CHEM 8M
Lab Manual
Organic Chem Lab II

Contents

1. **Functional Group Table**

2. **Experiments with the following components for each:**
   - Background reading
   - Procedures
   - How and what to do BEFORE, DURING, & AFTER lab
   - Pre-Lab Questions
   - Lab report guidelines: in-lab questions & experimental methods
   - lab notebook templates

3. **IR and NMR Spectroscopy Reference Tables**

Caitlin Binder, PhD
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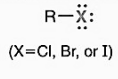
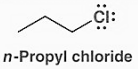
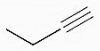
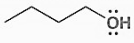
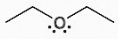
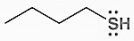
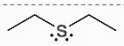
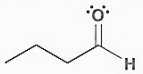
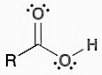
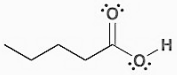
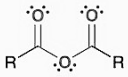
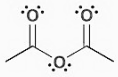
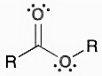
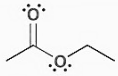
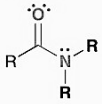
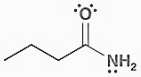
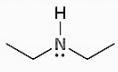
Department of Chemistry and Biochemistry

TABLE 2.1 EXAMPLES OF COMMON FUNCTIONAL GROUPS

FUNCTIONAL GROUP*	CLASSIFICATION	EXAMPLE	CHAPTER
 (X=Cl, Br, or I)	Alkyl halide	 *n*-Propyl chloride	7
	Alkene	 1-Butene	7, 8
	Alkyne	 1-Butyne	9
	Alcohol	 1-Butanol	12
	Ether	 Diethyl ether	13
	Thiol	 1-Butanethiol	13
	Sulfide	 Diethyl sulfide	13
	Aromatic (or arene)	 Methylbenzene	17, 18

FUNCTIONAL GROUP*	CLASSIFICATION	EXAMPLE	CHAPTER
	Ketone	 2-Butanone	19
	Aldehyde	 Butanal	19
	Carboxylic acid	 Pentanoic acid	20
	Acyl halide	 Acetyl chloride	20
	Anhydride	 Acetic anhydride	20
	Ester	 Ethyl acetate	20
	Amide	 Butanamide	20
	Amine	 Diethylamine	22

* The "R" refers to the remainder of the compound, usually carbon and hydrogen atoms.

Klein, D. (2019) Organic Chemistry, 3rd edition.

Experiment 1 – Separation of Excedrin Components *via* Column Chromatography

Revell, K. D. *Journal of Chemical Education.* **2011**, 88, 1413.

Learning Objectives

- Understand principles behind silica-based chromatography
- Critical analysis of column and thin-layer chromatography technique
- Analyze data to assess purity and success of experiment
- Understand the role of functional groups and polarity on separation
- Predict sources of error and understand their effects on results

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How to Prepare for Lab + Assignments - Follow Canvas Exp 1 Module…

Before Lab

- Read this PDF – background, procedure, safety, pre-lab and in-lab questions
  - Option: listen to Caitlin read this document in the **8M Exp 1 Podcast**
- Attend and/or watch **lab lecture** – we go over everything you need for your assignments!
- Practice the lab online *via* **Slugs@home platform** - sites.google.com/ucsc.edu/slugshome/home
- Complete the **pre-lab questions** at the end of this doc - incorporated into Canvas quiz ☺
  - **Quiz** due before your enrolled section – check Canvas for due date
- Download the **Exp 1 worksheet** on Canvas and prepare your **lab notebook**…

Lab Notebook Preparation – *worksheet = template / outline to copy by hand into lab notebook*

- **Purpose:** one-sentence summary of the main lab goals plus the structures of Excedrin components
- **Reagent Table** – add chemical properties; Wikipedia is a reliable source for chemical properties!
- **Procedure with Diagrams** – complete before starting lab; sample on Canvas
  - Use the procedure that follows to create your hand-drawn experimental instructions
    - Simple sketches & labels for all **equipment, chemical names** with **amounts**, & **transfers**
  - Format: Break it up with flow charts, bullet-points, comic strip, and/or whatever works for you!
    - Avoid copying the procedure word-for-word.
    - Make it easy for anyone to follow your procedure without referring to this document.
  - **Slugs@home Exp 1 website** - Equipment & Safety pages; pictures & videos of the whole lab
  - The **class notes** include useful diagrams as well

During Lab

- Check the **safety rules** to dress for lab and arrive a few minutes early to **Thimann Labs**
- **Pre-lab talk:** tips for success and open Q&A
- Show your **lab notebook pages** to your TA
- Perform the experiment with a partner, fill out data & observations in **lab notebook**

After Lab – each partner submits separate, individual assignments

- Upload **Notebook Pages** to Canvas by midnight on lab day – graded on completeness / participation
- Complete & upload the **Lab Report** on GradeScope (GS) – due date on Canvas
  - Guidelines at end of this document

Background: Principles & Theory of Silica Chromatography

Column chromatography is a type of *adsorption chromatography* used to separate components from a mixture based on selective affinity to stationary and mobile phases. The principles of column chromatography and thin-layer chromatography (TLC) are analogous. The separation of components from a mixture is based on **polarity**. The *stationary phase* is most commonly silica (SiO_2) and the *mobile phase* is an organic solvent or solvent mixture. SiO_2 is polar and has a greater affinity for polar compounds. Thus, *less polar compounds will always elute from a column earlier and move farther on a TLC plate than polar compounds.*

In TLC, the mobile phase moves up the SiO_2 plate by capillary action, against gravity (**Figure 1a**). Less polar compounds travel farther up the TLC plate (higher retention factor, R_f). Components remain on the plate and are analyzed by visual inspection. In column chromatography, the mobile phase is added to the top of the column and travels down with gravity, eluting components as a solution in the solvent (**Figure 1b**). Less polar compounds elute from the column first due to their low affinity for SiO_2. Components can be isolated from the mixture in column chromatography, whereas TLC separates components without collection.

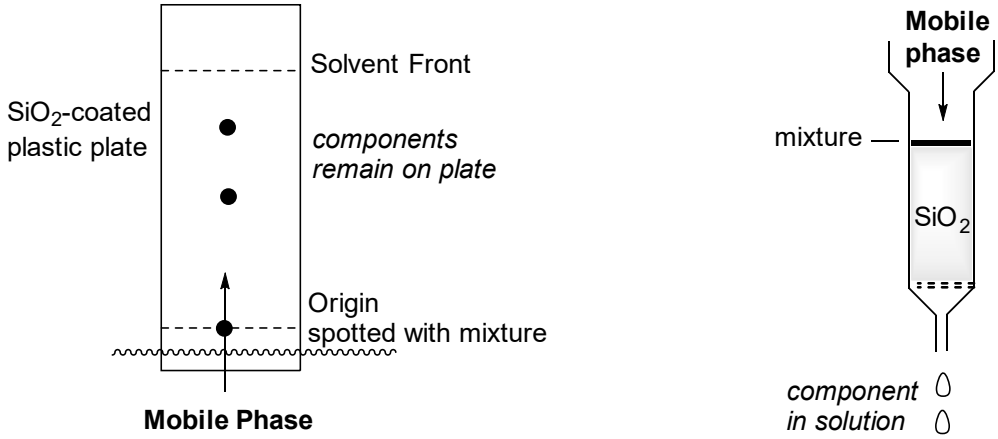

Figure 1. Diagrams of **(a)** TLC, **(b)** column chromatography

Students will use column chromatography to separate the active ingredients of Excedrin, an over-the-counter analgesic (**Figure 2**). A column is packed with SiO_2 then dry-loaded with an Excedrin-SiO_2 mixture. Increasingly polar solvents will be added to selectively elute aspirin (ASP), acetaminophen (ACE), then caffeine (CAF) based on their increasing polarities. This **solvent gradient** includes mixtures of hexanes and ethyl acetate (EtOAc) then the more polar acetone. Solutions of ASP, ACE, and CAF will be collected in fractions and analyzed by TLC. Pure fractions will be concentrated to isolate each component and compared to known values. Students will separate Excedrin components by a different method (acid-base extraction) and the results will be compared in Experiment 2.

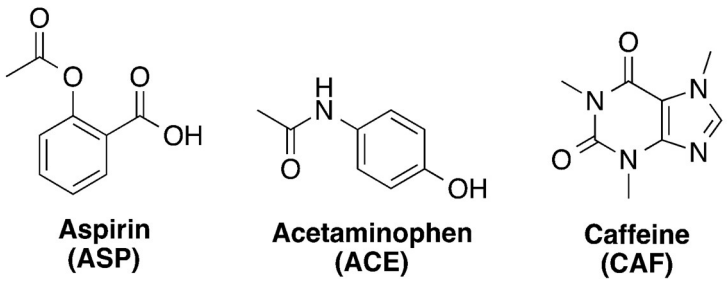

Figure 2. Active ingredients in Excedrin

PROCEDURE

1. Active Ingredients in Excedrin - Obtain the mass of an Excedrin® tablet then crush to a fine powder using a mortar and pestle. Add 20 mL of ethyl acetate (EtOAc) to the mortar and gently mix with a stir rod in the fume hood for 2 minutes. The three active components should dissolve but the starchy tablet binder (inactive ingredients) will not. Decant the solution into a small glass funnel with a small piece of cotton using a glass stir rod to aid in the transfer. Rinse with an additional 2 mL EtOAc. Collect the filtrate in a labeled 50-mL round-bottom flask (RBF).

2. Prepare & Load the Column - Add approximately 0.5 mL of SiO_2 to the RBF (compare to reference in the lab) and concentrate to dryness using a rotary evaporator (rota-vap). The result is Excedrin-coated SiO_2! Prepare the following solvent mixtures in the fume hood and keep in labeled, covered Erlenmeyer flasks. ***Prevent chemical exposure incidents and spills*** by using a funnel to transfer the majority of each solvent or mixture from the reagent container into a graduated cylinder, then use a pipet to bring the solution up to the proper volume.

(1) 30 mL of 1:1 hex / EtOAc = 15 mL hexanes, 15 mL ethyl acetate

(2) 30 mL of 1:2 hex / EtOAc = 10 mL hexanes, 20 mL ethyl acetate

(3) 35 mL of acetone

Label seven large test tubes for collection of the column fractions and keep in a test tube rack. Clamp a disposable polypropylene column (1.5 x 12 cm) to a ring stand and make sure there is a filter toward the bottom (add one if not present). Add approximately 3 g of SiO_2 to the column (reference provided in lab) followed by the Excedrin-SiO_2 mixture using a powder funnel. Add a level, ~2 mm layer of sand on top of the sample to prevent disturbing the stationary phase.

3. Run the microcolumn: Clamp the column to a ring stand in the fume hood and twist off the tip of the plastic column, if necessary. Carefully add the first solvent portion (1:1 hex / EtOAc) without disturbing the sand by *slowly swirling the pipet around the inside walls of the column* while gently applying pressure to the pipet bulb. Once the solvent level is high enough, the remaining solvent can be added more quickly. *Do not allow the column to run dry or test tubes to overflow*. Collect the eluent in the test tubes labeled “F1” and “F2,” switching approximately 15 mL per test tube. Switch to the next solvent mixture (1:2 hex / EtOAc) and collect each successive ~15 mL portion of solvent in test tubes “F3” and “F4.” Repeat with acetone, collecting in “F5” and “F6.” TLC analysis can be completed as fractions are obtained, space permitting.

4. TLC Analysis: *TLC analysis of the standards can be done at any time and shared as a lab*. Place a small amount (microspatula tip) of ACE, ASP, or CAF standard in a small test tube and dilute with 1 mL acetone. Analyze each column fraction by TLC in comparison to the standards. Carefully but quickly spot the plate once per each column fraction. These compounds are highly UV active and require only minimal amounts for visualization. The spot should be small enough for 2-3 lanes per plate without smearing. Rinse the capillary

tube with acetone to prevent cross-contamination between samples. Before placing the plate in the developing chamber, visualize the spots with a UV lamp to ensure you added enough sample to visualize but not so much to smear when run.

Keep the TLC chambers in the fume hoods and covered at all times. Use tweezers to carefully place the TLC plate into the developing chamber without disturbing the mobile phase. Place the cap on the jar upside down (screwing the cap on will likely disturb the mobile phase!). 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 in the hood before visualizing with the UV lamp. Circle the spots then calculate all R_f values at your bench (distance of spot from origin / distance of solvent front from origin). Dispose of the plates in solid waste.

5. Isolation of Components: Any fractions containing a single compound as determined by TLC can be concentrated using a rota-vap (*in vacuo*). If two fractions contain the same single compound by TLC, those fractions can be combined. Transfer the fraction(s) to an appropriately sized, pre-weighed RBF and remove the solvent. The compound may or may not solidify on the rota-vap but do keep it on the vacuum for a few extra minutes to ensure complete removal of solvent. Record the mass of each component isolated and determine the percent recovery compared to the initial mass of Excedrin tablet. Experimental success will be determined by comparison to your responses in pre-lab #1 (theoretical percent recovery).

Clean-up	**Safety**
Liquid waste: acetone, hexanes, EtOAc, and fractions	Acetone, hexanes, ethyl acetate are flammable
Solid waste: pipets, column with silica, dry silica, TLC plates, CAF, ASP, ACE	Caffeine is a *stimulant* and is NOT to be ingested or taken home
Thank you for cleaning your work station: Wash glassware, put away equipment, and wipe benchtops	Silica is an irritant

All used pipets & broken glass go in the glass waste box.

Please do not throw away glass in the trash as it creates an unexpected occupational hazard for our custodial staff.

Thank you for participating in community set up & clean up tasks ☺

Pre-lab Questions / Quiz – see your class notes!

1. Each Excedrin tablet contains 250 mg aspirin (ASP), 250 mg of acetaminophen (ACE), and 65 mg of caffeine (CAF). Calculate the **theoretical percent (%) recovery** of each component using the mass of one tablet (675 mg). Note: there are also inactive ingredients in the tablet.

   (a) ASP **(b)** ACE **(c)** CAF

2. **THE STATIONARY PHASE:** What stationary phase is used in the column and in TLC analysis? Is this substance considered polar or non-polar?

3. **THE MOBILE PHASE:** List each of the solvents / solvent mixtures with ratios used to run the column in order from least to most polar.

4. Go to pubs.acs.org to perform a citation search in the *Journal of Chemical Education*, volume *88*, page 1413 (proper reference format: Revell, K. D. *J. Chem. Ed.* **2011**, 88, 1413). This requires campus access or remote log-in to view the full article. Read this brief article and **report the order that the Excedrin components are expected to elute from the column.**

   - The article is also under Canvas Files > Experiment 1, but it's good practice to try and look it up yourself!

5. Use the *J. Chem. Ed.* Article above and **report the mobile phase for TLC** as well as the **expected R_f values** for each component.

6. **THE SAMPLE:** What **functional groups** do ASP and ACE each contain? Indicate the **intermolecular force (IMF)** associated with *each functional group*: ion-dipole, hydrogen-bonding, dipole-dipole, or dispersion / van der waals forces.

   a. Practice identifying IMFs in the free *Chirality-2* mobile app!

Take the **Canvas Exp 1 pre-lab quiz** *before* your enrolled section – see Canvas for due date

- The quiz incorporates the questions below - the questions may be reworded.
- **Be prepared with your responses to the pre-lab questions *before* starting the quiz.**
- There is a 20-minute time limit on the quiz and you get two attempts.
  - Make sure you have enough time to complete the quiz - you can't save and come back later.
  - If you choose to re-take the quiz, your grade will be the highest of the two attempts.

Though we encourage collaboration in this class, this is an individual quiz.

- The responses should be a product of your original work so that you are assessed on *your* understanding of the material.
- Sharing your quiz or your responses in any format (screenshots, email, CHEGG, social media, text, carrier pigeon, etc.) is in violation of the UCSC academic integrity policy.

LAB REPORT – see your class notes!

No abstract or 'experimental methods' section for the Exp 1 report.

In-lab Questions – numbered responses that incorporate the questions, no need to include the exact question

- Discuss with your partner during lab.
- Work on your own to type your responses in complete sentences for the individual lab report.
- Please **select pages** after uploading to GradeScope.

1. Report all TLC **retention factor (R_f)** values in one table (see recommended format below). **Identify** each spot as CAF, ASP, or ACE by entering the R_f values in the appropriate column for each sample. Account for all spots in each fraction if more than one was present, and indicate which spot was more prevalent (darker), if applicable. Show **R_f sample calculations** for ASP, ACE, and CAF standards.

TLC results for Excedrin column separation (R_f values)

	ASP standard	**ACE standard**	**CAF standard**	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**
ASP										
ACE										
CAF										

2. Discuss whether the column separation was successful using the TLC results. Report which **fractions were combined and/or concentrated** to obtain ASP, ACE, and CAF. All fractions should be accounted for, including those that were disposed of in the waste without concentration.

3. Report the **mass recovery** of each component after isolation. Calculate the **percent (%) recovery** of each component from the tablet (similar to pre-lab #1). Show your work.

(a) ASP **(b)** ACE **(c)** CAF

4. Comment on your **actual vs. theoretical recoveries**. List specific parts of the procedure where product may have been lost.

5. Explain the **order of separation** of Excedrin components on the column given what you know about functional groups, polarity, and acid-base chemistry (*hint: **hydrogen-bonding** and **ion-dipole interactions** should be included in your response).* Were the **results as expected**?

- For fun - Practice functional group and IMF identification in the free *Chirality-2* mobile app!

6. What role does the **acetic acid** play as part of the **TLC solvent mixture**?

Template – copy by hand into lab notebook

Name _____ Lab Partner _____

TA Name _____ Section Day _____ Time _____

Experiment 1 Worksheet – Column Chromatography

Use as reference for notebook preparation – everyone submits on Canvas individually after lab

Pre-Lab Requirements

1. **Dress for lab** – see safety rules – arrive a few minutes early
2. **Lab Notebook:** copy templates below into designated notebook
   - **Purpose, scheme,** and **reagent table**
   - **Procedure Diagrams** – must be complete before you can start the lab

A. Experimental Purpose and Structures of Excedrin Components

B. Reagent Table

* Fill in properties before lab; leave mass (mg) and millimoles (mmol) blank – fill in during lab

Name	Volume	Density	Mass	milli moles	Molecular Mass	Boiling or melting point	Hazards
Excedrin	-						
Silica	-						
Ethyl acetate			-	-			
Hexanes			-	-			
Acetone			-	-			
Aspirin	-						
Acetaminophen	-						
Caffeine	-						

See Slugs@home for pics & videos of the full lab!

C. Procedure Diagrams

- Use the **procedure from the lab PDF** create your hand-drawn experimental instructions
  - Simple sketches & labels for all **equipment, chemical names** with **amounts**, & **transfers**
  - Include clean-up & safety notes throughout your procedure and leave space for observations
- Format: Break it up with flow charts, bullet-points, comic strip, and/or whatever works for you!
  - Avoid copying the procedure word-for-word.
  - Make it easy for anyone to follow your procedure without referring to this document.
- **Slugs@home Exp 1 website** - Equipment & Safety pages; pictures & videos of the whole lab
- The **class notes** include useful diagrams as well
- *Use as many pages as needed* - at least 3 pages is typical

1. **Active ingredients in Excedrin -** Weigh tablet, crush, dissolve, filter
2. **Prepare & load the column** – Rota-vap, addition of SiO_2 and Excedrin- SiO_2 mixture
3. **Run the column** – add solvents and collect fractions
4. **TLC analysis –** spot, run, and visualize one representative plate
5. **Isolation of components** – combine and concentrate (rota-vap) one representative sample

See Slugs@home for pics & videos of the full lab!

E. Data

Mass of Excedrin tablet _____ g

Sketches of TLC plates and calculated R_f values for each spot:

Standards
(pure ACE, ASP, & CAF)

Column Fractions

TLC results for Excedrin column separation (Retention Factor, R_f values)

	ASP standard	**ACE standard**	**CAF standard**	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**
ASP										
ACE										
CAF										

Mass recoveries after concentration:

ASP _____ g ACE _____ g CAF _____g

Percent recoveries = (mass recovery) / (mass of tablet) x 100%

ASP _____ % ACE _____ % CAF _____%

See Slugs@home for pics & videos of the full lab!

Experiment 2 – Two Base Extraction of Excedrin Components

Learning Objectives

- Understand principles behind acid-base extraction
- Critical analysis of extraction techniques
- Analyze data to assess purity and success of experiment
- Understand the role of functional groups and acidity / basicity on separation
- Predict sources of error and understand their effects on results

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How to Prepare for Lab + Assignments - Follow Canvas Exp 2 Module…

Before Lab

- Read this PDF – background, procedure, safety, pre-lab and in-lab questions
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- Attend and/or watch **lab lecture** – we go over everything you need for your assignments!
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  - **Quiz** due before your enrolled section – check Canvas for due date
- Download the **Exp 2 worksheet** and prepare your **lab notebook**…

Lab Notebook Preparation – *worksheet = detailed template / outline to copy by hand into lab notebook*

- **Purpose:** one-sentence summary of the main lab goals plus the structures of Excedrin components
- **Reagent Table** – add chemical properties; Wikipedia is a reliable source for chemical properties!
- **Procedure with Diagrams** – complete before starting lab; sample on Canvas
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After Lab – each partner submits separate, individual assignments

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- Complete & upload the **Lab Report** on GradeScope (GS) – due date on Canvas
  - Guidelines at end of this document

Background: Acid-Base Extraction

The solubility of organic compounds is primarily dependent on polarity. You may recall "*like dissolves like,*" meaning 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 have limited solubility 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 utilize acid-base chemistry to separate a mixture based on preferential solubility in water or ethyl acetate (EtOAc), a polar organic solvent. Excedrin is an over-the-counter analgesic containing the active ingredients aspirin (ASP), caffeine (CAF), and acetaminophen (ACE) that can be separated through **acid-base extraction** (**Figure 1**).

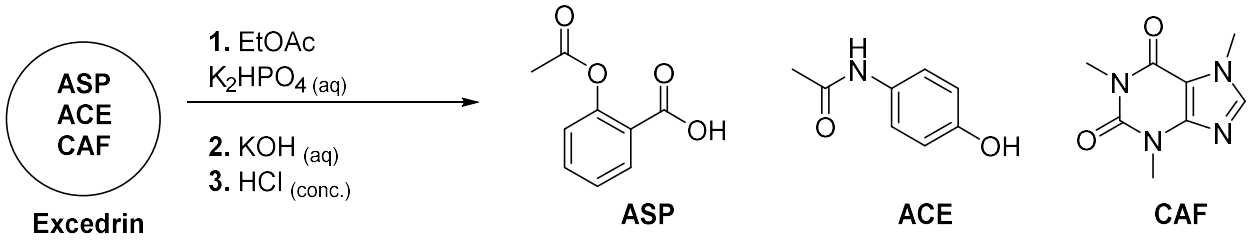

Figure 1. Separation of Excedrin components using acid-base extraction

Acids (HA) react with bases (B) to form a conjugate base (A^-) and a conjugate acid (^+BH) (**Figure 2**). 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.

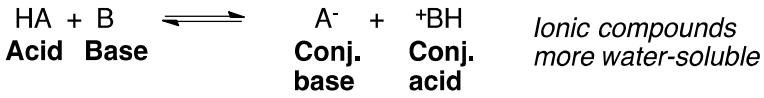

Figure 2. A generic acid-base reaction.

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 dibasic potassium phosphate (K_2HPO_4) and sodium hydroxide (NaOH), respectively. The by-products are different but both reactions form a **sodium carboxylate salt**, which is more water-soluble than the acid (**Figure 3**). In this experiment, the carboxylic acid in ASP is deprotonated with K_2HPO_4 to initiate separation from ACE and CAF. More on this later!

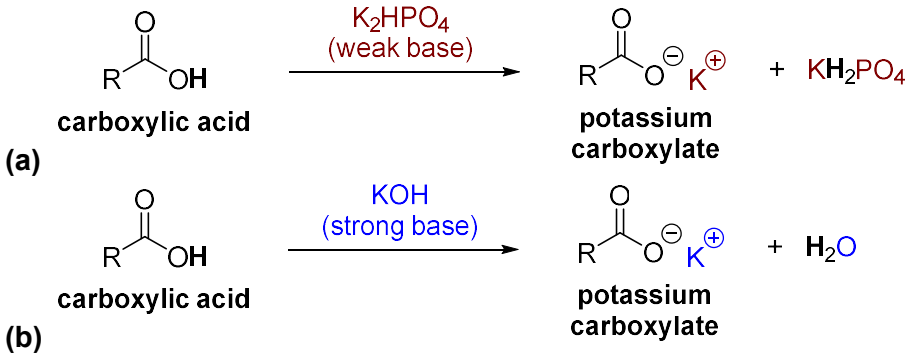

Figure 3. Reaction of carboxylic acids with **(a)** weak base and **(b)** strong base.

Phenols are significantly less acidic than carboxylic acids. Phenols do not react with weak bases. A strong base like potassium hydroxide (KOH) is required for the reaction to occur, resulting in a water-soluble **sodium phenoxide salt** (**Figure 3**). Note that the extraction cannot be started with KOH, as both ASP and ACE would react. Instead, the phenol in ACE is deprotonated with KOH *after* ASP has already been removed and separation from CAF is complete. Keep reading to see how that works!

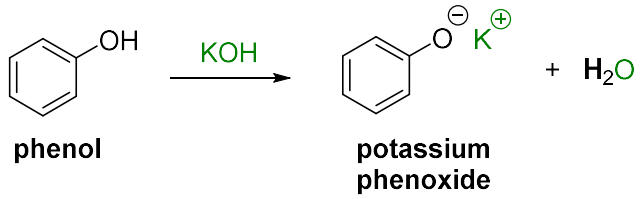

Figure 3. Reaction of phenol with strong base.

Nitrogen-containing organic compounds, also known as alkaloids, tend to be basic. Amines and imines react with strong acids to form water-soluble **ammonium chloride salts** (**Figure 4**). Note that the double-bonded N in the imidazole ring below is more basic and gets the hydrogen instead of the single-bonded N. The latter N is not basic because its lone pair is tied up in resonance and not available to grab the H. This is analogous to the structure of CAF. Though not utilized in this experiment, CAF could be separated from ACE and ASP by treatment with a strong acid.

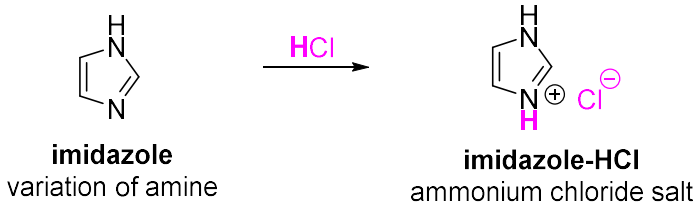

Figure 4. Reaction of imidazole with strong acid.

When both acids and bases are present in a mixture, a liquid-liquid extraction is carried out and at least one of the reactions above is performed. 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.

In this experiment, students will separate a mixture containing a carboxylic acid (ASP), phenol (ACE), and an amine (CAF). The extraction can be started in one of two ways: **(1)** react the carboxylic acid with a weak base or **(2)** react the amine with an acid. Either way will theoretically work, but let's work through the example that starts with a mildly basic extraction (**Figure 5**).

The mixture is dissolved in an appropriate organic solvent, in this case ethyl acetate (EtOAc), and this solution is extracted with a weak base. The organic layer (**ORG**) contains unreacted phenol and amine. The mildly basic aqueous layer (**AQ$_{basic}$**) contains the carboxylate salt (the conjugate base of a carboxylic acid). The carboxylate is reprotonated with acid, thus precipitating from the solution, and permitting isolation *via* filtration. The remaining organic layer is extracted with a strong hydroxide base to deprotonate the phenol, leaving the phenoxide salt (conjugate base of phenol) in the basic aqueous layer and the unreacted amine in the organic layer. The amine can be isolated by drying (ex. Sodium or magnesium sulfate), filtering off the drying agent, then evaporating the solvent in a rotary evaporator (rota-vap). The phenoxide salt must be acidified (reprotonated) and extracted into EtOAc before being dried, filtered, and concentrated.

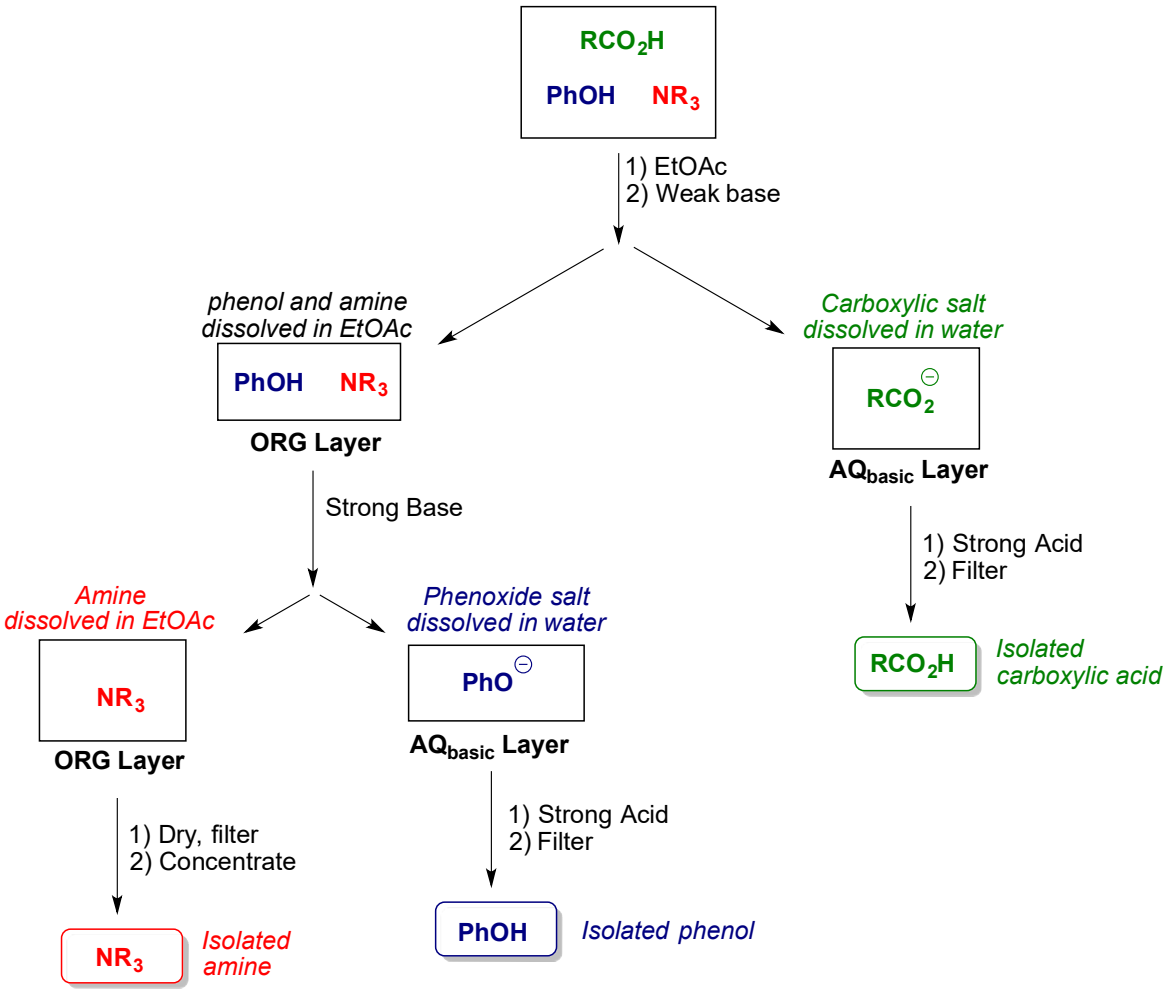

Figure 5. Flow chart for the acid-base extraction of a carboxylic acid from an amine.

A similar procedure is employed in the separation of the three active ingredients in Excedrin. The active components are separated from the inactive ingredients through solid-liquid extraction with EtOAc followed by filtration. Liquid-liquid extraction is used to separate ASP, ACE, and CAF. The solution of active ingredients in EtOAc is treated with $K_2HPO_{4\,(aq)}$, causing two layers to form in the separatory funnel. This weak base reacts with aspirin's carboxylic acid group, causing the extraction of ionized, deprotonated ASP into the **aqueous layer (ASP-AQ)**. This layer is separated from the **organic layer (ORG)**, which contains ACE and CAF as a solution in EtOAc. The **ASP-AQ** layer is treated with HCl to protonate and precipitate ASP from solution. ASP is then isolated by vacuum filtration.

The **ORG** layer is treated with aqueous potassium hydroxide ($KOH_{(aq)}$). This strong base reacts with ACE's phenol, creating phenoxide ions that are extracted into the AQ layer (**ACE-AQ**). This is separated from the **ORG** layer, which now contains only CAF. The **ORG** layer is dried ($MgSO_4$) to remove residual water, then concentrated to isolate solid CAF. The **ACE-AQ** layer is treated with strong acid (HCl) to reprotonate the phenoxide, but unfortunately ACE does not precipitate. Instead, an acidic aqueous extraction is performed. The acidic **ACE-AQ** layer is instead extracted with EtOAc. ACE migrates into the **ORG** layer, which is then dried, filtered, and concentrated to isolate solid ACE.

Keep in mind that in each liquid-liquid extraction, there is no guarantee that 100% of the compounds end up in the expected layer (refer to the pre-lab videos on liquid-liquid extraction). TLC will be used to determine the effectiveness of the separation of each component. IR spectroscopy will be used to confirm the identity of each compound.

PROCEDURE

Procedure Diagrams must be complete in your notebook before you can start the lab – worksheet on Canvas

** **All steps involving ethyl acetate (EtOAc) must be performed in the fume hood.** **

1. Solid-liquid extraction of Excedrin's active ingredients - Obtain the mass of a single tablet of Excedrin® and crush using a mortar and pestle. Add 20 mL of EtOAc to the mortar and mix with a stir rod in the fume hood for 5 minutes. The three active components will dissolve and the starch binder (inactive ingredients) will not. Decant the solution into a small glass funnel with a small piece of cotton using a glass stir rod to aid in the transfer. Collect the filtrate directly in a separatory funnel secured on a support ring on a ring stand.

2a. Extraction with weak base - Add 10 mL of $K_2HPO_{4\,(aq)}$ (aqueous dibasic potassium phosphate) to the separatory funnel. Cap then invert the funnel twice, holding onto the cap. Vent into the fume hood by holding the funnel upside-down and open the stop cock with the tip pointing *away from your face*. Continue to mix and vent frequently for at least 3 minutes. A chemical reaction is taking place and proper time must be given for components to travel to the preferred layer. Drain the mildly basic aqueous layer containing deprotonated aspirin into a labeled scintillation vial (**K_2HPO_4 – ASP AQ**) and set aside. The organic layer will remain in the separatory funnel. Extract the organic layer with an additional 3 mL of K_2HPO_4 (add 3 mL of $K_2HPO_{4(aq)}$, mix and vent for several minutes, then drain into the **K_2HPO_4 – ASP AQ** vial). The organic layer remains in the funnel. One student in the pair should move onto "**Isolation of Aspirin**" using the combined **K_2HPO_4 – ASP AQ** extracts.

2b. Extraction with strong base - Add 10 mL of 1 M KOH to the separatory funnel. Mix the layers for 3 minutes (vent early and often into the fume hood). Drain the aqueous layer containing deprotonated acetaminophen into a second small, labeled container (**KOH – ACE AQ**) and set aside. Extract the organic layer with an additional 3 mL of KOH (add 3 mL of KOH, mix & vent for a few minutes, then drain the aqueous layer into the **KOH – ACE AQ** vial). Keep the organic layer in the funnel.

2c. Isolation of caffeine - Wash the remaining organic layer with 10 mL of *aq*. NaCl (brine); add the brine to the funnel and mix for 1 minute before draining the AQ layer. Separate the layers, draining the organic layer into a small, labeled Erlenmeyer flask. The brine wash (aqueous) should be kept in a separate container labeled "waste" and transferred into the liquid waste at the end experiment. Use an additional 2 mL of EtOAc to rinse any residual **CAF** from the walls of the separatory funnel. Remove any visible water from the bottom of the Erlenmeyer using a pipet. Dry the organic layer by adding two spatula tips of anhydrous sodium sulfate (Na_2SO_4). Allow the capped organic layer to sit with occasional swirling for 5 minutes (move onto one of the isolation steps below while waiting). Decant the organic layer using a small glass funnel with loosely packed cotton into a pre-weighed 50 mL round-bottom flask (RBF). Concentrate the dried organic extracts using a rotary evaporator (rota-vap). This concentrated **CAF** extract may either be a liquid or solid, depending on purity. Obtain the mass of caffeine by difference with the original flask then transfer into a labeled vial.

2d. Isolation of Aspirin – This step may be performed on the benchtop. Tear one 2-inch piece of pH paper into many small squares to conserve. Determine the pH of the **K_2HPO_4 – ASP AQ** solution by dipping a stir rod into the solution then touching to a small piece of pH paper on a watch glass. Obtain 10 mL of 6 M HCl in a labeled test tube. Slowly add 6 M HCl drop-wise to the **ASP AQ** solution, swirling and taking pH readings after every 5-10 drops, until the solution is acidic (pH 2 or less). Do not rush this process! Re-label the vial "**Acidic ASP AQ.**" It may be necessary to get additional 10 mL portions of HCl. Please conserve and take only small amounts at a time. A significant amount of ASP should precipitate, creating an opaque solution. Collect the product by vacuum filtration. Allow the solid to dry with the vacuum on for 10-15 minutes. Obtain the mass of the solid then transfer into a capped vial labeled "**ASP + (initials)**."

2e. Acidic extraction and isolation of acetaminophen – Carry out the same acidification procedure used to isolate aspirin (add 6M HCl, take pH to 2 or less). Label the vial "**Acidic ACE AQ**." The neutral protonated compound acetaminophen is in the aqueous solution and will be extracted with EtOAc. Transfer the acidic aqueous solution to the separatory funnel and add 15 mL of EtOAc. Mix and vent for 3 minutes, then drain the aqueous and organic layers into separate flasks. Extract the aqueous layer with an additional 15 mL of EtOAc (add 15 mL EtOAc to the aqueous layer, mix & vent for several minutes, then remove the aqueous layer). Wash the combined organic extracts with 10 mL of brine.

Separate the layers and dry the organic layer over anhydrous Na_2SO_4 for 5 minutes (remove visible water from the organic layer by pipet, add the drying agent, and allow to sit with occasional swirling). Filter into a pre-weighed 50-mL RBF then concentrate using a rota-vap. The concentrated extracts may either be a liquid or solid, depending on purity. Obtain the mass of **ACE** by difference, transfer to a labeled vial, and proceed to analysis.

ANALYSIS PROCEDURE

3a. TLC - TLC standard R_f values were obtained in Exp 1 and can be referred to without repeating this part of the experiment. Dilute a small amount (microspatula tip) of each component isolated in this experiment with 1 mL of acetone in a test tube. Analyze by TLC using 1:2 hexanes / ethyl acetate with 1% acetic acid as the mobile phase. Visualize the plates under a UV lamp, circle the spots, and calculate all R_f values. Repeat as necessary to obtain optimal results (Ex. if spots are too large / smeared - dilute your samples; if lanes are slanted - be more careful when placing the plate in the jar and do not move the jar).

3b. IR – After TLC analysis, determine whether each of the isolated components are pure (1 spot). Do not attempt to take an IR spectrum of contaminated samples. Instead, take the IR of a standard. Compare your predicted IR spectra tables with labmates – instructions for predicting spectra are in the pre-lab questions. Obtain the IR of each pure compound using a Nujol mull (grind the mull for at least one minute). Identify any peaks within the expected ranges based on the functional groups and bonds within ASP, ACE, and CAF.

Table 1. Clean-up and Safety

Clean-up – leave the lab as you found it!	**Safety**
Glass waste: uncontaminated pipets only	HCl and KOH are *corrosive & toxic*.
Liquid waste: contents of rota-vap trap, TLC solutions	Acetone and ethyl acetate are *flammable*. Caffeine is a *stimulant* and is NOT to be ingested or taken home.
Solid waste: filter paper, used pipets	
Product waste bag: product vials	Do not look directly into the UV lamp.
All used pipets & broken glass go in the glass waste box. ***Please do not throw away glass in the trash as it creates an unexpected occupational hazard for our custodial staff.*** Thank you for participating in community set up & clean up tasks ☺	

References & Supplemental Reading

Mohrig 4th ed. Chapter 10.1-10.5 (Extraction), Drying agents (Chapter 11), TLC (Chapter 18)

Revell, K. D. *J. Chem. Ed.* **2011**, 88, 1413.

Pre-lab Questions / Quiz – see your class notes!

Take the **Exp 2 pre-lab quiz** *before* your enrolled section – see due date on Canvas

- The quiz incorporates the questions below - the questions may be reworded.
- **Be prepared with your responses to the pre-lab questions *before* starting the quiz.**
- There is a 20-minute time limit on the quiz and you get two attempts.
    - Make sure you have enough time to complete the quiz - you can't save and come back later.
    - If you choose to re-take the quiz, your grade will be the highest of the two attempts.

Though we encourage collaboration in this class, this is an individual quiz.

- The responses should be a product of your original work so that you are assessed on *your* understanding of the material.
- Sharing your quiz or your responses in any format (screenshots, email, CHEGG, social media, text, carrier pigeon, etc.) is in violation of the UCSC academic integrity policy.

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1. Classify ACE, ASP, and CAF as **acidic, basic, or neutral**. Indicate which **functional group** determines the acid-base properties of each.

2. What **reaction** takes place in the addition of **dibasic potassium phosphate (K_2HPO_4)** to the mixture of ASP, ACE, and CAF? Show the **chemical equation** with full structures in support of your answer. Indicate whether each component (ASP, ACE, and CAF) should be in the **aqueous** or **organic layer** after the reaction.

3. What **reaction** takes place in the addition of **potassium hydroxide (KOH)** to the organic layer (after pre-lab #2)? Show the **chemical equation** with full structures in support of your answer. Indicate in which layer (**AQ or ORG**) each component should be after the reaction.

4. What **volume of 6 M HCl** is required to react with (neutralize) **13 mL of 1 M K_2HPO_4**? …to neutralize **13 mL of 1 M KOH**? Show your work. Hint: $M_1V_1 = M_2V_2$

5. Predict the IR spectra of ASP, ACE, and CAF using the tables in the **Exp 2 Worksheet** and the steps below.

- Identify each functional group (FG) in ASP, ACE, and CAF.
- Use the **IR Tables** on Canvas to find the IR active bonds within each functional group (FG) and its expected wavenumber range.
    - **List all bonds and vibrations** for each FG, as there may be multiple.
        - Some bonds have two different vibrations (ex. C-H bonds in arenes stretch and bend).
    - Determine if double bonds are **saturated or conjugated** (resonance with another pi bond).
- The substitution patterns of the arene ring affect the **C-H bending** vibrations. Use **IR Table 2** to determine the specific range of C-H bending frequencies.

LAB REPORT

Canvas > **Experiment 2 Report** for submission details

Upload to GradeScope (GS) after both parts of the lab – see due date on Canvas

- **Select Pages** to correlate your responses to the GS outline ☺

In-Lab Questions – see your class notes! Discuss with your partner during lab. Many of these questions are included in the Exp 2 Worksheet. Type your responses in complete sentences for the lab report, leaving space to draw by hand where necessary.

1. Report the **mass recoveries of ACE, ASP, and CAF** after isolation. Calculate the **% recovery** of each component from the initial amount of Excedrin used. Show your work.

2. Compare the recoveries above to the theoretical recoveries (Exp 1, pre-lab #1) and list the specific parts of the procedure **where product may have been lost**.

3. Report and discuss the **TLC results**: Make a table with the **R_f values** for each spot in each sample (4 columns – sample, ACE, ASP, CAF). **Identify** each spot as ACE, ASP, or CAF by entering the R_f value in the appropriate column for each sample. Include standard R_f values from Exp 1. **Explain** whether or not the separation was effective.

4. Interpret the **IR spectra** of ACE, ASP, and CAF. Type all 3 completed IR tables from the **Exp 2 Worksheet** (no hand-written tables in the results section please). Use three sentences (one per compound) **to describe** how the IR spectra can be used to positively identify each individual compound (unique stretches in each).

5. Compare the results of Excedrin separation *via* column chromatography (Exp 1) and acid-base extraction (Exp 2) as follows. While one method may not be generally *better* than the other, there should be some differences in the points below.

(a) Restate the **recoveries** of each component by each method.

(b) Which method produced **greater amounts** of ASP, ACE, and CAF? Note that different methods could be more ideal for isolating different components.

(c) Which method yielded **higher purity** of each component as determined by TLC?

(d) Based on your results and discussion above, was **column chromatography or acid-base extraction** more effective for separation of Excedrin components?

Template – copy by hand into lab notebook

Name _____ Lab Partner _____

TA Name _____ Section Day _____ Time _____

Experiment 2 Worksheet – Column Chromatography

Each student submits this individually on Canvas after lab

Pre-Lab Requirements

1. **Dress for lab** – see safety rules – please arrive a few minutes early
2. **Lab Notebook:** copy templates below into designated notebook
   - **Purpose, scheme,** and **reagent table**
   - **Procedure Diagrams** – copy templates provided, follow instructions to complete diagrams

A. Experimental Purpose and Structures of Excedrin Components

B. Reagent Table

Name	Volume	Density	Mass	milli moles	Molecular Mass	Boiling or melting point	Hazards
Excedrin	-						
Ethyl acetate							
K_2HPO_4			**-**				
KOH			**-**				
HCl			**-**				
Aspirin	-						
Acetaminophen	-						
Caffeine	-						

Check out Slugs@home for pics & videos of the whole lab!

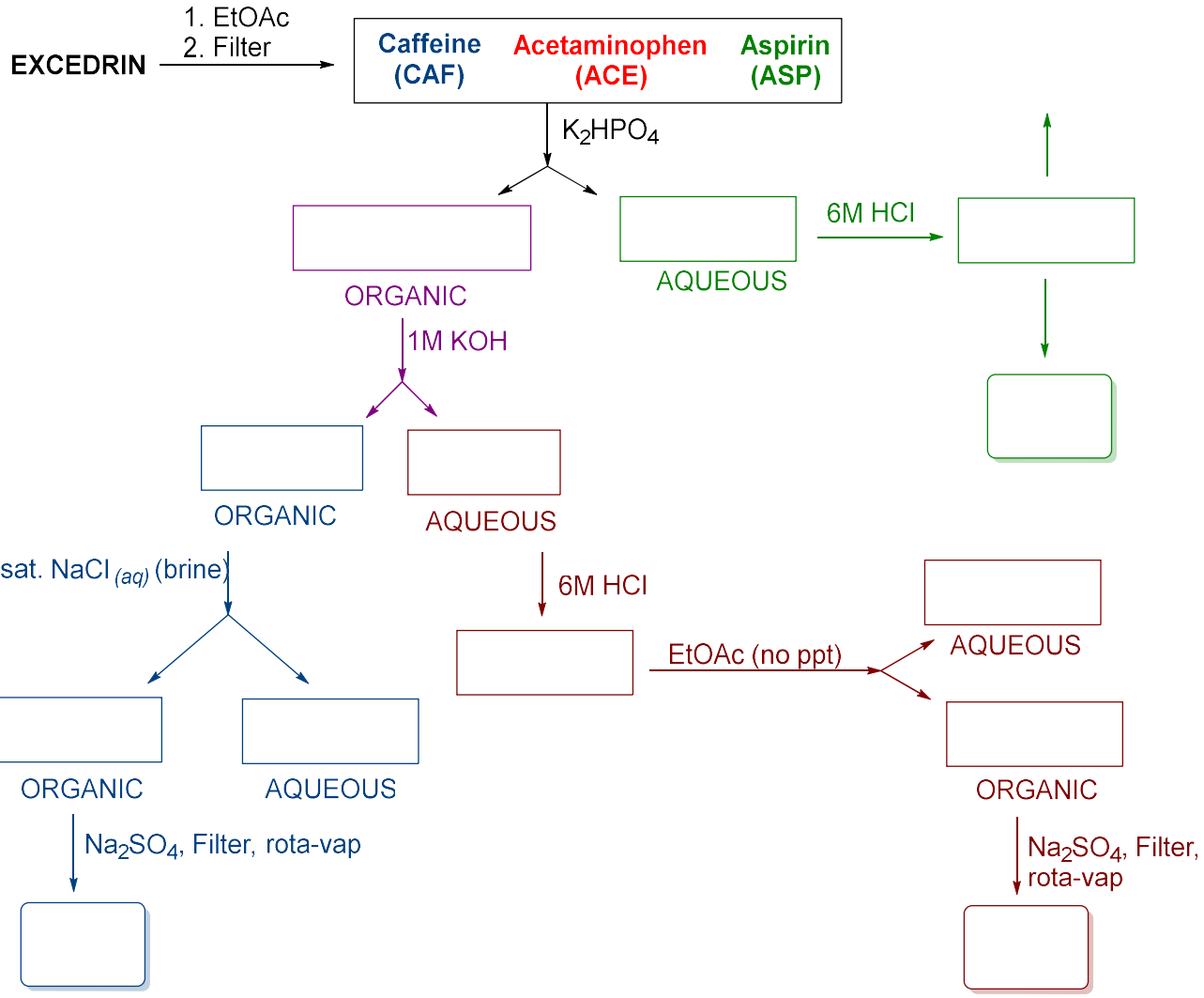
C. Procedure Diagrams of key procedural segments on provided templates below

- All **labeled equipment, chemical names** with **amounts**, and pertinent **safety notes** in every step.
- **Slugs@home Exp 2 website** - Equipment & Safety pages; pictures & videos of each part of the lab.
- The **class notes** include useful diagrams as well!

1. Active Ingredients in Excedrin

– crush, dissolve, & filter into separatory funnel

Fill in the boxes in this separation overview:

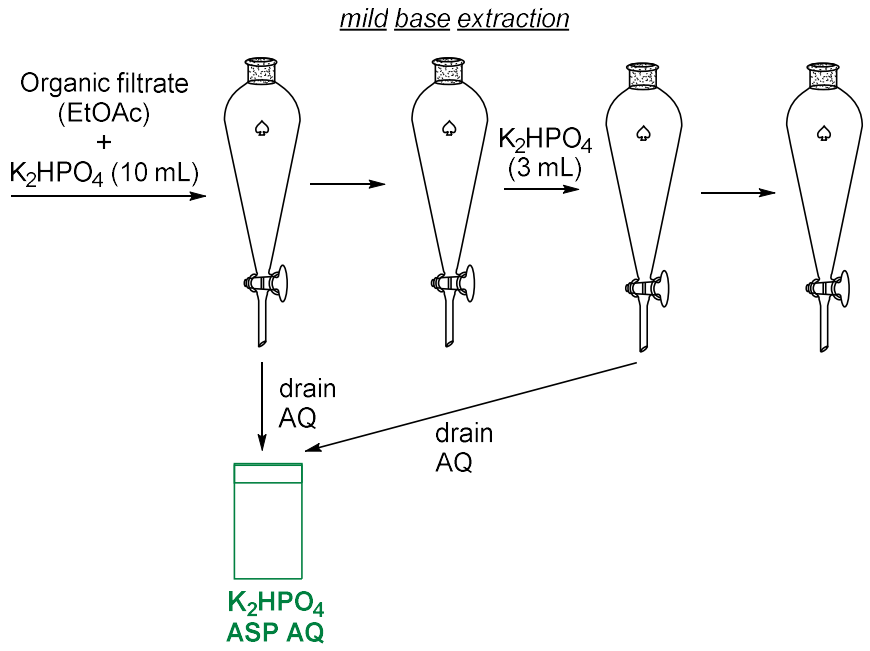


Check out Slugs@home for pics & videos of the whole lab!

Template – copy by hand into lab notebook

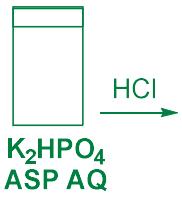
Indicate the layer(s) present in each separatory funnel diagram & label what components are in each layer

2a. Extraction with weak base

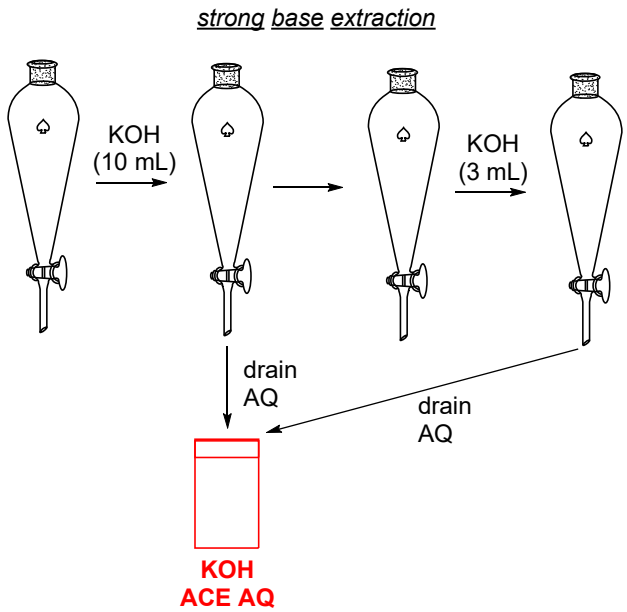


2d. Acidification & Isolation of Aspirin

* include pH testing and filtration



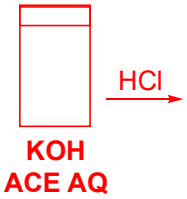
2b. Extraction with strong base



Check out Slugs@home for pics & videos of the whole lab!

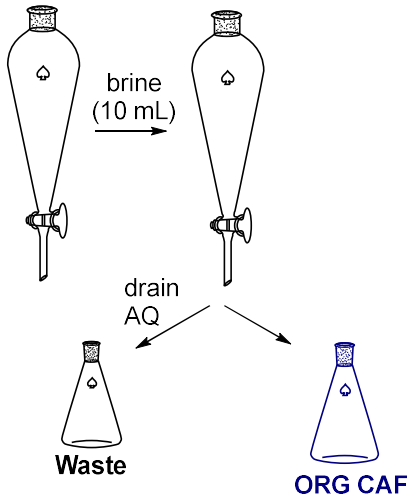
2e. Acidification of Acetaminophen

* include pH testing and filtration

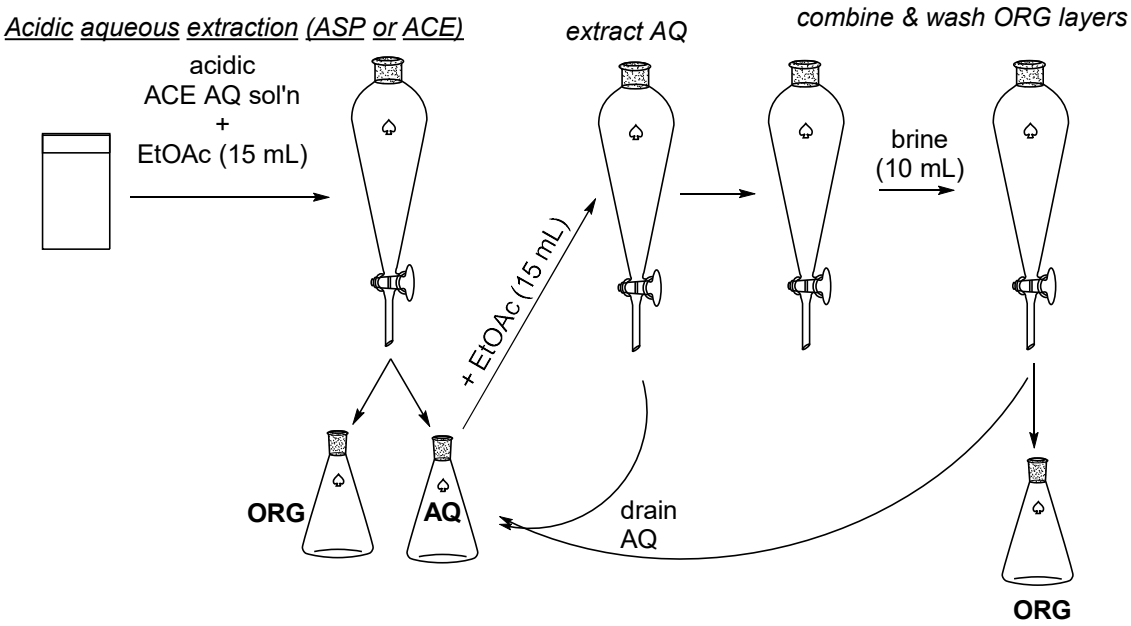


2c. Isolation of caffeine

* include steps to dry, filter, and concentrate CAF



2e. Acidic extraction and isolation of acetaminophen



* include steps to dry, filter, and concentrate ACE

Check out Slugs@home for pics & videos of the whole lab!

3. Analysis Procedure

(a) TLC – spot & run one plate; rough sketch of UV lamp and developed plates with labels

(b) IR – prepare and obtain the spectrum of one sample; rough sketch of IR spectrum

E. Data

Mass of Excedrin tablet _____ g

Sketches of TLC plates and calculated R_f values for each spot:

Standards
(pure ACE, ASP, & CAF)

Extracts

TLC results for Excedrin column separation (Retention Factor, R_f values)

	ASP standard	**ASP extract**	**ACE standard**	**ACE extract**	**CAF standard**	**CAF extract**
ASP						
ACE						
CAF						

Mass recoveries after concentration:

ASP _____ g ACE _____ g CAF _____g

Percent recoveries = (mass recovery) / (mass of tablet) x 100%

ASP _____ % ACE _____ % CAF _____%

Check out Slugs@home for pics & videos of the whole lab!

IR Analysis – see pre-lab questions for how to spectra from structure. Observe your IR spectrum and identify any signals within the expected range from the IR Tables. It is acceptable for a signal to be "not observed."

ASP

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

ACE

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

CAF

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

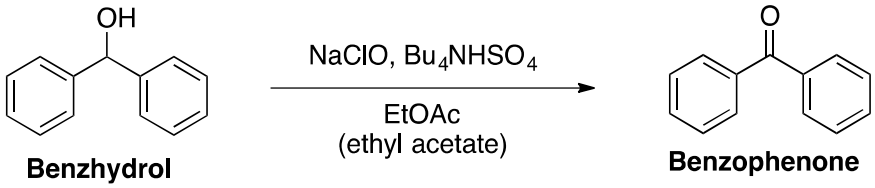
Check out Slugs@home for pics & videos of the whole lab!

Experiment 0 = Nuclear Magnetic Resonance (NMR) Spectroscopy

All NMR readings & videos are in the Canvas Exp 0 Module
(couldn't add them to this reader!)

Exp 0 assignments - see Canvas
1. Introductory Problems —> incorporated into Canvas Exp 0 Quiz
2. NMR Worksheet
Worksheet is posted on Canvas & included in "8M Workbook"

Experiment 3 – Oxidation of Benzhydrol



Benzhydrol **Benzophenone**

Learning Objectives

- Understand phase-transfer catalysis and organic oxidation reactions
- Apply TLC to monitor reaction progress
- Analyze IR spectra to assess purity and success of the reaction
- Assign signals on ^{1}H NMR spectra to the hydrogens in benzhydrol and benzophenone
- Predict sources of error and understand their effects on results

* Please find "How to Prepare for Lab & Assignments" after the procedure in this doc.

Background: Oxidation Reactions and Phase Transfer Catalysis

In this experiment, students will perform a simple oxidation reaction of a secondary, benzylic alcohol with commercial bleach. Recall that Oxidation Is a Loss of electrons while Reduction Is a Gain of electrons (OIL RIG). In order to apply this mnemonic, you need to know the oxidation states of each atom within the compound. Carbon can carry oxidation states ranging from -4 to +4. A few examples are shown in **Figure 1** below.

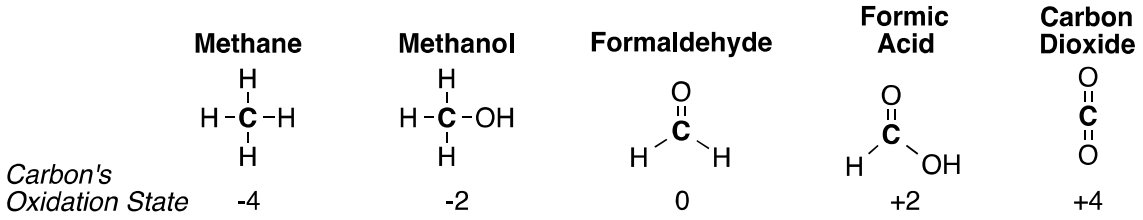


Figure 1. Examples of the oxidation levels of carbon

You may have noticed that all of the compounds in **Figure 1** are neutral and carbon has zero formal charge. The concept of oxidation state and formal charge are similar with one important difference in the calculation: *assuming whether the bonding electrons are shared equally or not*. Both are calculated by taking the difference between the valence electrons from the periodic table and the number of electrons belonging to that atom within the molecule.

The valence electrons of an atom will never change but the electrons 'belonging' to the atom in the molecule will vary depending on lone pairs of electrons and bonds to more or less electronegative atoms.

- **Oxidation states** assign bonding electrons to the more electronegative atom in a bond, except when the two atoms are the same and the bonding electrons are split equally.

- **Formal charge** splits bonding electrons equally between the two atoms.

In summary, the difference in the calculation of oxidation states and formal charge is based on the assignment of bonding electrons. This is how the highlighted carbon in ethanol can have an oxidation state of -1 but a formal charge of zero (**Figure 2**).

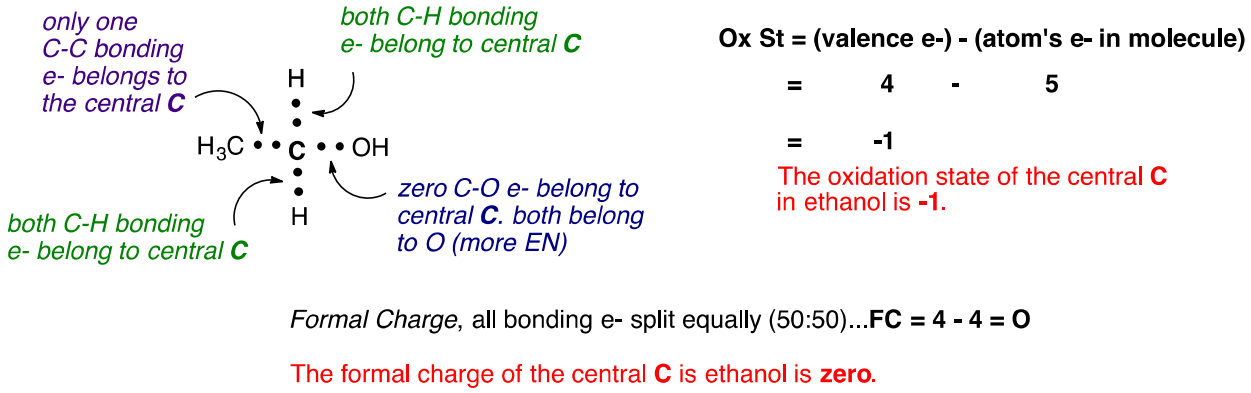


Figure 2. Calculation of oxidation state and formal charge of the central carbon in ethanol

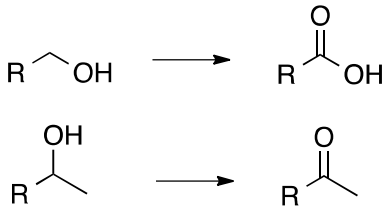
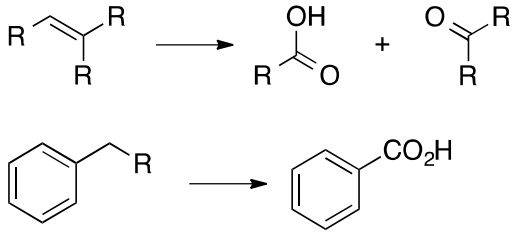
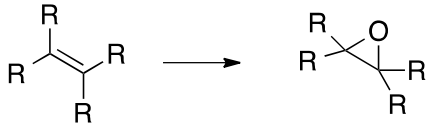
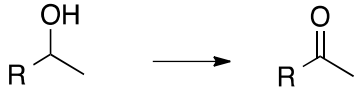
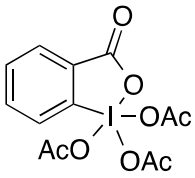
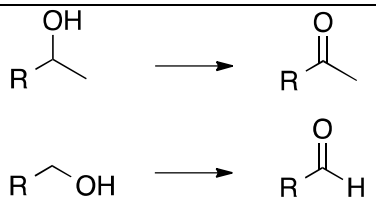
An oxidation reaction is one where an atom loses electrons. In other words, the atom gains a bond to a more electronegative atom (electron hogs!). The examples discussed in this experiment will involve oxygen-containing compounds (alcohols and carbonyl compounds) but there are many other examples of organic oxidation reactions that do not involve oxygen. You should be able to categorize whether the reactions learned in the CHEM 8 series qualify as oxidation or reduction based on the rules outlined above.

Table 1 on the following page highlights common oxidizing agents and their applications. The following issues should be addressed when choosing the appropriate oxidizing agent.

- *Reactivity* – does it react with the starting material? Is it too reactive or not reactive enough for the desired transformation?
- *Selectivity* – will it also react with other functional groups in the molecule?
- *Ease of use* – is it toxic and/or does it require special equipment? How is waste handled?
- *Availability* – is it commercially available or does it need to be made separately? Is it cost-effective?

In this experiment, the oxidation of a secondary alcohol (benzhydrol) is achieved with commercially available bleach. This reagent is inexpensive and easy to handle with typical personal protective equipment (PPE) including goggles and gloves. Most importantly, it works! However, one issue is presented in using bleach: *solubility*. Bleach is an aqueous solution of sodium hypochlorite (NaClO) but many organic compounds, including benzhydrol, are not water-soluble. Thus, a **phase transfer catalyst** (PTC) is employed to facilitate the reaction.

Table 1. Common oxidizing agents and applications

Oxidizing Agent	Main Application(s)	Comments
Jones Reagent: CrO_3, H_2SO_4		CrO_3 is highly toxic and a carcinogen. High waste disposal cost.
Pyridinium chlorochromate (PCC)		Suspected carcinogen, high waste disposal cost.
Potassium Permanganate ($KMnO_4$) with heat		Nonselective – many functional groups are oxidized (alkenes, alkynes, alcohols, etc.)
Peroxyacids (RCO_3H)		Common peroxyacid: *meta*-chloroperoxybenzoic acid (*m*CPBA)
Sodium Hypochlorite (bleach, NaClO)		Cheap and easy!
Dess-Martin Periodinane 		Easy to use but expensive reagent.

The mechanism employed by a PTC is similar to that used in soaps. Soaps contain both non-polar and polar (typically ionic) regions so they can absorb grease and also be washed away with water. Quaternary alkylammonium salts such as tetrabutylammonium hydrogen bisulfate ($Bu_4N^+HSO_4^-$) are common examples of PTCs. For the remainder of this discussion, this salt will be abbreviated by Q^+X^-. These salts are soluble in both water and organic solvents. When NaClO $_{(aq)}$ is mixed with an immiscible organic solvent such as ethyl acetate (EtOAc), little to none of the NaClO enters the organic phase. However, once a small amount of Q^+X^- is added, the salts participate in a dynamic equilibrium where ClO^- pairs with Q^+ and travels into the organic layer (**eq. 1**).

$$Q^+X^- + Na^+ClO^- \rightleftharpoons Q^+ClO^- + Na^+X^- \qquad \textbf{(1)}$$

Some of the hypochlorite (ClO^-) ion, the active oxidizing agent, is paired with the tetrabutylammonium cation Q^+. Because Q^+ is soluble in organic solvents, it can carry the ClO^- ion from the aqueous to the organic phase where the reaction can occur (**Figure 3**). As the ClO^- reacts in the organic phase, the equilibrium shifts to transport more ClO^- from the aqueous phase to reestablish equilibrium. It is important to note that the salts do not instantly transport from one layer to another. *Vigorous stirring is required to facilitate phase transfer.* This continues until the reaction is complete and the solubility issue is resolved! The applications of PTC are widespread to many other types of reactions, not just oxidations.

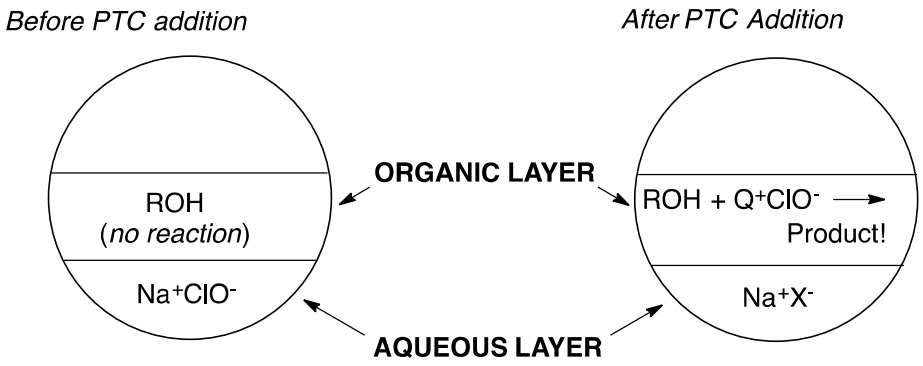


Figure 3. Phase-transfer catalysis (PTC) in an oxidation reaction.

The oxidation of benzhydrol is monitored by TLC to determine reaction progress. The product is isolated via liquid-liquid extraction to remove the aqueous layer and by-products. IR analysis is performed to observe the disappearance of the alcohol O-H stretch and appearance of the conjugated ketone C=O stretch. Proton nuclear magnetic resonance (^{1}H NMR) spectra of benzhydrol and benzophenone are provided for analysis. This valuable analytical tool provides information about the chemical environment of each hydrogen in the molecule. Each hydrogen in benzhydrol and benzophenone will be assigned to a signal on the ^{1}H NMR spectrum.

PROCEDURE

Procedure Diagrams must be complete in your notebook before you can start the lab.

1. Reaction Preparation and Set-up: TLC will be used to monitor reaction progress. Prepare TLC standards and plates before setting up the reaction. Make solutions of the standards (benzhydrol and benzophenone) in small test tubes. This does not require careful measuring, but do be conservative. Dissolve a small amount of the compound (microspatula tip) in ethyl acetate (EtOAc, 1 mL). Obtain three TLC plates, carefully handling by the edges without bending, and gently spot the plate at the origin with a capillary tube (not a melting point capillary). Create one lane for benzhydrol or benzophenone and leave a space for the reaction mixture to be spotted later (2 spots per plate). Be sure to record which lane is which in your notebook. Take note of the solvent in the TLC chambers.

In a 25-mL Erlenmeyer flask equipped with a magnetic stir bar, add 0.37 g (± 0.01 g)* of benzhydrol, 5 mL of commercial bleach (approximately 0.7 M NaClO), 5 mL of ethyl acetate (EtOAc), and 40 mg (± 5 mg)* of tetrabutylammonium hydrogen sulfate (Q^+X^- or $Bu_4N^+HSO_4^-$). Secure the flask to a ring stand, loosely stopper (check for correct size to avoid getting stuck), and *stir vigorously on a stir plate without heat*. Increase the stir speed if two layers are observed.

* It is acceptable to obtain 10 mg more or less benzhydrol and 5 mg more Q^+X^-. Record the exact mass obtained.

2. Monitoring Reaction Progress: After about 10 minutes, stop stirring to allow phase separation and remove a small aliquot of the upper layer of the reaction by touching the tip of a capillary tube to the top of the reaction solvent. Spot the TLC plate with this aliquot using a capillary tube alongside the standards. Run the TLC plate using the chambers provided in the fume hood. *Do not remove the chambers from the fume hood!* Develop the plate with a UV or fluorescence light after evaporating the solvent from the plate in the fume hood.

If starting material is still present in the reaction, continue stirring for another 10 minutes and take another TLC aliquot. A faint spot for benzhydrol may still appear on a visualized plate, even when the reaction is complete. When there is no *dark* spot for benzhydrol in the reaction mixture, you may consider the reaction to be complete. The 10 minutes is counted from the first aliquot (20 min total). By the time you run the first TLC plate, it's probably time to run the second! Continue taking aliquots at 10-minute intervals until the reaction is complete. If the reaction is taking longer than 40 minutes, make a note then proceed to the next step.

3. Reaction Work-Up (FUME HOOD): Transfer the completed reaction mixture to a screw-cap test tube and remove the aqueous layer with a pipet. Wash the organic layer with 3 mL of brine (sat. NaCl) followed by a wash with 2 mL of water – mix, invert, then remove the aqueous layer after each portion of brine or water is added. Dry the organic layer over $MgSO_4$, gravity filter using a pipet with cotton plug, and collect the filtrate in a pre-weighed 25-mL round-bottom flask (RBF). Concentrate using a rota-vap and weigh the product. Pro-tip: the product rarely crystallizes in the rota-vap bath. When the solvent appears to have evaporated, take the flask off the rota-vap and swirl in the ice bath to crystallize. You can still proceed with the product in liquid form.

4. Analysis: Obtain the IR spectrum of your product. Is an OH peak present? The IR of starting material is online and should also be posted in the instrument room. Record the identifying peaks in your notebook. Sketch the final TLC plate into your notebook and calculate the R_f values for each spot. Report your data in table format. Analyze the ^1H NMR spectra of benzhydrol and benzophenone (provided on Canvas) using the table format in the worksheet.

Table 2. Clean-up & Safety

Clean-up	**Safety**
Liquid waste: aqueous layers and contents of rota-vap trap	Ethyl acetate is *flammable*.
Solid waste: $MgSO_4$, pipets, filter pipets, capillary tubes, and TLC plates	Benzophenone, benzhydrol, and Bu_4NHSO_4 are *irritants*.
After analysis, dispose of your product in the liquid waste using a *very small amount* of ethanol from a wash bottle to aid the transfer.	Sodium hypochlorite is an *oxidizer*. It will bleach your clothes so consider your wardrobe for the day!
Wash all glassware and wipe down counters.	Wear gloves & goggles throughout the experiment.
All used pipets & broken glass go in the glass waste box. Please do not throw away glass in the trash as it creates an unexpected occupational hazard for our custodial staff. Thank you for participating in community set up & clean up tasks ☺	

References & Supplemental Reading

Oxidation reactions	Klein 12.10
^{1}H NMR	Klein 15.1-6 or Mohrig Chapter 22.1-22.7
Extraction	Mohrig Chapter 10
TLC	Mohrig Chapter 18

- **Klein**, D. "Organic Chemistry, 3rd Edition";
- **Mohrig**, J. R.; *et. al*. "Techniques in Organic Chemistry, 4th Edition."
- Palleros, D. R. *Experimental Organic Chemistry*, Wiley: New York, **2000**; pp. 255-257.

How to Prepare for Lab + Assignments - Follow Canvas Exp 3 Module…

Before Lab

- Read this PDF – background, procedure, safety, pre-lab and in-lab questions
  - Option: listen to Caitlin read this document in the **8M Exp 3 Podcast**
- Attend and/or watch **lab lecture** – we go over everything you need for your assignments!
- Practice the lab online *via* **Slugs@home platform** - sites.google.com/ucsc.edu/slugshome/home
- Complete the **pre-lab questions** at the end of this doc - incorporated into Canvas quiz ☺
  - **Quiz** due before your enrolled section – check Canvas for due date
- Download the **Exp 3 worksheet** and prepare your **lab notebook**…

Lab Notebook Preparation – *worksheet = template / outline to copy by hand into lab notebook*

- **Purpose:** one-sentence summary of the main lab goals plus the structures of Excedrin components
- **Reagent Table** – add chemical properties; Wikipedia is a reliable source for chemical properties!
- **Procedure with Diagrams** – complete before starting lab; sample on Canvas
  - Use the procedure on the previous pages to create your hand-drawn experimental instructions
    - Simple sketches & labels for all **equipment, chemical names** with **amounts**, & **transfers**
  - Format: Break it up with flow charts, bullet-points, comic strip, and/or whatever works for you!
    - Avoid copying the procedure word-for-word.
    - Make it easy for anyone to follow your procedure without referring to this document.
  - **Slugs@home Exp 3 website** - Equipment & Safety pages; pictures & videos of the whole lab
  - The **class notes** include useful diagrams as well

During Lab

- Check the **safety rules** to dress for lab and arrive a few minutes early to **Thimann Labs**
- **Pre-lab talk:** tips for success and open Q&A
- Show your **lab notebook pages** to your TA
- Perform the experiment with a partner, fill out data & observations in **lab notebook**

After Lab – each partner submits separate, individual assignments

- Upload **Notebook Pages** to Canvas by midnight on lab day – graded on completeness / participation
- Complete & upload the **Lab Report** on GradeScope (GS) – due date on Canvas
  - In-lab questions & experimental methods – see last page of this document

Pre-lab Questions / Quiz

Take the **Exp 3 pre-lab quiz** *before* your enrolled section – see Canvas for due date

- The quiz incorporates the questions below - the questions may be reworded.
- **Be prepared with your responses to the pre-lab questions *before* starting the quiz.**
- There is a 20-minute time limit on the quiz and you get two attempts.
    - Make sure you have enough time to complete the quiz - you can't save and come back later.
    - If you choose to re-take the quiz, your grade will be the highest of the two attempts.

Though we encourage collaboration in this class, this is an individual quiz.

- The responses should be a product of your original work so that you are assessed on *your* understanding of the material.

Sharing your quiz or your responses in any format (screenshots, email, CHEGG, social media, text, carrier pigeon, etc.) is in violation of the UCSC academic integrity policy.

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1. Which **atom is oxidized** in the reaction of benzhydrol with bleach? Draw the **structures** and indicate the **oxidation number** of that atom in the starting material and product (see page 1 of this document for a refresher on oxidation numbers).

2. Predict the **IR spectra of benzhydrol and benzophenone**: identify functional groups, bonds, and expected wavenumber ranges. What are the main **differences** you expect to find between the IR of the starting material and product?

3. Briefly explain how **phase transfer catalysts** work and why one is necessary in this experiment.

4. What are the **advantages of using bleach** as an oxidizing agent? What other **oxidizing agents** could be used to carry out the same transformation (see **table 1**)?

5. What are the **two solvents** used in the oxidation reaction? Will the aqueous layer be on the **top or bottom** in the reaction work-up?

6. Calculate the **mmoles** of each reagent used, identify the **limiting reagent**, and calculate the **theoretical yield** of benzophenone (recall that catalysts cannot be limiting since they are regenerated). Show your work.

LAB REPORT

Canvas > **Experiment 3 Report** for submission details

Upload to GradeScope (GS) after both parts of the lab – see due date on Canvas

- **Select Pages** to correlate your responses to the GS outline ☺

A. In-Lab Questions –Many of these questions are included in the Exp 3 Worksheet (notebook template).

1. Report the mass of benzhydrol used and the theoretical yield of benzophenone. Report the **yield of product (mg and %).** Briefly **discuss** any parts of the procedure that may have caused the yield to be lower than 100%, citing specific steps and transfers.

2. Report the **TLC results** (mobile phase, R_f values, and identification) of TLC analysis in table format and explain how you decided to stop the reaction. Briefly **explain** why the TLC separation of benzhydrol and benzophenone was successful by comparing the polarity of the samples and mobile phase.

3. Report **IR analysis** in table format. **Compare** the IR of the starting material and product. Briefly **explain** which peaks signify reaction completion, including functional group, bond, and stretching frequency. Include a photo of your IR product spectrum.

4. Interpret the **^{1}H NMR spectra of benzhydrol and benzophenone**: re-draw the structures with labeled hydrogens. Create the NMR tables into a word processing document. Answer the following in one sentence: **Which NMR peak(s) best distinguish starting material from product?**

B. Experimental Methods

How to Write the Methods Section:

- Review the 8M Writing Guidelines on Canvas and the **writing section of the Exp 3 worksheet**
  - Use a similar format and writing style to the sample provided in the 8M writing guidelines, incorporating necessary content from the Exp 3 writing worksheet.
- Organize the **key information** into **complete, concise sentences** to allow an experienced synthetic chemist to carry out this experiment.
- Note: the experimental methods section is an *abbreviated* version of the procedure and will omit many procedural details.

Template – copy by hand into notebook

Name _____ Partner Name _____

TA Name _____ Section Letter _____ Day _____ Time _____

Experiment 3 Worksheet – Oxidation of Benzhydrol

Each student submits this individually on Canvas after lab

Pre-Lab Requirements

1. **Dress for lab** – see safety rules – please arrive a few minutes early
2. **Lab Notebook:** copy templates below into designated notebook
   - **Purpose, scheme,** and **reagent table**
   - **Procedure Diagrams** – copy templates provided, follow instructions to complete diagrams

A. Experimental Purpose and Oxidation Reaction Scheme

B. Reagent Table

Refer to the procedure for amounts and safety table for hazards; find the chemical properties on Wikipedia!

Name	Volume	Density	Mass	MW	mmol	Equiv*	Boiling or melting point	Hazards
Benzhydrol	-					1		
Bleach (~0.7 M)		-						
Tetrabutyl ammonium sulfate, $Bu_4N^+HSO_4^-$								
Ethyl Acetate						M		
Benzophenone (product)	-					-		

*** Equiv** = molar equivalents of reaction components with respect to the limiting reagent (benzhydrol)

- Bleach & $Bu_4N^+HSO_4^-$ (reagents): divide the mmol of reagent by the mmol of benzhydrol

- Ethyl Acetate (solvent): approximate concentration = divide the mmol of benzhydrol by the volume of solvent

Check out Slugs@home for pics & videos of the full lab!

C. Procedure Diagrams – *worksheet = template / outline to copy by hand into lab notebook*

- Use the **procedure from the lab PDF** create your hand-drawn experimental instructions
  - Simple sketches & labels for all **equipment, chemical names** with **amounts**, & **transfers**
  - Include clean-up & safety notes throughout your procedure and leave space for observations
- Format: Break it up with flow charts, bullet-points, comic strip, and/or whatever works for you!
  - Avoid copying the procedure word-for-word.
  - Make it easy for anyone to follow your procedure without referring to this document.
- **Slugs@home Exp 3 website** - Equipment & Safety pages; pictures & videos of the whole lab
- The **class notes** include useful diagrams as well
- *Use as many pages as needed* - at least 3 pages is typical

1. **Reaction Preparation and Set-up** – chemicals added to flask, preparing TLC plates with standards
2. **Monitoring Reaction Progress –** representative aliquot from reaction and steps for spotting, running, and visualizing the TLC plate
3. **Reaction Work-Up** – include all transfers from one container to another
4. **Analysis** – steps for preparing IR sample and rough sketch of both IR spectra; NMR not included in this section

E. Data

Mass of benzhydrol _____ mg

Theoretical yield _____ mg

Calculation:

Sketches of TLC plates and calculated R_f values for each spot:

Standards

Reaction Aliquots (portions over time)

Notes on potential Product loss:

Product mass _____ mg

Percent recovery = (product mass) / (theoretical yield) x 100% = _____%

IR Analysis – Observe the IR spectrum in the website and identify any signals within the expected range. It is acceptable for a signal to be "not observed."

Benzhydrol

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

Benzophenone

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

^{1}H NMR analysis of spectra (Canvas)

Benzhydrol – add structure with H's labeled **A**-**E**

Signal	Integration (# of H's)	Expected Chemical Shift (ppm)	Observed Chemical Shift (ppm)
A			
B			
C			
D			
E			

Calculations for expected chemical shifts:

Benzophenone structure with H's labeled **A'** – **C'**

Signal	Integration (# of H's)	Expected Chemical Shift (ppm)	Observed Chemical Shift (ppm)
A'			
B'			
C'			

Calculations for expected chemical shifts:

F. Experimental Methods Writing Worksheet – provided in lab ☺

1. Draw the **reaction scheme** by hand (no copy/paste) and list the **name of the product**.
The reaction scheme includes reactant, reagents over arrow, solvent under arrow, and product.

2. What **glassware** and **equipment** was used for this reaction (aside from chemicals)?

3. How much **benzhydrol** was used? Convert **mass** to **mmol (xx g, xx mmol)**. Show your work, including units with every value. *Calculate or look up the molecular weight of benzhydrol (g/mol) = (mg/mmol).*

4. How much bleach (**NaClO**) was used and what was the **concentration (____ M, ____ mL)**? Fill in the blanks and calculate the quantity of **bleach in mmoles.** Show your work. *Recall Molarity = (moles / Liter) … M = (mol / L) = (mmol / mL).*

5. How much *tert*-butylammonium hydrogen sulfate (**Bu_4NHSO_4**) was used (**xx g**)? This is a catalyst – include only mass not mmol.

6. Determine the **limiting reagent** then calculate the **theoretical yield** (mmol and mg). Show your work, including units with every value. *Determine the mole ratio in the reaction (x mol benzyhydrol / x mol benzophenone). Calculate or look up the molecular weight of benzhydrophenone (g/mol) = (mg/mmol).*

F. Experimental Methods Writing Worksheet (cont'd)

7. What **solvent** was used in the oxidation reaction and in what **volume**?

8. What was the **reaction temperature** and **time**? Was the reaction stirred, refluxed, or standing?

9. What **technique** was used to monitor **reaction progress**? What **solvent(s)** were used during this analysis?

10. List the **identity** and **quantities** of the **chemicals (xx mL)** used in the **reaction work-up**. *Note: quantity of drying agent need not be included.*

11. What **additional processes** were involved in the final isolation of product?

12. What is the yield of **benzophenone (_____ g, _____ mmol, _____ % yield)**? Fill in the blanks and show your work below, including units on every value.

(a) Convert **benzophenone mass** (300 mg) to **mmol** using molecular weight (g/mol) = (mg/mmol).

(b) Calculate **percent (%) yield** using 300 mg as the actual yield and the th. yield from #6.

$$\% \text{ yield} = \frac{\text{actual yield (mg)}}{\text{Theoretical yield (mg)}} \times 100\%$$

Experiment 4 – Preparation of Fruity Fragrances

Learning Objectives

- Perform and understand Fischer esterification reactions
- Apply acid-base extraction in the reaction work-up
- Critical analysis of liquid-liquid extraction technique
- Observe and interpret hydroxamic acid tests for esters
- Interpret infrared (IR) spectra of starting materials and product to determine reaction success
- Predict and interpret ^{1}H NMR spectra of synthetic banana and apple oils

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* Please find "How to Prepare for Lab & Assignments" after the procedure in this doc.

Background: Esterification Reactions

Esters encompass a large family of organic compounds with broad applications in medicine, biology, and industry. Esters are represented by the structure R(C=O)OR', in which R and R' are alkyl or aryl groups. Esters are widespread in nature, occurring naturally in plants and animals. Small esters, in combination with other volatile compounds, produce the pleasant aroma of fruits. A symphony of chemicals is typically responsible for specific fruity fragrances, however, often one single compound plays the leading role. For example, artificial pineapple flavor contains more than twenty ingredients but ethyl butyrate is the major component. Examples of ester flavors and fragrances are shown in **Figure 1**. In contrast to previous experiments where students isolated compounds from plants, in this experiment, students will synthesize these compounds in the lab.

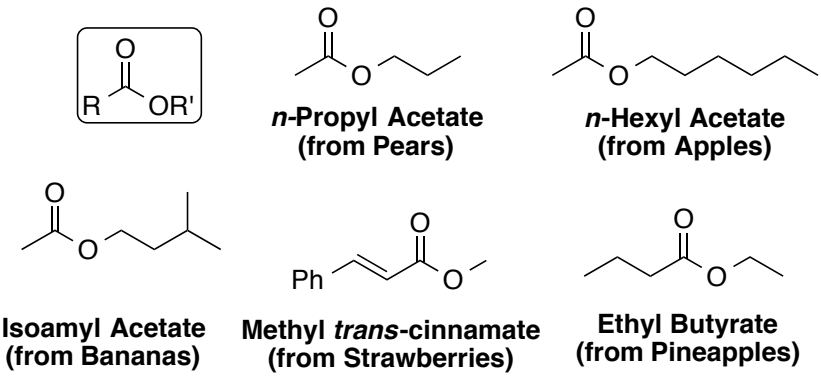

Figure 1. Examples of esters found in essential fruit oils.

Esters are carboxylic acid derivatives commonly synthesized by Fischer esterification (**Figure 2**). A carboxylic acid is reacted with an alcohol in the presence of catalytic amounts of mineral acids such as sulfuric or hydrochloric acids under refluxing conditions (heat to boiling). This reaction is reversible and thus is limited by its equilibrium constant and dictated by Le Chatelier's Principle. A large excess of either reactant pushes the equilibrium to favor products, thus increasing the yield. Constantly removing the product will also increase the yield, though this is not always possible or practical. A Fischer esterification is only recommended with primary and secondary alcohols and unhindered carboxylic acids. Steric hindrance near the reaction center slows down the esterification.

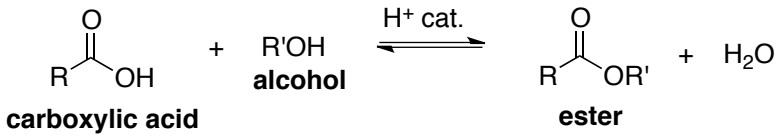

Figure 2. General scheme for a Fischer esterification reaction.

In this experiment, students prepare either banana oil from acetic acid and isoamyl alcohol or prepare sour apple oil from acetic acid and *n*-hexanol (**Figure 3**). Incidentally, isoamyl acetate is also the alarm pheromone of the honeybee and thus, it should be kept away from beehives! The reaction is performed at the microscale level using a Fischer esterification under refluxing conditions. A round-bottom flask is topped with a water-cooled condenser. The contents of the flask are heated to the boiling. Vapors travel up and inside the reflux condenser, where they condense back to a liquid and fall back into the round-bottom flask. This allows the system to remain open while heating, but without losing any reaction components. This particular reaction is run "neat" or without solvent. The acid and alcohol are both liquids and act as the solvent. It is important that the reaction flask does not run dry and that *cold water* be running through the condenser at all times.

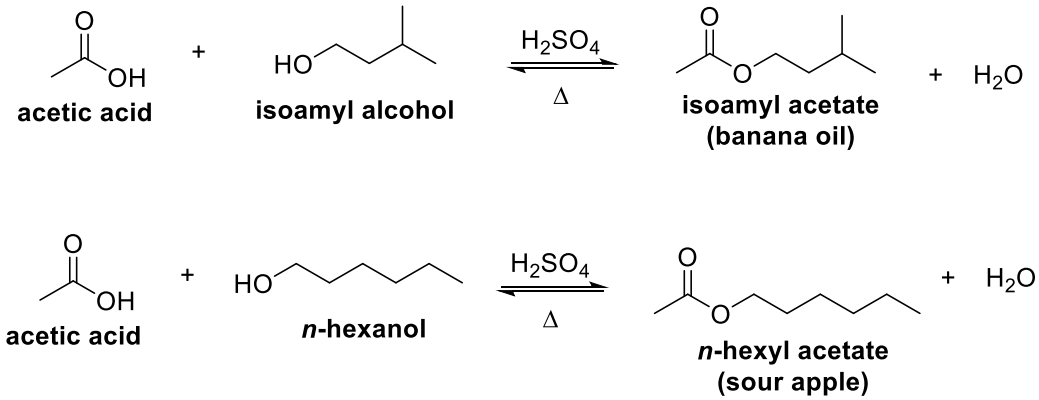

Figure 3. Reaction schemes for fruity fragrance synthesis *via* Fischer esterification

An acid-base extraction is performed with an aqueous bicarbonate (baking soda, $NaHCO_3$) solution to separate the ester from the unreacted acetic and sulfuric acid. This weakly basic solution also contains NaCl to improves phase separation in liquid-liquid extractions. This $NaHCO_3$-NaCl solution has a high ionic strength and draws residual water out of the organic layer. No additional organic solvent is necessary for the acid-base extraction because these esters are liquids and separate from the aqueous solution as an immiscible layer.

Time and quantity permitting, the ester product may be purified by microscale distillation using a Hickman still and a water-cooled condenser. Acid-base extraction is not an applicable method for separation of alcohol from ester, neither of which are acidic or basic! Column chromatography would be effective for separation since the alcohol and ester have very different polarities. The product is analyzed by IR and the hydroxamic acid test for esters and with comparison to alcohol starting materials. ^{1}H NMR spectra of banana and apple oil are provided for analysis.

PROCEDURE

Procedure Diagrams must be complete in your lab notebook before you can start the lab (see worksheet)

The statements in quotes are provided to give you guidance in writing the experimental methods section. One well-written sentence can explain an entire paragraph's worth of information!

1. Reaction Preparation and Set-Up

"To a 15-mL RBF was added…[chemical names (mmol, mL)]…and heated to reflux for 1 hour."

Pre-heat a sand bath on a hot plate at a medium setting. You may set this up as soon as you enter the lab, before the TA's pre-lab talk. Dispense 10 mmoles of the desired alcohol (isoamyl alcohol or *n*-hexanol) and 40 mmoles of glacial acetic acid into a 15-mL round-bottom flask (RBF) using a glass pipet and pluringe. Convert the *mmole quantities into volume (mL) before lab.* Add 3 drops of sulfuric acid and magnetic stir bar then attach a microscale water-jacketed condenser (figure on next page). Be sure the water is running through the condenser and reaction is stirring before heating. Heat to reflux with stirring in the sand bath and allow the reaction to reflux for one hour.

2. Reaction Work-up

"The reaction was quenched and washed with…"

Carefully lift the apparatus from the heat and allow the mixture to cool to ambient temperature. Disassemble the apparatus and turn off the water (clamp), but keep the hoses attached. Do not wash the condenser at this stage, as it may be used later. Transfer the liquid to a 16 x 125 screw-cap test tube with a pipet. Rinse the RBF with 2 mL of 5% $NaHCO_3$ in 15% NaCl solution. Slowly transfer the rinse to the screw-cap test tube. Stir the mixture with a microspatula until gas evolution (carbon dioxide) has subsided. Cap the tube and invert it several times to mix the layers. Frequently vent the system to release the pressure by momentarily unscrewing the cap. Let the system settle for about 10 minutes.

Use a pipet to transfer the lower aqueous layer to a labeled test tube. Keep this until the end of the experiment then discard it. Wash the organic layer remaining in the test tube twice with 1 mL of the $NaHCO_3$-NaCl solution. Invert and vent well in each wash. Collect the aqueous washes in the same labeled test tube as before.

"The combined organic layers were dried (Na_2SO_4) and filtered to afford..."

Remove any visible water from the product with a pipet. Dry the organic layer by adding a small microspatula-ful of anhydrous Na_2SO_4. Note that this drying agent is more granular than $MgSO_4$ and will create a similar but not identical snow-globe effect when sufficient drying agent is added. It may be necessary to add more, however, this may affect how much liquid can be obtained after filtration. Allow the product to dry for 5 minutes with occasional swirling. Filter using a pipet loosely packed with a small piece of cotton into a pre-weighed, labeled vial to obtain the mass of the crude product.

(No purification by distillation)

4. Analysis: Hydroxamic Acid Test

"Product formation was confirmed (or not) by the hydroxamic acid test for esters."

Perform this test with starting materials (alcohol and acetic acid), ethyl acetate (ester standard), and product in four separate test tubes. Add one drop of the sample to be tested to 1 mL of 0.5 M hydroxylamine hydrochloride (NH_2OH-HCl) in 95% ethanol in a test tube. Add 0.2 mL of a 6 M NaOH solution drop-wise and a boiling chip. Bring the mixture to a boil by heating in a water bath. Let the system cool and add 2 M HCl drop-wise until the pH is 2-3. If cloudiness develops, add 2 mL of 95% ethanol. Add 2 drops of 3% ferric chloride solution. A red-violet color is a positive test.

Analysis: IR and NMR spectroscopy spectroscopy

"The [crude or purified] product was analyzed by IR."

Analyze the IR spectrum of the alcohol (provided in lab, posted on Canvas). Obtain the IR spectrum of your product using NaCl plates and identify ester peaks. *Is there an OH peak in the product?*

Interpret the ^{1}H NMR spectra of <u>both ester products</u> (may be provided in lab, also posted on Canvas). Assign every hydrogen on the structure to a signal on the spectrum (integration, splitting, and expected & observed chemical shift).

Table 1. Clean-up & Safety

Clean-up	**Safety**
Liquid waste: aqueous layers and solutions from chemical test	H_2SO_4, HCl, hydroxamic acid, NaOH, and acetic acid are *corrosive*
Solid waste: Na_2SO_4, pipets, filter pipets	Acetic acid, ethyl acetate, and ethanol are *flammable*
After analysis, dispose of your product in the liquid waste using a *very small amount* of ethanol from a wash bottle to aid the transfer.	Isoamyl alcohol is an *irritant*
Wash all glassware and wipe down counters; return shared glassware to reagent counter	Wear gloves & goggles throughout the experiment.
Clean IR plates with acetone saturated with NaCl. Return plates to the desiccator after use.	Be careful not to burn or melt the water hoses on the hotplates!
All used pipets & broken glass go in the glass waste box. *Please do not throw away glass in the trash as it creates an unexpected occupational hazard for our custodial staff.* Thank you for participating in community set up & clean up tasks ☺	

<u>References and Supplemental Reading</u>

Palleros, D. R. "Preparation of Fruity Fragrances," *Experimental Organic Chemistry*, **2000**. Wiley: Hoboken.

Mohrig 4th edition: Chapter 7.1 (Reflux), 22.7-11 (NMR)

Klein 2nd edition: Chapter 15.1-6 (NMR), 20.10 & 20.15 (Fischer esterification)

McMurry 8th edition: Chapter 13.11 (^{1}H NMR splitting), 21.3 (Fischer Esterification), & 21.10 (^{1}H NMR of esters)

How to Prepare for Lab + Assignments

Follow Canvas Exp 4 Module…

Before Lab

- Read this PDF – background, procedure, safety, pre-lab and in-lab questions
  - Option: listen to Caitlin read this document in the **8M Exp 4 Podcast**
- Attend and/or watch **lab lecture** – we go over everything you need for your assignments!
- Practice the lab online *via* **Slugs@home platform** - sites.google.com/ucsc.edu/slugshome/home
- Complete the **pre-lab questions** at the end of this doc - incorporated into Canvas quiz ☺
  - **Quiz** due before your enrolled section – check Canvas for due date
- Download the **Exp 4 worksheet** and prepare your **lab notebook**…

Lab Notebook Preparation – *worksheet = template / outline to copy by hand into lab notebook*

- **Purpose:** one-sentence summary of the main lab goals plus the reaction schemes
- **Reagent Table** – add chemical properties; Wikipedia is a reliable source for chemical properties!
- **Procedure with Diagrams** – complete before starting lab; sample on Canvas
  - Use the procedure on the previous pages to create your hand-drawn experimental instructions
    - Simple sketches & labels for all **equipment, chemical names** with **amounts**, & **transfers**
  - Format: Break it up with flow charts, bullet-points, comic strip, and/or whatever works for you!
    - Avoid copying the procedure word-for-word.
    - Make it easy for anyone to follow your procedure without referring to this document.
  - **Slugs@home Exp 4 website** - Equipment & Safety pages; pictures & videos of the whole lab
  - The **class notes** include useful diagrams as well

During Lab

- Check the **safety rules** to dress for lab and arrive a few minutes early to **Thimann Labs**
- **Pre-lab talk:** tips for success and open Q&A
- Show your **lab notebook pages** to your TA
- Perform the experiment with a partner, fill out data & observations in **lab notebook**

After Lab – each partner submits separate, individual assignments

- Upload **Notebook Pages** to Canvas by midnight on lab day – graded on completeness / participation
- Complete & upload the **Lab Report** on GradeScope (GS) – due date on Canvas
  - In-lab questions & experimental methods – see last page of this document

Pre-lab Questions / Quiz – see your class notes!

1. Why is the reaction mixture extracted with **sodium bicarbonate ($NaHCO_3$)** and **sodium chloride (NaCl)** solution? What role does each salt play?

2. Calculate the **mass (mg)** and **volume (mL)** of alcohols and acetic acid that will be mixed from the mmol given in the procedure. Include these values in the reagent table in your notebook.

3. Determine the **limiting reagent** in the reactions. Calculate the **theoretical yield** of both syntheses in mg. Recall that catalysts cannot be the limiting reagent.

4. How is **Le Chatelier's Principle** on equilibrium used to increase the success of the esterification reaction?

5. Based on the techniques you have learned thus far in the organic chemistry lab, what are two methods that could be used to **separate unreacted alcohol from the ester**? Briefly explain **why** each would be expected to work. *Hint: you learned one of the techniques earlier this quarter; the other you learned in 8L.*

Take the **Exp 4 pre-lab quiz** *before* your enrolled section – check Canvas for due date

- The quiz incorporates the questions below - the questions may be reworded.
- **Be prepared with your responses to the pre-lab questions *before* starting the quiz.**
- There is a 20-minute time limit on the quiz and you get two attempts.
    - Make sure you have enough time to complete the quiz - you can't save and come back later.
    - If you choose to re-take the quiz, your grade will be the highest of the two attempts.

Though we encourage collaboration in this class, this is an individual quiz.

- The responses should be a product of your original work so that you are assessed on *your* understanding of the material.

Sharing your quiz or your responses in any format (screenshots, email, CHEGG, social media, text, carrier pigeon, etc.) is in violation of the UCSC academic integrity policy.

LAB REPORT

Canvas Modules > **Experiment 4 Report** for submission details

Upload to GradeScope (GS) – due date on Canvas

- **"Select Pages"** to correlate your responses to the GS outline ☺
- Option to submit with ONE partner – one person uploads then "Add Group Member"

A. In-Lab Questions – see your lecture notes!

1. Show the full arrow-pushing **mechanism** for the assigned ester (apple or banana), including charged reaction intermediates to account for all bonds broken and formed. Draw the **full structures of the starting alcohol and final product** (define "R groups" as use the abbreviation only in the intermediates).

2. Draw the chemical reactions that **sodium bicarbonate** facilitates in the reaction workup. The equations should include the gas formed. *Note: sodium bicarbonate participates in two different (though similar) reactions.*

3. Report the **yield (mg)** and calculate the **percent yield** of the assigned synthesis. Discuss 2-3 suspected sources of **product loss** (exact parts of the procedure, such as transfers between containers, when you most likely lost product).

4. Interpret the **IR of the assigned alcohol and product**. Include the functional group, bond, expected and observed absorbances (wavenumbers, cm^{-1}). Briefly discuss whether the reaction went to completion (or not).

5. Report and interpret the **hydroxamic acid test** results. Draw the **chemical reaction** that occurred with your product – no abbreviations. What do the chemical test results suggest about the **success** of the fruity fragrances synthesis?

6. Interpret the **^{1}H NMR spectra** provided in lecture for *both* **(a)** banana oil and **(b)** sour apple. Spectra provided in lecture notes and posted online. *Caitlin made supplemental videos on NMR interpretation of these esters - linked in the Canvas assignment for this report* ☺

- Re-create **separate typed tables for each ester** in your report, including **re-drawn structures** with each set of **H's labeled (A, B, C, etc.).**

B. Experimental Methods

Use the **bold headings within the Exp 4 procedure** to get an idea of the level of detail to include in the experimental methods section (you may use those exact words!). You will need to **fill in your own data and descriptions** in place of "…" Simply report whether the "presence of an ester was confirmed by the **hydroxamic acid test**" (no procedural details). **IR** is the only form of characterization to report, as you are not directly analyzing your sample by NMR.

Writing guidelines and **sample experimental methods** are available on Canvas. Remember the sample experimental contains way more information than is pertinent to CHEM 8M students!

Template – copy by hand into lab notebook

Name _____ Partner Name _____

TA Name _____ Section Letter _____ Day _____ Time _____

Experiment 4 Worksheet – Synthesis of Fruity Fragrances

Use as reference for notebook preparation – everyone submits on Canvas individually after lab

Pre-Lab Requirements

1. **Dress for lab** – see safety rules – please arrive a few minutes early
2. **Lab Notebook:** copy templates below into designated notebook
   - **Purpose, scheme,** and **reagent table**
   - **Procedure Diagrams** – copy templates provided, follow instructions to complete diagrams

A. Experimental Purpose and Reaction Scheme

B. Reagent Table

Refer to the procedure for amounts and safety table for hazards; find the chemical properties on Wikipedia!

Name	Volume	Density	Mass	MW	mmol	Boiling or melting point	Hazards
Isoamyl alcohol	-						
n-hexyl alcohol		-					
Sulfuric acid	3 drops	-	-		-		
Isoamyl acetate (banana product)	-						
n-hexyl acetate (apple product)	-						

See Slugs@home for pics & videos of the full lab!

C. Procedure Diagrams - use many pages as needed, at least 3 is typical

- Use the procedure in the lab PDF to create your hand-drawn experimental instructions
  - Simple sketches & labels for all **equipment, chemical names** with **amounts**, & **transfers**
- Format: Break it up with flow charts, bullet-points, comic strip, and/or whatever works for you!
  - Avoid copying the procedure word-for-word.
  - Make it easy for anyone to follow your procedure without referring to this document.
- **Slugs@home Exp 4 website** - Equipment & Safety pages; pictures & videos of the whole lab
- The **class notes** include useful diagrams as well

1. **Reaction Preparation and Set-up** – chemicals added to flask, components & assembly of reflux apparatus

2. **Reaction Work-Up** – all step-wise transfers of solutions, including components in each layer, drying, filtering, and isolation of product

3. **Distillation** – assembly and components of miscroscale distillation apparatus, including what material was added to and removed from each part

4. **Analysis: Hydroxamic Acid Test & IR –** labeled test tubes with contents and observations; IR sample preparation and sketch of spectrum

E. Data

Alcohol _____ Alcohol volume _____ mL Alcohol moles _____ mmol

Theoretical Yield _____ mg

Calculation:

Product Loss

Product Recovery _____ mg % Yield _____

Hydroxamic Acid Test

Sample	Observations	Interpretation
1. Alcohol		
2. Acetic Acid		
3. Ethyl acetate		
4. Product		

Draw the two chemical reactions that occurred in all positive chemical tests reported above: starting material, reagent & solvent (either sodium iodide in acetone or silver nitrate in ethanol), and product.

See Slugs@home for pics & videos of the full lab!

E. Data (cont'd)

IR Analysis – Predict each signal from the structure *before* analyzing provided spectra. Observe the IR spectrum and identify any signals within the expected range. It is acceptable for a signal to be "not observed."

Assigned Alcohol:

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

Assigned Ester

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

E. Data (cont'd)

^{1}H NMR Analysis of Isoamyl Acetate (Banana Oil) – posted on Canvas, provided in lab

Draw structure with labeled H's

Signal	Integration (# of H's)	Expected Chemical Shift (ppm)	Observed Chemical Shift (ppm)	# of 3-bond Neighbors (n)	Multiplicity/ Splitting (m = n+1) ex. Singlet, doublet, etc.
A			4.0		
B			2.0		
C			1.6		
D			1.4		
E			0.9		

^{1}H NMR Analysis of Hexyl Acetate (Apple Oil) – posted on Canvas, provided in lab

Draw structure with labeled H's

Signal	Integration (# of H's)	Expected Chemical Shift (ppm)	Observed Chemical Shift (ppm)	# of 3-bond Neighbors (n)	Multiplicity/ Splitting (m = n+1)
A	2H		4.0		triplet
B	3H		2.0		singlet
C	2H		1.5		pentet
D	6H		1.2	(Many)	multiplet
E	3H		0.8		triplet

See Slugs@home for pics & videos of the full lab!

Experiment 5 – Synthesis of Aspirin

Learning Objectives

- Perform and understand esterification reactions
- Purification – acidification & recrystallization
- Observe and interpret iron (III) chloride tests for phenols
- Interpret infrared (IR) spectra of starting materials and product to determine reaction success
- Predict and interpret ^{1}H and ^{13}C NMR spectra of aspirin

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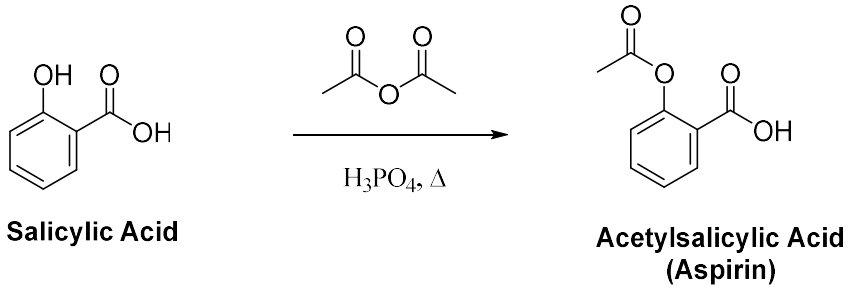
* Please find "How to Prepare for Lab & Assignments" after the procedure in this doc.

Lab Overview

In this experiment, students carry out the acid-catalyzed esterification of salicylic acid with acetic anhydride and isolate aspirin as a white solid (**Scheme 1**). The mechanism is similar to Fischer esterification (Exp 4). The difference is the use of an acid anhydride instead of an alcohol. Acetic anhydride loses its acetate group, which is removed in the reaction workup with a weak base extraction. Conversion to product is confirmed with iron (III) chloride chemical tests in comparison to standards. IR spectra of starting material and product as well as ^{1}H and ^{13}C NMR spectra of aspirin will be interpreted.



Salicylic Acid **Acetylsalicylic Acid (Aspirin)**

Scheme 1. Aspirin synthesis *via* acid-catalyzed esterification with acetic anhydride.

PROCEDURE

Procedure Diagrams must be complete in your notebook before you can start the lab (see worksheet).

1. Reaction Setup: Fill a small crystallizing dish half way with water. Place on a hotplate (medium setting) and bring to a gentle boil. You may do this when you enter the lab, before the TA's pre-lab talk. *The water bath must be pre-heating before obtaining reagents.* In the meantime, in a clean and **dry** 15-mL round-bottom flask add a small stir bar and approximately 200 mg of salicylic acid. Add 2 mL of acetic anhydride using the pluringe provided (keep this and all reagent bottles in the fume hood). Finally, add 2 drops of H_3PO_4 to catalyze the reaction.

Attach a microscale condenser using a small amount of grease and Keck clip. Place the apparatus half-way in the *boiling* water bath and let the system react for about 5 minutes. The reaction will not proceed if the water bath is not at a boil for the full 5 minutes. *Carefully* move the apparatus out of the water bath and allow the system to cool to room temperature. Add 1 mL of water through the top of the condenser to quench excess acetic anhydride. Place the system back in the water bath and allow this to react for an additional 5 minutes. There is no need to continue heating the water bath during this time - just the warm water bath is sufficient.

2. Reaction Workup: Carefully remove the water bath from the hot plate using a hot mitt and let the reaction apparatus cool to room temperature. Use a pipet to transfer the liquid to a labeled 50-mL beaker. Wash the walls of the RBF with 2 mL of water to facilitate transfer of any reaction mixture still in the flask. Add 3 mL of water to the beaker then cool the system in an ice-water bath for a few minutes. Once the solution has cooled, *scratch the bottom of the beaker with a glass stir rod to release small crystals attached to the glass* and promote further crystal growth. If crystals do not form within a few minutes after scratching, raise your hand to obtain a seed crystal from your TA. Allow crystals to form undisturbed in the ice-water bath for an additional 5 minutes (Pro-tip: crystals tend to form when you're not watching them!).

Set up the vacuum filtration apparatus while crystals continue to form and pre-weigh the filter paper. Vacuum-filter the product using a Buchner funnel. It is common for more crystals to form in the filtrate after filtration. If that is the case, transfer the funnel onto a different filter flask and filter again. Carefully collect a small amount of aspirin off the filter paper for the chemical test (microspatula tip). The effect on product yield is negligible. Let the solid dry on the filter paper with the vacuum on for 10 minutes while performing the chemical tests. Weigh the product and calculate the yield by subtracting the mass of filter paper. Calculate the % yield using the theoretical yield from the pre-lab.

4. Analysis: Iron (III) Chloride tests, IR, ^{1}H NMR, and ^{13}C NMR

Start early with the standards while the reaction is running, aspirin crystals are forming, or any other down time. Obtain reagents in the fume hood then bring the samples back to your workspace. Prepare 3 labeled test tubes each with 1 mL of a 0.1% aqueous ferric chloride solution in each. To one test tube, add a small amount of salicylic acid (microspatula tip). Add the aspirin product to another test tube. Add a drop of water to the third test tube. Observe any change in color. A red-purple color is a positive test for phenols; yellow is considered negative. Have your TA initial your exam to confirm that you have completed the chemical tests.

Analyze the IR spectrum of the alcohol (provided in lab, posted on Canvas). Obtain the IR spectrum of your product and identify ester peaks. Is there an OH peak in the product?

Interpret the ^{1}H and ^{13}C NMR of aspirin on Canvas. Assign every H on the structure to a signal on the spectrum. This is all covered in lab lecture ☺

Table 1. Clean up and safety instructions

Clean-up	*Safety*
Keep all reagents in the fume hood and clean up spills with spill mats, NOT the sponges from the sink.	**Label** all glassware (except for reflux setup).
	Phosphoric acid is corrosive – change gloves after use
Return all shared glassware, cleaned, to its original location.	**Acetic anhydride is a lachrymator** (induces tears) – wear goggles
Unplug hotplates. Disassemble the reflux and filtration apparatus – leave materials as you found them.	**Wear gloves, goggles, and lab coat at all times.**
Solid waste: Used pipets, filter paper, product	*** Allow reaction to cool (raise out of water bath) before quenching with water.**
Liquid waste: filtrates	

Adapted from Palleros, D. R. “Transforming Bengay into Aspirin” in *Experimental Organic Chemistry.* Wiley: New York, **2000**.

How to Prepare for Lab + Assignments

Follow Canvas Exp 5 Module…

Before Lab

- Read this PDF – background, procedure, safety, pre-lab and in-lab questions
- Attend and/or watch **lab lecture** – we go over everything you need for your assignments!
- Practice the lab online *via* **Slugs@home platform** - sites.google.com/ucsc.edu/slugshome/home
- Complete the **pre-lab questions** at the end of this doc - incorporated into Canvas quiz ☺
    - **Quiz** due before your enrolled section – check Canvas for due date
- Download the **Exp 5 worksheet** and prepare your **lab notebook**…

Lab Notebook Preparation – *worksheet = template / outline to copy by hand into lab notebook*

- **Purpose:** one-sentence summary of the main lab goals plus the reaction scheme
- **Reagent Table** – add chemical properties; Wikipedia is a reliable source for chemical properties!
- **Procedure with Diagrams** – complete before starting lab; sample on Canvas
    - Use the procedure on the previous pages to create your hand-drawn experimental instructions
        - Simple sketches & labels for all **equipment, chemical names** with **amounts**, & **transfers**
    - Format: Break it up with flow charts, bullet-points, comic strip, and/or whatever works for you!
        - Avoid copying the procedure word-for-word.
        - Make it easy for anyone to follow your procedure without referring to this document.
    - **Slugs@home Exp 5 website** - Equipment & Safety pages; pictures & videos of the whole lab
    - The **class notes** include useful diagrams as well

During Lab

- Check the **safety rules** to dress for lab and arrive a few minutes early to **Thimann Labs**
- **Pre-lab talk:** tips for success and open Q&A
- Show your **lab notebook pages** to your TA
- Perform the experiment with a partner, fill out data & observations in **lab notebook**

After Lab – each partner submits separate, individual assignments

- Upload **Notebook Pages** to Canvas by midnight on lab day – graded on completeness / participation
- Complete & upload the **Lab Report** on GradeScope (GS) – due date on Canvas
    - In-lab questions & experimental methods – see last page of this document

Pre-lab Questions / Quiz – see your class notes!

1. Convert the amounts of salicylic acid and acetic anhydride provided in the procedure into **mmoles**. Calculate the mmol of salicylic acid and acetic anhydride used in the reaction. Calculate the **theoretical yield** for the esterification reaction (synthesis of aspirin from salicylic acid). Show your work.

2. What would happen if the glassware were not **dry** during the esterification reaction? How is water used to **quench the reaction** after it is complete?

3. What differences would you expect to see in the IR and ^{1}H NMR spectra of salicylic acid and aspirin?

4. There are several periods of down time during this experiment. What / when are these periods and what can you do in your down-time to be efficient with your time?

Take the **Canvas Exp 5 pre-lab quiz by midnight Monday** *before* your enrolled section.

- The quiz incorporates the questions below - the questions may be reworded.
- **Be prepared with your responses to the pre-lab questions *before* starting the quiz.**
- There is a 20-minute time limit on the quiz and you get two attempts.
    - Make sure you have enough time to complete the quiz - you can't save and come back later.
    - If you choose to re-take the quiz, your grade will be the highest of the two attempts.

Though we encourage collaboration in this class, this is an individual quiz.

- The responses should be a product of your original work so that you are assessed on *your* understanding of the material.

Sharing your quiz or your responses in any format (screenshots, email, CHEGG, social media, text, carrier pigeon, etc.) is in violation of the UCSC academic integrity policy.

LAB REPORT

Upload to GradeScope (GS) – see due date on Canvas

- **Select Pages** to correlate your responses to the GS outline ☺
- OPTION to work with a partner – one person uploads the PDF then **"Add Group Member"** – gives both of you the same grade

A. In-Lab Questions – see your class notes!

1. Draw the arrow-pushing **mechanism** for the synthesis of aspirin from salicylic acid. You may abbreviate the aromatic ring ("Ar") in the intermediates; draw full structures of starting materials and products.

2. What are the two **roles of water** in the reaction work-up? Show the **chemical reaction** for the water-sensitive reagent.

3. Report the **mass of salicylic acid** given and the re-calculated **theoretical yield of aspirin** (mmol and mg). Report the **mass of product** and calculate the **% yield** of aspirin. Show your work.

Use the table format provided in the **Exp 5 Worksheet** to report data in addition to the prompts below.

4. Report the observations and interpretation of the **ferric chloride tests**. Was the reaction successful? Briefly explain.

5. Interpret the **IR** spectra of starting material and product in table format. Which peaks in each IR spectra be used to tell whether the reaction is complete?

6. Interpret the **^{1}H NMR** of aspirin on Canvas. Report integration, chemical shift (expected and observed), and splitting patterns for each signal in table format. Clearly assign each signal to the structure. You may list a range of expected chemical shifts where appropriate but you are graded on proper assignments of all signals to observed shifts.

7. Interpret the **^{13}C NMR** of aspirin on Canvas. Assign as many signals as possible on the spectrum to the structure (you're not expected to definitively assign each carbon, but you can get close!). Report the appropriate expected chemical shift range of each carbon using the NMR table of values.

B. Experimental Methods

Writing guidelines and sample experimental methods are available on Canvas. Remember the sample experimental contains way more information than is pertinent to CHEM 8M students! Apply the format used in previous reports:

Analysis: Report whether the absence of a phenol was confirmed by the **iron (III) chloride test** (no procedural details). **IR** is the only form of characterization to report, as you are not directly analyzing your sample by NMR.

Template – copy by hand into lab notebook

Name _____ Partner Name _____

TA Name _____ Section Letter _____ Day _____ Time _____

Experiment 5 Worksheet – Synthesis of Aspirin

Use as reference for notebook preparation – everyone submits on Canvas individually after lab

Pre-Lab Requirements

1. **Dress for lab** – see safety rules – arrive a few minutes early
2. **Lab Notebook:** copy templates below into designated notebook
   - **Purpose, scheme,** and **reagent table**
   - **Procedure Diagrams** – must be complete before you can start the lab

A. Experimental Purpose and Reaction Scheme

B. Reagent Table

Refer to the procedure for amounts and safety table for hazards; find the chemical properties on Wikipedia!

Name	Volume	Density	Mass	MW	mmol	Equiv*	Boiling or melting point	Hazards
Salicylic acid	-							
Acetic anhydride		-						
Phosphoric acid	2 drops	-	-		-			
Acetylsalicylic acid (aspirin, product)	-							

*** Equiv** = molar equivalents of reaction components with respect to the limiting reagent (salicylic acid)

- Acetic Anhydride (reagent): divide the mmol of reagent by the mmol of salicylic acid

See Slugs@home for pics & videos of the full lab!

C. Procedure Diagrams - use many pages as needed, at least 3 is typical

- Use the procedure in the lab PDF to create your hand-drawn experimental instructions
  - Simple sketches & labels for all **equipment, chemical names** with **amounts**, & **transfers**
- Format: Break it up with flow charts, bullet-points, comic strip, and/or whatever works for you!
  - Avoid copying the procedure word-for-word.
  - Make it easy for anyone to follow your procedure without referring to this document.
- **Slugs@home Exp 4 website** - Equipment & Safety pages; pictures & videos of the whole lab
- The **class notes** include useful diagrams as well

1. **Reaction Set-up** – chemicals added to flask, assembly of reaction apparatus

2. **Reaction Work-Up** – acidification and crystallization

3. **Filtration -** isolation of aspirin from solution

4. **Analysis: Iron (III) Chloride tests and IR Spectroscopy –** labeled test tubes with contents and observations; preparation of IR sample and sketch of IR spectrum

D. Accountability Buddy Contract: you have the OPTION to work with one PARTNER to submit one report and get the same grade in GradeScope. Add your name to one box in part **(a)** and schedule a time to collaborate after lab in part **(b).** If you prefer to work on INIDIVIDUALLY on this report, please include that in your notebook page submission.

(a) *Who's finalizing what?* Discuss the in-lab questions in the Exp 5 PDF with your partner during / after lab. Use the writing worksheet toward the end of this document for step-wise instructions on writing the experimental methods 😊 Decide who will type or draw the revised responses to which in-lab questions.

In-Lab Q's # _____ / Exp Methods	**In-Lab Q's #_____ / Exp Methods**

(b) "DO" Date: _____ = when / how you'll meet or exchange work to discuss & proofread, at least 1-2 days before the DUE date.

Who will combine both sets of in-lab questions and submit as one PDF to GradeScope? _____

E. Data

Salicylic acid mass _____ mg

Theoretical Yield _____ mg

Calculation:

Product Loss

Product Recovery _____ mg

% Yield _____

See Slugs@home for pics & videos of the full lab!

E. Data (cont'd)

Ferric Chloride Test Results

Sample	Observations & brief interpretation
Salicylic Acid	
Product	
Water	

IR Spectrum of Salicylic Acid

Functional Group	Bond Assignment (C=O, N-H, etc.)	Expected Wavenumber Range (cm^{-1})	Wavenumber (cm^{-1})

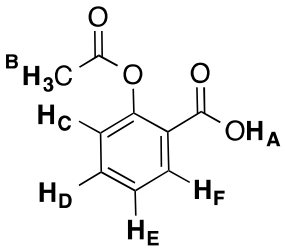
IR Spectrum of Aspirin

Functional Group	Bond Assignment (C=O, N-H, etc.)	Expected Wavenumber Range (cm^{-1})	Wavenumber (cm^{-1})

See Slugs@home for pics & videos of the full lab!

E. Data (cont'd)

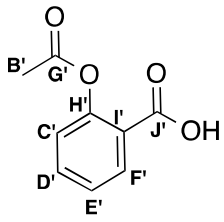
^{1}H NMR Analysis of Aspirin – posted on Canvas



Acetylsalicylic Acid (Aspirin)

Signal	Integration	Splitting	Expected Chemical Shift (ppm)	Observed Chemical Shift (ppm)
A	1 H	singlet	9.7 – 12.5	10
B				
C				
D				
E				
F				

^{13}C NMR Analysis of Aspirin – posted on Canvas



Acetylsalicylic Acid (Aspirin)

Assignments (B' – J')	Expected Chemical Shift Range (ppm)	Chemical Shift (Observed ppm)
		169 & 170
		152
		125 – 135 (4 peaks)
		122
		20

Experiment 6 – Colorful Chemistry: Synthesis & Application of Organic Dyes

Learning Objectives

- Synthesize ~~azo and~~ indigo dyes
- Dye fabric swatches containing multiple types of fibers to observe the different colors or qualities that can be obtained with one dye
- Perform and observe different dyeing methods: direct, mordant, and vat dyeing
- Observe the correlation between dye structure and its absorbance & emission properties (color)

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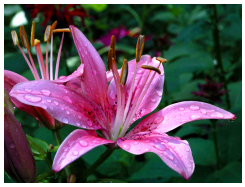
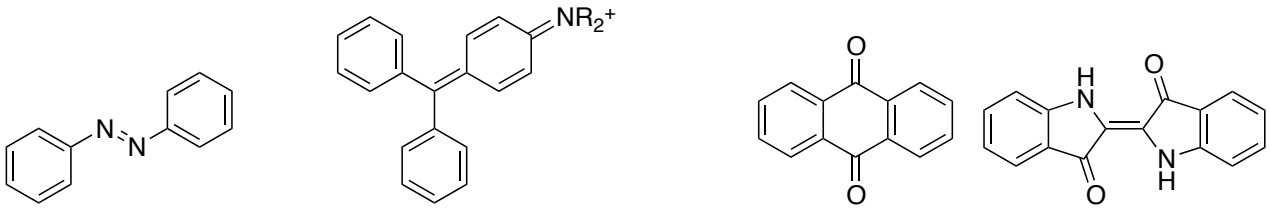
* Please find "How to Prepare for Lab & Assignments" after the procedure in this doc.



Background: Organic Dyes

DYES AND PIGMENTS are colorful compounds used to change the appearance of objects. Nature produces them to make flowers attractive to insects and to people, to tell predators to back off, and to catch the sunlight for energy. Humans have learned to use such naturally colored substances from a very early time, as cave paintings and ceramic artifacts testify. It was not until the past century or so that we have discovered how to make our own dye molecules. The creation of new colors and their applications in the textile and printing industries was at least partially responsible for bringing synthetic organic chemistry to the foreground of scientific research!

THE DIFFERENCE BETWEEN DYES AND PIGMENTS is that dyes are water-soluble and pigments are not. Dyes can be classified according to their structures and also based on their mode of application to fibers. According to structural differences, the most common dyes can be classified as *azo, cationic, anthraquinone,* and *indigo* (**Figure 1**). Depending on their mode of application, dyes can be grouped into the following types: *direct, mordant, ingrain, vat, disperse, reactive,* and *solvent*.



Azo Benzene (Parent of azo dyes) | **Alkylmmonium triphenylmethane** (Parent of some cationic dyes) | **Anthraquinone** | **Indigo**

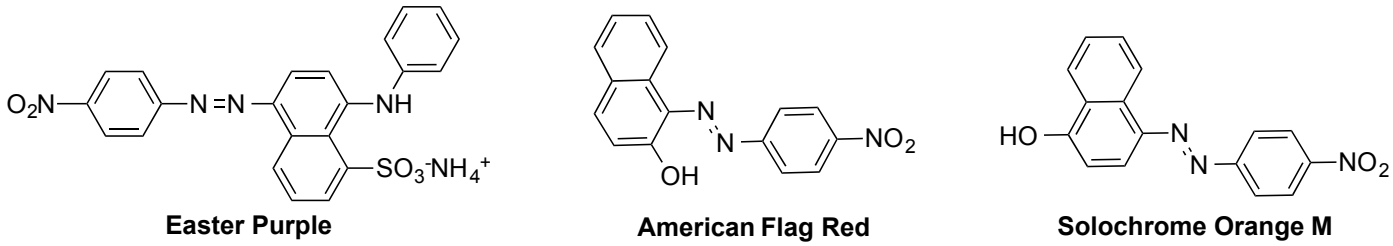
Figure 1. Structural families of dyes

THE NATURE OF COLOR. Objects appear a certain color to our eyes and brains because the materials absorb certain wavelengths of the visible spectrum (400 – 750 nm) and reflect the complementary colors. Thus, a compound that absorbs blue light will appear orange and one that absorbs red will appear green. But what is

it about the structures of these compounds that make them absorb certain wavelengths? A short explanation is the *extent and nature of the conjugation* present in the compound. A conjugated compound has a network of linked p-orbitals (forming pi-bonds), appearing structurally as alternating double and single bonds. This is apparent in all of the examples of dyes in **Figure 1** above. In general, the more extended a conjugated system (the larger the number of pi electrons involved), the longer the wavelength absorbed (towards red), and the shorter the wavelength emitted (towards violet). There are many other factors involved, as you will observe, including contribution of *ortho/para*-activators and *meta*-deactivators.

The azo dye synthesis is no longer performed in the teaching labs due to safety hazards.
Optional reading for fun…

Azo Dyes encompass the largest family of dyes. They contain an azo group, -N=N-, linking two aromatic rings. Because of their extended conjugated pi-orbital systems, these aromatic compounds absorb in the visible region of the electromagnetic spectrum and are deeply colored, often vibrant orange. This implies that azo dyes *absorb* relatively short wavelengths of light. TO BE USEFUL AS DYES, AZO COMPOUNDS MUST BE SOLUBLE IN WATER. This can be achieved by having polar and ionic groups attached to the aromatic rings. Sodium salts of sulfonic ($-SO_3Na$) and carboxylic ($-CO_2Na$) acids work well for this purpose. Easter purple and American flag red (AFR) are examples of ionic azo dyes (**Figure 2**). Recalls that nitro (NO_2) group contain a positively charged nitrogen and negatively charged oxygen. Simple changes in substituents and substitution patterns can make significant enough changes to be noticed by the naked eye, as evidenced by the comparison of **Solochrome Orange M** to **AFR**.



Easter Purple **American Flag Red** **Solochrome Orange M**

Figure 2. Examples of water-soluble azo dyes

THE SYNTHESIS OF AZO DYES is accomplished in two steps (**Figure 3**). In the first step, an aromatic amine (aniline) is transformed into a diazonium salt by the reaction of nitrous acid (HNO_2) obtained *in situ* by mixing sodium nitrite and a mineral acid. Diazotization reactions are usually performed at low temperatures to avoid the decomposition of the diazonium salts. These compounds are unstable at higher temperatures due to their tendency to expel nitrogen gas. Some **diazonium salts are explosive when dry and must be kept in solution**. In the second step, the diazonium salt is coupled to an aromatic compound, usually an aniline or phenol derivative, to yield an aromatic azo compound.

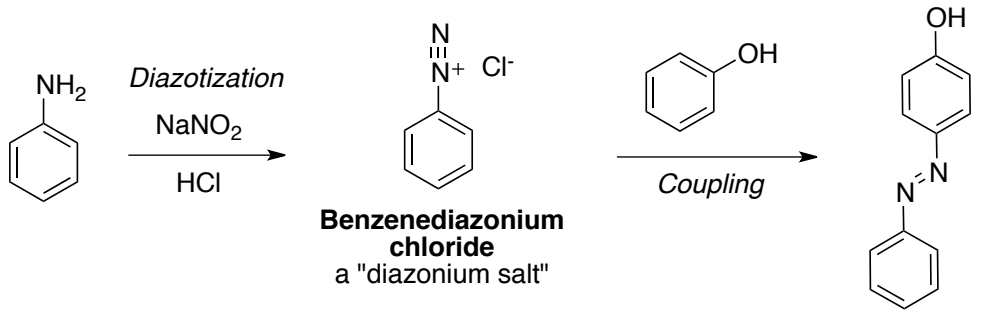


Figure 3. Synthesis of azo dyes.

The azo dye synthesis is no longer performed in the teaching labs due to safety hazards.

Cationic Dyes

THERE ARE SEVERAL CHEMICAL CLASSES OF *CATIONIC DYES*, the most important being the derivatives of triphenylmethane, such Malachite Green (**Figure 5**). In triphenylmethane dyes, three aromatic rings are directly attached to a central sp^2-hybridized carbon atom. At least two of the rings have a dialkylamino group ($-NR_2$) *para* to the central carbon. These molecules are highly conjugated and have the positive charge delocalized among all three aromatic groups. Notice that just one extra lone pair from the methyl amine group donating into the system drastically changes the color from green to violet!

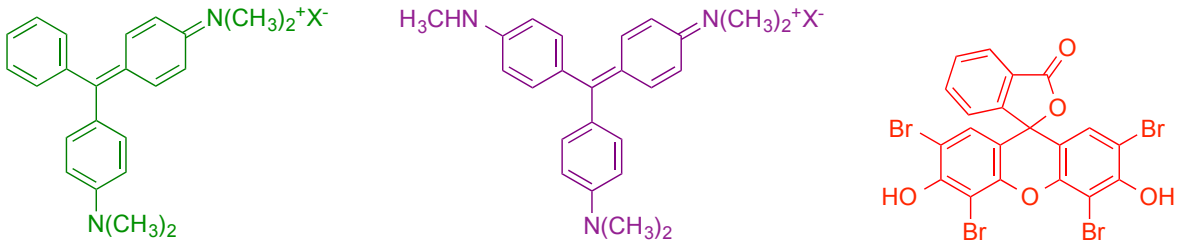


Figure 5. (a) Cationic green and violet dyes and (b) an uncharged dye

Mordant Dyeing

THESE DYES OF NATURAL ORIGIN were used for centuries to dye cotton and leather with beautiful red hues. The most important dye of this class is **alizarin**, which is the main component of the dyestuff obtained from the roots of the madder plant *Rubia tinctorum*. These dyes are applied to fabrics in the presence of metal ions such as aluminum, iron, tin, and chromium. This method is called *mordant dyeing*, where the fabric is pre-treated (soaked) in a specific salt solution before dyeing to create coordination complexes. The metal cation is the center of the complex while the dye and fiber molecules are bound as *ligands* through strong **ion-dipole interactions** (**Figure 6**).

When **alizarin** is used to dye cotton, a red hue is obtained if the metal is aluminum or tin, a deep violet shade with Fe^{2+}, and brown-black if Fe^{3+} is used instead. The connection between metal and dye is strongest

when the dye can be ionized (protonated or deprotonated). One of alizarin's phenol protons is removed in a basic dye bath. This creates a negatively charged conjugate base (**Figure 6b**), which is very happy sharing its extra electron with the metal in a stronger **ionic bond**! The difference in size and charge of the metal can drastically affect the conjugated electrons in the dye, causing different colors of dyed fabric. In this lab, you'll investigate the effects of pre-treating fabric with $CuSO_4$, $AlKSO_4$, and $FeSO_4$ on the observed colors of an alizarin dye swatch.

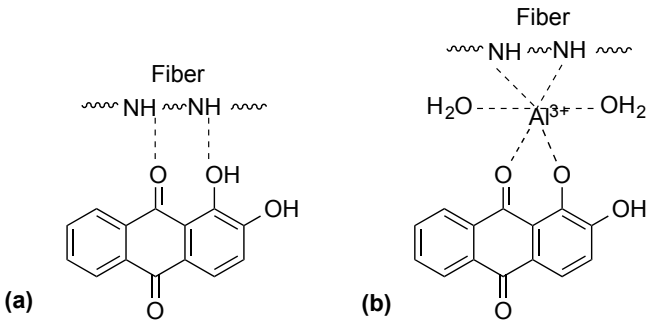


Figure 6. (a) Direct and (b) mordant dyeing with alizarin under basic conditions.

Indigo Dye

THE USE OF INDIGO, the dye of blue jeans, goes back at least 4000 years. The pigment was obtained from several indigenous plants from India and was introduced into the Middle East by Phoenician merchants. From there its use spread around the Mediterranean region and the rest of Europe. Indigo and its derivatives give blue-purple colors.

INDIGO IS SYNTHESIZED BY THE CONDENSATION of *o*-nitrobenzaldehyde and acetone under basic conditions (**Figure 7a**). The reaction is complete in a matter of minutes. *Vat dyes* such as indigo are insoluble in water but dissolve upon reduction with sodium dithionite ($Na_2S_2O_4$) under basic conditions. The reduced dye, called the *leuco* form, is soluble in water and is applied onto the fiber by immersion. Upon drying and exposure to atmospheric oxygen, the dye is re-oxidized and acquires its original color (**Figure 7b**). Notice that the carbonyl carbon of blue indigo is reduced (how many C-O bonds are in the reactant vs. product?). Dithionite is oxidized to sulfite in the process. While in the leuco-indigo solution, the fabric is yellow, but it quickly turns blue after it is removed.

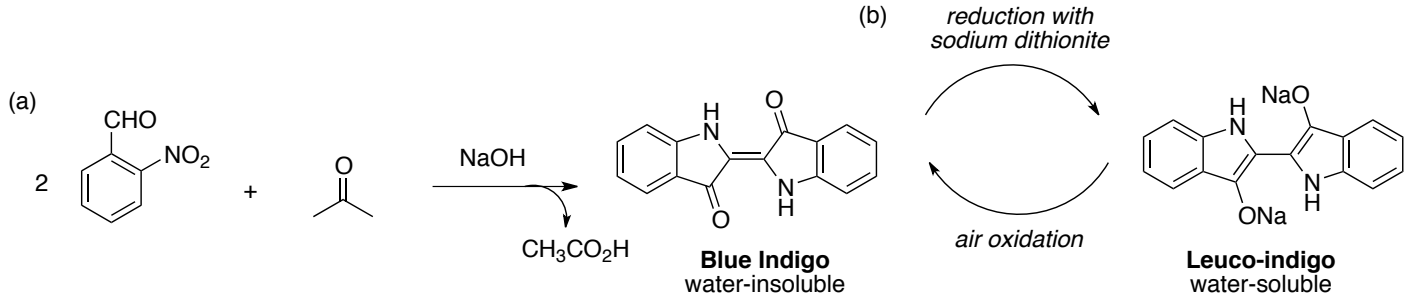


Figure 7. (a) Synthesis of Indigo and (b) reduction to leuco-indigo

Dying to Learn about Dyeing?

TO UNDERSTAND THE PROCESS OF DYEING we must consider the chemical nature of fibers and fabrics. Different fibers subjected to the same dyeing process produce different color shades because each type of fiber reacts with the dye molecules in a unique way. Fibers with an abundance of polar groups like the alcohol (OH) groups in cotton and wool, are easier to dye. Polyesters, acetates, and acrylics contain less polar functional groups like esters and nitriles. These synthetic fibers are generally less absorbent than natural ones and require special methods for color application. Polyesters dyes require high pressure and temperature to adequately adhere to the fabric.

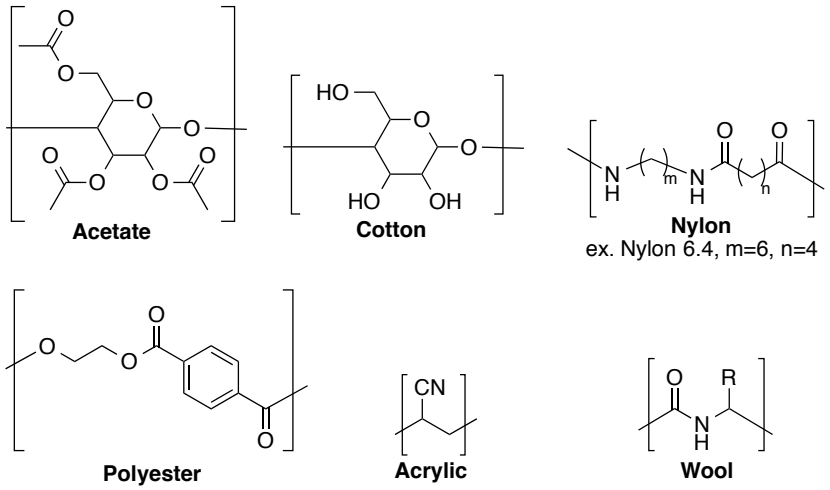


Figure 8. Structures of the repeating units of fibers

EXPERIMENT OVERVIEW

In this experiment, students synthesize dyes and use them to dye fabric swatches containing multiple types of fabric (**Figure 8**). The overall objective is to observe the different colors or qualities of fabrics that can be obtained with one dye, as well as comparison of different dyes and dyeing methods.

Thread a paperclip through the acetate (smoother) end of the fabric swatch *before* dyeing. The order is: acetate (smooth), cotton, nylon, polyester, acrylic, and wool (tan). Label each fabric strip with your name, the dye, mordant, or other conditions if applicable on a securely fastened tag. Attach this tag to the paperclip immediately after dyeing and rinsing.

Down time during reactions or dyeing? If you are prepared for the next steps of the experiment and looking for a way to kill time, take this opportunity to write a draft of the experimental methods section. It is to your benefit to do this in lab while you can ask your TA questions!

**** EXPERIMENTAL PROCEDURE ****

Parts A & B omitted due to safety concerns with the diazocoupling reaction.

Part C. Synthesis and Vat Dyeing with Indigo

Indigo requires a special dyeing process because it is not soluble in water. Once synthesized, **blue indigo** is made solution by a reduction reaction with a solution sodium dithionite ($Na_2S_2O_4$).

C.1. Synthesis of Blue Indigo

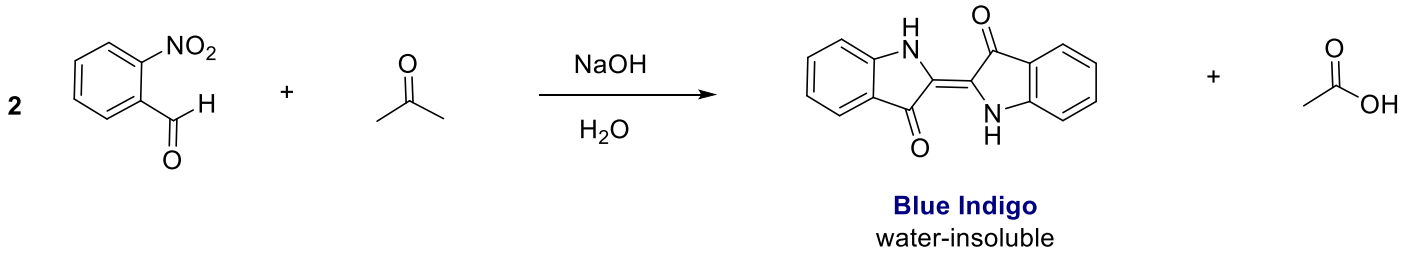


Figure 9. Synthesis of blue-indigo

Perform this reaction in the fume hood. In a 50-mL beaker add a stir bar, 100 mg of *o*-nitrobenzaldehyde, 1 mL of acetone, and 1 mL of water. Stir the suspension on a stir-plate and add 1 mL of a 2.5 M NaOH solution drop-wise. Dark blue indigo should start to form immediately as a black-blue sludge. Bring the beaker back to your bench-top and let the reaction mixture stand undisturbed at room temperature for 10 minutes. Transfer to an ice-water bath for an additional 10 minutes. Collect the solid by vacuum filtration onto pre-weighed filter paper, performed at your bench-top. Use a magnet to keep the stir bar from falling into the funnel.

Wash the solid on the filter with 2 mL COLD water, allowing all the liquid to pass through before following with 2 mL of ethanol.** Let the solid air dry with the vacuum on for 15 minutes, weigh the product, and calculate the % yield. If the yield is greater than 100%, place the filter paper with solid back on the funnel and dry for an additional 10 minutes. Rinse the stir bar over the liquid waste, then leave it in a shared dithionite bath for at least 10 minutes, which should remove any residual blue indigo and make for easier cleaning.

C.2. Dyeing with Indigo

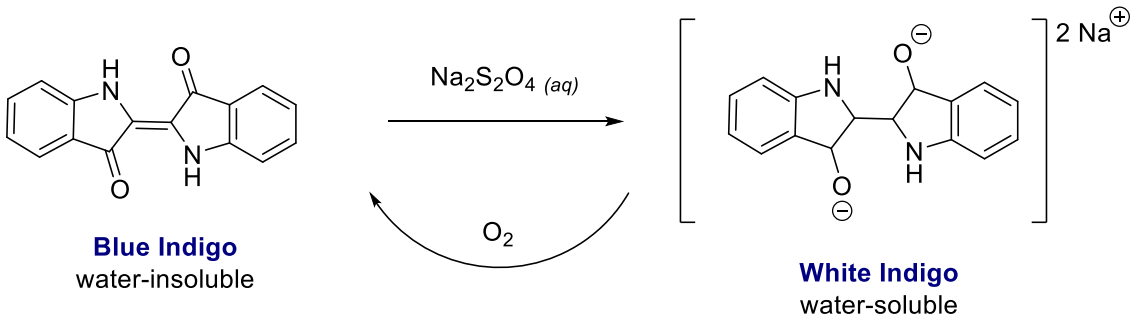


Figure 10. Vat dyeing: reduction of the carbonyl carbons in blue indigo and oxidation of white indigo

To a 100-mL beaker equipped with a magnetic stir bar, add 25 mL of water and dunk the filter paper containing indigo directly into the beaker with the aid of tweezers. If possible, take out the filter paper after most of the indigo has dissolved, otherwise the paper can remain in the beaker. Add 5 mL of 2.5 M NaOH and cover with a watch glass.** Boil on a hotplate with stirring with magnetic stir bar. Once the solution is boiling, add 7 mL of a freshly made solution of sodium dithionite. Boil and observe any color change. If the blue color persists add more sodium dithionite (1 mL at a time), allowing the solution to return to a boil between additions (up to 3 mL), until most of the solid has dissolved and solution turns yellow.** The solution may not be clear yellow. Once 10 mL is added and the solution is boiling, proceed to the next step.

Turn off the heat, add a strip of fabric (don't forget to paperclip the acetate side!) and let it sit in the hot bath for 3 minutes. Use tweezers to remove from heat. Rinse well into a labeled waste beaker, dry with paper towels, then let it air dry. Wait a few minutes to record observations, as it takes time for the indigo to dry and completely undergo oxidation in the air.

Part D. Direct Dyeing with Malachite Green and Eosin Y

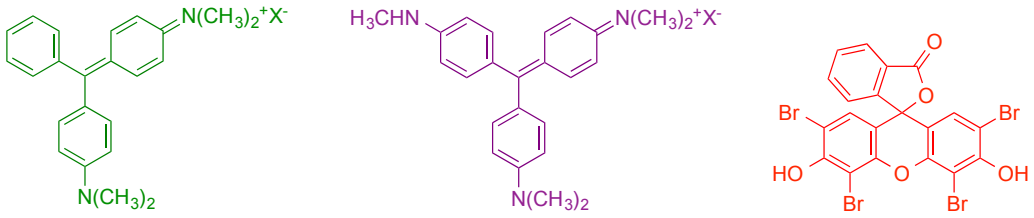


Figure 5. (a) Cationic green and violet dyes and (b) an uncharged dye

Perform this step in the fume hood. Obtain 20 mL of the Malachite Green or Eosin Y solution in a beaker and cover with a watch glass. Add a strip of fabric and bring the system to a *gentle* boil on a hot plate, keeping it covered.** After about 3 minutes of gentle boiling, use tweezers to remove from the heat and rinse the swatch into the waste beaker. Pat dry between paper towels and clean the tip of the squirt bottle.**

Part E. Mordant Dyeing with Alizarin

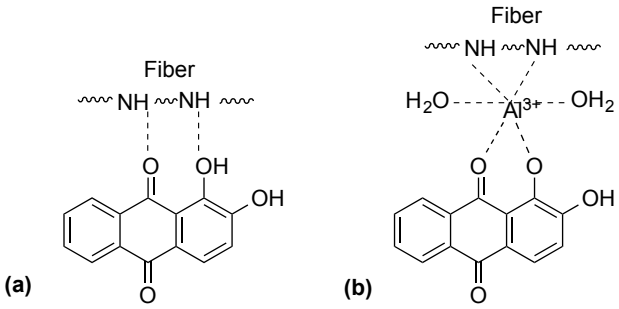


Figure 6. (a) Direct and (b) mordant dyeing with alizarin.

In a 100-mL beaker place 20 mg of alizarin and 20 mL of 0.5 % $NaHCO_{3\,(aq)}$. Warm on a hot plate to dissolve the dye, then bring to a gentle boil. Pre-treated mordant fabric swatches will be available in the lab. Add your assigned strip of fabric (untreated, $CuSO_4$, $AlKSO_4$, or $FeSO_4$) and gently boil for 5 minutes. Remove the strip from the bath with tweezers, soak in tap water for a minute, then rinse with tap water into the waste until the rinse water runs clear. Dry on paper towels. Dispose of the solutions in the liquid waste. Record your observations and those for the other three fabric swatches.

Table 1. Clean-up & Safety - *Copy the pertinent notes into the specific pages of your notebook.*

Clean-up	Safety
Keep isolated solids on the filter paper and dispose in solid waste after you're sure you're done with them!	4-nitroaniline, 2-naphthol, and malachite green are highly toxic – minimize exposure
Liquid waste: mother liquors, dye baths, and other liquids	Sodium nitrite is a toxic oxidizer
	Ethanol and acetone are flammable
Solid waste: filter papers, pipets, and contaminated paper towels	Hydrochloric acid and sodium hydroxide are corrosive
Part B: Rinse pipets or anything used with diazonium salts with water or liquid from ice baths and dispose in solid waste; wash glassware immediately!	Parts A & B: Diazonium salts are explosive in solid state! Wash this glassware immediately.
	Irritants: naphthols, salicylic acid, *o*-nitrobenzaldehyde, $Na_2S_2O_4$, and ANS

Experiment adapted from Palleros, D. R. "Dyes and Pigments," *Experimental Organic Chemistry*, **2000**. Wiley: New York. p. 611 - 634.

Pre-lab Questions / Quiz Prep

1. What structural characteristics give dyes their color? List two examples that fit this trend.

2. List the main **functional group** and associated **intermolecular force (IMF)** in the fibers of cotton, wool, nylon, polyester, acetate, and acrylic.
   - Examples of IMF's include hydrogen-bonding (H-bonding) and dipole-dipole interactions. "Polar" and "non-polar" are technically not IMF's!

3. Consider the dye **American Flag Red** and indicate its predominant IMF (**Figure 2**). Do you expect this dye to adhere better to cotton or to polyester? Base your response on the information in #2 above.

4. Briefly explain the difference between **ingrain and mordant dyeing**. What is the role of the mordant and of the sodium bicarbonate solution? Why do mordant-dyed fabrics keep their colors so well?

5. Explain the general process of **vat dyeing**. Which atom on indigo is being reduced in the vat dyeing process (**Figure 7b**)?

6. Calculate the **mmoles** of *o*-nitrobenzaldehyde and acetone used. Determine the **limiting reagent** and report the **theoretical yield** of blue indigo in mmol and mg. Show your work.

How to Prepare for Lab + Assignments

Follow Canvas Exp 6 Module…

Before Lab

- Read this PDF – background, procedure, safety, pre-lab and in-lab questions
- Attend and/or watch **lab lecture** – we go over everything you need for your assignments!
- Practice the lab online *via* **Slugs@home platform** - sites.google.com/ucsc.edu/slugshome/home
- Complete the **pre-lab questions** at the end of this doc - incorporated into Canvas quiz ☺
    - **Quiz** due the Monday before your enrolled section – check Canvas for due date
- Download the **Exp 6 worksheet** and prepare your **lab notebook**…

Lab Notebook Preparation – *worksheet = template / outline to copy by hand into lab notebook*

- **Purpose:** one-sentence summary of the main lab goals plus the reaction scheme
- **Reagent Table** – add chemical properties; Wikipedia is a reliable source for chemical properties!
- **Procedure with Diagrams** – complete before starting lab; sample on Canvas
    - Use the procedure on the previous pages to create your hand-drawn experimental instructions
        - Simple sketches & labels for all **equipment, chemical names** with **amounts**, & **transfers**
    - Format: Break it up with flow charts, bullet-points, comic strip, and/or whatever works for you!
        - Avoid copying the procedure word-for-word.
        - Make it easy for anyone to follow your procedure without referring to this document.
    - **Slugs@home Exp 6 website** - Equipment & Safety pages; pictures & videos of the whole lab
    - The **class notes** include useful diagrams as well

During Lab

- Check the **safety rules** to dress for lab and arrive a few minutes early to **Thimann Labs**
- **Pre-lab talk:** tips for success and open Q&A
- Show your **lab notebook pages** to your TA
- Perform the experiment with a partner, fill out data & observations in a **lab notebook**

After Lab – each partner submits separate, individual assignments

- Upload **Notebook Pages** to Canvas by midnight on lab day – graded on completeness/participation
- Complete & upload the **Lab Report** on GradeScope (GS) – due date on Canvas
    - In-lab questions only – see last page of this document

LAB REPORT

Canvas > **Experiment 6 Report** for submission details

Upload to GradeScope (GS) after both parts of the lab – see due date on Canvas

- **Select Pages** to correlate your responses to the GS outline ☺
- OPTION to work with a partner – one person uploads the PDF then **"Select Group Members"** – gives both students the same grade

In-lab Questions

1. Re-submit your **dye-fabric observations** from the worksheet. You do not need to type this table for the report but do make sure your observations are *neat and easy to read, please* ☺

3. Report the **yield** (in mg and %) for the **synthesis of indigo** *in one complete sentence*. Show your work.

4. *For any one dye under normal conditions (without mordant)*, briefly comment on the abilities of different fabrics to absorb the dye (color intensity). Include comments on the **structural features of both the fiber and the dye**.

5. Discuss the results of **mordant dyeing**. What were the differences using the dye with and without a mordant (metal salt)? What were the differences using the same dye with different mordants?

6. Comment on how the extent in **conjugation** (number of pi-electrons, electron withdrawing/donating groups) affects the observed **color** of the dyed fabric. Choose 2-3 examples that best exemplified this trend.

Name _____ Partner Name _____

TA Name _____ Section Letter _____ Day _____ Time _____

Experiment 6 Worksheet – Synthesis & Application of Organic Dyes

Each student submits this individually on Canvas after lab

Pre-Lab Requirements

1. **Dress for lab** – see safety rules – arrive a few minutes early
2. **Fill out every page's** purpose, structures, and reagent table
   - Print **this worksheet** or copy templates by hand
3. **Procedure Diagrams** – must be complete before you can start the lab

Part C. Purpose and Indigo Reaction Schemes: Synthesis & Dye

Part C Reagent Table

Refer to the procedure for amounts and safety table for hazards; find the chemical properties on Wikipedia!

Name	Volume	Density	Mass	MW	mmol	Equiv*	Boiling or melting point	Hazards
o-nitrobenzaldehyde	-					1		
acetone								
water								
NaOH, 2.5M								
Indigo	-					-		
Sodium dithionite, $Na_2S_2O_4$ (aq)					-	-		

III. Procedure Diagrams for Part C: Synthesis of Indigo and Vat Dyeing

- All **labeled equipment, chemical names** with **amounts**, and pertinent **safety notes** in every step.
- **Slugs@home Exp 6 website** - Equipment & Safety pages; pictures & videos of each part of the lab.
- The **class notes** include useful diagrams as well!

Part C Data

Synthesis of Indigo

Mass of o-nitrobenzaldehyde _____g Re-calculated theoretical yield _____g

Product loss

Mass of indigo _____g

_____ % Yield

**** Leave space to record observations of the vat dyeing process, it's pretty cool!**

Parts D-E Organic Dye Structures: Malachite Green, Eosin Y, and Alizarin

II. Parts D-E Reagent Table

Refer to the procedure for amounts and safety table for hazards; find the chemical properties on Wikipedia!

Name	Volume	Density	Mass	MW	mmol	Equiv*	Boiling or melting point	Hazards
Malachite Green								
Eosin Y								
Alizarin								
Sodium bicarbonate, 0.5 % $NaHCO_{3\,(aq)}$								

Procedure Diagrams for Parts C-D: Direct and Mordant Dyeing

- All **labeled equipment, chemical names** with **amounts**, and pertinent **safety notes** in every step.
- **Slugs@home Exp 6 website** - Equipment & Safety pages; pictures & videos of each part of the lab.
- The **class notes** include useful diagrams as well!

Data

Observations of Dyed Fabric Swatches – get creative in describing the color's depth & hue

Dye & conditions	Acetate	Cotton	Nylon	Polyester	Acrylic	Wool
Indigo						
Alizarin – untreated fabric swatch						
Alizarin Cu^{2+}						
Alizarin Fe^{2+}						
Alizarin w/ Al^{3+}						
Malachite Green						
Eosin Y						

D. Accountability Buddy Contract: You and your partner have the option work together to submit one report and get the same grade in GradeScope. Add your name to one box in part **(a)** and schedule a time to collaborate after lab in part **(b).**

(a) *Who's finalizing what?* Discuss the in-lab questions in the Exp 6 PDF with your partner during / after lab. Use the writing worksheet toward the end of this document for step-wise instructions on writing the experimental methods 😊 Decide who will type or draw the revised responses to which in-lab questions.

In-Lab Q's # _____ / Exp Methods	**In-Lab Q's #_____ / Exp Methods**

(b) "DO" Date: _____ = when / how you'll meet or exchange work to discuss & proofread, at least 1-2 days before the DUE date.

Who will combine both sets of in-lab questions and submit as one PDF to GradeScope? _____

Table 1. Characteristic IR Absorption Peaks of Functional Groups*

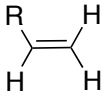
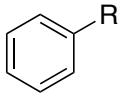
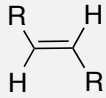
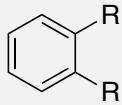
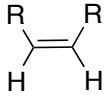
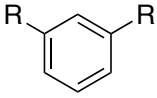
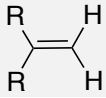
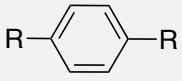
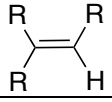
Vibration	Position (cm^{-1})	Intensity*	Notes
Alkanes			
C-H stretch	2990 – 2850	m to s	
Alkenes			
=C-H stretch	3100 – 3000	m	
C=C stretch	1680 – 1620 (sat.) 1650 – 1600 (conj.)	w to m	
=C-H bend	995 – 685	s	See Table 2 for detail
Alkynes			
≡C-H stretch	3310 – 3200	s	
C≡C stretch	2250 – 2100	m to w	
Aromatic Compounds			
C-H stretch	3100 – 3000	m to w	
C=C stretch	1625 – 1440	m to w	Hidden in fingerprint region
C-H bend	900 – 680	s	See Table 2 for detail
Alcohols**			
O-H stretch	3550 – 3200	br, s	Hydrogen bonded (typical)
Amines			
N-H stretch	3550 – 3250	br, m	Primary (two bands) Secondary (one band)
Nitriles			
C≡N stretch	2280 – 2200	s	
Aldehydes			
C-H stretch	2900 – 2800 & 2800 – 2700	s	H-C=O Fermi doublet
C=O stretch	1740 – 1720 (sat.) 1715 – 1680 (conj.)	s	
Ketones			
C=O stretch	1750 – 1705 (sat.) 1700 – 1665 (conj.)	s	
Esters**			
C=O stretch	1765 – 1735 (sat.) 1730 – 1715 (conj.)	s	
Carboxylic Acids**			
O-H stretch	3200 – 2500	br, m to w	
C=O stretch	1725 – 1700 (sat.) 1715 – 1680 (conj.)	s	
Amides			
N-H stretch	3500 – 3150	m	Primary (two bands) Secondary (one band)
C=O stretch	1700 – 1630	s	

Table 1 cont'd

Vibration	Position (cm^{-1})	Intensity	Notes
Anhydrides**			
C=O stretch	1850 – 1800 & 1790 – 1740	s	
Acid Chlorides			
C=O stretch	1815 – 1770	s	
Nitro Compounds			
NO_2 stretch	1570 – 1490 & 1390 – 1300	s	
Thiols†			
R-S-H stretch	2550 – 2600		
Alkyl & Aryl Halides†			
C-F stretch	1000 – 1400		Hidden in fingerprint region
C-Cl stretch	< 600 – 840		
C-Br stretch	< 700		
C-I stretch	< 600		

* Abbreviations: s = strong; m = medium; w = weak; br = broad; sat. = saturated; conj. = conjugated
** Alcohols, Esters, Carboxylic Acids, and Anhydrides also absorb in the fingerprint region due to the C-O stretch (1300 – 1000, s).

Table 2. Out-of-Plane C-H Bending Vibrations in Alkenes and Aromatics

Alkene Structure	Position (cm^{-1})	Phenyl Structure	Position (cm^{-1})
Mono-substituted 	997 – 985 & 915 – 905	Mono-substituted 	770 – 730 & 720 – 680
Disubstituted, *trans* 	980 – 960	Disubstituted, *ortho* 	770 – 735
Disubstituted, *cis* 	730 – 665	Disubstituted, *meta* 	810 – 750 & 725 – 680
Disubstituted, symm. 	895 – 885	Disubstituted, *para* 	860 – 800
Trisubstituted 	840 – 790		

* Adapted from…Mohrig, J. R.; Hammond, C. N.; Schatz, P. F. "Infrared Spectroscopy" in *Techniques in Organic Chemistry*. Freeman: New York, 2006.
† Palleros, D. R. "Infrared Spectroscopy" in *Experimental Organic Chemistry*. Wiley: New York, 2000. p. 688.

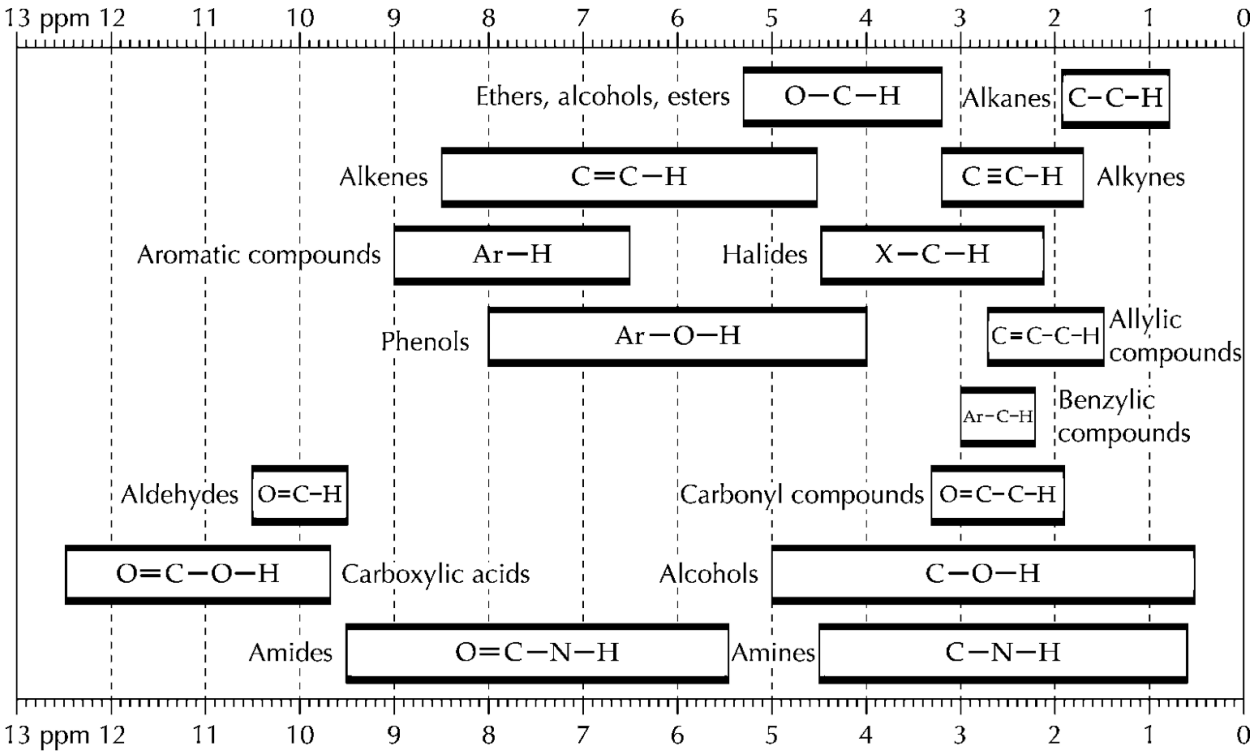


FIGURE 22.13 Approximate regions of chemical shifts for different types of protons in organic compounds.

TABLE 22.2 Characteristic ^{1}H NMR chemical shifts in $CDCl_3$

Compound	Chemical shift (δ, ppm)
TMS	0.0
Alkanes (C–C–**H**)	0.8–1.9
Amines (C–N–**H**)	0.6–4.5
Alcohols (C–O–**H**)	0.5–5.0
Alkenes[a] (C=C–C–**H**)	1.5–2.6
Alkynes (C≡C–**H**)	1.7–3.1
Carbonyl compounds (O=C–C–**H**)	1.9–3.3
Halides (X–C–**H**)	2.1–4.5
Aromatic compounds[b] (Ar–C–**H**)	2.2–3.0
Alcohols, esters, ethers (O–C–**H**)	3.2–5.3
Alkenes (C=C–**H**)	4.5–8.5
Phenols (Ar–O–**H**)	4.0–8.0
Amides (O=C–N–**H**)	5.5–9.5
Aromatic compounds (Ar–**H**)	6.5–9.0
Aldehydes (O=C–**H**)	9.5–10.5
Carboxylic acids (O=C–O–**H**)	9.7–12.5

a. Allylic protons.
b. Benzylic protons.

Figures from Mohrig's *Techniques in Organic Chemistry*, 3rd Edition.

TABLE 22.4 Additive parameters for predicting NMR chemical shifts of aromatic protons in $CDCl_3$

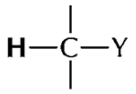
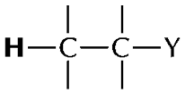
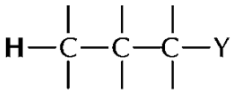
	Base value	7.36 ppm[a]	
Group	***ortho***	***meta***	***para***
—CH_3	–0.18	–0.11	–0.21
—$CH(CH_3)_2$	–0.14	–0.08	–0.20
—CH_2Cl	0.02	–0.01	–0.04
—$CH{=}CH_2$	0.04	–0.04	–0.12
—CH=CHAr	0.14	–0.02	–0.11
—$CH{=}CHCO_2H$	0.19	0.04	0.05
—CH=CH(C=O)Ar	0.28	0.06	0.05
Group	***ortho***	***meta***	***para***
—Ar	0.23	0.07	–0.02
—(C=O)H	0.53	0.18	0.28
—(C=O)R	0.60	0.10	0.20
—(C=O)Ar	0.45	0.12	0.23
—(C=O)CH=CHAr	0.67	0.14	0.21
—$(C{=}O)OCH_3$	0.68	0.08	0.19
—$(C{=}O)OCH_2CH_3$	0.69	0.06	0.17
—(C=O)OH	0.77	0.11	0.25
—(C=O)Cl	0.76	0.16	0.33
—$(C{=}O)NH_2$	0.46	0.09	0.17
—C≡N	0.29	0.12	0.25
—F	–0.32	–0.05	–0.25
—Cl	–0.02	–0.07	–0.13
—Br	0.13	–0.13	–0.08
—OH	–0.53	–0.14	–0.43
—OR	–0.45	–0.07	–0.41
—OAr	–0.36	–0.04	–0.28
—O(C=O)R	–0.27	0.02	–0.13
—O(C=O)Ar	–0.14	0.07	–0.09
—NH_2	–0.71	–0.22	–0.62
—$N(CH_3)_2$	–0.68	–0.15	–0.73
—NH(C=O)R	0.14	–0.07	–0.27
—NO_2	0.87	0.20	0.35

a. Base value is the measured chemical shift of benzene in $CDCl_3$ (1% solution).

TABLE 22.3 Additive parameters for predicting NMR chemical shifts of alkyl protons in $CDCl_3$[a]

Base values

Methyl	0.9 ppm
Methylene	1.2 ppm
Methine	1.5 ppm

Group (Y)	Alpha (α) substituent 	Beta (β) substituent 	Gamma (γ) substituent 
—R	0.0	0.0	0.0
—C=C	0.8	0.2	0.1
—C=C–Ar[b]	0.9	0.1	0.0
—C=C(C=O)OR	1.0	0.3	0.1
—C≡C–R	0.9	0.3	0.1
—C≡C–Ar	1.2	0.4	0.2
—Ar	1.4	0.4	0.1
—(C=O)OH	1.1	0.3	0.1
—(C=O)OR	1.1	0.3	0.1
—(C=O)H	1.1	0.4	0.1
—(C=O)R	1.2	0.3	0.0
—(C=O)Ar	1.7	0.3	0.1
—(C=O)NH_2	1.0	0.3	0.1
—(C=O)Cl	1.8	0.4	0.1
—C≡N	1.1	0.4	0.2
—Br	2.1	0.7	0.2
—Cl	2.2	0.5	0.2
—OH	2.3	0.3	0.1
—OR	2.1	0.3	0.1
—OAr	2.8	0.5	0.3
—O(C=O)R	2.8	0.5	0.1
—O(C=O)Ar	3.1	0.5	0.2
—NH_2	1.5	0.2	0.1
—NH(C=O)R	2.1	0.3	0.1
—NH(C=O)Ar	2.3	0.4	0.1

a. There may be differences of 0.1–0.5 ppm in the chemical shift values calculated from this table and those measured from individual spectra.
b. Ar = aromatic group.

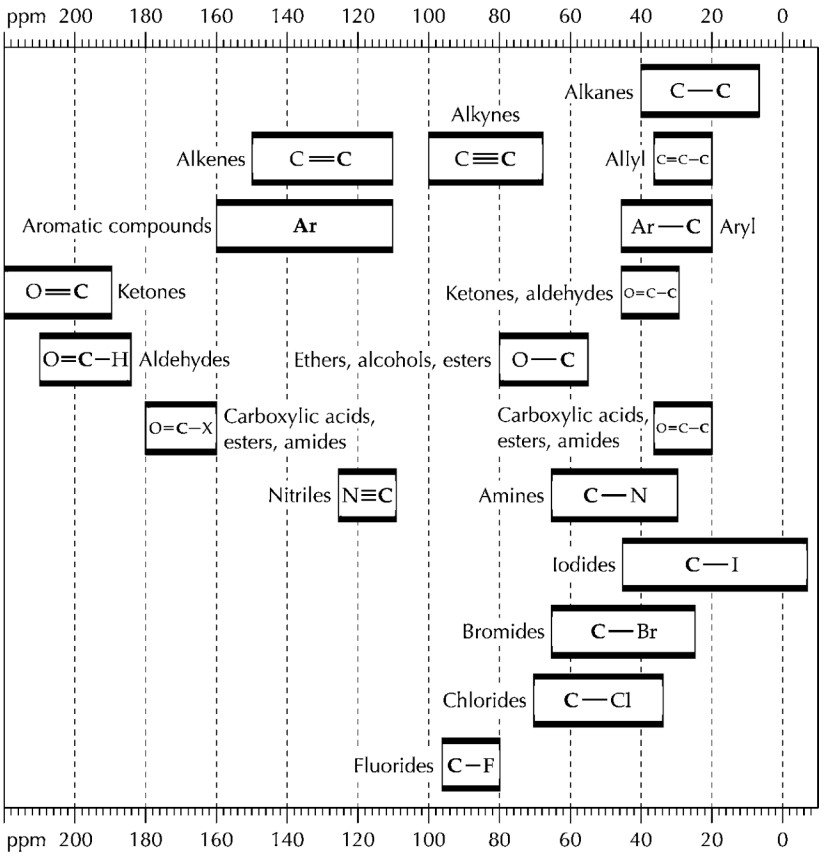


FIGURE 23.4 Approximate regions of ^{13}C chemical shifts for different types of carbon atoms in organic compounds.

TABLE 23.1 Characteristic ^{13}C NMR chemical shifts in $CDCl_3$

Compound	Chemical shift (ppm)
TMS	0.0
CDCl_3 (t)	77
Alkane (C–**C**H_3)	7–30
Alkane (C–**C**H_2)	15–40
Alkane (C–**C**H) and (C–**C**)	15–40
Carboxylic acids, esters, and amides (**C**–C=O)	20–35
Allyl (**C**–C=C)	20–35
Arene (**C**–Ar)	20–45
Ketones, aldehydes (**C**–C=O)	30–45
Amines (**C**–N)	30–65
Iodides (**C**–I)	–5–45
Bromides (**C**–Br)	25–65
Chlorides (**C**–Cl)	35–70
Fluorides (**C**–F)	80–95
Alcohols (**C**–OH), ethers (**C**–OR), esters (**C**–O[C=O]R)	55–80
Alkyne (**C**≡C)	70–100
Alkene (**C**=C)	110–150
Aromatic	110–160
Nitriles (**C**≡N)	110–125
Carboxylic acids, esters, and amides (**C**=O)	160–180
Aldehydes (**C**=O)	185–210
Ketones (**C**–O)	190–220

Figures from Mohrig's *Techniques in Organic Chemistry*, 3rd Edition.