Background

In this lab you will be given a mixture containing two compounds. Your task is to separate the two components and, using an assortment of instrumental and wet chemical methods, unambiguously establish their identities. Although the process of elimination might sometimes lead you to correctly guess the unknown without having to perform extensive tests, we think that such an approach denies you valuable learning opportunities. Therefore we require that for each unknown you record and analyze the following data:

**Mandatory Instrumental Methods:** $^1$H NMR, $^{13}$C NMR, IR, GC/MS and, if the unknown is a solid, CHN analysis.

**Mandatory Wet Chemical Methods:** At least one confirmatory test for functional group and the preparation of a derivative. See below for more details.

In addition, you will need to determine relevant physical properties such as melting or boiling points for your unknowns and their derivatives.

Each unknown will contain only one major functional group. For example, you will not have an alcohol that also contains an aldehydic functional group elsewhere in the molecule. For our purposes, however, halides, carbon-carbon double and triple bonds, and aromatic rings are not considered unique functional groups, so you might have an alcohol which also contains a halide and/or a phenyl group as substituents, for instance. Furthermore, your mixture will not contain two acids, two bases, or two neutral compounds. You also will not have a mixture of a carboxylic acid and a phenol.

Separation Protocol

**Step 1:** Dissolve the mixture in 25 mL of dichloromethane and pour into a 125 mL separatory funnel. Extract the organic solution three times with 15 mL portions of 5% NaOH and separate the layers after each extraction. Set aside the organic layer. Combine the aqueous extracts, cool in an ice-water bath and carefully add 6M HCl until the solution is strongly acidic. You may then proceed as follows depending on the outcome of acidification.

(a) If a solid precipitate forms, filter and recrystallize from a suitable solvent. Meanwhile, proceed to step 3. OR

(b) If two immiscible layers are produced, extract the acidified solution with three 10 mL portions of dichloromethane. Combine the organic layers, dry over anhydrous Na$_2$SO$_4$, filter or decant, and remove the solvent using a rotary evaporator. Meanwhile, proceed to step 3. OR

(c) If you find no product, go to step 2, below.

**Step 2:** Extract the organic layer, that you set aside in step 1, three times with 15 mL portions of 5% HCl and separate the layers after each extraction. Combine the aqueous...
extracts, cool in an ice-water bath and carefully add 6M NaOH until the solution is strongly basic. You may then proceed as follows depending on the outcome of basification.

(a) If a solid precipitate forms, filter and recrystallize from a suitable solvent. Meanwhile, proceed to step 3. OR

(b) If two immiscible layers are produced, extract the basified solution with three 10mL portions of dichloromethane. Combine the organic layers, dry over anhydrous Na$_2$SO$_4$, filter or decant, and remove the solvent using a rotary evaporator. Meanwhile, proceed to step 3.

**Step 3:** Wash the organic layer remaining after the acid or base extraction with two 10 mL portions of water followed by one 10 mL portion of saturated NaCl (brine). Dry the organic layer over sodium sulfate, filter or decant, and remove the solvent using a rotary evaporator.

**A. Physical Characteristics (Record for Each Unknown)**

1. Solid or liquid
   - Color
   - Odor

2. Boiling or melting point. Take care that an accurate measurement is made and that you report your value as a range. This becomes an important clue to the identity of your unknown.

**B. Functional Group Tests (Always run a known compound along with your unknown to make sure that the test itself is working properly.)

1. **Aromatic Ring**
   Aromatic compounds often burn with a sooty flame. The presence of heteroatoms (such as oxygen) may result in a negative test, even though the compound is aromatic.
   
   *Place a small amount on a spatula and put the tip into a flame.*
   *(BACK HOOD ONLY)*

   The following tests can be done on spot plates:

2. **Unsaturation (for alkenes or alkynes)**
   The color of a dilute bromine solution should be discharged.
   
   **CAUTION! Avoid getting bromine on your skin. Do not breathe vapors.**
   
   *Dissolve a drop (or a few crystals) of your unknown in a mL of dichloromethane. Add a drop of bromine solution.*

3. **Aldehydes and Ketones**
   a. Preparation of a 2,4-dinitrophenylhydrazone. A positive test is the immediate formation of a yellow to red precipitate.
   
   **CAUTION! Contains sulfuric acid. Handle with care.**
Dissolve a small amount of your compound in a minimum amount of 95% ethanol, then add a small amount of the 2,4-dinitrophenylhydrazine (2,4-D) solution.

b. Chromic acid oxidation. This test differentiates between aldehydes and ketones. Aldehydes react to give an immediate green precipitate, but ketones do not react. The first step is the formation of a chromate ester, followed by an elimination reaction. For the reaction to proceed, there must be a hydrogen on the carbon bearing the oxygen atom (see 5. Alcohols as well).

**CAUTION!** Strongly acidic. Chromium reagents are strong oxidizing agents and toxic. Handle with care.

Add a small amount of your unknown to acetone in one of the wells of a spot plate. Add a few drops of the chromic acid reagent (Jones Reagent).

4. Phenols

Most phenols are only weakly acidic. They do not react with bicarbonate, but will react with sodium hydroxide. A colored (gray-purple) complex is formed in a reaction with ferric chloride. A brown, ferric chloride colored, solution or precipitate is NOT a positive test.

Dissolve a few drops (or crystals) of unknown in dichloromethane. Add a drop of pyridine and a couple of drops of iron(III) solution.

5. Alcohols

Chromic acid will oxidize primary and secondary alcohols. Tertiary alcohols do not react. See 3b.
C. Preparation of Derivatives

Once you know the functional group in your compound, you need to characterize it by preparing a derivative.

1. Alcohols and Phenols
   A 3,5-dinitrobenzoate derivative usually provides a solid compound having a characteristic melting point.

   ![Chemical reaction]

   Place about 0.5 gram of 3,5-dinitrobenzoyl chloride in approximately 1.5 mL of dry pyridine. Add about 0.5g or 0.5 mL of alcohol or phenol, and heat for 10 - 15 minutes. Cool the mixture, and pour into a solution of 3 mL of 5% sodium bicarbonate, 3 mL of water, and some crushed ice. Keep the mixture cool until a product crystallizes. Collect and recrystallize from ethanol-water as follows. Add enough hot ethanol to dissolve the compound; allow to cool. If crystallization does not take place, add water a drop at a time until the solution becomes cloudy.

2. Aldehydes and Ketones
   Prepare a 2,4-dinitrophenylhydrazone.
   On a larger scale than your spot test (see 3a. of Functional Group Tests), prepare enough of the derivative to recrystallize and take its melting point. Ethanol-water is often used for recrystallization.

3. Carboxylic Acids
   Prepare an amide derivative.
   CAUTION! Thionyl chloride is a lachrymator. It reacts violently with water to give HCl.

   ![Chemical reaction]

   Under your hood, add about 0.5g of the acid to about one mL of thionyl chloride. Heat under reflux for 30 minutes. Cool. Still under the hood, pour the reaction mixture into a beaker containing about 5 mL of cold concentrated ammonia (ammonium hydroxide) solution. Note: Your product should be the solid material in your beaker, not the white solid (NH₄Cl) that may deposit on the glass above the solution. The product can be recrystallized from ethanol - water.

   OR
Prepare an anilide derivative. On occasion, amide derivatives are difficult to prepare successfully. If you wish, you may try to prepare an anilide instead.

Follow the procedure for converting your acid into its acid chloride as outlined for the amide derivative. Cool the mixture and carefully and add to it 1 gm of aniline which has been dissolved in 25 mL of toluene. Warm for about 5 minutes on a hot plate, then transfer to a separatory funnel. Wash this solution sequentially with 5 mL of water, 5 mL of 5% HCl, 5 mL of 5% NaOH, and finally with another 5 mL water. Dry the toluene layer over anhydrous Na₂SO₄ and evaporate to dryness. Recrystallize the resulting anilide from water or ethanol-water.

4. Amines
Prepare a picrate derivative.

CAUTION! Dry picric acid explodes above 300°, or by percussion.

Dissolve about 0.2g of your compound in a minimum of ethanol. Slowly add about 5 mL of a solution of saturated picric acid. Collect the product by vacuum filtration, and rinse with cold ethanol.
(1) Review the Chemically Active Extraction experiment from last semester. Prepare a flow chart that clearly outlines the separation protocol for your mixture of unknowns.

(2) Answer the following questions.
   (a) Meredith and Greg have an unknown that is either a ketone or an aldehyde. What signal in a $^1$H NMR spectrum could distinguish between an aldehyde and a ketone?
   
   (b) Jenny and Justin also have either an aldehyde or a ketone. Which wet chemical test differentiates between these two compounds?
   
   (c) The IR spectrum of Graham and Margaret’s unknown shows a strong, sharp peak at 1725 cm$^{-1}$. Disregarding any other peaks that may be present, name four functional groups that might give this peak.
   
   (d) Ivan and Stan have either an alcohol or a phenol. Their proton NMR shows a doublet at 1.3 ppm, a septet at 2.8 ppm, a doublet at 3.7 ppm, and a singlet at 4.1 ppm. Do they have an alcohol or a phenol? How did you decide on your answer?
   
   (e) Amy and Andrew have an alcohol. What kind of derivative should they make?
   
   (f) Nick and Eric were accidentally given a double unknown containing a carboxylic acid and a phenol. How can they separate this mixture? Briefly explain your reasoning. [HINT: Carboxylic acids are considered strong organic acids, and most phenols are considered weak organic acids.]
   
   (g) DMT and JPMe really messed up! They inadvertently put the product of their acidic extraction into the waste container under the hood (at least they didn’t throw it down the sink!). The label on the container indicated that the bottle already contained fluorene, fluorenone, benzoic acid and biphenyl. Would they be able to successfully extract that mixture and recover their product? Why or why not?
REPORT

MIXTURE CODE: __________

Provide the following information for each unknown
(Do not use the same form for both unknowns)

A. Physical Characteristics

1. Solid or liquid

Color

Odor

2. Boiling or melting point. Take care that an accurate measurement is made and that you report your value as a range.

GENERAL SCHEME OF SEPARATION

FUNCTIONAL GROUP TESTS
Results:
DERIVATIVE
Results:

NMR (submit copies of the $^1$H and $^{13}$C NMR spectra)

IR (submit a copy of the spectrum)

GC-MS (submit a copy of the printout)

CHN Analysis (for solids only, submit a copy of the printout)
UNKNOWN IS: