Exp 2 – Acid-Base Extraction and Isolation of Excedrin Components

Reading Assignment: Mohrig Chapter 10.1-10.5 (Extraction)
Review Topics: Drying agents (Chapter 11), TLC (Chapter 18)

The solubility of organic compounds is primarily dependent on polarity. The "like dissolves like" rule applies in most cases – polar compounds dissolve in polar solvents and non-polar compounds dissolve in non-polar solvents. It is safe to assume that most organic compounds of medium to low polarity are insoluble in water. More polar compounds like alcohols are more likely to be soluble in water, but are only sparingly soluble when there are six or more carbons present in the molecule. In this lab, students will carry out simple acid-base extractions to effect the separation of Excedrin components. Excedrin is an over-the-counter analgesic containing the active ingredients aspirin, caffeine, and acetaminophen.

Acids (HA) react with bases (B) to form a conjugate base (A^-) and a conjugate acid (^+BH). It is likely that one or both of the products are ionic compounds, making them significantly more soluble in water than their non-charged counterparts. In this experiment, we will learn how to take advantage of this change in solubility for the separation of a mixture of acids and bases.

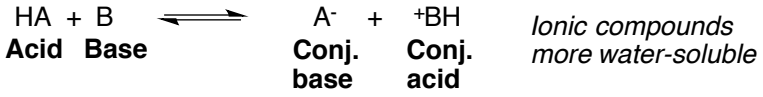


Figure 1. A general acid-base reaction.

The functional groups of interest in organic acid-base chemistry are strongly acidic carboxylic acids, weakly acidic phenols, and basic amines. Carboxylic acids are deprotonated equally well by weak and strong bases such as $NaHCO_3$ and NaOH, respectively. The by-products are different but both reactions form a **sodium carboxylate salt**, which is likely water-soluble (**Figure 1a**). Phenols do not react with $NaHCO_3$ and instead require a strong base for reaction to occur, resulting in a water-soluble **sodium phenoxide salt** (**Figure 1b**). Amines react with strong acids to form water-soluble **ammonium chloride salts** (**Figure 1c**).

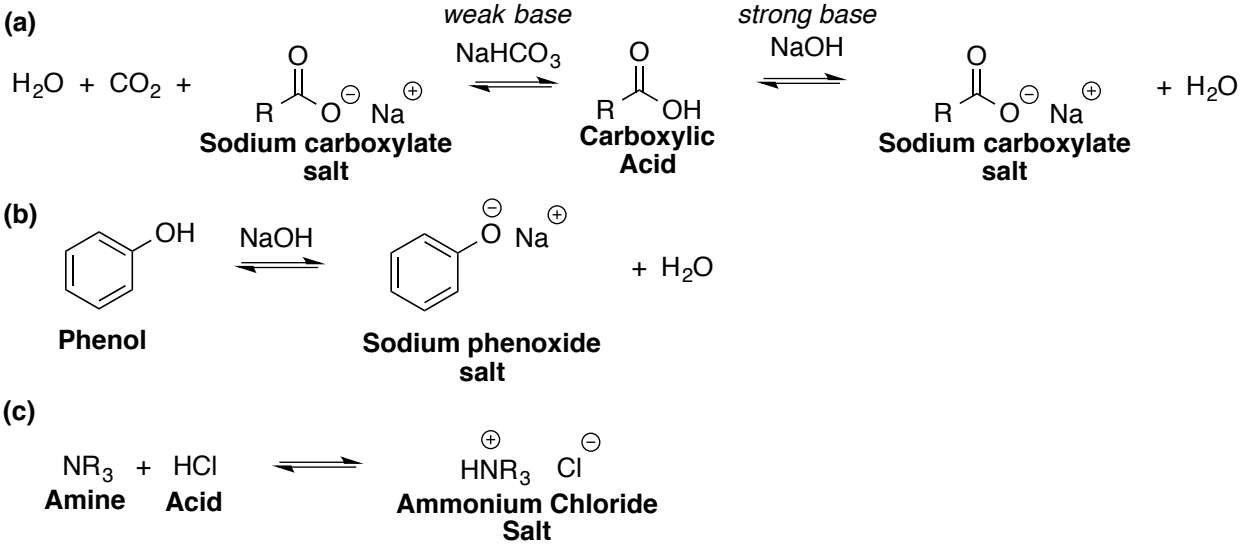


Figure 2. Reactions between **(a)** carboxylic acids with a weak and strong base; **(b)** phenols with a strong base; and **(c)** amines with a strong acid.

When both acids and bases are present in a mixture, a liquid-liquid extraction is carried out and one of the reactions above is performed. It would be wise to review your notes from the caffeine extraction lab in CHEM 8L! The mixture is dissolved in an organic solvent and a solution of either acid or base is added. The unreacted component is extracted in the organic layer and the reacted component, a salt, is transferred to the aqueous layer.

Suppose you're separating a mixture containing a carboxylic acid and an amine. The extraction can be started in one of two ways: (1) react the carboxylic acid with a base or (2) react the amine with an acid. Either way will theoretically work, but let's work through the example that starts with an acidic extraction (**Figure 3**).

The mixture is dissolved in an appropriate organic solvent, in this case dichloromethane (DCM), and this solution is extracted three times with aqueous HCl. The organic layer (**ORG_{acid}**) contains unreacted carboxylic acid and the acidic aqueous layer (**AQ_{acid}**) contains the ammonium chloride salt. The carboxylic acid can be isolated by drying ($MgSO_4$) and concentrating (rota-vap) the organic layer. The ammonium salt, however, must be deprotonated before isolation so a second acid-base extraction is performed. A solution of NaOH is added to make the aqueous layer basic, thus deprotonating the ammonium salt back to its neutral amine form. The basic aqueous layer (**AQ_{base}**) is then extracted three times with DCM. The organic layer (**ORG_{base}**) contains the amine, which is isolated after the solution is dried and concentrated.

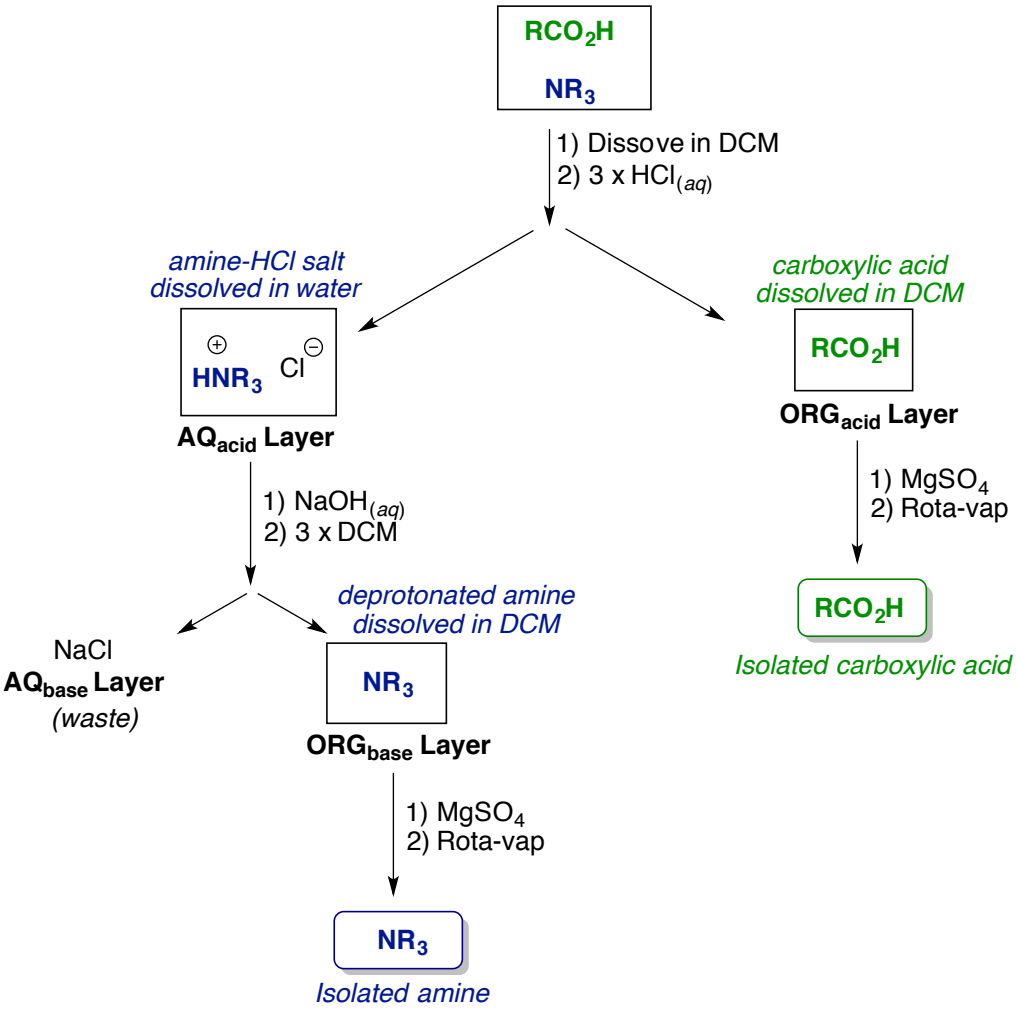
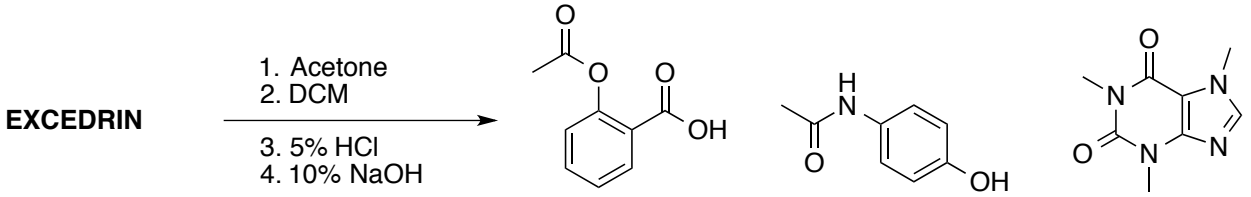


Figure 3. Flow chart for the acid-base extraction of a carboxylic acid from an amine.

A similar procedure will be carried out in the separation of the three active ingredients in Excedrin. Keep in mind that in each extraction, there is no guarantee that 100% of the compounds end up in the expected layer (refer to the reading on Partition Coefficients). Three extractions are carried out to maximize yield. TLC will be used to determine the effectiveness of the separation of each component and IR spectroscopy will be used to confirm the identity of each compound.

Notebook Preparation

- *Purpose* – one-sentence description of the purpose in addition to the following scheme:



- *Reagent table* – Amount (mg or mL), MW, bp or mp, density, and one-word hazards found in the clean-up/safety table for each of the chemicals in the scheme above. For Excedrin, list only the amount to be used and leave space to write down the actual mass used in lab.
- *Procedure* – hand-written, step-by-step procedure. **Copy the completed flow charts from lecture into your notebook after the extraction procedure** (blank Lecture 2 handout online). Include a list of materials (chemicals, labeled glassware, equipment, etc.)
- *Safety & Clean-up* – copy the table at the end of the procedure into your notebook.

EXPERIMENTAL PROCEDURE – Students work in pairs

**This experiment includes many different clear, colorless liquids. Containers must be labeled with the contents, your initials, and experiment date before the material is inside.

ACID-BASE EXTRACTION ***Frequently refer to flow charts along with written procedure.***
Active ingredients in Excedrin: *"The active ingredients in Excedrin were separated,…"*

Weigh a single tablet of Excedrin or copy the mass of a tablet from the board. You will need approximately 1.5 tablets for the experiment (three tablets between you and the pair next to you). One pair will grind two tablets and the other will grind one tablet using a mortar and pestle. Do your best to not make annoying tapping sounds! Weigh out *approximately 1 g* of powder onto a piece of tared weighing paper folded on a diagonal, borrowing from the pair that ground two tablets if needed, and record the mass. Do not dispose of the Excedrin powder until you are sure other groups have what they need. Transfer the powder into a dry screw-cap test tube (check that it's clean, wash & dry only if needed). Add 10 mL of acetone, cap the tube, and mix well for 5 minutes with frequent venting to ensure the bulk of the tablet has dissolved. Filter the acetone-insoluble inactive ingredients (tablet binder) using a pipet with small cotton plug into a pre-weighed 25-mL round bottom flask (RBF). Use an additional 1 mL of acetone to rinse the test tube and pipet.

Transfer a few drops of the filtrate (liquid) to a capped vial labeled "ORIGINAL MIXTURE + (your initials) + (date)" and keep for TLC analysis next week. Evaporate the remaining ORIGINAL MIXTURE using a rota-vap and record the mass of the concentrated extracts, containing aspirin, caffeine, and acetaminophen. Compare this to the expected mass of active ingredients (in-lab #1) to determine percent recovery (in-lab #2). Your TA will perform and demonstrate the first time you need to use the rota-vap. Please pay attention to these instructions, as you will need to do this independently later in this experiment.

Isolation of Acetaminophen:
"…acetaminophen was filtered from a solution in DCM,…"

Acetaminophen is insoluble in DCM and this will be used to your advantage! Add 15 mL of DCM to the solid residue in the RBF. The aspirin and caffeine in the mixture will dissolve but acetaminophen should remain in suspension. After swirling the flask for 5 minutes, use a pipet to transfer the suspension to a vacuum-filtration apparatus with pre-weighed filter paper. Wash the walls of the flask with an additional 1-2 mL of DCM and transfer the rinses to the filter. Only turn on the vacuum enough to allow the solvent to run through. If the vacuum is too high, you will evaporate the DCM and will need to add more to re-dissolve aspirin and caffeine. Obtain the mass of the solid then transfer and save in a capped vial with the label "ACE."

Acidic Extraction of Caffeine from Aspirin: *"…and an acid-base extraction was carried out with aqueous HCl and NaOH to separate caffeine from aspirin."*

Acidification and Extraction of Caffeine (refer to flow charts and written procedure)

Perform this step in the fume hood. *Demonstrate proper mixing and venting to your TA using water in a separatory funnel before proceeding.* Use a pipet to transfer the contents of the filter flask into a 125-mL separatory funnel and extract the organic layer with 3 x 7 mL of 5% $HCl_{(aq)}$ according to the following procedure: Add 7 mL of 5% HCl, cap the funnel, and invert repeatedly (~20 times) with *frequent* venting. Accidents happen when students do not vent early and often. To vent, turn the funnel upside-down and open the stopcock *with the tip pointing away from your face* and into the hood. Drain the lower organic layer and place it in a 50-mL Erlenmeyer flask labeled "ORG - ASP." Drain the remaining aqueous layer into a 50-mL beaker labeled "AQ - CAF." Transfer the DCM layer back into the funnel and extract it two more times with 7 mL of the HCl solution. Collect all the aqueous layers in the "AQ - CAF" beaker. The protonated caffeine should be in the aqueous layer and neutral aspirin in the organic (DCM).

Isolation of Aspirin

Dry the DCM layer (ORG – ASP) with a couple microspatula-fuls of $MgSO_4$. This should create a snow-globe effect after mixing the appropriate amount. Wipe down the counter to clean up the inevitable snowstorm that occurs near the $MgSO_4$ containers. Allow the solution to dry for about 5 minutes covered in the fume hood. In the meantime, move on to the neutralization step below. Filter through a pipet with a *loose* cotton plug into a dry and pre-weighed RBF. Concentrate using the rota-vap and record the mass of aspirin. *Accurate self-assessment* – ask your TA for help if unsure of how to use the rota-vap. Transfer the solid to a capped vial labeled "ASP." It will not be possible to scrape out every bit of solid from the RBF. Do your best!

Neutralization and Isolation of Caffeine

Treat the acidic "AQ - CAF" layer with 10% $NaOH_{(aq)}$ until the pH is basic (>10). **DO NOT DUNK** the pH paper into the solution as the dyes will leach into your sample. Place a few small pieces of pH paper on a watch glass. Dip a stir rod into the solution then touch it to the pH paper. Extract the aqueous layer three times with 10 mL of DCM in the separatory funnel. Use the same precautions as above – inverting repeatedly with frequent venting into the fume hood. Take your time in between separation - caffeine does not instantly transport itself from the aqueous to organic phase! Collect all the organic layers in an Erlenmeyer flask ("ORG – CAF"). Dry with $MgSO_4$ and filter after 5 minutes using a glass funnel with loose cotton plug. Collect the filtrate in a pre-weighed RBF and evaporate the solvent using a rota-vap. Weigh the product and transfer to a vial labeled "CAF." **Check the drawer equipment list and go through the contents with the TA before leaving (2 points per missing, extra, or dirty item).**

Copy the completed flow charts (lecture 2 handout) into your notebook here (after the extraction procedure). The underlined parts of the procedure above are described in the lecture handout using diagrams of separatory funnels, beakers, and flasks.

ANALYSIS:

"The identity of each component was confirmed by TLC, IR, and melting point analysis."

Time permitting, melting points and some IR spectra may be obtained in the first week then continued in the second week. Pay close attention to timing and stop wet lab work at least 20 minutes early to leave time for clean up. Legally, no students can be present in the lab after the scheduled lab period. TLC must be completed during the second week of the experiment.

Melting point – Obtain the melting point of acetaminophen and aspirin only.

IR – Follow TA instructions on facilitating a proper rotation for students using the IR spectrometer (sign-up sheet on the board). Obtain the IR of each fraction using a Nujol mull (grind the mull for at least one minute). Honest self-assessment – ask the TA for a refresher on how to use the IR if needed.

TLC (week 2, fume hood only)

In separate, labeled test tubes, make solutions of each of the solid extracts from week 1 in acetone (pick up a little solid with the tip of a microspatula and add about 1 mL of acetone): ACE, ASP, and CAF. You will analyze these extracts alongside the standards provided and the ORIGINAL MIXTURE from the beginning of week 1. A few students can make standard solutions in clearly labeled test tubes to share with the rest of the section, leaving these test tubes in the reagent hood until the end of the lab. The ORIGINAL MIXTURE need only be spotted once.

Carefully but quickly spot the TLC plates with 2 lanes per plate at the origin using a capillary tube (not a melting point capillary). Best results are obtained when the spots are very small and tight – one spot per sample – and when the plate is very carefully placed into the jar without disturbing the solvent. Rinse the capillary to prevent cross-contamination by dipping it into acetone then pressing onto a kim wipe several times in between samples. Before placing the plate in the developing chamber, visualize the spots with a UV lamp to ensure you added enough sample.

Using tweezers, carefully place the TLC plate into the developing chamber. Be sure not to disturb the mobile phase as the sample should not dissolve in the solvent. Allow the TLC plate to run until the solvent is approximately 1 cm from the top of the plate. Remove the plate with tweezers, quickly draw the solvent front on the plate, and wait until the solvent evaporates before visualizing with the UV lamp. Circle the spots, calculate all R_f values, then dispose of the plates in solid waste.

Before leaving week 2: Check with your TA to be sure you've completed your analysis and NMR problems (see next page). Also, check the drawer equipment list and go through the contents with the TA before leaving (3 points per missing, extra, or dirty item this week).

Table 1. Clean-up and Safety

Clean-up – leave the lab as you found it!	**Safety**
Glass waste: uncontaminated pipets only	HCl and NaOH are *corrosive & toxic*.
Liquid waste: contents of rota-vap trap, TLC solutions	Acetone, DCM, and ethyl acetate are *flammable*. Caffeine is a *stimulant* and is NOT to be ingested or taken home.
Solid waste: filter paper, used pipets	DCM is a *potential carcinogen*.
Product waste bag: product vials	Do not look directly into the UV lamp.

Palleros, D. R. *Experimental Organic Chemistry*, Wiley: New York, **2000**; pp. 255-257.

Introduction: Pre-Lab Questions, Week 1

1. Classify the following compounds as acidic, basic, or neutral: acetaminophen, aspirin, and caffeine. Name the functional groups present in each molecule and determine which ones affect their acid-base properties.

2. Which would be more effective in separating aspirin from acetaminophen: $NaHCO_3$ or NaOH? Include a chemical reaction as part of your answer (hint: see **Figure 2**). Indicate whether each of the products of the acid-base reaction would be in the aqueous or organic layers.

3. What role does HCl play in the extraction of caffeine? Include a chemical reaction.

4. Could a mixture of salicylic acid and aspirin be separated by acid-base extraction? Explain.

Week 2

*** Re-produce 3 copies of the following table in your lab notebook**, one per compound, and fill in all but the observed stretches. You will not be permitted into the lab without these tables.

Table x. IR Analysis of (Compound Name)

Functional Group	**Bond**	**Expected (cm^{-1})**	**Observed (cm^{-1})**

(add more rows as needed)

****** Bring a **draft of the abstract using the results obtained thus far** (*5 points* for bringing a reasonable draft – typed or hand-written is OK). Use the technical writing guidelines in addition to the lab-specific details below.

- The purpose of this experiment was to _____ so that _____.
- The procedure sentences are written for you in quotes on the previous pages!
- The main results for this experiment are the recoveries of each component (mg and %) along with a statement reflecting whether each sample was pure/as expected by TLC and IR analysis. It is not necessary to list the R_f values or IR stretches in the abstract.
- The conclusion sentence should tie the theory behind the experiment (acid-base extraction) back to the results: did the acid-base extraction effectively separate the mixture as expected?

******* Complete **problems 14,16,17,18** in **Chapter 13** of McMurry's Organic Chemistry, 8th Edition. This can be started before lab and shown to your TA for credit before leaving (*5 points*). These NMR spectroscopy problems are unrelated to the Excedrin lab, but will be a useful introduction to this form of analysis in future labs.

Results: In-Lab Questions

1. Each Excedrin tablet contains 250 mg aspirin, 250 mg of acetaminophen, and 65 mg of caffeine. Calculate the theoretical % recovery of each component using the mass of one whole tablet. **These expected recoveries (mg and %) should be reported in the abstract conclusion.**

Th. % Recovery of Aspirin = (250 mg / xx mg tablet) x 100%

2. Report the mass of the solid mixture after evaporation of acetone. Compare this mass with the combined amount of acetaminophen, aspirin, and caffeine that should be present in 1 g of Excedrin powder. Was the solid-liquid extraction of the active ingredients effective?

3. Report the masses of acetaminophen, aspirin, and caffeine after isolation, including estimated uncertainty in balance measurements (ILE). Calculate the % recovery of each component from the initial amount of Excedrin used (~1 g). **These recoveries (mg and %) should be reported in the results sentence of the abstract.** Compare to in-lab #1 and list the specific part(s) of the procedure where product may have been lost.

4. Report the melting points of aspirin and acetaminophen. Compare to literature values. Are your samples relatively pure?

5. Report and discuss the TLC results. Make a table with the R_f values for each spot in each sample. Identify each spot as caffeine, aspirin, or acetaminophen. Was the separation effective?

6. Interpret the IR spectra of aspirin, acetaminophen, and caffeine. Reproduce the IR tables into the word processing document (no hand-written tables in the results section). Use no more than three sentences to describe how the IR spectra can be used to positively identify the compound present in the solid.

Exp 2 - Acid-Base Extraction (Excedrin) Name _____
Due Date in Syllabus

Section Day _____ Time _____ TA Name _____

CHEM 8M GRADING RUBRIC - Use as cover page for report

SECTION	INSTRUCTOR COMMENTS	POINTS ASSIGNED
IN-LAB QUIZ		**/ 5**
LAB REPORT		
ABSTRACT One paragraph, typically four-six sentences: Purpose, procedure, main result(s), and conclusion(s).		**/ 30**
INTRODUCTION Each pre-lab question is addressed in its own paragraph using complete sentences. Structures and calculations are hand-written, where appropriate.		/ **40**
RESULTS The main results are stated, as outlined in the in-lab questions, using complete sentences.		/ **50**
EXPERIMENTAL SECTION The experimental details (including final amount used and obtained) are *briefly* described in a few sentences.	NONE	0 / 0
NOTEBOOK PAGES Proper format: reaction scheme, chemical info table, procedure, flow charts, waste and clean-up procedure.		/ **30**
NEATNESS AND ORGANIZATION Proper grammar and format per instructions in syllabus and writing guidelines		**/ 10**
LAB TECHNIQUE & CLEAN UP Lab space left clean, proper technique, instructions followed, checked in with TA before leaving.		/ **10**
	LAB REPORT TOTAL	**/ 175**