Chapter 17: Alcohols and Phenols

Alcohols contain an OH group connected to a saturated carbon (sp\(^3\))

Phenols contain an OH group connected to a carbon of a benzene ring

Alcohols are classified as primary (1°), secondary (2°) or tertiary (3°), which refers to the carbon bearing the hydroxy group

Water           Alcohol           Ether           Peroxide

Thiols           Thioether         Disulfides

Alcohols are classified as primary (1°), secondary (2°) or tertiary (3°), which refers to the carbon bearing the hydroxy group.
17.1: Nomenclature:

1. In general, alcohols are named in the same manner as alkanes; replace the -ane suffix for alkanes with an -ol for alcohols

\[
\begin{align*}
\text{butane} & : \text{CH}_3\text{CH}_2\text{CH}_3 \\
1\text{-butanol} & : \text{CH}_3\text{CH}_2\text{CH}_2\text{OH} \\
2\text{-butanol} & : \text{OH}
\end{align*}
\]

2. Number the carbon chain so that the hydroxyl group gets the lowest number

3. Number the substituents and write the name listing the substituents in alphabetical order.

4. For phenols, follow benzene nomenclature and use phenol as the parent name. The carbon bearing the -OH group gets number 1.

Many alcohols are named using non-systematic nomenclature:

- 2-methyl-2-pentanol
- 3-phenyl-2-butanol
- 3,4-dinitrophenol

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)
17.2: Properties of alcohols and phenols: Hydrogen bonding:
The structure around the oxygen atom of an alcohol or phenol is similar to that in water and is sp\(^3\) hybridized.

Alcohols and phenols have much higher boiling points than similar alkanes and alkyl halides:

<table>
<thead>
<tr>
<th></th>
<th>H(_2)O</th>
<th>CH(_3)CH(_2)CH(_2)CH(_3)</th>
<th>CH(_3)CH(_2)CH(_2)Cl</th>
<th>CH(_3)CH(_2)CH(_2)OH</th>
</tr>
</thead>
<tbody>
<tr>
<td>MW</td>
<td>18</td>
<td>58</td>
<td>92.5</td>
<td>74</td>
</tr>
<tr>
<td>bp</td>
<td>100° C</td>
<td>-0° C</td>
<td>77° C</td>
<td>116° C</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>C(_6)H(_6)</th>
<th>C(_6)H(_6)OH</th>
<th>C(_6)H(_6)CH(_3)</th>
<th>C(_6)H(_6)CH(_2)OH</th>
</tr>
</thead>
<tbody>
<tr>
<td>MW</td>
<td>78</td>
<td>94</td>
<td>92</td>
<td>108</td>
</tr>
<tr>
<td>bp</td>
<td>80° C</td>
<td>182° C</td>
<td>110° C</td>
<td>203° C</td>
</tr>
</tbody>
</table>

Alcohols and phenols, like water, can form hydrogen bonds: non covalent interaction between a hydrogen atom (δ\(^+\)) involved in a polar covalent bond, with the lone pair of a heteroatom (usually O or N), which is also involved in a polar covalent bond (δ\(^-\)):

Hydrogen-bonds are broken when the alcohol reaches its bp, which requires additional energy.
17.3: Properties of alcohols and phenols: acidity and basicity:

Like water, alcohols are weak Brønsted bases and weak
Brønsted acids. The nature of the R group can
significantly influence the basicity or acidity

\[
\begin{align*}
\text{R-OH} + \text{H}^+ & \rightarrow \text{R-O}^+ + \text{H}_2\text{O} \\
\text{R-O}^- + \text{H}^+ & \rightarrow \text{R-OH} + \text{H}_2\text{O}
\end{align*}
\]

<table>
<thead>
<tr>
<th>CH₃OH</th>
<th>CH₃CH₂CH₂CH₂OH</th>
<th>CH₃CH₂CH(OH)CH₃</th>
<th>(CH₃)C-OH</th>
</tr>
</thead>
<tbody>
<tr>
<td>MW = 32</td>
<td>MW = 74</td>
<td>MW = 74</td>
<td>MW = 74</td>
</tr>
<tr>
<td>bp = 65° C</td>
<td>bp = 116° C</td>
<td>bp = 99° C</td>
<td>bp = 82° C</td>
</tr>
<tr>
<td>pKa ~ 15.5</td>
<td>pKa ~ 16</td>
<td>pKa ~ 17</td>
<td>pKa ~ 18</td>
</tr>
</tbody>
</table>

The steric environment around the oxygen atom can
influence the physical properties of an alcohol

Solvation: upon acid dissociation the alkoxide ion is stabilized by
solvation through hydrogen bonding between water and
the negatively charge oxygen. The steric environment
around the negatively charge oxygen influences the
solvation effect

\[
\begin{align*}
\text{R-OH} + \text{H}^+ & \rightarrow \text{R-O}^+ + \text{H}_2\text{O} \\
\text{R-O}^- + \text{H}^+ & \rightarrow \text{R-OH} + \text{H}_2\text{O}
\end{align*}
\]

Acidity: methanol > 1° alcohol > 2° alcohol > 3° alcohol
Reflects the ability water to stabilized the resulting alkoxide
though solvation
Electronic factors that influence acidity:
inductive and resonance effect

<table>
<thead>
<tr>
<th></th>
<th>CH₃CH₂OH</th>
<th>FCH₂CH₂OH</th>
<th>F₂CHCH₂OH</th>
<th>F₃CCH₂OH</th>
<th>(F₃C)₃CCH₂OH</th>
</tr>
</thead>
<tbody>
<tr>
<td>pKₐ ~</td>
<td>16.0</td>
<td>14.4</td>
<td>13.3</td>
<td>12.4</td>
<td>5.4</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>X</th>
<th>pKₐ ~</th>
<th>X</th>
<th>pKₐ ~</th>
<th>X</th>
<th>pKₐ ~</th>
<th>X</th>
<th>pKₐ ~</th>
<th>X</th>
<th>pKₐ ~</th>
</tr>
</thead>
<tbody>
<tr>
<td>-OCH₃</td>
<td>10.21</td>
<td>-NH₂</td>
<td>10.46</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Phenols are much more acidic than aliphatic alcohols:
a benzene ring is generally considered electron withdrawing (inductive effect)
the benzene ring stabilizes the negative charge of the phenoxide ion through resonance

(Fig. 17.3, p. 595)
Electron-withdrawing substituents make a phenol more acidic by stabilizing the phenoxide ion through delocalization of the negative charge and through inductive effects. Electron-donating substituents make a phenol less acidic by destabilizing the phenoxide ion (resonance effect). The location of the substituent relative to the phenol is important.

### 17.4: Preparation of alcohols:

- **Markovnikov addition**
  - [Diagram showing Markovnikov addition with specific reagents: B₂H₆, THF; NaOH, H₂O₂; Hg(OAc)₂, H₂O; NaBH₄; OsO₄; NaHSO₃.]
  - **Hydration of alkenes** (Ch. 7.4)
  - **Oxymercuration of alkenes** (Ch. 7.4)
  - **Hydroboration of alkenes** (Ch. 7.5)
  - **Di-hydroxylation of alkenes** (Ch. 7.8)
17.5: Alcohols from reduction of carbonyl compounds

Figure 10.5 (Chapter 10.10)

Increasing oxidation state

\[
\begin{align*}
\text{C} & \quad \text{C} & \quad \text{C} \\
\text{C} & \quad \text{O} & \quad \text{H} \\
\text{C} & \quad \text{O} & \quad \text{O} \\
\text{C} & \quad \text{Cl} & \quad \text{Cl} \\
\text{C} & \quad \text{NH}_2 & \quad \text{C} \\
\end{align*}
\]

17.5: Alcohols from reduction of carbonyl compounds
add the equivalent of \( \text{H}_2 \) across the \( \pi \)-bond of the carbonyl to give an alcohol

\[
\text{aldehyde (R or R' = H)} \rightarrow 1^\circ \text{ alcohol} \\
\text{ketone (R and R' ≠ H)} \rightarrow 2^\circ \text{ alcohol}
\]

[H]: sodium borohydride: \( \text{NaBH}_4 \), ethanol reduces aldehydes to \( 1^\circ \) alcohols and ketones to \( 2^\circ \) alcohols

lithium aluminum hydride (LAH): \( \text{LiAlH}_4 \), ether reduces aldehydes, carboxylic acids, and esters to \( 1^\circ \) alcohols and ketones to \( 2^\circ \) alcohols

In general, \( \text{NaBH}_4 \) and \( \text{LiAlH}_4 \) will not reduce C=C.
17.6: Alcohols from reaction of carbonyl compounds with Grignard reagents

Alkyl halides will react with some metals (M^0) in ether or THF to form organometallic reagents

Grignard reagent- organomagnesium

\[ R-X + Mg^{(0)} \xrightarrow{\text{ether or THF}} R-Mg^{(II)}-X \]

X= Cl, Br, or I

R can be a variety of groups: 1°-, 2°-, 3°-alkyl, aryl or vinyl

Grignard reagents react with aldehydes or ketones to give alcohols

If, carbonyl = H₂C=O → 1° alcohol
= aldehyde → 2° alcohol
= ketone → 3° alcohol

\[ \text{H}_3\text{O}^+ \]
Grignard reagents react with esters to give 3° alcohols

\[
\begin{align*}
\text{Grignard reagents react with esters to give 3° alcohols} \\
\text{Some functional groups are incompatible with Grignard reagents} \\
\text{Grignard reagents are very strong bases as well as highly reactive nucleophiles} \\
\text{Carboxylic acids are simply deprotonated by Grignard reagents and do not give addition products}
\end{align*}
\]

Grignard reagents will deprotonate alcohols

\[
\begin{align*}
\text{Grignard reagents will deprotonate alcohols} \\
\text{Other incompatible groups:} \\
\text{Reactive functional groups:}
\end{align*}
\]

Other incompatible groups:
- \(-\text{CO}_2\text{H}, -\text{OH}, -\text{SH}, \text{NH}_2, \text{CONHR}\) (amides)

Reactive functional groups:
aldehydes, ketones, esters, amides, halides, -\(\text{NO}_2\), -\(\text{SO}_2\text{R}\), nitriles
17.7 Some reactions of alcohols

A. Reactions involving the C-O bond

Dehydration to alkenes:

- E1 mechanism (reactivity: $3^\circ > 2^\circ >> 1^\circ$)
- requires strong acid catalyst ($\text{H}_2\text{SO}_4$)
- water is a much better leaving group than $\text{HO}^-$
- usually follows Zaitzev’s rule

Dehydration to alkenes with $\text{POCl}_3$

- E2 mechanism - requires an anti-periplanar conformation between leaving group and the hydrogen that is being lost
- mild conditions, requires a base (pyridine)
Conversion of an alcohol to an alkyl halide (R-OH → R-X) (Chapter 10.7)

1. Substitution reaction of alcohols with HX

\[ \text{R-OH} + \text{HX} \rightarrow \text{R-X} + \text{H}_2\text{O} \]

Works better with more substituted alcohols

\[ \text{Methyl} < \text{Primary (1°)} < \text{Secondary (2°)} < \text{Tertiary (3°)} \]

Increasing reactivity

\[ \text{S}_\text{N}1 \text{ mechanism involving a carbocation intermediate: rearrangements, stereochemistry (racemization)} \]

2. Preparation of alkyl chlorides by the treatment of alcohols with thionyl chloride (SOCl$_2$)

\[ \text{R-OH} + \text{SOCl}_2 \rightarrow \text{R-Cl} + \text{SO}_2 + \text{HCl} \]

3. Preparation of alkyl bromides by the treatment of alcohols with phosphorous tribromide (PBr$_3$)

\[ \text{R-OH} + \text{PBr}_3 \rightarrow \text{R-Br} + \text{P(OH)}_3 \]

\[ \text{S}_\text{N}2 \text{ mechanism: works best with 1° and 2° alcohols, but not with 3° alcohols. stereochemistry: inversion} \]
B. Reaction involving the O-H bond
Conversion of an alcohol to a tosylate (ROTos)

Reaction of an alcohol with p-toluenesulfonfyl chloride (tosyl chloride, p-TosCl) in pyridine gives a tosylates

Formation of the tosylate does not involve the C–O bond so the stereochemistry of the carbon attached to the alcohol is not affected
Tosylates are good leaving groups and their reactivity is similar to alkyl halides
Oxidation of primary alcohols with Cr(VI)
exact structure of the chromium reagent depends on solvent and pH

\[
R_2CHOH + Cr(VI)O_3 \rightarrow \text{chromate ester} + Cr(IV)
\]

pyridinium chlorochromate (PCC)- oxidizes 1° alcohols to aldehydes; and 2° alcohols to ketones. Solvent: CH₂Cl₂

chromic acid (Jones reagent):
\[
CrO₃ (or Na₂Cr₂O₇) + H₂O + H₂SO₄ \rightarrow H₂CrO₄
\]
\[
2 \ H₂CrO₄ \rightarrow H₂Cr₂O₇ + H₂O
\]
oxidizes 1° alcohols to carboxylic acids; and 2° alcohols to ketones. Solvent: H₃O⁺ and acetone
17.9 Protection of Alcohols

Hydroxyl groups are weak protic acids and can transfer a proton to a basic reagent, which may prevent a desired reaction.

Protecting group: Temporarily convert a functional group that is incompatible with a set of reaction conditions into a new functional group (with the protecting group) that is compatible with the reaction. The protecting group is then removed giving the original functional group (deprotection).
17.10 Preparation of phenols
alkali fusion reaction (Chapter 16.2)

Chapter 24.8: anilines (Ar-NH$_2$) → phenols (Ar-OH)

17.11 Reactions of Phenols:
- electrophilic aromatic substitution (Chapter 16.5-16.7)
  - phenols are highly activated toward electrophilic aromatic substitution and are o,p-directors
Oxidation of phenols to quinones (please read)
phenols can be oxidized by strong oxidants to give hydroquinones and quinones

\[
\text{OH} \quad \text{(KSO}_3\text{)}_2\text{NO, H}_2\text{O (Fermy's salt)} \quad \text{OH} \\
\begin{align*}
\text{hydroquinone} & \quad \text{semiquinone} \\
\text{quinoine} & \quad \text{quinoine} (\text{oxidized})
\end{align*}
\]

Ubiquinones (n= 1-10): Coenzyme Q

\[
\begin{align*}
\text{hydroquinone} & \quad \text{semiquinone} \\
\text{quinoine} & \quad \text{quinoine} (\text{oxidized})
\end{align*}
\]

α−tocopherol (vitamin E)

17.12 Spectroscopy of Alcohols and Phenols:
Infrared (IR): Characteristic O–H stretching absorption at 3300 to 3600 cm\(^{-1}\)
Sharp absorption near 3600 cm\(^{-1}\) except if H-bonded: then broad absorption 3300 to 3400 cm\(^{-1}\) range
Strong C–O stretching absorption near 1050 cm\(^{-1}\)
\(^1\text{H NMR:}\)
protons attached to the carbon bearing the hydroxyl group are deshielded by the electron-withdrawing nature of the oxygen, \(\delta\) 3.5 to 4.0

Usually no spin-spin coupling between the O–H proton and neighboring protons on carbon due to exchange reaction

The chemical shift of the -OH proton occurs over a large range (2.0 - 5.5 ppm). This proton usually appears as a broad singlet. It is not uncommon for this proton not to be observed.
\[ ^{13}\text{C NMR: The oxygen of an alcohol will deshield the carbon it is attached to. The chemical shift range is 50-80 ppm} \]