Chapter 24: Phenols. Alcohols contain an OH group bonded to an sp^3-hybridized carbon. Phenols contain an OH group bonded to an sp^2-hybridized carbon of a benzene ring.

24.1: Nomenclature (please read)
24.2: Structure and Bonding (please read)
24.3: Physical Properties (please read). Like other alcohols the OH group of phenols can participate in hydrogen bonding with other phenol molecules and to water.

24.4: Acidity of Phenols. Phenols are more acidic than aliphatic alcohols

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{OH} & \quad \text{pK}_a \approx 16 \\
\text{FCH}_2\text{CH}_2\text{OH} & \quad 14.4 \\
\text{F}_2\text{CHCH}_2\text{OH} & \quad 13.3 \\
\text{F}_3\text{CCH}_2\text{OH} & \quad 12.4 \\
\text{(F}_3\text{C})_3\text{COH} & \quad 5.4
\end{align*}
\]

Factors that influence acidity:
Inductive effect:

Electron-withdrawing groups make an alcohol a stronger acid by stabilizing the conjugate base (alkoxide).

A benzene ring is generally considered electron withdrawing and stabilizes the negative charge through inductive effects.
Resonance effect: the benzene ring stabilizes the phenoxide ion by resonance delocalization of the negative charge.

24.5: Substituent Effects on the Acidity of Phenols.
Electron-donating substituents make a phenol less acidic by destabilizing the phenoxide ion (resonance effect).

\[
\begin{array}{cccc}
X &=& \text{-H} & \text{-CH}_3 & \text{-OCH}_3 & \text{-NH}_2 \\
pK_a^* &= 10 & 10.3 & 10.2 & 10.5
\end{array}
\]

Electron-withdrawing substituents make a phenol more acidic by stabilizing the phenoxide ion through delocalization of the negative charge and through inductive effects.

\[
\begin{array}{cccc}
X &=& \text{-H} & \text{-Cl} & \text{-Br} & \text{-NO}_2 \\
pK_a^* &= 10 & 9.4 & 9.3 & 7.2
\end{array}
\]

The influence of a substituent on phenol acidity is also dependent on its position relative to the -OH.

\[
\begin{array}{cccc}
pK_a^* & X &=& \text{-Cl} & 9.4 & 9.1 \\
& \text{-NO}_2 & 7.2 & 8.4 \\
& \text{-OCH}_3 & 10.2 & 9.6 \\
& \text{-CH}_3 & 10.3 & 10.1
\end{array}
\]
The effect of multiple substituents on phenol acidity is additive.

\[
\begin{align*}
\text{pK}_a \quad & 10 & 7.2 & 8.4 & 7.2 \\
pK_a \quad & 4.0 & 0.4 & 6.7
\end{align*}
\]

24.6: Sources of Phenols. (Table 24.3)

From aryl diazonium ion

From aryl ketones

24.7: Naturally Occurring Phenols. (please read) Phenols are common in nature.

Resveratrol
**24.8: Reactions of Phenols: Electrophilic Aromatic Substitution.** Table 24.4 (a review from Chapter 12). The hydroxyl group of phenols is a strong activator and o-/p-director.

a. Halogenation. Phenols are so activated that they often react with Br\(_2\) and Cl\(_2\) without a catalyst.

\[
\text{Halogenation: } \text{PhOH} + \text{X}_2 \rightarrow \text{PhX} + \text{HX}
\]

b. Nitration.

\[
\text{Nitration: } \text{PhOH} + \text{HNO}_3 \rightarrow \text{PhNO}_2 + \text{H}_2\text{O}
\]

c. Sulfonation.

\[
\text{Sulfonation: } \text{PhOH} + \text{H}_2\text{SO}_4, \Delta \rightarrow \text{PhSO}_3\text{H} + \text{H}_2\text{O}
\]

d. Friedel-Crafts alkylation

\[
\text{Friedel-Crafts alkylation: } \text{PhOH} + \text{R}^+\text{Cl}^- \rightarrow \text{PhR} + \text{HCl}
\]

e. Friedel-Crafts acylation

\[
\text{Friedel-Crafts acylation: } \text{PhOH} + \text{R}^+\text{Cl}^- \rightarrow \text{PhR} + \text{HCl}
\]

**24.9: Acylation of Phenols.** In the absence if AlCl\(_3\), phenols react with acid chlorides to afford phenyl esters.

\[
\text{Acylation: } \text{PhOH} + \text{R}^+\text{Cl}^- \rightarrow \text{PhOR} + \text{HCl}
\]

Note: The Fischer esterification works poorly for the preparation of phenyl esters

\[
\text{C}_6\text{H}_5\text{OH} + \text{CO}_2 \underset{(100 \text{ atm})}{\xrightarrow{\text{H}^+}} \text{C}_6\text{H}_5\text{O}^- \xrightarrow{\text{H}_2\text{C}-\text{O}^=\text{CH}_3} \text{C}_6\text{H}_5\text{CO}_2\text{H}
\]

24.11: Preparation of Aryl Ethers. The phenoxide ion is a good nucleophile and reacts with 1° and 2° alkyl halides and tosylates afford aryl ethers (Williamson ether synthesis)

\[
\begin{align*}
\text{C}_6\text{H}_5\text{OH} + \text{NaH} & \underset{\text{THF}}{\xrightarrow{\text{K}_2\text{CO}_3, \text{acetone}, \Delta}} \text{C}_6\text{H}_5\text{O}^- \overset{\text{R}_2\text{C}-\text{Br}}{\underset{\text{THF}}{\xrightarrow{\text{NaBr}, \text{acetone}, \Delta}}} \\
\text{C}_6\text{H}_5\text{OH} + \text{K}_2\text{CO}_3 & \xrightarrow{\text{acetone}, \Delta} \text{C}_6\text{H}_5\text{O}^- \overset{\text{R}_2\text{C}-\text{OH}}{\underset{\text{\Delta}}{\xrightarrow{\text{KF}, \text{acetone}, \Delta}}} \\
\text{C}_6\text{H}_5\text{F} + \text{K}_2\text{CO}_3 & \xrightarrow{\text{acetone}, \Delta} \text{C}_6\text{H}_5\text{F} \overset{\text{R}_2\text{C}-\text{OH}, \Delta}{\underset{\text{\Delta}}{\xrightarrow{\text{NaBr}, \text{acetone}, \Delta}}}
\end{align*}
\]

24.12: Cleavage of Aryl Ethers by Hydrogen Halides. Aryl alkyl ethers can be cleaved by HX to give phenols.

\[
\text{C}_6\text{H}_5\text{O}-\text{CH}_2\text{R} + \text{HX} \underset{\Delta}{\xrightarrow{\text{HX}}} \text{C}_6\text{H}_5\text{OH} + \text{X}-\text{CH}_2\text{R}
\]

24.13: Claisen Rearrangement. Thermal rearrangement of an aryl allyl ether to an o-allyl phenol.

\[
\begin{align*}
\text{C}_6\text{H}_5\text{OH} & \xrightarrow{\text{K}_2\text{CO}_3, \text{acetone}, \Delta} \text{C}_6\text{H}_5\text{C}^\text{2} \underset{\Delta}{\xrightarrow{(-200^\circ\text{C})}} \text{C}_6\text{H}_5\text{O}^\text{1}
\end{align*}
\]
The Claisen rearrangement involves a concerted, pericyclic mechanism, which is related to the Diels-Alder reaction.

24.14 Oxidation of Phenols: Quinones (please read)

\[
\begin{align*}
\text{hydroquinone} & \quad \text{quinone} \\
\text{Coenzyme Qn (Ubiquinone)} & \quad \text{P450}
\end{align*}
\]

24.15: Spectroscopic Analysis of Phenols. Largely the same as for alcohols (Ch 15.14).

**IR**: broad O-H stretch \(\sim 3600 \text{ cm}^{-1}\). C-O single bond stretch is \(\sim 1200-1250 \text{ cm}^{-1}\), which is shifted from that of aliphatic alcohols (1000-1200 cm\(^{-1}\)).

**\(^1H\ NMR**: Like aliphatic alcohols, the O-H proton resonance is observed over a large chemical shift range as a broad singlet.

**\(^{13}C\ NMR**: The \(sp^2\)-carbon directly attached to the OH has a chemical shift of \(\sim 150-160 \text{ ppm}\).