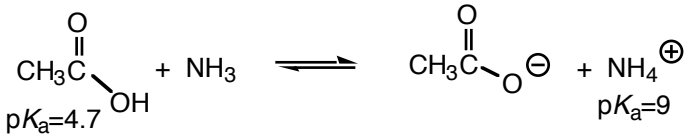
Name(s): _____ Section_____

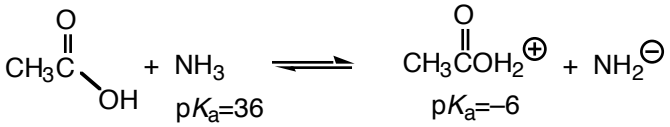
Chem 226 / Dr. Rusay
ORGANIC MOLECULES (III) WORKSHEET
Acids and Bases

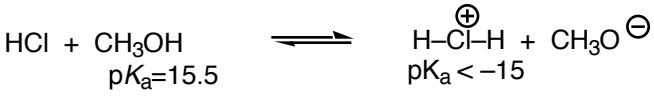
Turn-in answers neatly written on a separate piece of paper.

(Collaboration is encouraged. Turn-in one sheet per group being sure to list <u>all</u> collaborators who contributed.)

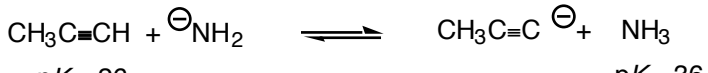
1. For each of the following reactions, designate the acids and the bases and use curved arrows to show the flow of electrons as the reaction proceeds from left to right. Circle the major species at equilibrium. Start by drawing complete Kekulé structures showing all bonding and nonbonding electron pairs at the reaction centers.

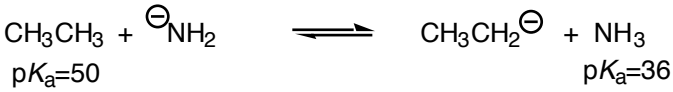
a. 

b. 

c. 

d. 

e. 

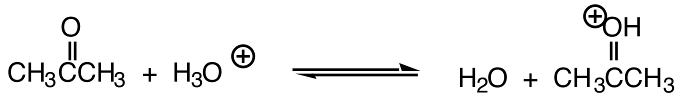
f. 

2. Draw complete Kekulé structures of reactants and products using lines for bonds, show nonbonding electron pairs, and indicate formal charges on atoms. Identify the acid and the base for each reaction. Use curved arrows to show the movement of electron pairs as the reactions proceed from left to right. Where appropriate identify and name the reactive species: carbocation, cabanion or free radical.

   a. $CH_3SCH_3 + BF_3 \rightleftharpoons (CH_3)_2\overset{\oplus}{S}{-}\overset{\ominus}{B}F_3$

   b. $^{\oplus}CH_3 + H_2O \rightleftharpoons CH_3\,\overset{\oplus}{O}H_2$

   c. $CH_3O^{\ominus} + CH_3SH \rightleftharpoons CH_3OH + CH_3S^{\ominus}$

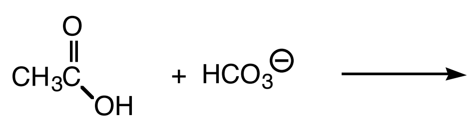
   d. 

   e. $HC{\equiv}C^{\ominus} + H_2C{=}O \rightleftharpoons HC{\equiv}C{-}CH_2{-}O^{\ominus}$

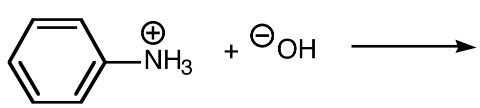
   f. $CH_2{=}CH_2 + HCl \rightleftharpoons {}^{\oplus}CH_2{-}CH_3 + Cl^{\ominus}$

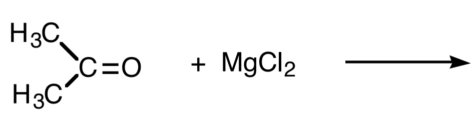
   g. $I^{\ominus} + CH_3Br \rightleftharpoons ICH_3 + Br^{\ominus}$

3. Predict the product(s) for the following reactions. The ideas that you used in the previous problems will be useful.

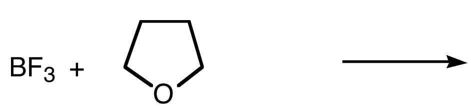
   a. 

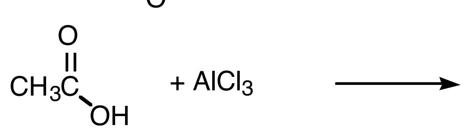
   b. $B(CH_3)_3 + (CH_3)_3N \longrightarrow$

   c. 

   d. 

   e. $H_2SO_4 + CH_3OCH_3 \longrightarrow$

   f. 

   g. 

4. For each of the following pairs, one reaction proceeds to the specified products and the other does not. Predict which is which and *clearly explain your choice*. It will help to start with curved arrows to show which bonds are made and which bonds are broken in each reaction.

a. $HO^{\ominus} + Br{-}CH_3 \longrightarrow HO{-}Br + {}^{\ominus}CH_3$

a 2. $HO^{\ominus} + Br{-}CH_3 \longrightarrow HO{-}CH_3 + Br^{\ominus}$

b. $H{-}C{\equiv}C^{\ominus} + H_2C{=}O \longrightarrow H{-}C{\equiv}C{-}CH_2{-}O^{\ominus}$

b 2. $H{-}C{\equiv}C^{\ominus} + H_2C{=}O \longrightarrow H{-}C{\equiv}C{-}O{-}CH_2^{\ominus}$

c, ${}^{\ominus}NH_2 + H{-}OCH_3 \longrightarrow H_2N{-}OCH_3 + {}^{\ominus}H$

c 2. ${}^{\ominus}NH_2 + H{-}OCH_3 \longrightarrow H_2N{-}H + {}^{\ominus}OCH_3$

5. Acid-Base chemistry is extremely important in medicinal chemistry and pharmacology. The basis of time release capsules relies on the stomach's highly acidic pH (~ 2-3) to dissolve a non-biologically active onion-like basic coating to release the active ingedient and then use the intestine's basic pH to dissolve a second acidic onion-like coating to continue the release of the active ingredient as it passes through the colon.

Chemically this is because:
Charged (ionized) molecules dissolve in water (eg. Salt, NaCl).
An acid in an acid solution will not ionize.
An acid in a basic solution will ionize.
A base in a basic solution will not ionize.
A base in an acid solution will ionize.

Now consider a drug, the active ingredient, not the biologically inactive layered acid-base binders, and the adage *oil and water don't mix*.

Ionized molecules = water soluble = poor absorption through tissue (such as the stomach or a placenta).

Non-ionized = lipid (oil) soluble = good absorption (Transports well across tissue membranes. Cell membranes are composed of lipids and remember "likes dissolve likes".)

A drug will not be absorbed or transported equally in the stomach, colon or blood depending on the drug's acid-base character, which can be determined from its pKa.

Basic Rules of acid-base drugs and their membrane penetration and transport

Comparing the pKa of a drug with its surrounding's pH (such as the stomach, pH<7, or the intestine, pH>7, or blood, pH≈7[though slightly greater], will determine the drug's behavior.

- *If pKa - pH = 0, then 50% of drug is ionized and 50% is un-ionized*
- *If pKa - pH = 0.5, then the solution is 75% ionized / 25% unionized or 75% un-ionized/ 25% ionized*
- *If pKa - pH > 1 then the solution is 99-100% ionized or 99-100% un-ionized*

Percent Ionized Formula

$$\frac{100}{1+10^{x\,(pH - Pka)}}$$

where x = -1 if the drug is acidic or 1 if basic

QUESTIONS:

Assume that the pH of the stomach is 2.5. The pKa of a general anesthetic, sodium pentothal, is 7.4 and it is acidic. If a patient is given sodium pentothal orally instead of *iv*, will it put the patient to sleep? *a)* Show your calculation to explain your answer, and *b)* Draw a line structure for sodium pentothal.

A basic drug has a pKa of 7.8 and is a known teratogen. If given *iv* to a pregnant woman whose blood pH is 7.4, will this drug cross the placenta and affect the baby? *c)* Define teratogen *d)* Show your calculation to explain your answer.