Alcohols, and Phenols
Alcohols and Phenols

- Alcohols contain an OH group connected to a 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
Alcohols and phenols may be viewed as organic derivatives of water.

![Chemical structures]

- **Alcohols**
  - A hydroxyl group attached to an alkyl group, \(-R\).

- **Phenols**
  - A hydroxyl function attached to an aromatic ring, \(-Ar\).

**Classification and Nomenclature of Alcohols**

Alcohols are subdivided into three classes: depends on the number of alkyl groups bonded to the carbon bearing the \(-OH\), the so-called carbinol carbon.

- **Primary (1°)**
  - One alkyl group bonded to the carbinol carbon.

- **Secondary (2°)**
  - Two alkyl groups bonded to the carbinol carbon.

- **Tertiary (3°)**
  - Three alkyl groups bonded to the carbinol carbon.

![Alcohol types]

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The **common names** for the simplest alcohols consist of

- alkyl group attached to the hydroxyl function followed by the word *alcohol*.

**Alkyl alcohol**

- *Primary alcohols*
  - CH₃OH: Methyl alcohol
  - CH₃CH₂OH: Ethyl alcohol
  - CH₂=CHCH₂OH: Allyl alcohol

- *Secondary alcohols*
  - \( \text{CH}_3\text{CHCH}_3 \): Isopropyl alcohol
  - \( \text{C}_2\text{H}_5\text{OH} \): Cyclopentyl alcohol

- *Tertiary alcohol*
  - \( \text{CH}_3\text{C}_2\text{H}_4\text{OH} \): \( t \)-Butyl alcohol

- In the **IUPAC system**, alcohols are named according to the following rules.
  1. Select the longest continuous carbon chain that *contains the -OH group*.
     - Drop the \(-e\) ending of the parent alkane and replace it by the suffix \(-ol\).

**Examples**

- CH₃OH (Methanol, *primary alcohol*)
- CH₃CH₂OH (Ethanol, *primary alcohol*)
- CH₂=CHCH₂OH (Cyclopentanol, *secondary alcohol*)
- CH₃C₂H₄OH (Cyclohexanol, *secondary alcohol*)
2. When isomers are possible, the chain is numbered so as to give the functional group (-OH) the *lowest possible number*.

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}_2\text{OH} & \quad \text{OH} \\
1\text{-Propanol} & \quad \text{(not 3-Propanol)} \\
\text{CH}_3\text{CH}_2\text{CH}_2\text{CHCH}_3 & \\
2\text{-Pentanol} & \quad \text{(not 4-Pentanol)}
\end{align*}
\]

3. When alkyl side chains or other groups are present, they are named alphabetically and their positions are indicated by a number.

The position of the functional group (-OH) is always given the *lowest possible number* at the end of the name.

\[
\begin{align*}
\text{CH}_2\text{CH}_3 & \\
\text{CH}_3\text{CH}_2\text{CHCH}_2\text{CHCH}_3 & \quad \text{Cl} \\
\text{OH} & \\
4\text{-Ethyl-2-hexanol} & \quad \text{(not 3-Ethyl-5-hexanol)} \\
\text{CH}_3\text{CH}_2\text{CHCH}_2\text{CHCH}_2\text{OH} & \\
\text{CH}_3 & \\
5\text{-Chloro-2-methyl-1-heptanol} & \quad \text{(not 3-Chloro-6-methyl-7-heptanol)}
\end{align*}
\]
For cyclic alcohols, numbering always starts from the carbon bearing the -OH group.

4. If a molecule contains both an -OH group and a C=C or C-C triple bond, the -OH group takes preference before the double or triple bonds in getting the lower number. The name should include (if possible) both the hydroxyl and the unsaturated groups, even if this does not make the longest chain the parent hydrocarbon.
Some alcohols contain more than one hydroxyl group.

- The suffix **-dial** is added to the name of the parent hydrocarbon when two hydroxyl groups are present, and the suffix **-triol** is added when there are three -OH groups.

- those containing two -OH groups on adjacent carbons are known as 1,2-glycols.

- Alcohols that contain more than three hydroxyl groups per molecule are known as polyols.
Phenols are generally named as derivatives of the simplest member of the family, phenol.

Several important hydroxysubstituted phenols also have common names.
The simplest alcohol, methanol, is a liquid at room temperature. The lower alcohols are completely miscible with water.

As the number of carbons in the alcohol increases, the solubility in water decreases.

Series of normal alcohols,

The boiling points increase with increase in molecular weights and decreased as the number of branched alkyl group increased.

A comparison of boiling points among isomeric alcohols;

- 1-Butanol: \( \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH} \) (mol wt = 74; bp = 118°C)
- 2-Methyl-1-propanol: \( \text{CH}_3\text{CHCH}_2\text{OH} \) (mol wt = 74; bp = 108°C)
- 2-Butanol: \( \text{CH}_3\text{CH}_2\text{CHCH}_3 \) (mol wt = 74; bp = 99.5°C)
- 2-Methyl-2-propanol: \( \text{CH}_3\text{CCH}_3 \) (mol wt = 74; bp = 83°C)
The straight-chain isomers have larger molecular surfaces than do their branched-chain isomers. Therefore, they have higher intermolecular interactions and, as a result, higher boiling points.

The high values of the boiling points of alcohols compared with alkanes of similar molecular weights.

The \( \text{O-H} \) bond and not to the presence of oxygen can be proved by comparing the boiling point of ethanol with Alcohols, Phenols, that of its structural isomer, methyl ether:

Therefore, the large increase in boiling points of alcohols compared with alkanes (or ethers) also must be due to the \( \text{O-H} \) group.
Alcohols 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.
• **Hydrogen Bonding**

The effect of the OH group on the physical properties of alcohols can be explained as follows.

The O—H bond is *highly polar*.

The oxygen, a highly electronegative atom carries a partial negative charge ($\delta^-$), and the hydrogen a partial positive charge ($\delta^+$).

Hydrogen bonding accounts also for the differences in physical states between lower alcohols and lower alkanes.

Hydrogen bonding also explains the solubility of the lower alcohols in water.

When those alcohols are mixed with water,

They dissolve because of hydrogen bonding between the OH bond of the alcohol and the hydroxyl group of the water.

As the number of carbons in an alcohol increases,

The nonpolar alkyl group becomes more and more important and the polar OH group becomes less important.
Phenol is a colorless, crystalline, low-melting solid, with a high boiling point, that is moderately soluble in water.

Most other phenols also are solids, with slight solubility in water and high boiling points.

The most significant physical property that distinguishes alcohols from phenols is the *acidity* of phenols.

**Acidities of Phenols and Alcohols Compared**

Why is the phenoxide ion more stable?

Because the negative charge on the oxygen is *dispersed* by *resonance* through the benzene ring.

No such delocalization of charge can take Place for the conjugate base of cyclohexanol.
Properties of Alcohols and Phenols: Acidity and Basicity

- Weakly basic and weakly acidic
- Alcohols are weak Brønsted bases
- Protonated by strong acids to yield oxonium ions, $\text{ROH}_2^+$

\[ \text{An alcohol} + \text{HX} \rightleftharpoons \text{An oxonium ion} \]

[or \( \text{ArOH} + \text{HX} \rightleftharpoons \text{ArOH}_2^+ \text{X}^- \)]
• Can transfer a proton to water to a very small extent
• Produces $\text{H}_3\text{O}^+$ and an alkoxide ion, $\text{RO}^-$, or a phenoxide ion, $\text{ArO}^-$
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

\[
\text{Methoxide ion, } \text{CH}_3\text{O}^- \\
pK_a = 15.54
\]

\[
\text{tert-Butoxide ion, } (\text{CH}_3)_3\text{CO}^- \\
pK_a = 18.00
\]
Electron-withdrawing groups make an alcohol a stronger acid by stabilizing the conjugate base (alkoxide).

Electron-withdrawing groups stabilize alkoxide and lower $pK_a$

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

\[pK_a = 5.4 \quad \text{versus} \quad pK_a = 18\]
Generating Alkoxides from Alcohols

- Alcohols are weak acids — requires 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

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

Electron-withdrawing groups (EWG) stabilize phenoxide anion, resulting in increased phenol acidity

Electron-donating groups (EDG) destabilize phenoxide anion, resulting in decreased phenol acidity
Nitro-Phenols

- Phenols with nitro groups at the ortho and para positions are much stronger acids.
- The pKa of 2,4,6-trinitrophenol is 0.6, a very strong acid.
Alcohols are derived from many types of compounds. The alcohol hydroxyl can be converted to many other functional groups, making alcohols useful in synthesis.
A. Hydration of Alkenes

1. Addition of water to a double bond in the presence of an acid catalyst, $H^+$. 

$$RCH=CHR + H\text{-}OH \xrightarrow{H^+} RCH\text{CHR}$$

2. The addition follows Markovnikov’s rule.

$$\text{CH}_3\text{CH}=\text{CH}_2 + H\text{-}OH \xrightarrow{H^+} \text{CH}_3\text{CHCH}_3$$

3. It is not possible to prepare primary alcohols except Ethanol.

B. Hydroboration-Oxidation

The addition of diborane, $\text{B}_2\text{H}_6$, followed by oxidation with alkaline hydrogen peroxide.

$$\text{CH}_3\text{CH}=\text{CH}_2 \xrightarrow{(1) \text{B}_2\text{H}_6} \xrightarrow{(2) \text{H}_2\text{O}_2, \text{NaOH}} \text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$$

The net result is the addition of $\text{H}_2\text{O}$ across $\text{C}=$ in an anti-Markovnikov manner.
• Reduction of a carbonyl compound in general gives an alcohol
• Note that organic reduction reactions add the equivalent of H₂ to a molecule

\[
\text{[H]} \quad \text{C} = \text{O} \quad \rightarrow \quad \text{C} - \text{OH}
\]

where [H] is a generalized reducing agent

\textit{A carbonyl compound} \quad \textit{An alcohol}
• NaBH₄ is not sensitive to moisture and it does not reduce other common functional groups
• Lithium aluminum hydride (LiAlH₄) is more powerful, less specific, and very reactive with water
• Both add the equivalent of “H⁻”
Alcohols from Reaction of Carbonyl Compounds with Grignard Reagents

- Alkyl, aryl, and vinylic halides react with magnesium in ether or tetrahydrofuran to generate Grignard reagents, RMgX
- Grignard reagents react with carbonyl compounds to yield alcohols

**Grignard formation**

\[ \text{R—X} + \text{Mg} \rightarrow \text{R—MgX} \]

R = 1°, 2°, or 3° alkyl, aryl, or vinylic
X = Cl, Br, or I

A Grignard reagent

\[ \text{C} \quad \text{O} \quad 1. \text{RMgX, ether} \quad \text{OH} \quad 2. \text{H}_3\text{O}^+ \quad \text{C—OH} \quad \text{RMgX} + \text{HOMgX} \]
Examples of Reactions of Grignard Reagents with Carbonyl Compounds

**Formaldehyde reaction**

\[
\text{MgBr} + \text{H}_2\text{C}==\text{H} \rightarrow \text{CH}_2\text{OH}
\]

Cyclohexylmagnesium bromide + Formaldehyde \(\rightarrow\) Cyclohexylmethanol (65%) (a 1° alcohol)

**Aldehyde reaction**

\[
\text{CH}_3\text{CHCH}_2\text{CH} = \text{O} + \text{MgBr} \rightarrow \text{CH}_3\text{CHCH}_2\text{CH} = \text{O}
\]

3-Methylbutanal + Phenylmagnesium bromide \(\rightarrow\) 3-Methyl-1-phenyl-1-butanol (73%) (a 2° alcohol)

**Ketone reaction**

\[
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}=\text{O} \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH} \text{OH}
\]

Cyclohexanone + Ethylmagnesium bromide \(\rightarrow\) 1-Ethylcyclohexanol (89%) (a 3° alcohol)
Reactions of Esters and Grignard Reagents

- Yields tertiary alcohols in which two of the substituents carbon come from the Grignard reagent
- Grignard reagents do not add to carboxylic acids – they undergo an acid-base reaction, generating the hydrocarbon of the Grignard reagent

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{COCH}_2\text{CH}_3 & \quad \xrightarrow{1. \text{2 CH}_3\text{MgBr}} \quad \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CCH}_3 + \text{CH}_3\text{CH}_2\text{OH} \\
\text{Ethyl pentanoate} & \quad \xrightarrow{2. \text{H}_3\text{O}^+} \\& \quad \text{2-Methyl-2-hexanol (85%)} \\
& \quad \text{(a 3° alcohol)}
\end{align*}
\]
Grignard Reagents and Other Functional Groups in the Same Molecule

- Can't be prepared if there are reactive functional groups in the same molecule, including proton donors.

\[
\text{Br} \quad \text{Molecule} \quad \text{FG}
\]

where \( \text{FG} = \quad \text{OH}, \text{NH}, \text{SH}, \text{CO}_2\text{H} \)

\[
\text{FG} = \quad \text{CH}, \text{CR}, \text{CNR}_2, \\
\text{C} = \text{N}, \text{NO}_2, \text{SO}_2\text{R}
\]

The Grignard reagent is protonated by these groups.

The Grignard reagent adds to these groups.
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
• Since alcohols are weaker acids than water
  it is not possible to form the salt of an alcohol in aqueous alkaline solutions.

\[
R-OH + Na^+ OH^- \rightarrow \text{No reaction}
\]

• It is possible to form the salt by the action of active metals such as Na or K.

\[
2 \text{CH}_3\text{O}-\text{H} + 2 \text{Na} \rightarrow 2 \text{CH}_3\text{O}^\text{-} \text{Na}^+ + \text{H}_2\uparrow
\]

- Methanol
- Sodium methoxide

• The action of metallic sodium on an alcohol is similar to the reaction of metallic sodium with water.

• **Alkoxides** are strong bases, even stronger than hydroxides. Alkoxides are used extensively in the synthesis of ethers.

• It is possible to obtain **phenoxide** salts from aqueous solutions of alkali.
Reactions Involving Carbon-Hydroxyl Bond Breaking

\[
\begin{align*}
HONO_2 & \quad \text{(nitric acid)} \quad \Rightarrow \quad RONO_2 \\
& \quad \text{Alkyl nitrate} \\
HONO & \quad \text{(nitrous acid)} \quad \Rightarrow \quad RONO \\
& \quad \text{Alkyl nitrite} \\
ROH & \quad \text{(sulfuric acid)} \quad \Rightarrow \quad RO-SO_3H \\
& \quad \text{Alkyl hydrogen sulfate} \\
ROH & \quad \Rightarrow \quad RO-SO_3R \\
& \quad \text{Dialkyl sulfate} \\
ROH & \quad \text{(phosphoric acid)} \quad \Rightarrow \quad RO-P-OH \\
& \quad \text{Alkyl dihydrogen phosphate} \\
ROH & \quad \Rightarrow \quad RO-P-OR \\
& \quad \text{Dialkyl hydrogen phosphate} \\
ROH & \quad \Rightarrow \quad RO-P-OR \\
& \quad \text{Trialkyl phosphate}
\end{align*}
\]
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.
• Tertiary alcohols are readily dehydrated with acid
• Secondary alcohols require severe conditions (75% H₂SO₄, 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
Phosphorus oxychloride in the amine solvent pyridine can lead to dehydration of secondary and tertiary alcohols at low temperatures.

An E2 via an intermediate ester of POCl$_2$ (see Figure 17.6).
Conversion of Alcohols into Alkyl Halides

- 3° alcohols are converted by HCl or HBr at low temperature
- 1° and alcohols are resistant to acid – use SOCl₂ or PBr₃ by an S₃-N₂ mechanism
The hydroxyl group of alcohols can be replaced by halide to form alkyl halides.

\[ \text{R—OH} \longrightarrow \text{R—X} \quad (X = \text{Cl, Br, or I}) \]

Alcohol \quad \text{Alkyl halide}

The replacement of OH by halogen is applicable only to chlorides, bromides, and iodides.

Alkyl fluorides, R—F, are not prepared from alcohols.

**Reaction with hydrogen halides: Lucas test.**

Treatment of alcohols with aqueous concentrated hydrogen halides H-X, or with anhydrous H-X, give alkyl halides.

\[ \text{R—OH} + \text{H—X} \rightleftharpoons \text{R—X} + \text{H}_2\text{O} \quad (\text{HX}=\text{HCl, HBr, or HI}) \]

The reaction of halogen acids with various alcohols proceeds at different rates.

**Tertiary alcohols** react rapidly with hydrogen halides.

**Secondary alcohols** react somewhat slower.

**Primary alcohols**, even more slowly.
Lucas test for distinguishing among the three classes of alcohols.

The Lucas test is carried out as follows.
An alcohol is mixed, at room temperature, with concentrated HCl and ZnCl₂ (catalyst).

The alkyl chloride, as it is formed, is insoluble in the medium and causes the solution to become cloudy before it separates as a distinct layer.

Tertiary alcohols react almost immediately.

\[
R_3\text{COH} + \text{HCl} \xrightarrow{ZnCl_2, 25^\circ C} R_3\text{CCl} + \text{H}_2\text{O}
\]

A 3° alcohol

(immediate cloudiness)

Secondary alcohols, the cloudiness appears after about five minutes.

\[
R_2\text{CHOH} + \text{HCl} \xrightarrow{ZnCl_2, 25^\circ C} R_2\text{CHCl} + \text{H}_2\text{O}
\]

A 2° alcohol

(cloudiness in 5 min)

Primary alcohols do not react under these conditions.

\[
R\text{CH}_2\text{OH} + \text{HCl} \xrightarrow{ZnCl_2, 25^\circ C} \text{No visible reaction}
\]

A 1° alcohol

(solution remains clear)
Conversion of Alcohols into Tosylates

- Reaction with \( p \)-toluenesulfonyl chloride (tosyl chloride, \( p \)-TosCl) in pyridine yields alkyl tosylates, ROTos.
- Formation of the tosylate does not involve the C–O bond so configuration at a chirality center is maintained.
- Alkyl tosylates react like alkyl halides.

\[
\begin{align*}
\text{An alcohol} & \quad \text{Pyridine} \quad \text{A tosylate (ROTos)} \\
\text{\( p \)-Toluenesulfonyl chloride} & \quad \text{\( + \) Pyridine \cdot HCl}
\end{align*}
\]
Oxidation of Alcohols

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

**Primary alcohol**

\[
\begin{align*}
\text{Primary alcohol} & \quad \text{OH} \\
& \quad \text{[O]} \quad \text{O} \\
& \quad \text{A carboxylic acid} \\
\end{align*}
\]

**Secondary alcohol**

\[
\begin{align*}
\text{Secondary alcohol} & \quad \text{OH} \\
& \quad \text{[O]} \quad \text{O} \\
& \quad \text{A ketone} \\
\end{align*}
\]

**Tertiary alcohol**

\[
\begin{align*}
\text{Tertiary alcohol} & \quad \text{OH} \\
& \quad \text{[O]} \quad \text{NO reaction} \\
\end{align*}
\]
Oxidation of Primary Alcohols

- To aldehyde: pyridinium chlorochromate (PCC, \( \text{C}_5\text{H}_6\text{NCrO}_3\text{Cl} \)) in dichloromethane
- Other reagents produce carboxylic acids

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

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

\[
\text{4-tert-Butylcyclohexanol} \xrightarrow{\text{Na}_2\text{Cr}_2\text{O}_7, \text{H}_2\text{O}, \text{CH}_3\text{CO}_2\text{H}, \text{heat}} \text{4-tert-Butylcyclohexanone (91%)}
\]

\[
\text{Testosterone (steroid; male sex hormone)} \xrightarrow{\text{PCC, CH}_2\text{Cl}_2, 25^\circ\text{C}} \text{4-Androstene-3,17-dione (82%)}
\]
Summary - Alcohols

- Synthesis
  - Reduction of aldehydes and ketones
  - Addition of Grignard reagents to aldehydes and ketones
- Protection of OH as TMS) ether
- Reactions
  - Conversion to alkyl halides
  - Dehydration
  - Oxidation