CHEM 321 Organic Chemistry I - Professor Kathleen Kilway

"Organic Chemistry" by Maitland Jones, 3rd edition

Chapter 6 – 1, 2, 4, 5, 7, 8, 14, 15, 19, 20, 21, 23, 24, 26, 27.

CHAPTER 6: ALKYL HALIDES, ALCOHOLS, AMINES, ETHERS, AND THEIR SULFUR-CONTAINING RELATIVES

Section 6.1

I. Preview

Section 6.2

II. Alkyl Halides: Nomenclature and Structure

A- Alkyl Halides

- a- Alkyl iodides, bromides, chlorides, and fluorides.
- b- They have the formula C_nH_{2n+1}, where X = F, Br, Cl, or I.
- c- Follow IUPAC rules for naming alkyl halides.
- a- Minimize the number given to the substituent.
- b- Name multiple substituents in alphabetical order.
- c- Names are based on longest straight chain that contains the halogen.
- d- Double bonds take precedence over halogen in assigning numbers.
- e- See Table 6.1 on page 233 for some examples.

4- Some common names that are often used:
- a- Haloform: CHX_3.
- b- Vinyl halides: $H_2C{=}CHX$.
- c- Allyl halides: $H_2C{=}CH\text{-}CH_2X$.

5- Allyl halides are classified as methyl, primary, secondary, and tertiary.
- a- See Figure 6.2 on page 234 for an illustration.
- b- CH_3X, CH_3CH_2X, $(CH_3)_2CHX$, $(CH_3)_3CX$

6- Alkyl halides are polar molecules and have a dipole moment.

7- The carbon to which the halogen is attached is approximately sp^3 hybridized.

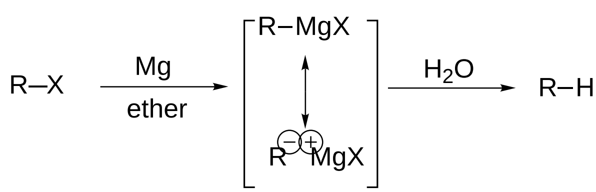
Section 6.3

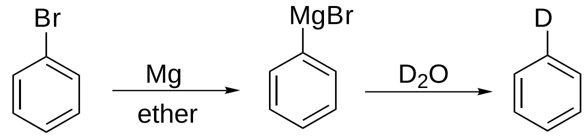
III. Alkyl Halides as Source of Organometallic Reagents: A Synthesis of Hydrocarbons

A- Organometallic Reagents

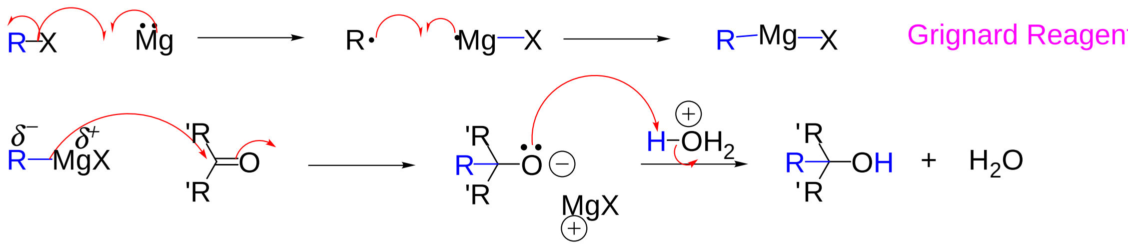
1- Molecules containing carbon-metal bonds.

2- Formed when an alkyl halide (X = Cl, Br, or I) is added to a cold mixture of magnesium or lithium and an ether solvent.





3- The end result is either a Grignard reagent (RMgX) or an organolithium reagent (RLi).
   a- See Figure 6.5 on page 236 for an example of a Grignard and an organolithium reagent.
   b- The mechanism of Grignard reagents involves a radical-transfer reaction in which a transient alkyl radical is formed in the presence of a magnesium-centered radical.
   c- See Figure 6.7 on page 237 for the mechanism with arrow formalism.

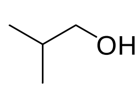


B- Reaction of Organometallic Reagents

1- Both organometallic reagents are strong bases.
2- They are sources of R:⁻.
3- Polar carbon-metal bond attacks Lewis and Brønsted acids.
   a- Water can be used to protonate a organometallic reagent.
   b- The product is a hydrocarbon.
   c- See Figure 6.9 on page 237 for an example of the reaction.

Section 6.4
IV. Alcohols

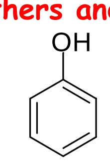
Remaining part of the chapter: Alcohols, diols, ethers and thiols
Section 6.4



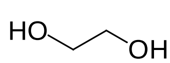
2-methyl-1-propanol

CH_3OH

methanol



phenol



ethylene glycol

R–O–R

ethers

R–SH

thiol

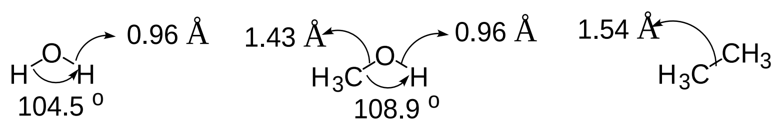
IV. Alcohols

A- Nomenclature

1- There are two ways of naming alcohols.
   - a- IUPAC system: drop final "e" of parent hydrocarbon and add suffix "ol".
     - i- OH takes precedence over other groups and is given the lowest possible number.
     - ii- The longest carbon is identified and substituents numbered appropriately.
   - b- Smaller alcohols (less than 5 carbons) are usually named by adding alcohol to the proper group name, (e.g. ethyl alcohol).
     - i- One exception: the correct name for hydroxybenzene is benzenol, but retains the common name of phenol.
   - c- See Figure 6.11 on page 239 for some examples.

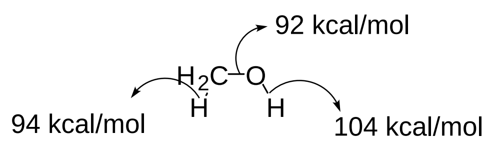
B- Structure of Alcohols

1- Alcohols are structurally similar to water.



C-O < C-C

   - a- Bond angle is slightly larger in alcohol: 109° in alcohol, 104.5° in water.
   - b- Bond length between O-H is almost the same.
   - c- Bond length between O-C is shorter than C-C in ethane.
     - i- Electronegative oxygen gives a stronger bond for O-C than C-C in ethane.
     - ii- An electron in an orbital near oxygen is more stable than it would be near carbon (Figure 6.14 on page 240).

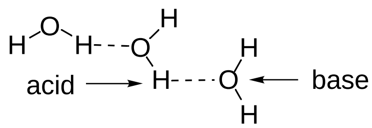


BDEs

C- Physical Properties of Alcohols

1- The electronegative oxygen causes strongly polarized bonds with substantial dipole moments.

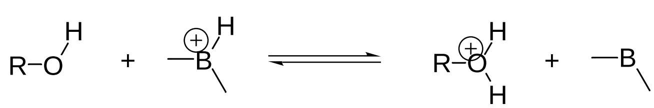
a- Alcohols are strongly associated in solution because of:
   i- Dipole-dipole interactions, and
   ii- **Hydrogen bonding**.



b- Alcohols and water are both Brønsted acid and Brønsted base.
   i- The basic oxygen partially bonds with acidic proton, causing boiling points to be much higher than parent alkane.
   ii- Alcohols are relatively water soluble, due to polarity.
   iii- See Table 6.3 for physical properties of alcohols (Compare with Table 2.4 on page 73).

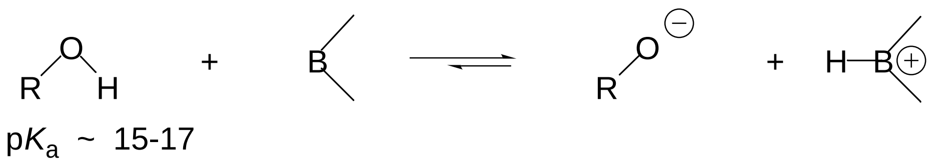
D- Acid and Base Properties of Alcohols

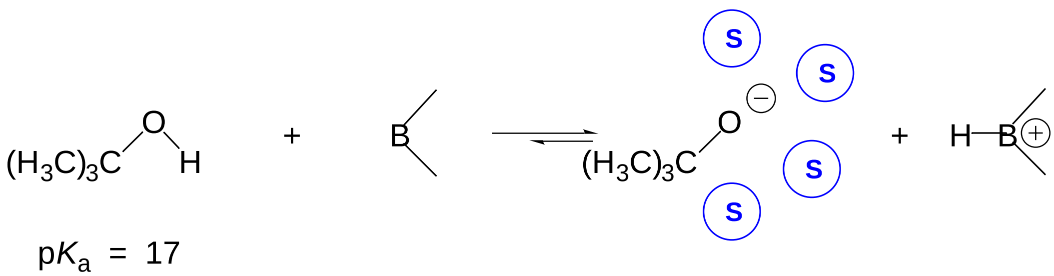
1- A Brønsted acid is any compound that can donate a proton.
   a- A Brønsted base is any compound that can accept a proton.
   b- Example:
      $K^+ HO^-$ + HCl   HOH + $Cl^- K^+$
      i- Brønsted bases: Cl^- and HO^-.
      ii- Stronger base HO^- wins the competition.
      iii- HCl is the conjugate acid of Cl^-, while Cl^- is the conjugate base of HCl.
2- Alcohols can act as Brønsted acids and bases.
   a- See Figure 6.18 on page 243.
3- Strong acids are better able to donate a proton than weaker acids.
   a- The stronger the acid, the lower the pK_a value.
   b- Table 6.4 on page 243 gives some examples of pK_a values.
      i- Acids with pK_a values lower than about +5 are regarded as strong acids; those with pK_a values below 0 are very strong acids.

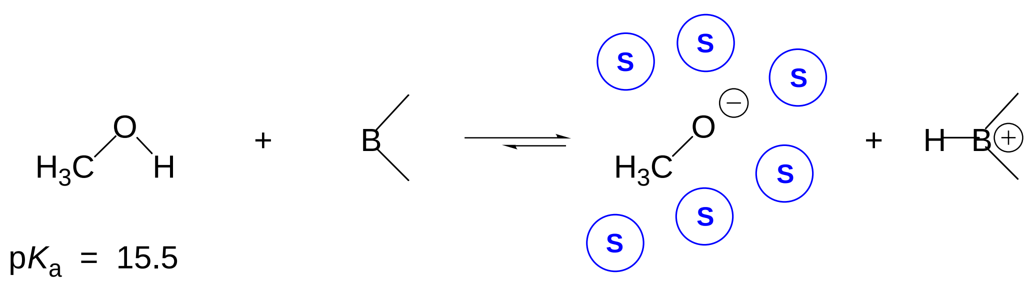


4- Brønsted basicity is centered on the lone-pair electrons of the oxygen atom.
   a- They want to bond to acids, including the O-H hydrogens of other alcohols (hydrogen bonding).
   b- Protonation of the oxygen gives an oxonium ion (RO^+H_2).
      i- See Figure 6.19 on page 244.
   c- HO^- is a poor leaving group, but after protonation HO^- becomes water (H_2O) and is a good leaving group.

5- Protonated alcohols are strong Brønsted acids.
   a- A very strong acid is required to protonate an alcohol.
   b- The conjugate base of the protonating acid must be a weaker base than the alcohol.
6- Oxonium ions are better proton donors than alcohols (See Table 6.5 on page 244).
7- Characteristics of Brønsted acidity depend on the hydroxyl hydrogen.
   a- Loss of this hydrogen to a Brønsted base gives an **alkoxide ion** (RO^-).
   b- Alcohols are similar to water in acidity (See Table 6.6 on page 245).
   c- Inductive effects are responsible for acidity in solvent, and alkyl groups seem to be electron-donating. Acidity decreases the more alkyl groups there are.
   d- In the gas phase, the alkyl groups seem to be electron-withdrawing, and acidity is reversed from the solvent phase.







Section 6.5
V. Solvents in Organic Chemistry

A- Polar Solvents

1- Solvation: stabilization by solvent.
2- Protic solvents: solvents that can donate a proton; usually quite polar.

3- Aprotic solvents: solvents without available protons; can be either polar or nonpolar.
4- Table 6.7 on page 247 gives some examples of polar solvents.

B- Solubility: "Like Dissolves Like"

1- Sodium chloride (Na^+Cl^-) dissolves in polar solvent water (H_2O), but nonpolar solvents cannot solvate ions efficiently and therefore don't dissolve Na^+Cl^-.
   a- See Figure 6.25 on page 248.
2- Hydrocarbons are insoluble in water, but are very soluble in other hydrocarbons.

Section 6.6

VI. Diols or Glycols

A- A diol or glycol (the common name for diol) is a molecule with two OH groups.

B- Naming

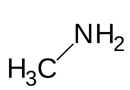
1- The final "e" of the alkane parent compound is not dropped and the suffix "diol" is added, (e.g. propanediol).

Section 6.7

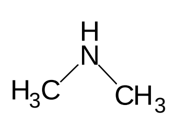
VII. Amines

A- Nomenclature

1- Parent of all amines: NH_3 is called ammonia.
   a- Successive replacement of the hydrogens leads to primary, secondary, and tertiary amines (NH_3, NH_2R, NHR_2, and NR_3, respectively).
   b- Quaternary nitrogen compounds are positively charged and are called ammonium ions ($^+NR_4$, tetraethylammonium chloride).
   c- See Figure 6.29 on page 249 for some examples.
2- Common names
   a- Primary amines are named by using the name of the substituent and appending the suffix "amine", (e.g. methylamine).
   b- Secondary and tertiary amines in which the substituent groups are all the same are named as di- and trialkylamines, (e.g. dimethylamine).
   c- Amines with different substituent groups are named by ordering the groups alphabetically, (e.g. ethylmethylamine).

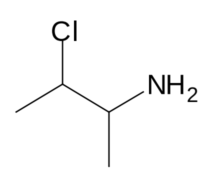


Methylamine
Methanamine
Aminomethane



Dimethyl amine

$N(CH_2CH_3)_3$
Triethylamine



2-Amino-3-chlorobutane

B- Structure and Physical Properties of Amines

1- Carbon-nitrogen bond distance is a little shorter than the corresponding carbon-carbon bond distance in alkanes.

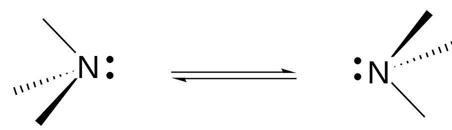
CH_3-OH (1.43 Å); CH_3-NH_2 (1.47 Å); CH_3-CH_3 (1.54 Å)

2- Simple amines are hybridized approximately *sp*^{3} at nitrogen and thus pyramidal.

3- The bond angles are close to the tetrahedral angle of 109.5°.

4- The pair of nonbonding electrons on nitrogen acts as a fourth substituent on the pyramid.

   a- Amines can undergo an "umbrella flip", amine inversion, forming the mirror-image pyramid.



   b- Figure 6.40 on page 253 illustrates the inversion process with planar transition state.

   c- Barriers to inversion in simple amines are very low, about 5-6 kcal/mol and therefore inversion is rapid (~5 kcal/mol for ethylmethylamine but 18.5 for 1,2,2-trimethylaziridine).

5- Amines have higher boiling points than hydrocarbons of similar molecular weight, because of hydrogen bonding.

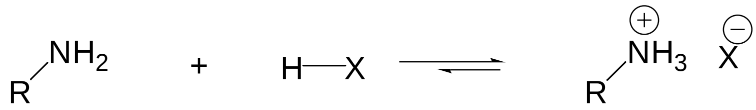
   a- See Table 6.8 on page 255 for some physical properties of amines and related alkanes.

6- Amines have a smell ranging from fishy to truly vile.

C- Acid and Base Properties of Amines

1- Amines are both Brønsted bases and nucleophiles.

   a- Brønsted basicity results in the formation of ammonium ions through proton transfer.



pK_a ~ 9-11

R = H; pK_a = 9.24
R = Me; pK_a = 10.63

b- See Figure 6.43 on page 256.

c- pK_a of ammonium ion is a common measure of the basicity of the related amine [$^+NH_4$ < $^+NRH_3$ < $^+NR_2H_2$ < $^+NR_3H$; from lowest pK_a to highest pK_a in gas-phase].

   i- Ammonium ions with high p$K_a$values (weak acids) are related to strongly basic amines.

   ii- Ammonium ions with low pK_a values (strong acids) are related to weakly basic amines.

   iii- Table 6.9 on page 256 gives pK_a values for some simple ammonium ions.

d- An irregular trend of basicity of amines in solution is observed.

   i- An alkyl substituent group stabilizes the ion by helping to disperse the charge.

   ii- But an alkyl group also destabilizes the ion by interfering with solvation.

   iii- These two effects operate in different directions, which leads to the observed irregular trend of basicity of amines in solution.

e- In the gas phase, basicity of amines increases with substitution (See Figure 6.45 on page 257).

   i- There is no solvation in the gas phase, therefore only the stabilizing effects remain.

$$HN(CH_2CH_3)_2 \xrightarrow{BuLi} Li^+\ {}^-N(CH_2CH_3)_2 + BuH\ (g)$$

pK_a ~36 pK_a > 50

2- Removal of a proton from an amine gives an amide in which the less electronegative nitrogen carries the minus charge.

   a- See Figure 6.50 on page 259.

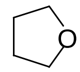
Section 16.8

VIII. Ethers

A- Nomenclature

1- Name the two groups joined by the oxygen in alphabetical order and add the suffix "ether", (e.g. ethyl methyl ether).

2- See Figure 6.52 on page 260 for some examples of ethers.

CH_3-O-CH_3	CH_3-O-CH_2CH_3	$(CH_3)_3C$-O-CH_3	
Dimethyl ether	Ethyl methyl ether	*tert*-butyl methyl ether	Tetrahydrofuran (THF)

B- Physical Properties

1- The polarity of ethers only affects the physical properties of the very smallest molecules in this class.

2- The larger ones have similar properties of the comparable alkane (See Table 6.10 on page 261).

C- Structure

1- C-O bond length is similar to alcohols.

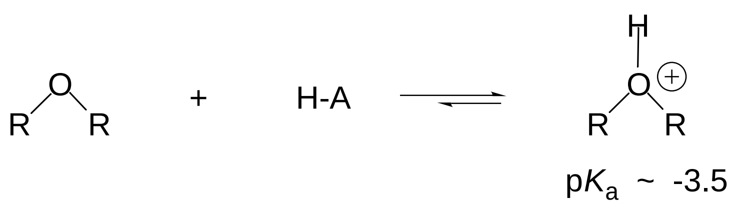
2- The R-O-R bond angle is ~112°, slightly wider than H-O-H (104.5°) and R-O-H (~109°).

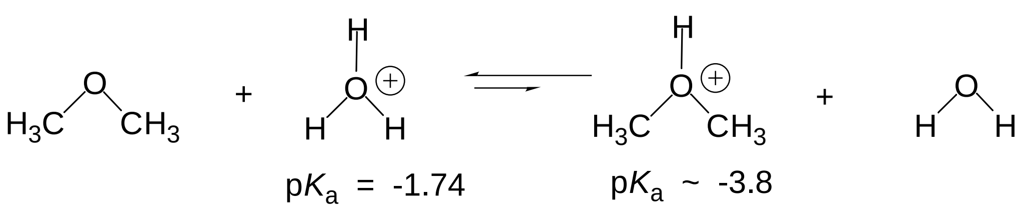
3- Oxygen is hybridized approximately sp^3.

D- Acidity and Basicity

1- Ethers are weak Brønsted and Lewis bases.

a- Protonated ethers have a pK_a similar to the comparable alcohol.





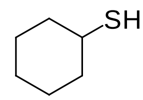
b- This means they are similarly strong bases (See Figure 6.53 on page 262).

2- The nucleophilic ethers are stabilizing to Lewis acidic species (e.g. Grignard reaction, page 236).

Section 16.9
IX. Special Topic: Thiols (Mercaptans) and Thioethers (Sulfides)

A- Nomenclature

1- Thiols are named by adding the suffix "thiol" to the parent hydrocarbon name. The final "e" is not dropped (e.g. methanethiol).

CH_3SH	$CH_3CH_2CH_2CH_2SH$	
Methanethiol (methyl mercaptan)	Butanethiol (butyl mercaptan)	Cyclohexanethiol

a- See Figure 6.56 on page 263 for an example.

2- The sulfur counterparts of ethers, **sulfides**, are named just like ethers (e.g. dimethyl sulfides).

CH_3SCH_3	$CH_3SHCH_2CH_3$
Dimethyl sulfide	Ethyl methyl sulfide

3- Disulfides are similar to peroxides and are named just like the sulfides. (See Figure 6.57 on page 263).

B- Acidity

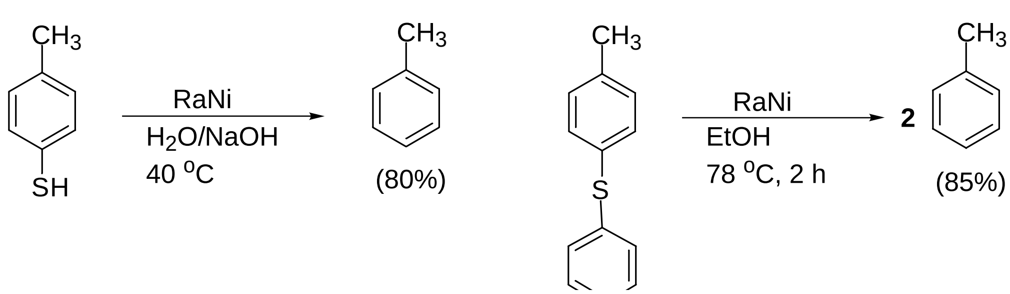
1- Thiols are stronger acids than alcohols (pK_a = 9-12).

$$\underset{pK_a = 10}{H_3C{-}S{-}H} + CH_3O^- \ Na^+ \rightleftharpoons H_3C{-}S^- \ Na^+ + \underset{pK_a = 15.2}{CH_3OH}$$

C- Reduction of Sulfur Compounds with Raney Nickel: A New Alkane Synthesis

1- The catalyst called Raney nickel reduces thiols and thioethers to produce alkanes.

a- See Figure 6.59 on page 264 for an example.



Section 16.10

X. Special Topic: Crown Ethers

A- Cyclic ethers have many uses

1- Cyclic polyethers have a somewhat crown-shaped structure and are called **crown ethers**.
2- They have the ability to capture certain metal ions, depending on the size of the cavity.
3- They are named by using the number of atoms in the ring first and the final number shows the number of heteroatoms in the ring, such as 12-crown-4.
4- Host-guest chemistry has exciting potential for research.

Section 16.11

XI. Special Topic: Complex Nitrogen-Containing Biomolecules - Alkaloids

A- Alkaloids

1- Any nitrogen-containing compound extracted from plants.
2- Among the most useful medicinal agents known.
   a- For example: morphine and quinine.
   b- But also addictive drugs: heroine and cocaine.
3- See Figure 6.64 on page 267 for some example pictures.