12. Alcohols and Phenols

Based on McMurry’s *Organic Chemistry, 6th edition*
Alcohols and Phenols

- Alcohols contain an OH group connected to a saturated C (sp\(^3\))
- They are important solvents and synthesis intermediates

- Phenols contain an OH group connected to a carbon in a benzene ring

- Methanol, CH\(_3\)OH, called methyl alcohol, is a common solvent, a fuel additive, produced in large quantities

- Ethanol, CH\(_3\)CH\(_2\)OH, called ethyl alcohol, is a solvent, fuel, beverage

- Phenol, C\(_6\)H\(_5\)OH ("phenyl alcohol") has diverse uses - it gives its name to the general class of compounds
Naming Alcohols

- **General classifications** of alcohols based on substitution on C to which OH is attached
  - Methyl (C has 3 H’s)
  - Primary (1°) (C has two H’s, one R)
  - Secondary (2°) (C has one H, two R’s)
  - Tertiary (3°) (C has no H, 3 R’s),

A primary alcohol (1°)       A secondary alcohol (2°)       A tertiary alcohol (3°)

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IUPAC Rules for Naming Alcohols

- Select the longest carbon chain containing the hydroxyl group, and derive the parent name by replacing the -e ending of the corresponding alkane with -ol.
- Number the chain from the end nearer the hydroxyl group.
- Number substituents according to position on chain, listing the substituents in alphabetical order.

- 2-Methyl-2-pentanol
- cis-1,4-Cyclohexanediol
- 3-Phenyl-2-butanol
Many Alcohols and Phenols Have **Common Names**

- Benzyl alcohol (Phenylmethanol)
- Allyl alcohol (2-Propen-1-ol)
- tert-Butyl alcohol (2-Methyl-2-propanol)
- Ethylene glycol (1,2-Ethanediol)
- Glycerol (1,2,3-Propanetriol)

- Phenol (also known as carbolic acid)
- Methyl salicylate
- Urushiols (R = different C₁₅ alkyl and alkenyl chains)
Naming Phenols

- Phenol is used both as the name of a specific substance (hydroxy-benzene) and as the family name for all hydroxy-substituted aromatic compounds.
- Name substituents on aromatic ring by their position from OH.
Properties of Alcohols and Phenols: Hydrogen Bonding

- The structure around O of the alcohol or phenol is similar to that in water, sp³ hybridized.
- Alcohols and phenols have much higher boiling points than similar alkanes and alkyl halides.

![Graph showing boiling points of alkanes, chloroalkanes, and alcohols](https://via.placeholder.com/150)

Phenol: bp = 181.7°C  
Toluene: bp = 110.6°C
Alcohols and Phenols Form Hydrogen Bonds

A positively polarized —OH hydrogen atom from one molecule is attracted to a lone pair of electrons on a negatively polarized oxygen atom of another molecule.

This produces a force that holds the two molecules together.

These *intermolecular attractions* are present in solution but not in the gas phase, thus elevating the boiling point of the solution.
Acidity: $pK_a$ Values for Typical OH Compounds

<table>
<thead>
<tr>
<th>Alcohol or phenol</th>
<th>$pK_a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$(\text{CH}_3)_3\text{COH}$</td>
<td>18.00</td>
</tr>
<tr>
<td>$\text{CH}_3\text{CH}_2\text{OH}$</td>
<td>16.00</td>
</tr>
<tr>
<td>HOH (water)</td>
<td>(15.74)</td>
</tr>
<tr>
<td>$\text{CH}_3\text{OH}$</td>
<td>15.54</td>
</tr>
<tr>
<td>$\text{CF}_3\text{CH}_2\text{OH}$</td>
<td>12.43</td>
</tr>
<tr>
<td>$p$-Aminophenol</td>
<td>10.46</td>
</tr>
<tr>
<td>$p$-Methoxyphenol</td>
<td>10.21</td>
</tr>
<tr>
<td>$p$-Methylphenol</td>
<td>10.17</td>
</tr>
<tr>
<td>Phenol</td>
<td>9.89</td>
</tr>
<tr>
<td>$p$-Chlorophenol</td>
<td>9.38</td>
</tr>
<tr>
<td>$p$-Bromophenol</td>
<td>9.35</td>
</tr>
<tr>
<td>$p$-Nitrophenol</td>
<td>7.15</td>
</tr>
<tr>
<td>2,4,6-Trinitrophenol</td>
<td>0.60</td>
</tr>
</tbody>
</table>

Weaker acid

Stronger acid
Relative Acidities of Alcohols

- Simple alcohols are about as acidic as water
- Alkyl groups make an alcohol a weaker acid
- The more easily the alkoxide ion is solvated by water the more its formation is energetically favored
- Steric effects are important

Methoxide ion, $\text{CH}_3\text{O}^-$  
($pK_a = 15.54$)

$\text{tert}$-Butoxide ion, $(\text{CH}_3)_3\text{CO}^-$  
($pK_a = 18.00$)
Inductive Effects

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

Electron-withdrawing groups stabilize alkoxide and lower $pK_a$

\[
\begin{align*}
\text{CF}_3 & \xrightarrow{\text{CF}_3} \text{C} \xrightarrow{\text{O}^-} \text{CF}_3 \\
\text{CH}_3 & \xrightarrow{\text{CH}_3} \text{C} \xrightarrow{\text{O}^-} \text{CH}_3
\end{align*}
\]

$pK_a = 5.4$ versus $pK_a = 18$

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Generating Alkoxides from Alcohols

- Alcohols are weak acids – require a strong base to form an alkoxide such as NaH, sodium amide NaNH$_2$, and Grignard reagents (RMgX)

- Alkoxides are bases used as reagents in organic chemistry

\[
\begin{align*}
2 \text{H}_3\text{C} &-\text{C}-\text{OH} + 2 \text{K} \rightarrow 2 \text{H}_3\text{C} &-\text{C}-\text{O}^- \text{K}^+ + \text{H}_2 \\
\text{CH}_3 & & \text{CH}_3 & & \text{CH}_3 \\
\text{tert-Butyl alcohol} & & \text{Potassium tert-butoxide} \\
\text{CH}_3\text{OH} + \text{NaH} & \rightarrow \text{CH}_3\text{O}^- \text{Na}^+ + \text{H}_2 \\
\text{Methanol} & & \text{Sodium methoxide} \\
\text{CH}_3\text{CH}_2\text{OH} + \text{NaNH}_2 & \rightarrow \text{CH}_3\text{CH}_2\text{O}^- \text{Na}^+ + \text{NH}_3 \\
\text{Ethanol} & & \text{Sodium ethoxide} \\
\text{OH} + \text{CH}_3\text{MgBr} & \rightarrow \text{OH}^- + \text{MgBr} + \text{CH}_4 \\
\text{Cyclohexanol} & & \text{Bromomagnesium cyclohexoxide}
\end{align*}
\]
Phenol Acidity

- Phenols (pK$_a$ ~10) are much more acidic than alcohols (pK$_a$ ~ 16) due to resonance stabilization of the phenoxide ion.

- Phenols react with NaOH solutions (but alcohols do not), forming soluble salts that are soluble in dilute aqueous.

- A phenolic component can be separated from an organic solution by extraction into basic aqueous solution and is isolated after acid is added to the solution.

$$\text{Phenol} + \text{NaOH} \rightarrow \text{Sodium phenoxide}$$
Substituted Phenols

- Can be more or less acidic than phenol itself
- An electron-withdrawing substituent makes a phenol more acidic by delocalizing the negative charge
- Phenols with an electron-donating substituent are less acidic because these substituents concentrate the charge
Nitro-Phenols

- Phenols with nitro groups at the *ortho* and *para* positions are much stronger acid
- The pKₐ of 2,4,6-trinitrophenol is 0.6, a very strong acid
Preparation of Alcohols: an Overview

- Alcohols are derived from many types of compounds
- The alcohol hydroxyl can be converted to many other functional groups
- This makes alcohols useful in synthesis
Review:
Preparation of Alcohols by Hydration of Alkenes

Hydration of an alkene is the addition of H-OH to the C=C to give an alcohol.

Reaction of an alkene with acid (HA) yields a carbocation intermediate.

Water acts as a nucleophile, using a lone pair of electrons on oxygen to form a bond to carbon. The oxygen atom, having donated electrons, is now trivalent and has the positive charge.

Loss of an H⁺ from oxygen then yields the neutral alcohol product and regenerates the acid catalyst HA.

1-Methylcyclopentene → 1-Methylcyclopentanol (92%)
Some Reactions of Alcohols

- Two general classes of reaction
  - At the carbon of the C–O bond
  - At the proton of the O–H bond
Dehydration of Alcohols to Yield Alkenes

- The general reaction: forming an alkene from an alcohol through loss of O-H and H (hence dehydration) of the neighboring C–H to give π bond

- Specific reagents are needed

A dehydration reaction

\[
\begin{align*}
\text{C–C} & \quad \text{H} \quad \text{OH} \\
\text{C–C} & \quad \text{C} \quad \text{C} \\
& \quad \text{H}_2\text{O}
\end{align*}
\]
Acid-Catalyzed Dehydration

- Tertiary alcohols are readily dehydrated with acid
- Secondary alcohols require severe conditions (75% H$_2$SO$_4$, 100°C) - sensitive molecules don't survive
- Primary alcohols require very harsh conditions – impractical
- Reactivity is the result of the nature of the carbocation intermediate

\[
\text{2-Methyl-2-butanol} \xrightarrow{\text{H}_3\text{O}^+, \text{THF}, 25^\circ\text{C}} \text{2-Methyl-2-butene (trisubstituted)} + \text{2-Methyl-1-butene (disubstituted)}
\]

Major product

Minor product
Acid-Catalyzed Dehydration: mechanism

Two electrons from the oxygen atom bond to $H^+$, yielding a protonated alcohol intermediate.

The carbon-oxygen bond breaks, and the two electrons from the bond stay with oxygen, leaving a carbocation intermediate.

Two electrons from a neighboring carbon-hydrogen bond form the alkene $\pi$ bond, and $H^+$ (a proton) is eliminated.
Conversion of Alcohols into Alkyl Halides

- 3° alcohols are converted by HCl or HBr at low temperature
- 1° and 2° alcohols are resistant to acid – use SOCl₂ or PBr₃ by an $S_N2$ mechanism
Oxidation of Alcohols

Can be accomplished by inorganic reagents, such as KMnO₄, CrO₃, and Na₂Cr₂O₇ or by more selective, expensive reagents.

Primary alcohol

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<tbody>
<tr>
<td></td>
<td></td>
<td>OH</td>
<td></td>
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</tr>
</tbody>
</table>

An aldehyde
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A carboxylic acid

Secondary alcohol

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<table>
<thead>
<tr>
<th>R</th>
<th>R'</th>
<th>H</th>
<th>[O]</th>
<th>C</th>
<th>R'</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>OH</td>
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</tbody>
</table>

A ketone

Tertiary alcohol

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<table>
<thead>
<tr>
<th>R</th>
<th>R'</th>
<th>R&quot;</th>
<th>[O]</th>
<th>C</th>
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<tbody>
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NO reaction
Oxidation of Primary Alcohols

- To aldehyde: pyridinium chlorochromate (PCC, C₅H₆NCrO₃Cl) in dichloromethane

- Other reagents produce carboxylic acids

\[\text{CH}_3\text{(CH}_2\text{)}_8\text{CH}_2\text{OH} \xrightarrow{\text{CrO}_3, \text{H}_3\text{O}^+, \text{acetone}} \text{CH}_3\text{(CH}_2\text{)}_8\text{COH}\]

1-Decanol → Decanoic acid (93%)
Oxidation of Secondary Alcohols

- Effective with inexpensive reagents such as Na$_2$Cr$_2$O$_7$ in acetic acid
- PCC is used for sensitive alcohols at lower temperatures

4-tert-Butylcyclohexanol → 4-tert-Butylcyclohexanone (91%)

Testosterone (steroid; male sex hormone) → 4-Androstene-3,17-dione (82%)
Laboratory Preparation of Phenols

- From aromatic sulfonic acids by melting with NaOH at high temperature
- Limited to the preparation of alkyl-substituted phenols

Toluene $\xrightarrow{\text{SO}_3, \text{H}_2\text{SO}_4} p$-Toluenesulfonic acid $\xrightarrow{1. \text{NaOH, 300°C, 2. H}_3\text{O}^+} p$-Methylphenol (72%)
Reactions of Phenols

- The hydroxyl group is a strongly activating (ortho- and para-directing) substituent, making phenols substrates for electrophilic halogenation, nitration, sulfonation, and Friedel–Crafts reactions.

- Reaction of a phenol with strong oxidizing agents (such as sodium dichromate) yields a quinone (or cyclohexadienedione).

- Quinones can be easily reduced to hydroquinones (p-dihydroxybenzenes) by NaBH₄.

\[
\text{OH} \quad \xrightarrow{\text{Na}_2\text{Cr}_2\text{O}_7, \text{H}_3\text{O}^+} \quad \text{O} \quad \text{O} \\
\text{Phenol} \quad \text{Benzoquinone}
\]
**Quinones in Nature**

- **Ubiquinones** mediate electron-transfer processes involved in energy production through their redox reactions.
- Within the mitochondria of cells, they mediate the respiration process in which electrons are transported from the biological reducing agent NADH to molecular oxygen.

**Step 1**

\[
\text{NADH} + \text{H}^+ + \text{Reduced form} \rightarrow \text{Oxidized form} + \text{NAD}^+ 
\]

**Step 2**

\[
\text{CH}_3\text{O} \quad \text{CH}_3 \quad \text{CH}_3 \quad \text{OH} \quad \text{CH}_3\text{O} \\
\text{CH}_3\text{O} \quad \text{R} \quad \text{OH} \quad \text{CH}_3\text{O} \\
+ \frac{1}{2} \text{O}_2 \quad \text{Net change: } \text{NADH} + \frac{1}{2} \text{O}_2 + \text{H}^+ \rightarrow \text{NAD}^+ + \text{H}_2\text{O} \quad \text{(+ energy production)}
\]

(+ energy production)
End of chapter 12