituted benzene undergoes further substitution mostly at the *ortho* and *para* positions, the original substituent is called an **ortho, para-directing group**. Thus, bromine is an *ortho, para*-directing group, because all electrophilic substitution reactions of bromobenzene occur at the *ortho* and *para* positions.

In contrast, some substituted benzenes react in electrophilic aromatic substitution to give mostly the *meta* disubstitution product. For example, the bromination of nitrobenzene gives only the *meta* isomer.



Other electrophilic substitution reactions of nitrobenzene also give mostly the *meta* isomers. If a substituted benzene undergoes further substitution mainly at the *meta* position, the origi-