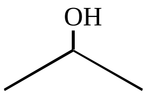
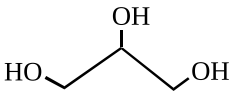
Chapter 13 – Alcohols, Phenols, Ethers, and Thioethers

Earlier you saw that an alcohol is an organic molecule containing an –OH group bound to a saturated carbon atom. Phenols are benzene rings that have attached –OH groups. Ethers are organic molecules with an oxygen bound to two organic groups. The prefix “thio-” means “sulfur containing” and usually means an oxygen atom has been replaced by a sulfur atom. Thus, thioethers are ethers where sulfur has substituted for the oxygen. The term “thioethers” is uncommon, however, and the term “sulfides” is more commonly used.

13.1 Occurrence, Types, and Names of Alcohols

The term “alcohol” has an interesting origin. Like many words in science beginning with “al-,” this term has an Arabic origin. “Al-“ means “the.” (Thus alchemy is “the chemistry.”) The last two syllables come from the word for an early eye shadow made of antimony powder. The word for the process by which this powder was made is very similar to the word for the powder itself. The process is essentially distillation. Medieval Europeans learned of distillation through the operation of making liquor. Of course, the active ingredient of liquors is ethanol, but at the time the name of the process by which ethanol was concentrated was given to the chemical itself. Hence the original name of ethanol was alcohol.

Molecules containing one or more –OH groups are common in nature. Their use is so widespread that many have common names. For example:

CH_3OH	CH_3CH_2OH			
wood alcohol	grain alcohol	rubbing alcohol		glycerin
methyl alcohol	ethyl alcohol	isopropyl alcohol	ethylene glycol	glycerol
methanol	ethanol	2-propanol	1,2-ethanediol	1,2,3-propanetriol

Since the vast majority of alcohols have their –OH groups attached to alkanes, their names are most easily generated by using those alkanes as their base.

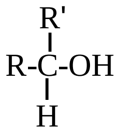
1) Find the longest carbon chain which includes the carbon to which the –OH group(s) is attached.
2) Name the molecule as if it were an alkane. Start counting from the end closest to the –OH group.
3) Change the final "-e" to "-ol" and put the –OH location prior to that chain name using numbers (if required to remove ambiguity). The examples just given also include their systematic names. When more than one –OH functionality is present, use the endings "-diol", "-triol," etc. Common names for the alcohols shown on p. 1 are also provided you.

The common name for alcohols is generated simply by taking the name of the alkane chain (see p. 11 of Chapter 11 notes) and adding alcohol to the end. The isopropyl alcohol molecule shown on p. 1 provides an example. (This is how common names are usually generated. For example $CH_3CHClCH_3$ (replace the -OH in isopropyl alcohol with Cl) is isopropyl chloride.)

Alcohols fall into 3 major structural category types. These categories are important because the types of reaction an alcohol may undergo depends on what else is attached to its carbon. If the carbon to which the –OH group binds also binds to 1 carbon atom, the alcohol is designated primary (1°). If only two carbons are attached to that carbon, the alcohol is secondary (2°). If three carbons are attached the alcohol is tertiary (3°). The R groups below represent any fragment attaching through a carbon atom, including aromatic units.

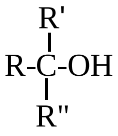
$R\text{-}CH_2\text{-}OH$

primary, 1°



$$R\text{-}\overset{R'}{\underset{H}{C}}\text{-}OH$$

secondary, 2°



$$R\text{-}\overset{R'}{\underset{R''}{C}}\text{-}OH$$

tertiary, 3°

Please note that this classification scheme does not affect the naming of an alcohol, all it does is allow you decided quickly what kinds of reactions the alcohol in question may participate in.

13.2 Physical Properties of Alcohols

Alkanes interact with one another exclusively through London Forces (p. 161 of textbook). The addition of an –OH group makes the molecule polar (allowing for dipole-dipole interactions) and, more importantly, provides sites for hydrogen bonding (pp. 165-169 of textbook). Recall that hydrogen bonding is an unusually strong dipole-dipole interaction. This means that alcohols tend to stick together much more strongly than alkanes and this affects their physical properties.

Before going further, please remember that the effects of the –OH group decrease as the alkane chain becomes longer. Thus, any hydrogen bonding effects in methanol are much larger than those in 1-pentanol. This was illustrated in the table of alcohol solubilities in water on p. 7 of the Chapter 11 notes.

A major effect that hydrogen bonding causes is a significant increase in boiling point. On that same page of the notes is a table of the boiling points of 3 different species. As you can see adding –OH groups causes substantial increases in boiling point. Your book does a similar table (13.2, p. 408) where it keeps the molecular weights roughly the same, but the major point in either case is that hydrogen bonding causes large increases in boiling points. Stronger intermolecular forces make it more difficult to separate the molecules. Again, this effect drops off as the molecules get bigger.

Other properties, not of biochemical interest, are also affected. For example, the viscosity of small alcohols is much higher than the viscosity of alkanes. Viscosity is the resistance to flow by a liquid. In other words, at the same temperature alcohols are “thicker” than alkanes. It is difficult (but possible) to see this comparing ethanol and pentane (the lightest alkane that is a liquid at room temperature). You can see this by simply swirling a flask containing each. If you have ever seen glycerin, though, it is as thick as warm maple syrup and it is only a little heavier than pentane.

13.3 Chemical Properties of Alcohols

Two types of reactions alcohols are prone to engage in are discussed in this chapter. One is essentially the reverse of addition of water to an alkene. This is called dehydration (the loss of water from an alcohol). The other is called oxidation. This reaction results in loss of hydrogen and the conversion of the C-O single bond to a double bond.

Dehydration

Your book gives you as an example the dehydration of ethanol (p. 410):

$$CH_3CH_2OH \xrightarrow[170\ ^\circ C]{H^+} H_2C{=}CH_2 + H_2O$$

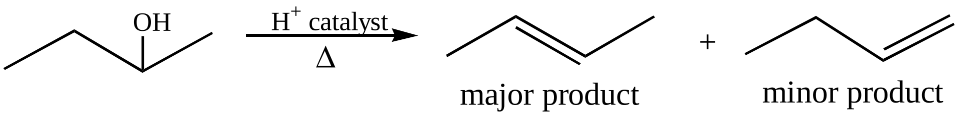
At this point you may well remember that the book used the same reaction (in reverse) as an illustration of addition reactions! (p. 376 textbook, p. 7, Chapter 12 notes)

$$H_2C{=}CH_2 + H_2O \xrightarrow[240\ ^\circ C]{H^+} CH_3CH_2OH$$

The same reaction shown in both directions?! On the surface this is a contradiction. Fortunately, a chemical principle from CHM 203 steps in and explains this apparent contradiction. Can you guess it?

In Chapter 6 (p. 163-65) you learned about equilibria. (This is an extremely important topic that we will revisit several more times this semester and you need to review it if you have forgotten it.) Le Châtelier’s principle reminds us that when a system at equilibrium is disturbed, it will adjust so as restore the equilibrium. Although the temperatures at which these reactions are conducted are different, this is not the principal cause of the direction of reaction. For a hydrolysis reaction (alcohol formation) there is a very large excess of water present to ensure that all of the alkene is converted to alcohol. In the case of dehydration either water is removed as the reaction progresses or the equilibrium already so favors alkene production that the small amount of water produced doesn't really affect the position of the equilibrium very much.

This reaction proceeds by a path essentially the reverse of the water addition path presented in the previous chapter. Given that, it is probably not surprising that for interior –OH groups, the final location of the C=C bond depends on the branching of the alkane. For example:



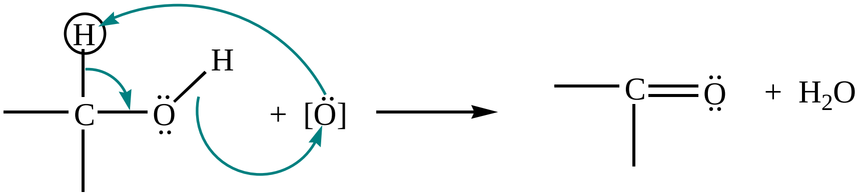
In general, the double bond will locate on the carbons with the most branching, although frequently there will be some of the other product present. As your book notes, when this reaction occurs biochemically, only one product forms (which one depends on the enzyme). This is because enzymes have stringent spatial requirements that allow the reactant alkene to bind in only one way before the reaction begins. This ensures only one product comes out and that product may not be the one preferred by standard organic methods.

<u>Oxidation</u>

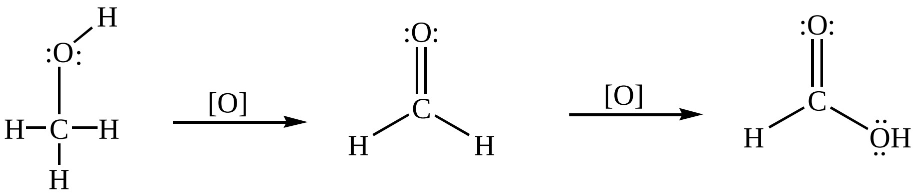
In an oxidation one of two things will happen. Either an external reagent will remove two hydrogen atoms (resulting in the conversion of a C-O bond to a C=O bond) or the reagent will transfer an oxygen atom to the molecule (added as a =O). Sometimes both reactions occur, although in a stepwise fashion. The reverse of these processes is called a <u>reduction</u>. Oxidations that occur via the removal of 2 hydrogen atoms are frequently called <u>dehydrations</u>, although the end product is still an oxidation product. It is important to remember that an organic oxidation is formally the same as an inorganic oxidation. We'll see how they are the same in the next few paragraphs.

For reasons that will soon be obvious, only 1° and 2° alcohols can be oxidized to other organic compounds. (Although if you provide harsh enough conditions they can be oxidized all the way to CO_2 and H_2O.)

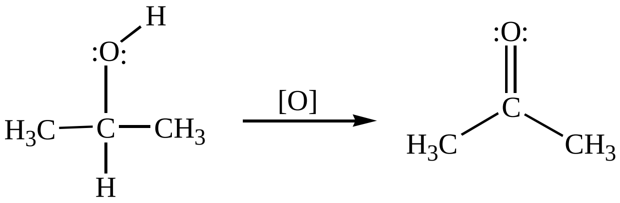
When the oxidant ([O]) reacts with an alcohol it effectively pulls the hydrogen atom bound to the oxygen off. It also takes a hydrogen bound to the carbon (bound to the –OH) off as well. The net effect is that it pulls two electrons out of the bonding system. Since adding electrons (negative charges) is a reduction, the reverse process (removing electrons) must be an oxidation. This can be see pictorially:



Now, if the reactant is a primary alcohol, we should wind up with an aldehyde. As it turns out, aldehydes are usually quite unstable to further oxidation. What this means is that the aldehyde reacts more rapidly with oxidant than does the parent 1° alcohol. Thus if one mixes one equivalent of primary alcohol with one equivalent of oxidant, instead of getting one equivalent of aldehyde, one obtains a mixture containing a substantial amount of the corresponding carboxylic acid. In other words, this is a poor way to make aldehydes, but a good one to make carboxylic acids. Secondary alcohols react to form ketones. Examples of each type of reaction include:



methanol formaldehyde formic acid



2-propanol 2-propanone (acetone)

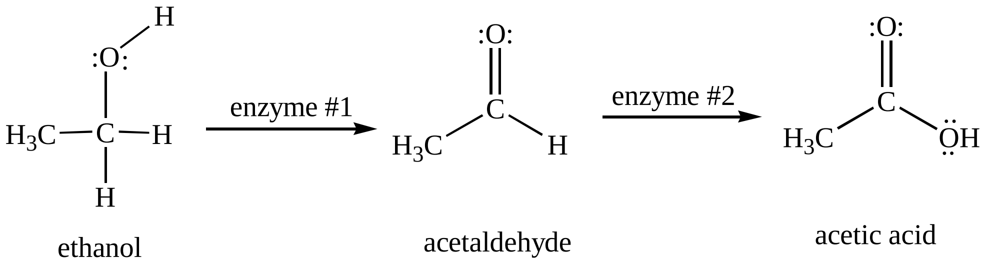
Two common oxidants are permanganate ion (MnO_4^-) and dichromate ion ($Cr_2O_7^{2-}$). As you learned in Chapter 4 (p. 85) whenever an oxidation occurs, a reduction must also proceed. Does it here? Let's look at the balanced chemical equation for the oxidation of 1-propanol to propanoic acid on p. 413 of your book. Can you assign oxidation numbers to each element below?

$$3\ CH_3CH_2CH_2OH\ +\ 2\ Cr_2O_7^{2-}\ +\ 16\ H^+ \rightarrow 3\ CH_3CH_2CO_2H\ +\ 4\ Cr^{3+}\ +\ 11\ H_2O$$

In this reaction a Cr^{6+} in $Cr_2O_7^{2-}$ is reduced to Cr^{3+} when the 1-propanol is oxidized to propanoic acid. The oxidation number of the carbon bound to oxygen goes from +1 in 1-propanol to +3 in propanoic acid. This is the oxidation.

As you've probably guessed, strong oxidants (like MnO_4^-) can't exist in your body. We have to use enzymes to accomplish the same types of reactions *in vivo*. As mentioned earlier, because enzymes are very specific, they can oxidize an alcohol to an aldehyde with no carboxylic acid by-product. This is a reaction manifested in human bodies across college campuses on a nightly basis. Since most of you are not yet 21 years old, you will (of course) not know of this from personal experience, but you may have heard of the "hangover" from classmates.

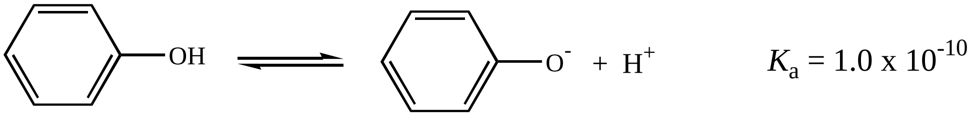
Not being a natural material found in the body, your body seeks to rid itself of ethanol in the bloodstream. It first decomposes ethanol to acetaldehyde, then to acetic acid, then carbon dioxide and water. Ethanol itself does not give you a hangover. The next morning the pain from the hangover results from the acetaldehyde floating through the bloodstream (and in many cases memories of what you said or did the previous evening). Inspection of acetaldehyde and formaldehyde (p. 6 and 7 of notes) shows them to be remarkably similar. As you may know, formaldehyde used to be used as embalming fluid and is still used today in biology labs as a preservative. (Its use as embalming fluid ceased, in large part, because it imparted an unnatural color to skin, a feeling many party goers feel is also true of acetaldehyde the next morning.) The acetic acid that forms from the acetaldehyde is not a problem for your body as you know from eating salads (vinegar is a 5% solution of acetic acid in water). In any event, drinking too much alcohol has a similar effect to injecting a small amount of formaldehyde into your blood stream.



13.4 Phenols

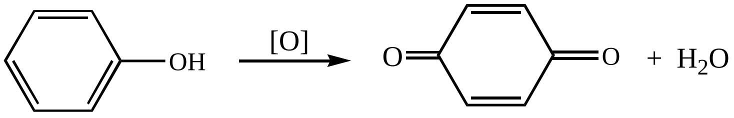
There is a tendency for students to think of phenols as aromatic alcohols, but this would be a mistake. Despite their outward similarities, they behave quite differently from one another. For example, while almost all aliphatic alcohols show negligible acidity or basicity in aqueous solution, phenols are weakly acidic. A 0.10 *M* phenol solution has a pH = 5.50 (for comparison:

0.10 *M* acetic acid (CH_3CO_2H) solution has a pH =2.87 and 0.1 *M* methanol solution has a pH = 7.00). While this solution is very weakly acidic, electron withdrawing substituents (e.g. F) can make phenols as acidic as many carboxylic acids.



The acidity of phenols comes from the fact that they can spread the negative charge onto the carbon atoms of the benzene ring. Recall from Chapter 12 (p. 12-13 of notes) that the *p*-orbitals π bond and form a ring around the benzene. Thus any of the negative charge that is spread from the oxygen to the benzene carbon to which it binds is spread all the way around the ring. In contrast, any negative charge on an alcohol stays on the carbon and oxygen because there is no way to spread it around. The result is that more of the negative charge can be removed from the oxygen. In general, substituents that spread charge around stabilize charged systems. Trivia question: In what over-the-counter medication is phenol the active ingredient?

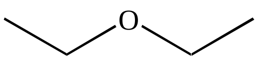
Phenols also easily undergo oxidation reactions. There are two reasons for this. First removing one of the hydrogen atoms is very easy as we have just seen. The second is that the C=O bond that forms is unusually stable.



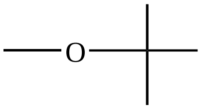
The ring on the right has a double bond to each of the carbon atoms, just like each of the carbons in the starting benzene ring. Thus each has a *p*-orbital overlapping its neighbors as was described in Chapter 12 (p. 12-13 of notes). By extending the number of orbitals in the π-system beyond the normal two in a ketone, extra stability is generated. The additional stability of the product is what makes the reactant easier to oxidize. The product on the right is called quinone (and is one of several related materials produced when phenol is oxidized). Answer: Chlorasceptic®. Curiously, despite the name, there is no chlorine containing substance in the ingredient list.

13.5 Ethers

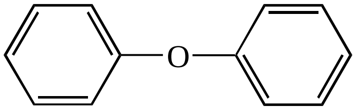
Ethers are compounds with two organic groups attached to an oxygen atom (R-O-R´). The carbon attached to the oxygen can't also be doubly bonded to oxygen. These compounds are called esters and we'll discuss them in Chapter 15. Some typical ethers include:



diethyl ether
"ether"



methyl 1,1-dimethylethyl ether
methyl *tert*-butyl ether (MTBE)



diphenyl ether

Diethyl ether is frequently just called "ether." Diethyl ether was the first general anesthetic developed by physicians and was used well into the 20th century. (Prior to this, anesthesia frequently consisted of getting the patient drunk ("feeling no pain").) It fell out of use because it causes incredible headaches in patients when they woke up (not to mention killing them if the dose was wrong). Also, it's a very flammable substance and not safe to keep around a doctor's office.

You won't know the second ether by its IUPAC name or by its common name, but the initials generated from its common name might look familiar. This is because MTBE is one of the two most common gasoline additives used to increase the amount of oxygen in gasoline (ethanol is the other). Without additives, gasoline consists only of hydrocarbons. Gasoline burns cleaner when oxygen containing organic molecules are mixed with it. By cleaner, we mean that more of the gasoline is burned and less unburned vapor escapes into the atmosphere. Clean Air regulations require that, in locations with too much smog, oxygen containing molecules be added to improve the burning of gasoline. Because it has been shown recently to be a carcinogen, it is being phased out of use.

Ethers have water solubilities intermediate between alkanes and alcohols. Because ethers have no O-H bonds, they cannot participate in hydrogen bonding to the same extent that alcohols do. Nevertheless, the oxygen in the ether can form a hydrogen bond to the hydrogen in water. The presence of only single site on the ether for a limited kind of hydrogen bonding interaction means that ethers generally have significantly smaller solubilities in water than do alcohols. Still they have higher solubilities than any hydrocarbon. Incidentally, you will frequently hear MTBE described as "highly soluble in water." What does this mean? Its water solubility is 5.1 g per 100 mL of water. This is falls between 1-butanol and 1-pentanol and by almost any standard is significant.

Preparation

Symmetrical ethers (R-O-R) can be prepared by gently heating an alcohol in the presence of an acid catalyst. This process is very similar to that used to dehydrate an alcohol to an alkene. The primary difference is that dehydration uses somewhat higher temperatures.

$$CH_3CH_2OH \xrightarrow[140\ ^{o}C]{H^+} CH_3CH_2OCH_2CH_3 + H_2O$$

Comparison of the hydration of an alkene and the dehydration of an alcohol to either an alkene or an ether shows the reactions to proceed over a relatively narrow temperature range (*ca*. 100^o for ethanol). Such a narrow range of conditions suggests that when these reactions are done one may obtain more than one product and such is frequently the case.

As you might imagine, this isn't the way ethers are usually made. Since one of the principal methods is very simple, we'll discuss it here. The following substitution reaction permits the convenient synthesis of both symmetrical and non-symmetrical ethers. This type of reaction happens in two steps, done separately. In the first the alcohol reacts with sodium (or some other substance that removes a proton from the alcohol –OH):

$$CH_3CH_2OH + Na \longrightarrow CH_3CH_2O^- + Na^+ + \tfrac{1}{2} H_2$$

Then an haloalkane is added to a solution of the resulting anion.

$$CH_3CH_2O^- + CH_3CH_2Cl \longrightarrow CH_3CH_2OCH_2CH_3 + Cl^-$$

where the Na^+ ion is a spectator ion (see p. 214 of textbook). For ethers with different R groups bound to oxygen, all one has to do is use an alcohol with one organic group and organic chloride with a different group.

Again, when the generation of an ether linkage occurs biochemically only one product forms. This raises the question "So if you only get one product in 100% yield biochemically, why fool with doing the reaction by standard chemical methods?" The principal answer deals with the selectivity of enzymes. Let's assume some plant has an enzyme that makes dimethyl ether (CH_3OCH_3). One must first identify the plant and the enzyme, then extract the enzyme and come up with reaction conditions that don't denature it (render it inactive). Sometimes the product of an enzyme denatures it in high concentration (which is what we will have if we seek to use the enzyme as a preparative catalyst). As you might imagine, all of this takes time and lots of money. So for chemicals with low profit margins, this method isn't practical. The other problem involves the inherent nature of enzymes. Enzymes are efficient because they work for only one molecule, thus your enzyme that converts methanol (CH_3OH) to dimethyl ether with 100% efficiency probably won't work at all to convert ethanol to diethyl ether. So the answer to the question posited above is that where chemists can they use enzymes because of the advantages they provide, but usually there is no enzyme that will do the job under practical conditions.

13.6 Thioalcohols and Disulfides

Thioalcohols are more properly called thiols. The old name for this class of molecules is the mercaptans. These are alcohols where the oxygen has been replaced by sulfur and they smell incredibly bad. Natural gas (methane) has no odor. A small amount (a few parts per million) of “mercaptan gas” is added and that is what you smell when some natural gas gets into the room. Mercaptan gas is any one of a number of volatile thiols (e.g. methane thiol (CH_3SH) or *t*-butyl thiol (Me_3CSH)).

Sulfides (thioethers) are ethers where a sulfur has replaced an oxygen atom (e.g. dimethyl thioether CH_3SCH_3). Another class of sulfur containing molecule has important biological implications, the disulfides. The molecules have the generic formula R-S-S-R and correspond to the peroxide class of oxygen containing molecules. Organic peroxides are high energy molecules, not found in nature. Hydrogen peroxide (H_2O_2, H-O-O-H) is the inorganic analogue and if you’ve ever put some on an open wound to disinfect it, you have some understanding by what is meant by the phrase “high energy molecule.”

While still comparatively reactive, disulfides are much more stable than peroxides and are found in nature. They form from the oxidation of thiols.

$$2\ RSH + [O] \rightarrow R\text{-}S\text{-}S\text{-}R + H_2O$$

In the presence of a reducing agent (source of hydrogen) the reaction runs basically in reverse:

$$R\text{-}S\text{-}S\text{-}R + 2[H] \rightarrow 2RSH$$

Protein molecules frequently contain disulfide linkages. When a perm is done, two solutions are used. The first reduces the disulfide linkages to thiols, the hair is then set, and an oxidizing solution is then used to generate new disulfide bonds to hold the hair in place. We will discuss these reactions further in the protein chapter.

January 3, 2002