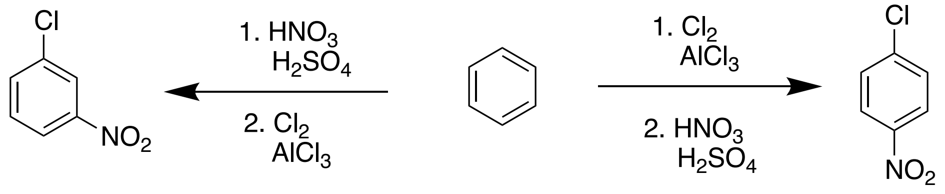
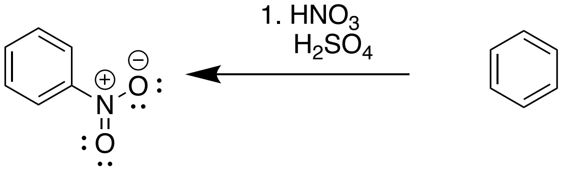
CHEM 261 **Dec 4, 2017**

REVIEW:

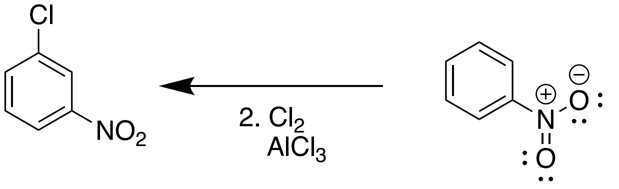


I **II**

For the left hand reaction, I

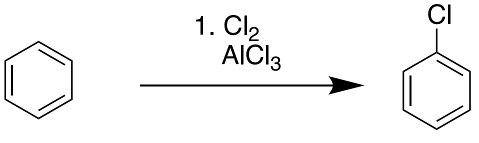


- to create a *meta* positioned Cl, the first molecule to be subsituted should be NO$_2$, resulting in *meta*-directing

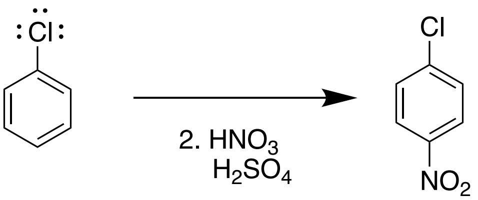


- NO$_2$ substitution results in resonance withdrawing electrons, making partial positive charges on the *ortho* and *para* positions, hence the electrophile Cl atom will substitute in the *meta* position.

For the right hand reaction, II



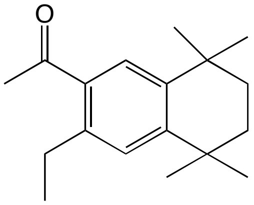
- To create a *para* subtituted NO$_2$, the chlorine should be added first,



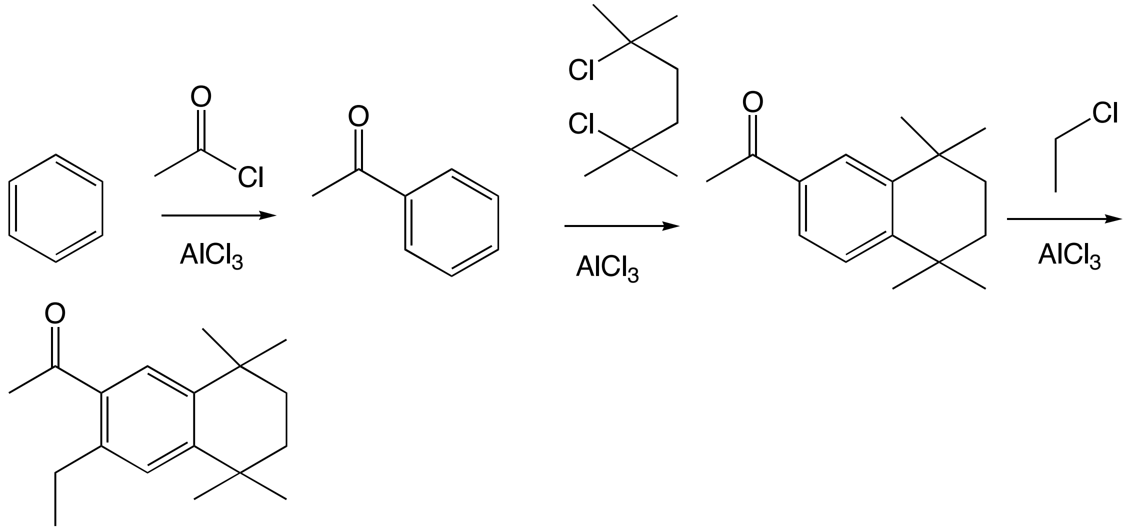
- the chloro group is an electron withdrawing group, inductively, but it is a resonance donator which then gives an *ortho* or a *para* substitution.

REVIEW: Versalide (a perfume component) Synthesis

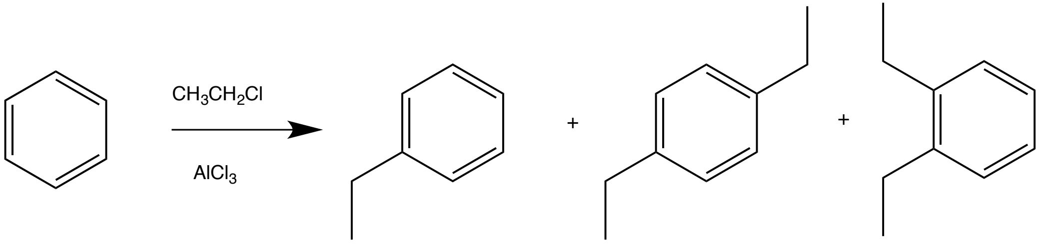
Synthesis Example: The sequence of steps is critical
How to make versalide, shown below, from benzene?



The answer is below. Be able to rationalize this sequence.



If you start to add ethyl group first, polyalkylation happens:

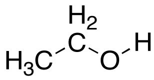


Alkylation must also be last because the acetyl group will direct to the meta position.

Lecture Outline 5: Alcohols, Ethers, Stereochemistry, Ketones, and Aldehydes

Nomenclature of Alcohols

Alcohols are compounds that have a hydroxyl group (-OH) bonded to a carbon atom (but not a carbonyl C=O). Alcohols can be thought of as organic derivatives of water in which one of the hydrogens is replaced by an organic group: H-O-H versus R-O-H. Alcohols occur widely in nature and have many industrial and pharmaceutical applications. Ethanol is one of the simplest alcohols, finding use as a fuel additive, an industrial solvent, and key ingredient in many beverages (beer, wine etc).

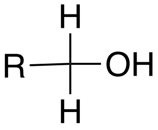


H_3C-CH_2-O-H

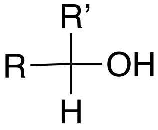
Ethanol

Naming Alcohols

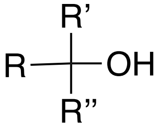
Alcohols are classified as primary (1°), secondary (2°), or tertiary (3°), depending on the number of organic groups bonded to the hydroxyl bearing carbon.



primary alcohol (1°)



secondary alcohol (2°)



tertiary alcohol (3°)

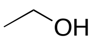
Simple alcohols are named using the IUPAC system as derivatives of the parent alkane, using the suffix *ol*:

1) Select the longest carbon chain containing the alcohol, and derive the parent name by replacing the *-e* ending of the corresponding alkane with *–ol.*
2) Number the alkane chain, beginning at the end closest to the hydroxyl group.
3) Number the substituents according to their position on the chain.

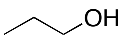
Examples:

H_3C-OH

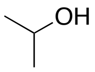
methanol
or methyl alcohol
or wood alcohol



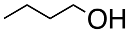
ethanol
or ethyl alcohol
or grain alcohol



n-propanol
or 1-propanol

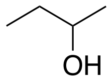


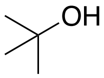
2-propanol
propan-2-ol
or isopropanol
rubbing alcohol



butanol
1-butanol
n-butanol (n means normal or straight chain)

butan-1-ol





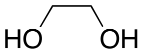
2-butanol

2-methyl-2-propanol
tert-butyl alcohol

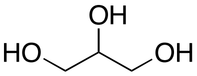
<u>If there is more than 1 OH group:</u>

2 OH's	diol (glycol)
3 OH's	triol
4 OH's	tetraol
5 OH's	pentaol

Some simple and widely occurring alcohols have common names that are accepted by IUPAC. For example:



ethylene glycol
or 1,2-ethanediol
(antifreeze)

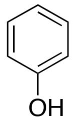


glycerol or glycerine
or 1,2,3-propanetriol
or propane-1,2,3-triol (better)

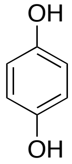
the freezing point is lower if mixed with water

Glycerol is a precursor to fats (fatty acid esters in cell membranes) and is used in personal lubricants such as KY jelly

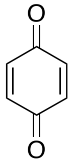
You need to know the following structures:



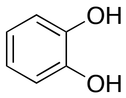
phenol



4-hydroxyphenol
or p-hydroxyphenol
or hydroquinone

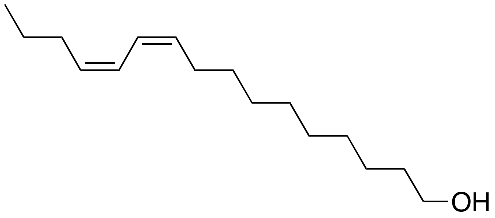


quinone



catechol

A nomenclature example is the name of the sex pheromone from the silkworm moth shown below.



hexadeca-10Z,12Z-dien-1-ol

The longest chain is 16 carbons long, which is a hexadecane. The *-e* ending is dropped, and replaced with *–ol* to become hexadecan-1-ol. There are two cis double bonds present at positions 10 and 12. This information allows the compound to be named a 10,12-diene. Putting the overall name together then gives hexadeca-10Z, 12Z-dien-1-ol.

This molecule was discovered by Adolf Butenandt in 1959.
The word pheromone comes from Greek pherein (to carry) and horman (excitement)

Physical Properties of Alcohols and Acidity

Look at the following comparisons:

Name	Methanol	Ethane
Formula	CH_3OH	CH_3CH_3
Molecular Weight (g/mol)	32	30
Boiling Point (° C)	65	-89
State (at room temp)	liquid	gas

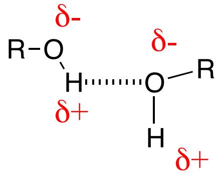
Ethane has almost the same molecular weight as methanol. However, the boiling point is much lower than methanol.

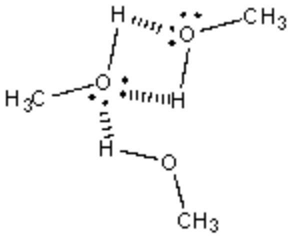
Similarly, propane has approximately the same molecular weight as ethanol, but the boiling point is significantly lower than ethanol:

Name	Ethanol	Propane
Formula	CH_3CH_2OH	$CH_3CH_2CH_3$
Molecular Weight (g/mol)	46	44
Boiling Point (° C)	78.5	-44.5

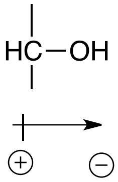
Why are the boiling points so different?
Answer: Alcohols are polar and able to form hydrogen bonds.

Hydrogen Bond





Dipole



Alcohols are strongly associated with each other both through dipole-dipole attraction (weaker intermolecular force) and hydrogen bonding (a stronger intermolecular force). The presence of the electronegative oxygen atom polarizes the bonds, and produces a dipole moment. The basic oxygen atoms also form partial bonds to the acidic hydroxyl hydrogens of another molecule (shown as dotted line in the figure above). Together, these factors raise the boiling points of alcohols far above their parent alkanes, with the hydrogen bonding being the most significant and powerful factor.

Review from previous section, there are **three** fundamental non-covalent bonding forces:

1. Hydrogen bonding (occurs with hydrogen attached directly to electronegative atoms such as O, N, or halogen). Linus Pauling described this.
2. Dipole-dipole interaction
3. London dispersion forces (temporary dipole interactions, which is the basis for hydrophobic forces). This is comparatively a weak intermolecular force on a per atom basis, but large hydrophobic (non-polar) sections of molecules interact strongly and can overcome hydrogen bonding between two atoms in the same molecules.

Physical Properties:

1. The **polarity** of alcohols make them quite soluble in (or miscible with) water if the number of carbons on the alcohol is less than 4. Butanol and higher alcohols are still soluble in water, but no longer infinitely miscible (completely soluble at all concentrations).
2. The **melting point** and **boiling point** for an alcohol is higher than its parent alkane (as seen from our comparison above).
3. The **density** of alcohol is less than 1 g/cm^3 (and hence less than water. If the given alcohol is not miscible with water (carbons >4), it will be floating on top of water)

ACIDITY

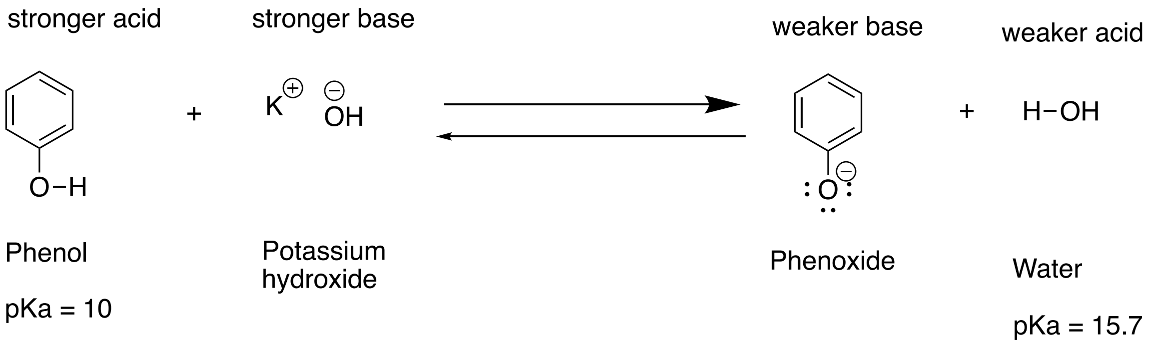
$$\mathbf{HA} \rightleftharpoons \overset{\oplus}{\mathbf{H}} \qquad :\overset{\ominus}{\mathbf{A}}$$

HA is the conjugate acid of A$^-$, and A$^-$ is the conjugate base of HA.

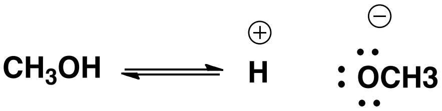
The equilibrium constant, or acidity constant, K_a, for this reaction can be expressed as:

$K_a = [H^+] [A^-] / [HA]$

For example: The dissociation of phenol



For example: the dissociation of methanol



$K_a = [H^+][CH_3O^-] / [CH_3OH] = 10^{-16}$

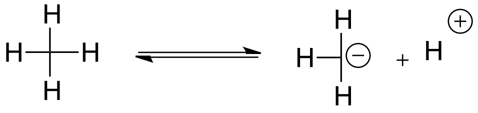
The oxygen of the OH group in methanol is partially negatively charged and the hydrogen is partially positively charged. The O-H bond is easy to break and it can break spontaneously. When methanol with OH is put in a solution of methanol with O-D (deuterium), the hydrogen will exchange rapidly against deuterium.

By analogy with pH, we can define a quantity pK_a, which is often used.
pK_a = -log K_a

Generally, the stronger the acid, the lower the pK_a.
The pK_a value for methanol is 16, for water is 15.7 (know these values). Since the pK_a value of water is less than methanol, the dissociation of methanol is harder than water and water is a stronger acid than methanol.

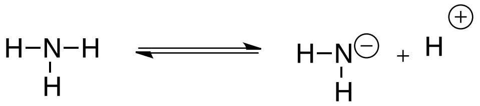
Remember that the pK_a and pK_w for water are not the same.
$K_w = [H^+][OH^-]$,
$K_a = [H^+][OH^-]/(H_2O]$

Examples:



The pK_a value of methane is about 46. It is not acidic.

What happens when we replace the carbon with nitrogen, a heteroatom?

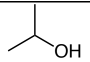
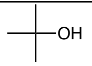


The pK_a value of ammonia is 36, which is 10 orders of magnitude (10^{10}) more acidic than methane. This is because the nitrogen atom is more electronegative than carbon and able to stabilize the negative charge better. However, ammonia is still a very weak acid. The acidity of ammonia (NH_3) should not be confused with the acidity of the ammonium ion (NH_4^+) which has a pK_a of 9.26.

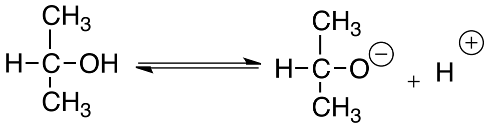
Based on pK_a *values, is oxygen more or less electron withdrawing than nitrogen?*
Answer: Oxygen is more electron withdrawing. It has lower pKa value, and is able to stabilize the negative charge more.

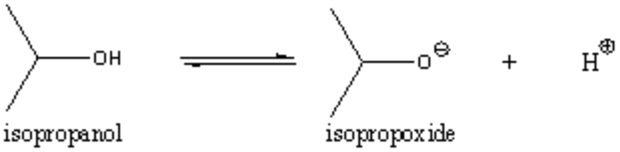
Name	Structure	pKa	Less acidic
methane	CH_4	46	
ammonia	NH_3	36	
water	HOH	15.7	
hydrofluoric acid	HF	3.2	More acidic

Recall from last term, **the stability of the conjugate anion determines the acidity of a compound**. The more stabilized the anion is, more acidic the molecule is.

Name	Structure	pKa	
methanol	$H_3C\text{-}OH$	16	More acidic
ethanol	$CH_3\text{-}CH_2\text{-}OH$	17	
isopropyl alcohol		18	
tert-butanol		19	Less acidic

What do these pK_a values mean in reactions?

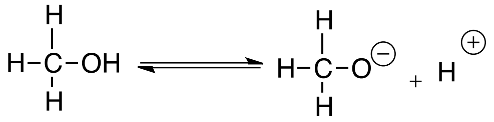




Isopropanol dissociates to from isopropoxide anion and a proton. However, the dissociation constant is 1 x 10^{-18}. Most of the molecules exist in the isopropanol form and only one part in 10^{18} is ionized. The equilibrium for this reaction lies far to the left.

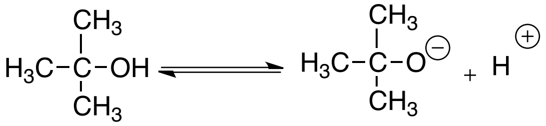
There are two alkyl groups attached to the central carbon bearing oxygen in isopropanol. The alkyl groups (methyls) donate electron density to that carbon (an inductive effect) that is already next to a negative charged center (O^-). Since negative charges repel each other, the anion is less stabilized. Therefore, the anion is even less likely to form (less stabilized than if the alkyl groups (methyls) in isopropanol were missing.

Methanol (pK_a 16) is 100 times (10^2) more acidic than isopropanol, since it has only hydrogens (a less donating group) attached to the carbon bearing the negative oxygen in the corresponding anion)



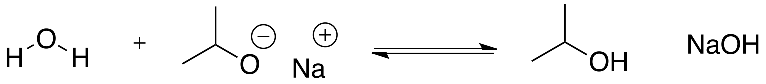
$$\mathrm{H{-}\overset{H}{\underset{H}{C}}{-}OH} \rightleftharpoons \mathrm{H{-}\overset{H}{\underset{H}{C}}{-}O^{\ominus}} + \mathrm{H^{\oplus}}$$

For *tert*-butanol (tert-butyl alcohol), there are three alkyl groups (methyls) that donate electron density to the carbon next to a negative charged group (inductive donation of electrons destabilizes the anion). Therefore, it is less likely to dissociate (pK_a 19) and the molecule is even less likely to ionize (less acidic).



$$\mathrm{H_3C{-}\overset{CH_3}{\underset{CH_3}{C}}{-}OH} \rightleftharpoons \mathrm{H_3C{-}\overset{CH_3}{\underset{CH_3}{C}}{-}O^{\ominus}} + \mathrm{H^{\oplus}}$$

Consider the example below:



Where does the equilibrium lie in the above reaction?
Answer: It lies far to the right.

The reaction of a stronger base (isopropoxide) **and a stronger acid** (water) **to a weaker base** (sodium hydroxide) **and weaker acid** (isopropanol) **is very fast**.