

Nuggets of Knowledge for Chapter 14 – Alcohols (I)

Chem 2320

I. Introduction to Alcohols

Definition and Examples of Alcohols and Thiols

- Alcohols are compounds which contain an OH functional group which is not connected to a C=O.
 - If the same carbon has a double bond to oxygen and an OH, this is a carboxylic acid.
 - Some common alcohols include methanol, ethanol, and isopropanol.
 - Methanol, CH_3OH , is often called wood alcohol. It is one of the first flammable gases given off when wood is heated. It is sometimes used as a race car fuel. It is poisonous, and causes blindness or death when ingested because it is oxidized to formaldehyde by the liver. Treatment involves intravenous administration of ethanol to overwhelm the oxidizing enzymes and allow the methanol to be excreted.
 - Ethanol, $\text{CH}_3\text{H}_2\text{OH}$, is often called grain alcohol. It can be obtained by fermenting sugar from a fruit or grain source. This is what people usually mean when they use the word “alcohol” in ordinary conversation. The ethanol that we use in the lab has been made unfit for drinking by adding one of several possible toxic compounds – this is called “denatured alcohol”. Ethanol is also poisonous, either in large doses at one time, or smaller doses over a longer time.
 - Isopropanol, $\text{CH}_3\text{CHOHCH}_3$, is found in rubbing alcohol. It is used for disinfecting in medicine.
- Thiols are compounds which contain an SH functional group. They are also known by an older name, mercaptans, because of their ability to “capture” mercury (or bind tightly to it).
 - Since oxygen and sulfur are in the same family on the Periodic Table, they have similar reactivity. However, sulfur is a larger atom than oxygen, so it is more acidic as well as more nucleophilic.
 - One of the most noticeable properties of thiols is their strong, disagreeable odor, often described as the smell of rotting cabbage. Ethyl thiol is added to natural gas to give it a detectable odor, and to other thiols are found in skunk spray. Not all thiols have this property however – grapefruit contains a thiol called grapefruit mercaptan which has pleasant citrus odor that is largely responsible for the aroma of grapefruit.

Classification of Alcohols

- Alcohols in which the OH is connected to an sp^3 carbon are classified as 1° , 2° , or 3° based on the number of carbons attached to the alcohol carbon (just like alkyl halides).

- Alcohols in which the OH are connected to an sp^2 carbon are classified as enols or phenols.
 - If the OH is attached to a single $C=C$, then it is an enol. Enols tautomerize to form a $C=O$, either an aldehyde or ketone. We will discuss them in Chapter 18.
 - If the OH is attached to a benzene ring, then it is an aryl alcohol. We will discuss them in this chapter along with regular alcohols.
 - Aryl alcohols are sometimes called phenols (accent on the last syllable), because of their relationship to phenol, the simplest aryl alcohol.
 - Alcohols which contain a $C=C$ or a benzene ring, but in which the OH is not directly attached to it, are simply called unsaturated or aromatic alcohols.

Physical Properties

- Alcohols have higher boiling points than alkyl halides or hydrocarbons because of the stronger intermolecular force of hydrogen bonding.
- Alcohols with one to four carbons are soluble in water, while those with more than four carbons have limited water solubility. Adding more OH groups increases the number of carbons a compound can have and still be soluble.

IR Spectra

- Alcohols are often easy to identify by IR spectroscopy.
 - The O-H band occurs at $3400-3200\text{ cm}^{-1}$, and is usually broad and rounded.
 - The C-O band occurs at $1300-1000\text{ cm}^{-1}$, and is usually visible in alcohols.

NMR Spectra

- Alcohols have two characteristic chemical shifts in NMR spectra.
 - The H attached to the O may occur anywhere from 1-5 ppm, depending on the concentration of the sample. These peaks may be broad or sharp, depending on the degree of hydrogen bonding that is occurring. They are nearly always singlets.
 - This band may be removed by adding D_2O to the sample.
 - The H's attached to the carbon with the OH occur from 3-4 ppm.

II. Acid-base Behavior of Alcohols

- Alcohols are amphoteric – they can react with acids or bases.
- Alcohols react with acids to form protonated alcohols, in which the oxygen has a positive charge and two hydrogens.
 - The pKa of a protonated alcohol is -2.4.
 - Only acids which are stronger than this (pKa less than -2.4) have a favorable equilibrium constant for forming the protonated alcohol. These acids include HI, HBr, HCl, H₂SO₄, and H₃PO₄.
 - Protonated alcohols are very acidic, and will react with any base whose conjugate acid pKa is lower than -2.4. They cannot exist in any solution that contains a strong base.
- Alcohols react with bases to form alkoxides, in which the oxygen has a negative charge.
 - The pKa of an alcohol is between 16 and 18.
 - Primary alcohols are on the more acidic end of the range (around 16), while tertiary alcohols are on the less acidic end of the range (around 18).
 - Only bases which are stronger than this (conjugate acid pKa greater than 18) will have a favorable equilibrium constant for forming the alkoxide.
 - The base most commonly used for this purpose is NaH. NaOH is not sufficiently strong for this purpose.
 - Sodium or potassium metals are also used to form alkoxides, but this takes place through an oxidation-reduction reaction rather than a simple acid/base reaction.
 - Sodium is effective for methyl and primary alcohols, but is too slow for secondary and tertiary alcohols. In this case, potassium is used instead.
 - Alkoxides are strong bases, and will react with any acid whose pKa is lower than 16. They cannot exist in any solution that contains a strong acid.
- Aryl alcohols will also react with bases to form alkoxides, which are often called phenoxides.
 - Aryl alcohols are much more acidic than aliphatic alcohols because their conjugate base is stabilized by resonance. Aryl alcohols have pKa's around 10. NaOH is the most commonly used base to deprotonate an aryl alcohol.
- Thiols will also react with bases to form thiolate ions.
 - Thiols are more acidic than alcohols because of the larger size of sulfur. They also have pKa's around 10, and can be effectively deprotonated by NaOH.

III. Nomenclature of Alcohols

Common Names

- Simple alcohols can be named using common names. The common name consists of the name of the alkyl substituent, then the word “alcohol” as two separate words.
 1. For example, CH_3OH is called methyl alcohol.
 2. Phenyl alcohol is not used – it is contracted to the common name “phenol.”

IUPAC Names

- The same basic steps are used in naming alcohols as all other organic compounds:
 1. Label any stereochemistry present in the molecule.
 2. Choose the principle chain, and name it.
 3. Number the principle chain.
 4. Name and order the substituents, and add them to the name.
- Stereochemistry in an alcohol is labeled R or S just as in any other chiral molecule. If the alcohol is unsaturated, then it may also need to be labeled cis or trans, or E or Z.
- Priorities for choosing the principle chain include an additional priority:
 1. The principle chain must contain the carbon connected to the OH. If there is more than one OH, the principle chain must contain as many of them as possible.
 2. If more than one chain is possible, the principle chain should include any double or triple bonds.
 3. If more than one chain is still possible, the principle chain should include as many carbon atoms as possible.
 4. If more than one chain is still possible, the principle chain should include the highest number of substituents.
- When the principle chain contains an alcohol, the name of the alkane is changed to reflect this. The “e” on the end is dropped, and “ol” is added. For example, methane becomes methanol.
 - If there is also a double or triple bond in the principle chain, the “en” or “yn” ending stays the same, but “ol” is added to it. For example, cyclopentene become cyclopentenol.

- If there is more than one OH, then the entire alkane name is used, and “diol”, “triol”, etc, is added to the end. For example, pentane becomes pentanediol. (Note that this is different from the way the name is changed for more than one double or triple bond.)
- Priorities for numbering the chain include an additional priority:
 1. Give the lowest number to the carbon with the alcohol.
 2. If there is still more than one way to number the chain, give the lowest number to the first carbon of any double or triple bonds.
 3. If there is still more than one way to number the chain, give the lowest number to the first substituent; if these are the same, then the second, etc.
 4. If there is still more than one way to number the chain, give the lowest number to the substituent which comes first in the alphabet.
- If an OH group must be named as a substituent, it is called a hydroxyl group.

IV. Synthesis of Alcohols

Reactions from Previous Chapters

- The following reactions that we have previously learned may be used to synthesize alcohols. Make sure to review these reactions, as you will be responsible for them in this chapter.
 - S_N2 reactions between primary alkyl halides and sodium hydroxide (Ch 8)
 - Acid-catalyzed hydration of alkenes, accomplished by treating an alkene with a catalytic amount of sulfuric or phosphoric acid and water (Ch 9)
 - Oxymercuration-reduction of alkenes, accomplished by treating an alkene with mercuric acetate and water, followed by sodium borohydride. (Ch 10)
 - Hydroboration-oxidation of alkenes, accomplished by treating an alkene with borane-THF, followed by hydrogen peroxide and sodium hydroxide. (Ch 10)
 - Hydroxylation of alkenes, accomplished by treating an alkene with potassium permanganate, water, and hydroxide, or with osmium tetroxide and hydrogen peroxide (Ch 10)
- In this chapter, we will add two more very useful ways of making alcohols. One begins with an aldehyde, ketone, carboxylic acid, or ester and reduces it to an alcohol. The other begins with an aldehyde, ketone, ester, acid chloride, or epoxide, and adds a carbon group as well as reducing it to an alcohol.

Reduction of C=O Groups to Form Alcohols

- Oxidation and reduction are not quite as clear-cut in organic chemistry as they are in inorganic chemistry. Because they have no charge, it is difficult to assign an oxidation number to an atom in a neutral organic compound.
- Definitions of oxidation and reduction in organic chemistry rely on changes to the number of bonds to oxygen and hydrogen.
 - Oxidation: an atom gains bonds to oxygen (or loses bonds to hydrogen)
 - Reduction: an atom loses bonds to oxygen (or gains bonds to hydrogen)
- If one or more atoms in a compound are oxidized, then we say that the compound has been oxidized. If one or more atoms in a compound are reduced, then we say that the compound has been reduced. If one atom is reduced, and another is oxidized, then there is no net change in the oxidation state of the molecule.
- Several different functional groups containing a C=O (often called a carbonyl group) can be reduced to form alcohols.
 - Aldehydes and carboxylic acids are reduced to primary alcohols.
 - Ketones are reduced to secondary alcohols.
 - Esters are reduced to two alcohols, one primary, the other whatever was attached to the ester.
- There are several reagents that can be used to accomplish these reductions. Each has different reactivity toward different functional groups, and so they are useful in different situations.
 - H₂, Pd/C is only useful for reducing double and triple bonds between carbons. It will not affect C=O's.
 - Sodium borohydride, NaBH₄, does not affect double and triple bonds between carbons, but does reduce the C=O of aldehydes and ketones. It is not strong enough to affect carboxylic acids or esters. It is the most common reagent for converting aldehydes and ketones to alcohols.
 - Lithium aluminum hydride, LiAlH₄, also does not affect double and triple bonds between carbons, but does reduce the C=O of aldehydes, ketones, carboxylic acids, and esters. It is the most common reagent for converting esters and carboxylic acids to alcohols.
 - LiAlH₄ is more reactive than NaBH₄ because of the increased electronegativity of Al compared to B, causing the Al-H bond to be weaker than the B-H bond.

- NaBH_4 can be used in an alcohol solvent, typically methanol, but LiAlH_4 is too reactive, and must be used in a dried solvent such as ether.
 - Since LiAlH_4 reacts with water to produce hydrogen, lab fires are a danger with this reagent.
- Raney nickel, usually written as Raney Ni, is a reagent that contains hydrogen absorbed onto a nickel catalyst. It is named after the scientist who invented it. It will reduce both carbon-carbon double and triple bonds and carbon-oxygen double bonds of aldehydes and ketones, but will not reduce esters and carboxylic acids.
 - Like Pd/C, Raney Ni is pyrophoric, and can spontaneously combust when exposed to air.
- The mechanism of NaBH_4 and LiAlH_4 reduction involves two steps:
 - step 1: nucleophilic attack of one of the H's attached to the B or Al with its electrons to the carbon of the $\text{C}=\text{O}$, pushing one pair of electrons onto the oxygen and forming an alkoxide. (This could be called attack-push up.)
 - step 2: the alkoxide takes a hydrogen, forming the alcohol. In the case of NaBH_4 , the H comes from the solvent, methanol. In the case of LiAlH_4 , a mildly acidic solution is added as a second step (after carefully quenching the unreacted LiAlH_4).

Addition of Organometallic Reagents to $\text{C}=\text{O}$ groups to form alcohols

- Reduction of a carbonyl group forms an alcohol with the same carbon structure. However, addition of an organometallic reagent also converts a $\text{C}=\text{O}$ to an alcohol, but also adds an additional carbon group to the compound.
- Organometallic reagents contain a bond between a carbon atom and a metal. The ones we will typically encounter are:
 - Grignard (grin-yard) reagents, which have a carbon-magnesium bond
 - organolithium reagents, which have a carbon-lithium bond
- The carbon-metal bond is highly polar, with the metal having a partial positive charge, and the carbon having a partial negative charge. Since carbon is not very electronegative, these compounds are highly reactive.
- Organometallic reagents are formed by reacting an alkyl, vinyl, or aryl halide with the appropriate metal – magnesium metal in an ether solution for Grignards, and lithium metal in ether or hexanes or organolithium reagents.

- Grignards and organolithium reagents can react as bases or as nucleophiles. The pair of electrons in the bond between the carbon and the metal is the attacker, and it connects the carbon with whatever is attacked, leaving the metal free as a positive ion (in the case of Grignards, a halide ion is also generated).
- The conjugate base of a Grignard or organolithium reagent is an alkane, the least acidic acid on our chart. This makes Grignards and organolithium reagents the strongest bases in organic chemistry. They react rapidly with any acidic hydrogens available, including water, alcohols, amines, amides, carboxylic acids, and even terminal alkynes.
 - This is usually a reaction we are trying to avoid, since it destroys the organometallic reagent. However, it can occasionally be useful. It can convert an alkyl halide to an alkane, or add a deuterium by using D_2O in place of H_2O .
- If all hydrogen sources are carefully excluded, Grignards and organolithium reagents will react as nucleophiles.
 - They attack partially positive carbons of aldehydes and ketones to form alkoxides, then when mild, aqueous acid is added, an alcohol is formed.
 - Addition of an organometallic reagent to an aldehyde gives a secondary alcohol.
 - If the aldehyde has only one carbon (formaldehyde) then a primary alcohol is formed.
 - Addition of an organometallic reagent to a ketone gives a tertiary alcohol.
 - They attack partially positive carbons of esters and acid chlorides to form an intermediate which loses the chlorine or alkoxy group to form a ketone. A second equivalent of the organometallic reagent then reacts with the ketone to form an alkoxide. When mild, aqueous acid is added, an alcohol is formed.
 - Addition of 2 equivalents of an organometallic reagent to an acid chloride gives a tertiary alcohol with two identical groups.
 - Addition of 2 equivalents of an organometallic reagent to an ester gives a tertiary alcohol with two identical groups.
 - They react with either of the two carbons on an epoxide, usually ethylene oxide, to give an alkoxide, which can be protonated with mild, aqueous acid to form an alcohol.
 - Addition of an organometallic reagent to an epoxide gives a primary alcohol with two carbons more than the reagent had.
- When using this reaction for synthesis, you can't tell from the product which carbon group was added, and which were already there. This often gives more than one option for which carbons were originally part of the organometallic reagent and which were part of the $C=O$ compound or epoxide.