Ortho-quinones are not aromatic, but the catechol addition products are; the aromatic stabilization of the product makes the reaction irreversible. These reactions result in an irreversibly modified protein, which is now sensed as "foreign" by the immune system. The resulting biological response is the all-too-familiar allergic reaction—the skin eruptions and the intense itch.

**PROBLEMS**

18.34 Given the structure of phenanthrene, draw structures of
(a) 9,10-phenanthraquinone  
(b) 1,4-phenanthraquinone

![phenanthrene]

Indicate whether each is an o- or a p-quinone.

18.35 Complete the following reactions.
(a)  
(b)  

18.36 Draw the important resonance structures of the radicals formed when each of the following react with \( \text{R}^+ \), a general free radical.
(a) vitamin E  
(b) BHT

18.37 (a) Give the structure of the product formed in the reaction of urushiol with \( \text{K}_2\text{CO}_3 \) and a large excess of methyl iodide.  
(b) Would this compound be likely to provoke the same allergic skin response as urushiol? Explain.

---

**18.9 ELECTROPHILIC AROMATIC SUBSTITUTION REACTIONS OF PHENOLS**

Phenols are aromatic compounds, and they undergo electrophilic aromatic substitution reactions such as those described in Sec. 16.4. In some of these reactions, the —OH group has special effects that are not common to other substituent groups.

Because the —OH group is a strongly activating substituent, phenol can be halogenated once under mild conditions that are totally ineffective for benzene itself.

\[
\begin{align*}
\text{H} & \quad \text{phenol} \\
\text{H} & \quad \text{Br}_2 \quad \text{Br} \\
\text{O} & \quad \text{OH} \quad \text{OH} \\
\text{phenol} & \quad \text{p-bromophenol}
\end{align*}
\]

\[
\text{Br} + \text{H} \quad \text{Br} \quad \text{Br} + \text{H} \quad \text{Br} \\
\text{O} & \quad \text{OH} \quad \text{OH} \\
\text{phenol} & \quad \text{p-bromophenol}
\]

\[
\text{Br} + \text{H} \quad \text{Br} \quad \text{Br} + \text{H} \quad \text{Br} \\
\text{O} & \quad \text{OH} \quad \text{OH} \\
\text{phenol} & \quad \text{p-bromophenol}
\]

Notice the mild conditions of this reaction. A Lewis acid such as FeBr₃ is not required. (A solution of Br₂ in CCl₄ is the reagent usually used for adding bromine to alkenes.) But when phe-
nol reacts with Br₂ in H₂O (bromine water), more extensive bromination occurs and 2,4,6-tri-
bromophenol is obtained.

\[
\text{phenol} + 3 \text{Br}_2 + \text{H}_2\text{O} \rightarrow \text{2,4,6-tribromophenol} + 3\text{HBr}
\]  

(18.76)

This more extensive bromination occurs for two reasons. First, bromine reacts with water to
give protonated hypobromous acid, a more potent electrophile than bromine itself.

\[
\text{Br}_2 + \text{H}_2\text{O} \rightarrow \text{Br}^- + \text{Br}^+\text{OH}_2 \text{HBr} + \text{Br}^-\text{OH} \quad (18.77)
\]

Second, in aqueous solutions near neutrality, phenol partially ionizes to its conjugate-base
phenoxide anion. Although only a small amount of this anion is present, it is very reactive and
brominates instantly, thereby pulling the phenol–phenolate equilibrium to the right.

\[
\text{OH} + \text{H}_2\text{O} \rightarrow \text{O}^- + \text{H}_3\text{O}^+ \text{very rapid} \quad \text{H}_3\text{O}^+ \rightarrow \text{Br}^-\text{Br} \quad \text{OH} \quad \text{(more acidic than phenol)}
\]

(18.78)

Phenoxide ion is much more reactive than phenol because the reactive intermediate is not a
carbocation, but is instead a more stable neutral molecule (red structure).

\[
\text{Br}^-\text{OH} \quad \text{Br}^-\text{OH} \quad \text{Br}^-\text{OH} \quad \text{Br}^-\text{OH} \quad (18.79)
\]
$p$-Bromophenol is also in equilibrium with its conjugate base $p$-bromophenoxide anion, which brominates again until all ortho and para positions have been substituted. Notice in Eq. 18.78 that in the second and third substitutions the powerful ortho, para-directing and activating effects of the $-\text{O}^-\text{Cl}^-$ group override the weaker deactivating and directing effects of the bromine substituents. In strongly acidic solution, in which formation of the phenolate anion is suppressed, bromination can be stopped at the 2,4-dibromophenol stage.

$$\begin{array}{c}
\text{phenol} \\
\text{OH} + 2\text{Br}_2 \rightarrow \text{Br}^- \text{OH} + 2\text{HBr}
\end{array}$$

(18.80)

Phenol is also very reactive in other electrophilic substitution reactions, such as nitration. Phenol can be nitrated once under mild conditions. (Notice that $\text{H}_2\text{SO}_4$ is not present as it is in the nitration of benzene; Eq. 16.10, p. 754.)

$$\begin{array}{c}
\text{phenol} \\
\text{OH} \rightarrow 15^\circ \text{C} \text{HNO}_3 \text{CHCl}_3
\end{array}$$

(18.81)

Because phenol is activated toward electrophilic substitution, it is also possible to nitrate phenol two and three times. However, direct nitration is not the preferred method for synthesis of di- and trinitrophenol, because the concentrated $\text{HNO}_3$ required for multiple nitrations is also an oxidizing agent, and phenols are easily oxidized (Sec. 18.8). Instead, 2,4-dinitrophenol is synthesized by the nucleophilic aromatic substitution reaction of 1-chloro-2,4-dinitrobenzene with $\text{^\text{3}OH}$ (Sec. 18.4A).

$$\begin{array}{c}
\text{chlorobenzene} \\
\text{Cl} \rightarrow \text{HNO}_3 \text{H}_2\text{SO}_4
\end{array}$$

(18.82)

The basic conditions of this reaction result in formation of the conjugate-base anion of the product; the $\text{H}_2\text{O}^+$ is added following the reaction to give the neutral phenol.

The great reactivity of phenol in electrophilic aromatic substitution does not extend to the Friedel–Crafts acylation reaction, because phenol reacts rapidly with the $\text{AlCl}_3$ catalyst.

$$\begin{array}{c}
\text{phenol} \\
\text{OH} + \text{AlCl}_3
\end{array}$$

(18.83)

The adduct of phenol and $\text{AlCl}_3$ is much less reactive than phenol itself in electrophilic aromatic substitution reactions because, as shown in Eq. 18.83, the oxygen electrons are delocalized onto the electron-deficient aluminum. Because of their delocalization away from the benzene ring, these electrons are less available for resonance stabilization of the carbocation.
intermediate formed within the ring during Friedel–Crafts acylation (Eq. 16.24, p. 760). Thus, Friedel–Crafts acylation of phenol occurs slowly, but can be carried out successfully at elevated temperatures. Because it is not highly activated, the ring is acylated only once.

\[
\text{Ph} - \text{OH} + \text{AlCl}_3 + \text{CH}_3(\text{CH}_2)_5\text{C} = \text{Cl} \xrightarrow{140^\circ \text{C}, \text{PhNO}_2} \xrightarrow{\text{H}_2\text{O}} \text{Ph} - \text{O} - \text{C} - (\text{CH}_2)_5\text{CH}_3
\]

(as a complex)

\[
\text{(34\% yield)} \quad \text{(47\% yield)}
\]

Friedel–Crafts alkylation of phenol is also possible.

\[
\text{Ph} - \text{OH} + \text{H}_3\text{C} - \text{C} - \text{OH} \xrightarrow{70\% \text{H}_2\text{SO}_4, 80^\circ \text{C}} \text{H}_3\text{C} - \text{C} - \text{OH} + \text{H}_2\text{O}
\]

\[
\text{p-\text{tert}-butylphenol (80\% yield)}
\]

**PROBLEMS**

18.38 Give the principal organic product(s) formed in each of the following reactions.

(a) \(\text{o-} + \text{Br}_2\text{in CCl}_4\)
(b) \(\text{m-Cl} + \text{HNO}_3\text{, low temperature}\)
(c) \(\text{p-} + \text{HCl}\)

18.39 Give a curved-arrow mechanism for the reaction in Eq. 18.85. Be sure to identify the electrophilic species in the reaction and to show how it is formed.

**18.10 REACTIVITY OF THE ARYL–OXYGEN BOND**

**A. Lack of Reactivity of the Aryl–Oxygen Bond in \(S_N1\) and \(S_N2\) Reactions**

Just as the reactions of alcohols that break the carbon–oxygen bond have close analogy to the reactions of alkyl halides that break the carbon–halogen bond, the carbon–oxygen reactivity of phenols follows the poor carbon–halogen reactivity of aryl halides. (That is, we can think of phenols as “aryl alcohols.”) Recall that aryl halides do not undergo \(S_N1\) or \(E1\) reactions (Sec. 18.3); for the same reasons, phenols also do not react under conditions used for the \(S_N1\) or \(E1\) reactions of alcohols. Thus, phenols do not form aryl bromides with concentrated \(\text{HBr}\); they do not dehydrate with concentrated \(\text{H}_2\text{SO}_4\). (Instead, they undergo sulfonation; see Sec.