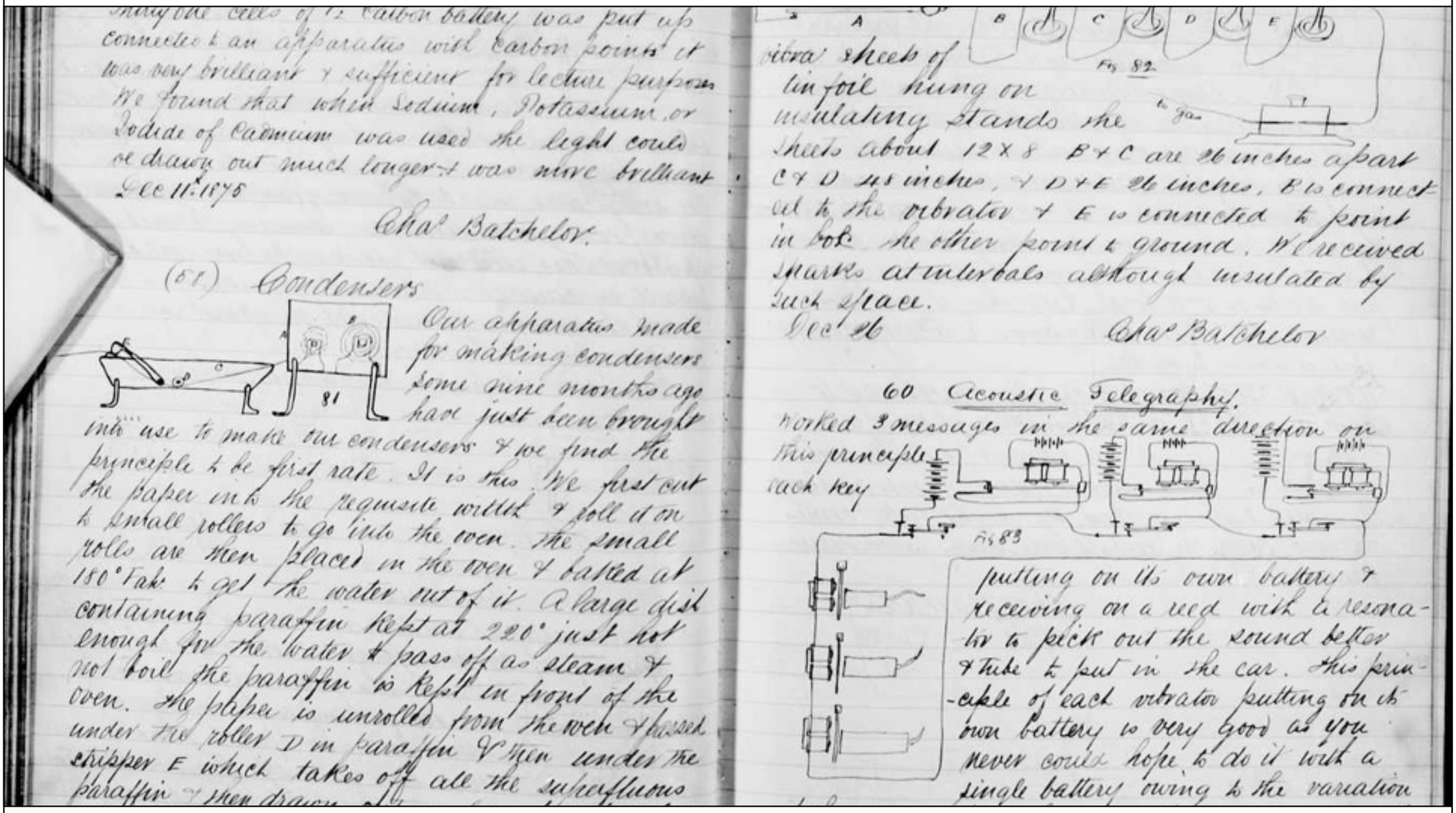
LABORATORY TECHNIQUES & EXPERIMENTS

Organic Chemistry I

William Collins & Kenny Miller

The Lab Notebook and Grading



Incandescent cells of 12 carbon battery was put up connected to an apparatus with carbon points it was very brilliant & sufficient for lecture purposes We found that when Sodium, Potassium or Iodide of Cadmium was used the light could be drawn out much longer & was more brilliant Dec 11. 1878

Chas Batchelor.

(61) Condensers

Our apparatus made for making condensers some nine months ago have just been brought into use to make our condensers & we find the principle to be first rate. It is this We first cut the paper into the requisite width & roll it on rolls to enter into the oven. The small rolls are then placed in the oven & baked at 180° Take to get the water out of it. A large dish containing paraffin kept at 220° just hot enough for the water & pass off as steam & not boil the paraffin is kept in front of the oven. The paper is unrolled from the oven & passed under the roller D in paraffin & then under the stripper E which takes off all the superfluous paraffin & then drawn

vibrating sheets of tin foil hung on insulating stands the sheets about 12 × 8 B & C are 26 inches apart C & D 18 inches, & D & E 26 inches. B is connected to the vibrator & E is connected to point in box the other point to ground. We received sparks at intervals although insulated by such space.

Dec 26 Chas Batchelor

60 Acoustic Telegraphy.

Worked 3 messages in the same direction on this principle each key

putting on its own battery & receiving on a reed with a resonator to pick out the sound letter & tube to put in the ear. This principle of each vibrator putting on its own battery is very good as you never could hope to do it with a single battery owing to the variation

A copy of Edison's lab notebook.

Chemistry 250-251 Lab Policies

The lab is an integral and essential part of the Organic Chemistry course. It must be completed satisfactorily in order for the student to receive credit for the course. Please note the following FLC policies.

- The student must attend his/her scheduled lab section and carry out the experiment in the week that it is scheduled. Under extenuating circumstances, the student may attend a "make-up" lab section at another time during the same week with the prior approval of the scheduled instructor and the make-up instructor. Otherwise, credit will not be given for that experiment.
- If the student fails to satisfactorily complete any experiment or fails to properly check out of lab at the end of the course, he/she may be assigned an incomplete (I) for the course or a failing grade (F).
- In order to insure your safety in the laboratory, it is important to come well prepared to the lab each week:

  a) Please read all assigned material in this manual before each experiment.

  b) Bring this lab manual with you to every laboratory session.

  c) Be aware of all safety precautions discussed in each experiment and in the prelab safety lecture.

  d) Pay particular attention to proper ways of cleaning equipment and disposing of chemical wastes.

  e) Keep your drawer and equipment clean and organized for efficient laboratory work.

- All lab work should be written up and reported in a manner described in this lab manual. Late lab books will receive lower grades. Please consult your laboratory instructor for further instructions.

KEEPING A LABORATORY NOTEBOOK FOR ORGANIC CHEMISTRY

Notes on your laboratory experiments or exercises are to be kept in a bound notebook with numbered pages. Put a table of contents at the front of the notebook that lists each experiment by title, date, and page. Your notebook must be legible, of course, but neatness and organization are also strongly encouraged. All entries should be recorded in ink. **Begin each new lab write-up on the right side of the page. Use the first left page to take notes, write down data, and make observations during the experiment. We will not grade the first left page, only the following right page and the pages thereafter.**

Each lab report must include the following:

1. **Date and title:** The date and title should be at the top of a new page.
2. **Purpose statement:** Below the title, include a sentence describing the goal or purpose of the experiment in your own words.
3. **Synthesis table (if required):** Directly below the purpose statement provide the full chemical transformation with clearly drawn structures of all reagents, catalysts, solvents, and products. Below the reaction draw the synthesis table. The table must include the following information: Reactants, molecular weight MW (g/mol), Density (g/mL), melting or boiling mp/bp (°C), Mass (g), Volume (mL), Moles, and % yield. If an entry is not possible (e.g., a density of a solid) put a dash through the box.
4. **Detailed procedure:** The procedure follows the table of chemical information (if required) and is always written in the past tense, third person, passive voice. This must be detailed enough that the experiment could be reproduced by one of your peers using only your notebook. Below are a few examples of poorly and well-written procedures:

Bad: "Weigh an empty 10-mL graduated cylinder and record its weight. Place approximately 5.0 mL of isopentyl alcohol in the graduated cylinder and reweigh it to determine the weight of the alcohol." This is not written in third person or past tense.

Good: Isopentyl alcohol (5 mL) was placed in a preweighed graduated cylinder (weight = 5.76 g) and the final mass was 10.23 g.

Bad: "I transferred the crude ester to a clean, dry 25 mL Erlenmeyer flask and added 1.0 g of anhydrous sodium sulfate." This is written in first person, active voice.

Good: The crude ester was transferred to a clean, dry 25 mL Erlenmeyer flask and anhydrous sodium sulfate (1.0 g) was added.

4. **Data and results:** Include the data you collected during the experiment such as calculations of percent yield, melting and boiling points, TLC data, important IR and NMR data, color change,

etc. If your experiment did not proceed as planned, discuss how you could have improved your results. Compare your data to what was given or expected. For example: How close was your melting point to that expected? What does your measured melting point tell you about the purity of your solid? Etc.

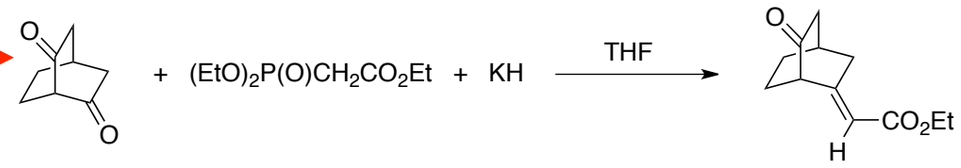
Title

07-08-2011

Preparation of Bicyclo[2.2.2]octane-2-one-6-methylidene Acetic Acid Methyl Ester

Purpose: To investigate the use of stabilized ylide reagents in the Wittig olefination of bicyclic diketones.

Drawn Reaction



Reaction Table

REACTANT	MW (G/MOL)	DENSITY (G/ML)	MP/BP	MASS (G)	VOLUME (ML)	MOLES	% YIELD
Bicyclo[2.2.2]octane-2-dione	138.1	---	195-196	0.150	---	0.0011	---
Potassium Hydide	40.1	---	---	0.044	---	0.0011	---
Triethylphosphonoacetate	224.2	1.130	134/8 mm	0.256	0.226	0.0014	---
Tetrahydrofuran	72.1	0.889	66	---	5.5	---	---
Bicyclo[2.2.2]octane-2-one-6-methylidene Acetic Acid	208.2	---	140-142	0.201	---	0.0011	89%

For solvents, you only need a volume, no mass is necessary

For the product, give the isolated mass and subsequent yield for the reaction

Procedure written in 3rd person passive voice! Make sure to include all observations and amounts of reagents added. DO NOT COPY THE PROCEDURE IN THE LAB MANUAL!

Procedure: Potassium hydride (0.044 g), suspended in tetrahydrofuran (3 mL) was transferred to a dry 10 mL round bottom flask equipped with a stir bar. Triethylphosphonoacetate (0.226 mL) was added slowly to the suspension of KH at room temperature over a 10 minute period. During the course of the addition a considerable amount of gas evolution was observed.

Procedure Cont: Stirring at room temperature was continued for 0.5 h. After this time, the bicyclo[2.2.2]octane-2-dione (0.150 g) was added. The subsequent slurry was stirred at room temperature for an additional 1.5 h

Middle of the procedure omitted for brevity

The crude product was purified by recrystallization. The solid was placed in a 125 mL Erlenmeyer flask. Hot (nearly boiling) water was added a few mL at a time until the solid was completely dissolved (roughly 2.5 mL). The flask was stopped and allowed to cool to room temperature over 1 h.

Copious crystals formed in the recrystallization flask. The crystals were collected by suction filtration through a Buchner funnel fitted with a filter paper. The crystals were rinsed 3 times with 5 mL of ice cold water, and dried for 1 h. The weight of the material was 0.201 g.

A capillary tube was filled with this material and a melting point was obtained = 140-142 oC.

Data and Results: 0.220 g of crude product was initially isolated, which would indicate a good yield of the transformation. Unfortunately , melting point analysis of this material (134-140 oC) indicated a depressed and broadened melting point range when compared to the literature values. Therefore, further purification in the form of a recrystallization was deemed necessary. After recrystallization from water 0.201 g of needle-like, translucent crystals could be isolated. This material had a near identical mp value (140-142 oC) when compared to the literature value (140-142 oC) indicating that the purification technique was successful.

Typically, each experiment will have a DATA PRESENTATION section which will ask you to include additional pieces of data/ observations from the experiment. Please put this info here.

Data and Results Cont:

If you are asked to provide information that requires calculations (e.g., theoretical yields, yields) please write out the calculations in full in this section. Show your work for credit!

Overall, it was shown in this experiment that through careful stoichiometric control it is possible to selectively olefinate a single ketone when using stabilized ylide reagents. It is possible that in this particular reaction, over- or under-olefination occurred to a small extent as evidenced by a an observable mp depression in the crude material. Nevertheless, after recrystallization of this material, pure mono-olefinated product was obtained in 89% yield. This high yield indicated that this was the predominant product.

It is important to finish the Data and Results section with a concluding paragraph that summarizes your experiment (whether it was successful, things you would change if you would do the experiment over, interesting results, ect...)

GRADING

Although each lab instructor might use a different grading scale, the average lab student's performance in each section will be used to put all grades on a single scale at the semester's end.

Grading of each lab will be based on three things:

1.) Lab performance and lab notebook (5/10 points)

Your lab performance will be based on observation of your preparedness for lab, your efficiency in lab, your ability to solve problems that arise, and your results. The quality of your written report will be most important. Your instructor will look for a detailed description of what you did in the experiment and evidence of your understanding of the principles involved.

Notebooks will be graded on a 0-5 scale as follows:

5 – Excellent: The lab report is written neatly and legibly. All required sections of the lab report are included (title and date, purpose, synthesis table if required, detailed procedure, results). The procedure is written in third person, past tense, passive voice and in sufficient detail that the experiment could be reproduced using only the notebook. The results are correctly summarized and interpreted. The results are compared to known or expected outcomes.

4 – Good: As described above, but with one of the following: Lack of neatness and legibility of the lab report; title, date, or purpose statement missing; procedure is not in the correct format or detail; insufficient summary of results and comparison to hypothesized outcomes.

3 – Average: As described above, but with two of the following: Lack of neatness and legibility of the lab report; title, date, or purpose statement missing; procedure is not in the correct format or detail; insufficient summary of results and comparison to hypothesized outcomes.

2 – Significant deficiencies: One or more of the following is lacking any detail or completely missing: procedure, results.

1 – Major deficiencies: The lab report is severely incomplete and several sections lack substance or are completely missing.

0 – No report but attended lab.

-5 – Missed lab.

2.) Cleanliness/ lab safety adherence (2/10 points)

Lab safety and adherence to lab policies will be evaluated throughout the lab period by the teaching assistant and the lab instructor. In particular, failure to wear safety glasses and/or carelessness while handling caustic/toxic materials will result in loss of lab points. Additionally, the cleanliness of the hood, bench, balances and instrumentation will be evaluated at the end of the lab period.

Failure to clean up after your experimentations will result in the loss of lab points.

3.) Pre-lab questions (3/10 points)

Finally, three pre-lab questions will be given at the beginning of each lab period. The three questions will be taken **directly** from the lab procedure that you are about to perform in lab (each experiment has ~10 possible pre-lab questions highlighted in green). The purpose of these questions are to make sure that you have read and reviewed the necessary material to perform the experiments in lab. You will have approximately 5 minutes to complete the three questions. A notecard will be provided for you (make sure you put your name on top). No additional resources (lab notebook, notes, ect...) can be used to answer the questions.

Note: Whether or not a lab report is accepted late is at the discretion of the lab instructor. Nevertheless, you should expect that an automatic deduction of **4-6 points** will be taken for any late lab reports.

Introduction to Synthetic Laboratory Techniques

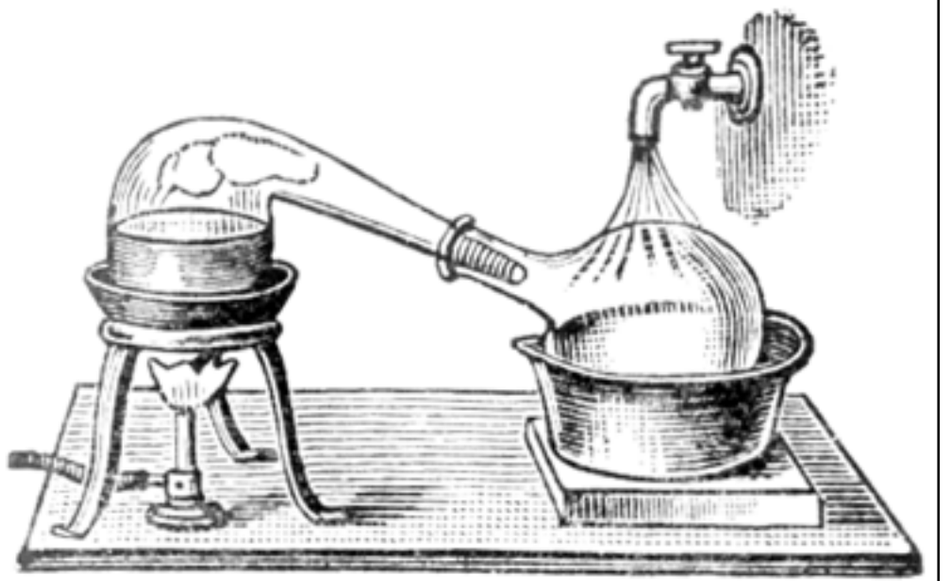


Diagram of alchemic distillation apparatus. Image

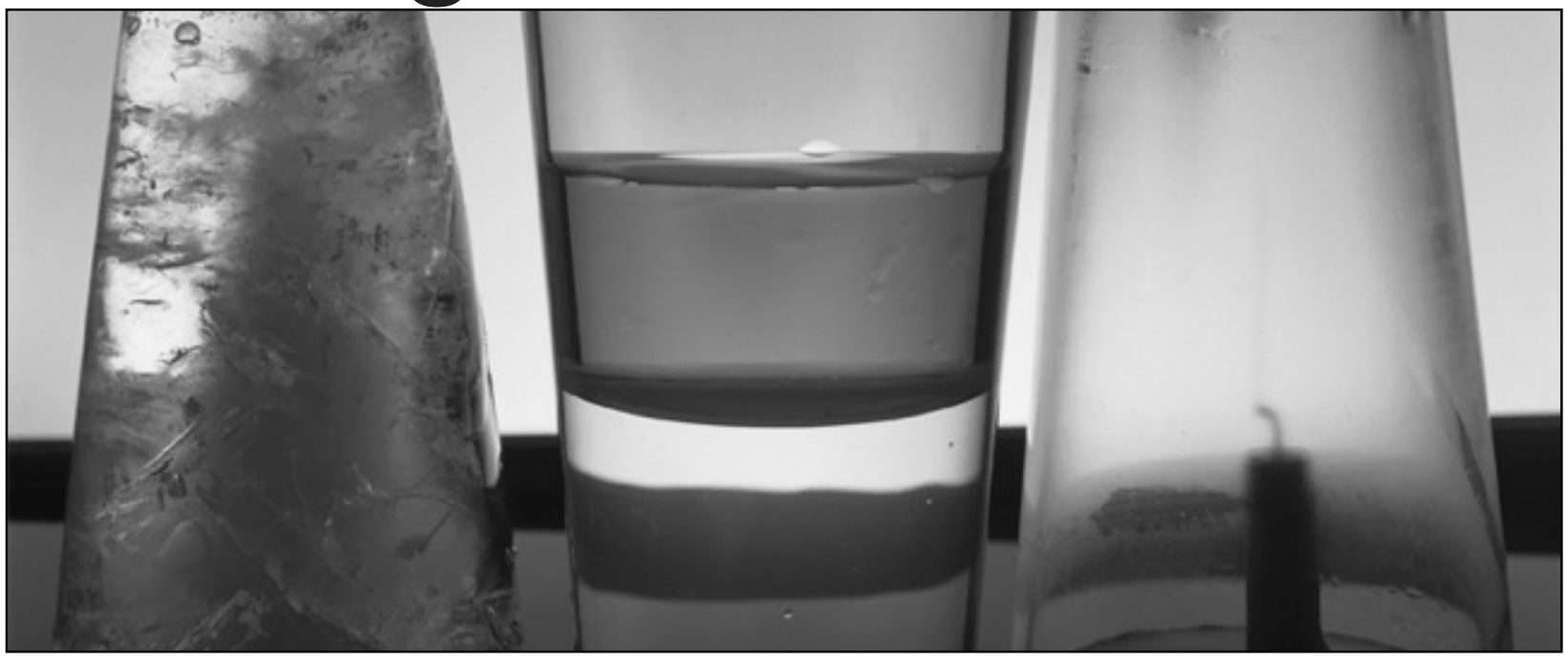
Despite the fact that synthetic, organic molecules influence nearly every aspect of modern day life, most of the techniques that are utilized to make and purify these molecules were in fact invented long ago by self-proclaimed alchemists. To this end, we will be stepping back in time to learn the ancient art of distillation, recrystallization, liquid separation, as well as the more modern techniques of chromatography, polarimetry, and FTIR. Once we have mastered these basic techniques, we will use them to isolate organic molecules from reactions that we learn in class.

"The Alchemist Discovering Phosphorus" by Joseph Wright (1771), Image

Determination of Physical Properties: Melting and Boiling Points

Laboratory Techniques:

1. Measurement of melting points in a capillary tube within a melting point apparatus.
2. Determination of purity by melting point ranges.
3. Identification of unknown compounds by melting point analysis.
4. Measurement of boiling points *via* micro-bp apparatus.
5. Identification of unknown compounds by boiling point analysis.



Example of Solid, Liquid and Gas Phase (solid ice, triphasic liquid mixture, and encapsulated candle). Image

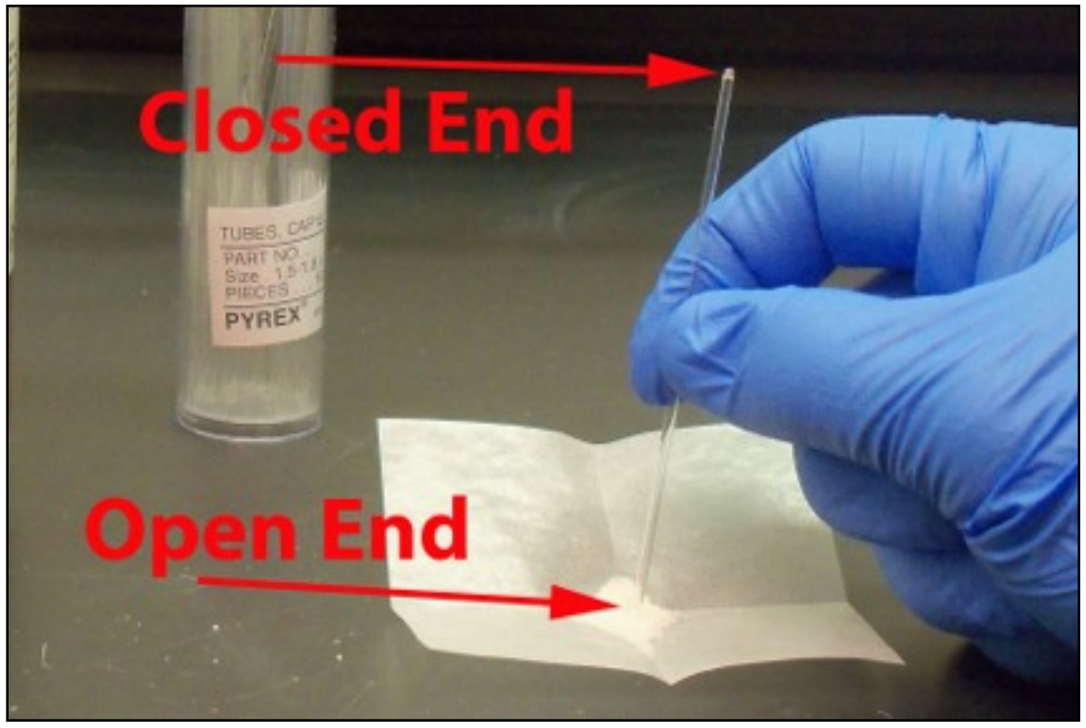
Organic chemists regularly face the challenge of **identifying unknown compounds**. While electronic techniques, such as spectroscopy, have become universally applied, and we will be using them later in this course, **physical properties** remain the first line of identification.

Melting points (mp) and boiling points (bp) of compounds are routinely reported, and serve as criteria both for identification and for purity. The mp of a solid is the pressure/temperature at which it changes state from solid to liquid. Similarly, the bp of a liquid is the pressure/temperature at which a liquid becomes a gas.

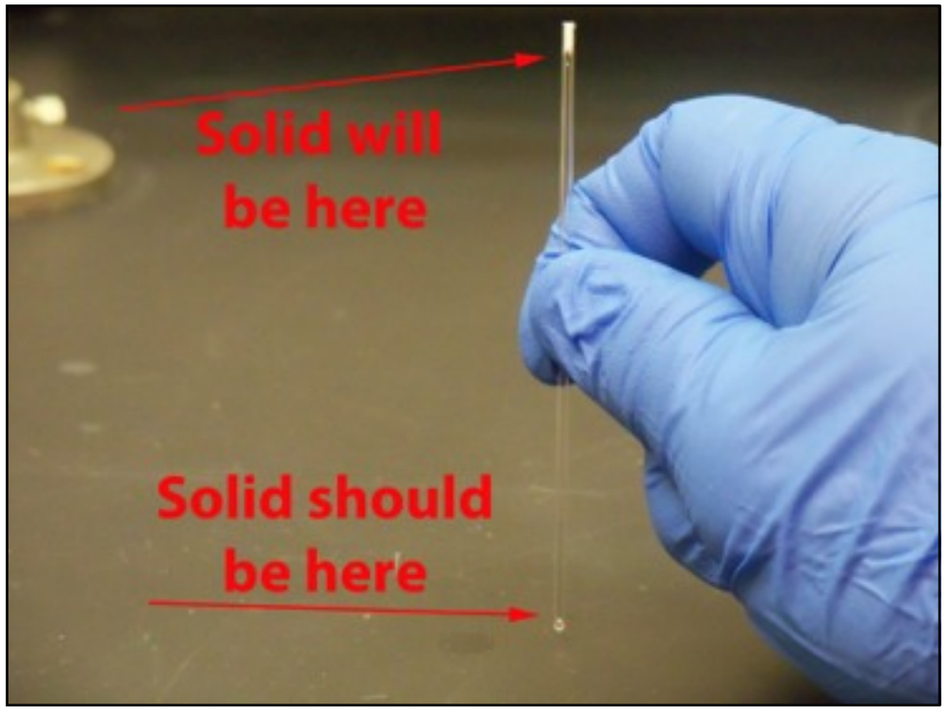
You will learn to make, purify, and identify organic compounds in this course, and so the determination of basic **physical properties** is a logical place to begin.

TECHNIQUE: Melting Points

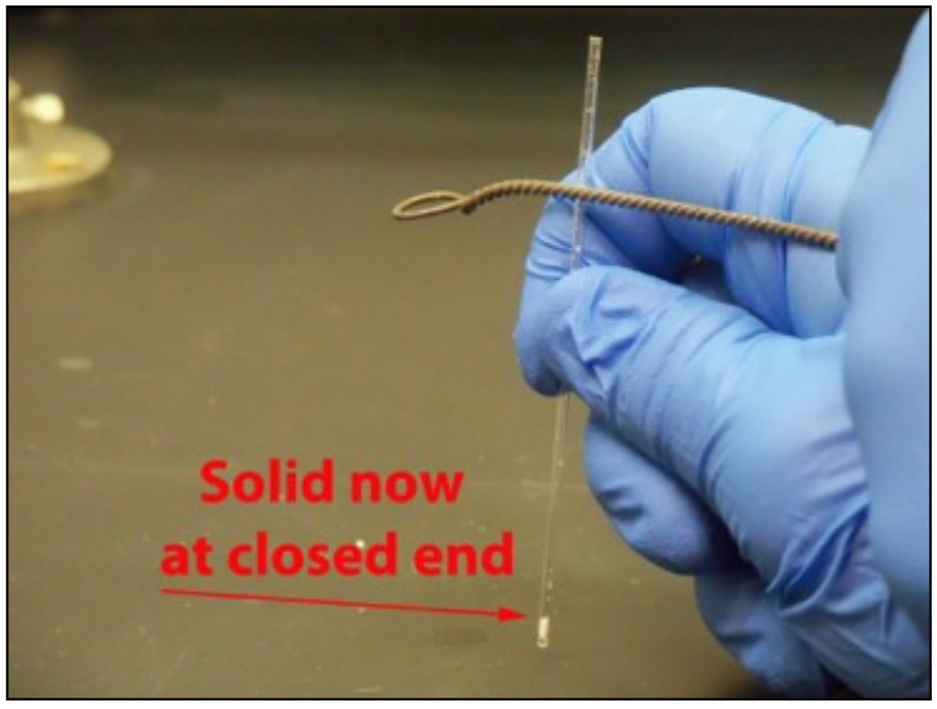
Melting points of crystalline organic compounds are determined by placing a small amount of the sample into a melting point capillary tube and inserting the tube into a melting point apparatus. The temperature of the apparatus is then increased rapidly until the temperature is within about 20 °C of the expected melting point. At this point, the heat is turned down sufficiently so that the rate of increase is only 2 °C per minute until complete melting has occurred. **The temperature range is recorded from the beginning of melting** (when the crystals start to glisten and move around) **to total formation of a liquid**. Melting point measurements do not vary with atmospheric pressure, so correction for varying atmospheric pressures is unnecessary.



Invert the capillary tube and pack the solid into the end of the capillary.

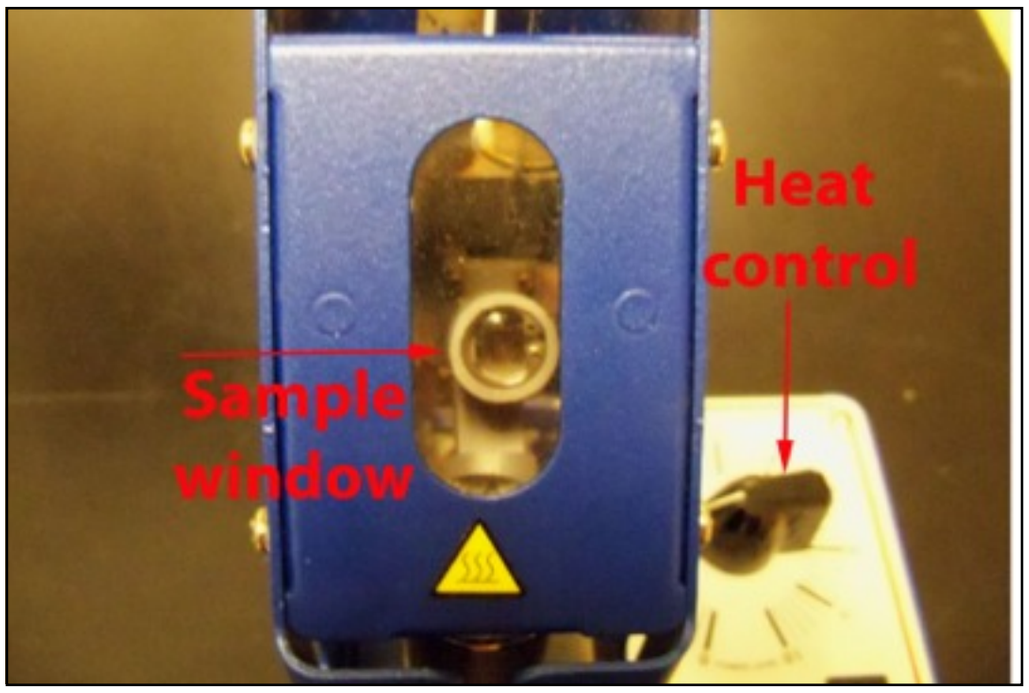


The solid should now be solidly packed into the top of the capillary.

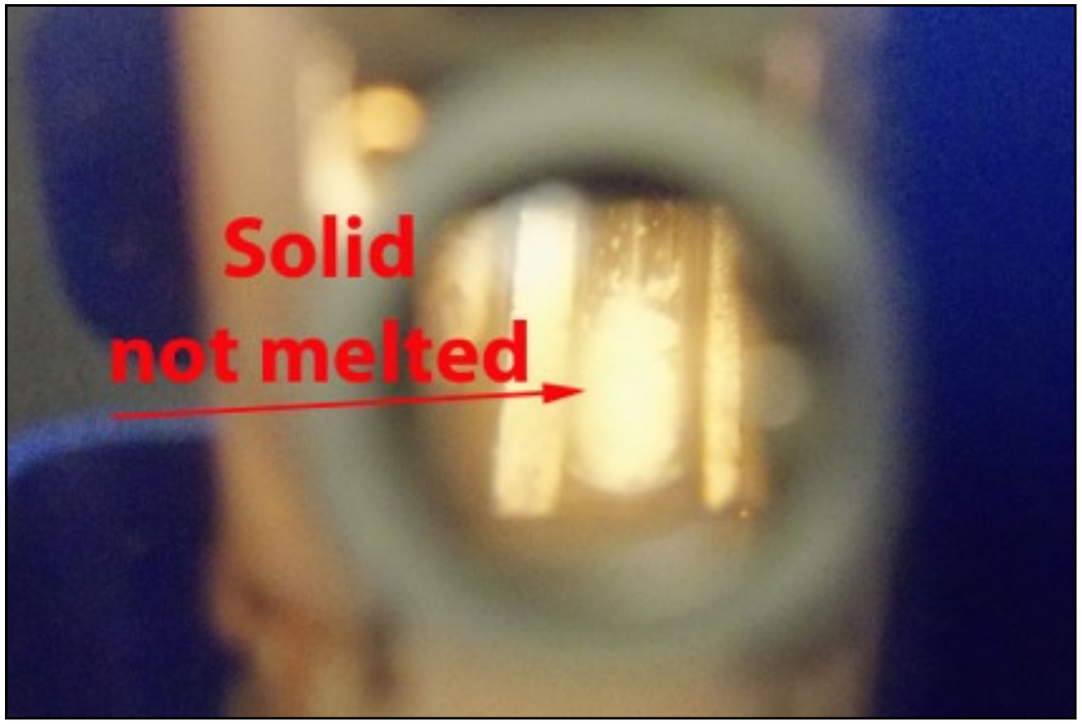


Either by gently tapping the bottom of the capillary onto a hard surface or by rubbing the side of the capillary, move the solid to the bottom of the tube.

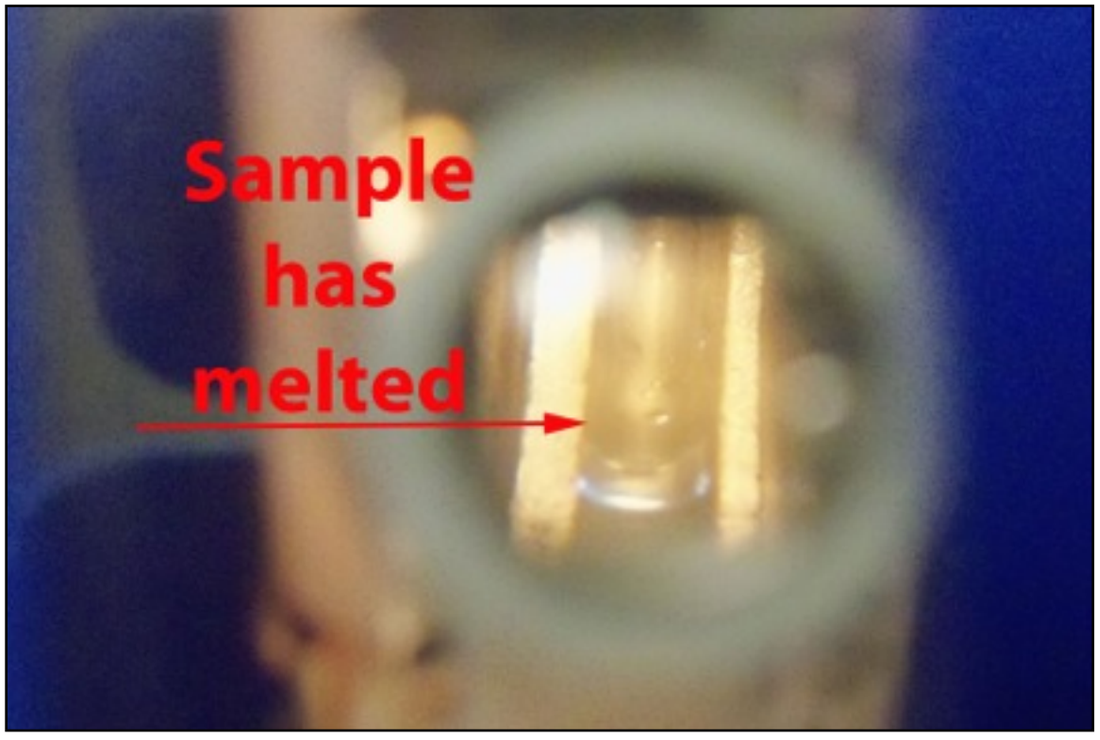
Place the capillary into the slot. Up to four tubes can fit in the mp apparatus at one time.



Use the heat control dial to speed up or slow down the heating process.



This is an example of a solid that is not yet melted.



This is complete melting. Record the temperature range that it takes to get to this point.

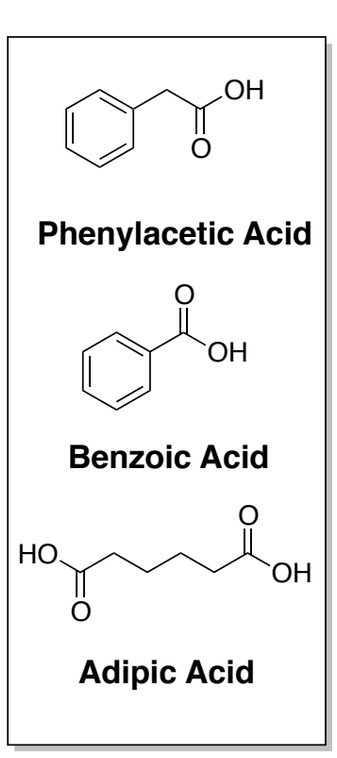
EXPERIMENTAL PROCEDURE:

A. **Melting Point Range of Phenylacetic Acid, a Mixture of Solids, and an Unknown Solid**

- Put a small amount (a few crystals) of phenylacetic acid into a melting point capillary tube, tap the tube to bring the crystals to the bottom, and insert the capillary tube into a melting point apparatus. Turn on the instrument and adjust the dial to achieve the desired heating rate (see Melting Point Technique). Record the temperature range from the start of melting to complete liquification. Turn off the instrument and remove and discard the used capillary tube. Record the melting point range (both the start and end of melting) and compare the high end of the range with the literature value of 77 °C.

- Mix a small amount of phenylacetic acid with a similar amount of either benzoic acid or adipic acid. Notice that the melting range of the mixture is below that of either pure compound. If the melting range of a mixture is depressed and broad, the two materials are not the same; if there is no depression, then they are the same, i.e., a single compound.

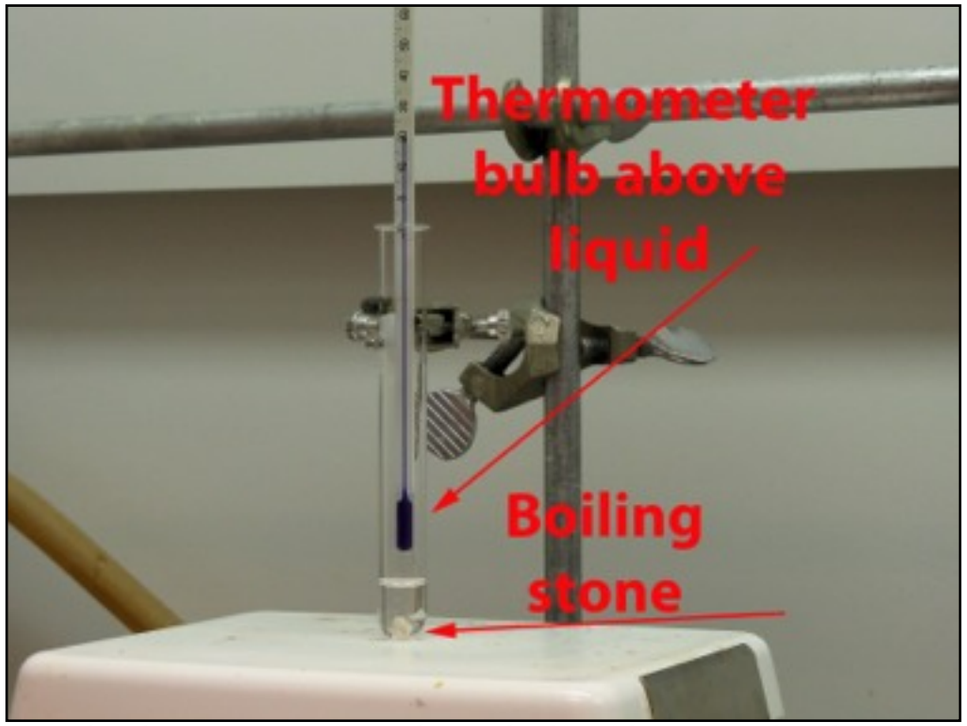
- Obtain a solid unknown from the stockroom. Carefully determine the melting point range of your solid. Be sure and record your unknown solid number in your lab notebook



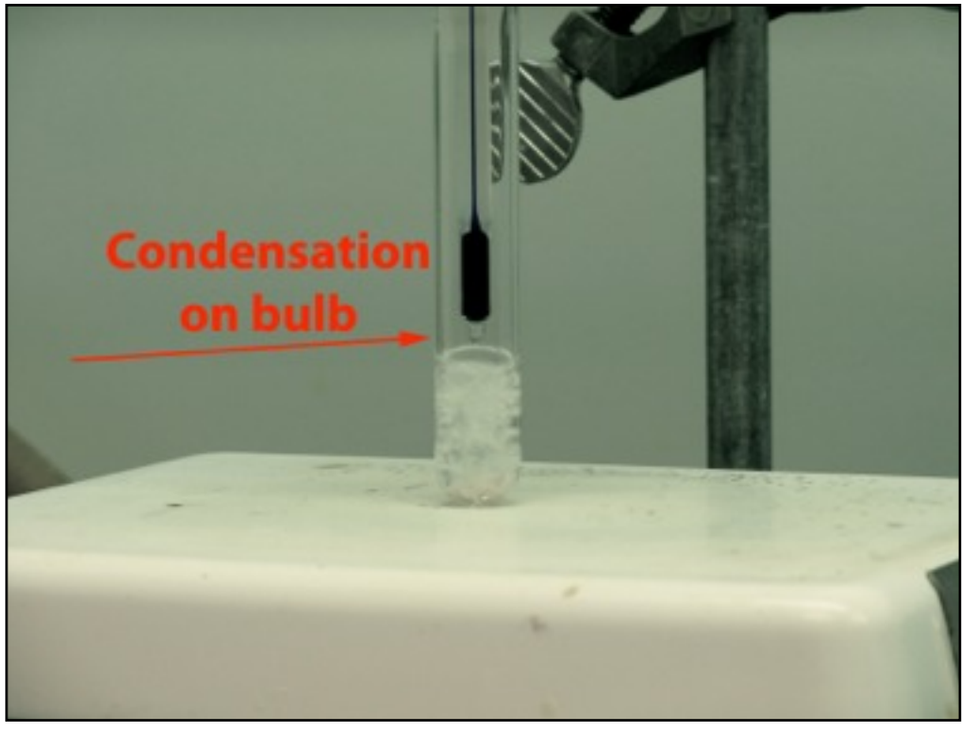
TECHNIQUE: Micro-Boiling Points

Boiling points of pure liquids are measured simply by pipetting a small amount (1/2 to 1 inch) of the liquid into a small test tube and clamping a thermometer slightly above the level of the liquid. The test tube can be heated over a hot plate until vigorous bubbling occurs. Make sure to look for a reflux ring above the bulb of the thermometer and drops of liquid condensing on the side of the test tube. Record the observed boiling point when the temperature reading on the thermometer has remained constant for ~ 2-3 minutes.

Pipette a small amount of the liquid into a test tube.



Clamp the thermometer just above the liquid. Do not let the thermometer touch the liquid or the side of the test tube. A boiling stone helps control the boil of the liquid.



The boiling liquid is condensing on the thermometer and dripping back down. Do not let the boiling liquid touch the thermometer.

After stabilization (2-3 minutes) you can record the boiling point (make sure to account for atmospheric pressure correction).

Remember that the boiling point of a liquid is the temperature at which the vapor pressure of the liquid equals the surrounding atmospheric pressure. It is important to note that atmospheric pressure varies from day to day, from place to place, and especially with elevation. At high elevation, the atmospheric pressure (600 torr at 6800 ft elevation in Durango) is lower than at sea level (760 torr). For this reason, boiling points of liquids are lower in Durango than "standard" boiling points that are measured at sea level (760 torr). Atmospheric pressure effects are very significant at nearly 7000 feet above sea level where measured boiling points are 6-8 degrees below the standard boiling points.

Atmospheric pressure correction: To convert an observed boiling point to its standard value at 760 *mm* Hg, a correction factor, T, is used. The correction factor is calculated using the following equation:

$$\Delta T = \frac{T(observed)}{C} \times \frac{760 - P(observed)}{10}$$

where:

- T observed = boiling temperature **in Kelvin**
- P observed = atmospheric pressure in *mm* Hg (600 *mm* Hg in Durango)
- C is a correction factor:
  - C = 850 if the liquid is non-hydrogen bonding (e.g., hexanes, dichloromethane, benzene, toluene)
  - C = 1020 if the liquid is hydrogen bonding (e.g., water, alcohols)

Note: You can just add six degrees to most boiling point you measure to compensate for the atmospheric pressure difference at this elevation.

EXPERIMENTAL PROCEDURE:

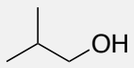
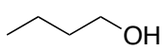
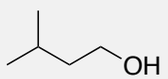
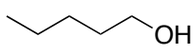
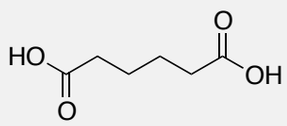
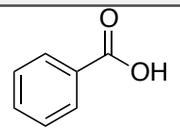
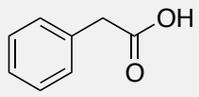
B. Boiling point of 2-Butanol, and the Identification of an Unknown Liquid

- Add about 1 mL of 2-butanol to a small test tube and set up the boiling point apparatus (see Micro-Boiling Point Technique). Use a hot plate for the heat source. Be careful not to overheat the liquid. Watch for the liquid condensation line to rise up slowly on the test tube wall as you heat the liquid to its boiling point. Keep the condensation line below the top of the tube or the liquid will evaporate from the test tube. When you are finished, pour the 2-butanol into the flammable waste container and rinse the test tube with a little acetone into the waste bottle.

- Obtain a liquid unknown from the stockroom. Determine the boiling point of your liquid unknown using the same boiling point method and apply the necessary atmospheric pressure corrections. Identify your unknowns from the list of possibilities provided below. Be sure and record your unknown liquid number in your lab notebook.

C. Experiment 2 Prep: Begin Ethanol Generation from Molasses

- **GO TO EXPERIMENT 2, AND BEGIN THE PROCEDURE LABELED: "WEEK 1"**. Do not include this experimental in your notebooks for this week. Include it in the write-up for experiment 2.

COMPOUND	STRUCTURE	BOILING POINT [°C/760 TORR)	MELTING RANGE [°C]
cyclohexane		81	-
isobutyl alcohol		108	-
n-butyl alcohol		118	-
isoamyl alcohol		130	-
n-pentyl alcohol		138	-
adipic acid		-	152- 154
benzoic acid		-	120 - 122
phenylacetic acid		-	77 - 79

WASTE DISPOSAL

Flammable waste for all organic liquids. You may return your unknown vials to the stockroom after recording their numbers in your lab report.

DATA PRESENTATION:

Include the following in your formal laboratory report discussion:

- Please include a drawing of the boiling point apparatus and your record of all temperature measurements made while determining the boiling points of 2-butanol and your unknown liquid.
- The identity of your solid unknown. You may measure the mixture melting range of your solid unknown with the authentic compound if you wish to give additional evidence of your correct identification.
- Calculation of the atmospheric pressure correction factor (T) for 2-butanol. Note that 2-butanol is hydrogen bonded. Add the correction factors to the observed boiling point.
- Calculation of the atmospheric pressure correction factor (T) for your liquid unknown. Note that all of the unknowns are hydrogen bonded except cyclohexane. Add the correction factor to the observed boiling point. What is your liquid unknown?

Preparation of Rum: Simple and Fractional Distillation

Laboratory Techniques

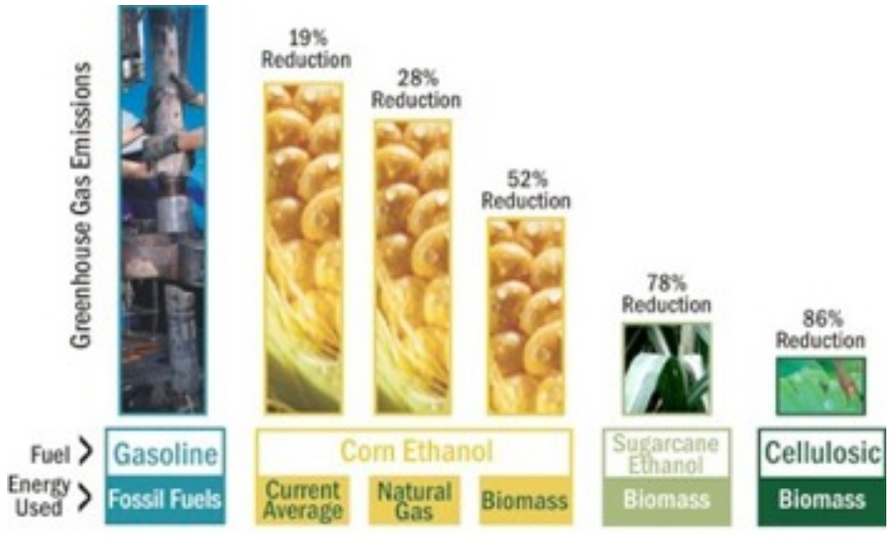
1. The assembly and operation of a distillation apparatus.
2. Simple and fractional distillation of a liquid as a purification technique.
3. Analysis of liquid compositions by refractometry.

The Montanya Rum Company's distillation apparatus (Silverton, CO). The crude material is added to the copper pot (on left) and allowed to reflux before the enriched alcohol vapor is transferred into the condenser on the right to form rum. Image

People have produced ethanol for millennia via the fermentation of sugars with yeast. Some historians have hypothesized that agriculture and human civilization began as an attempt to produce a consistent supply of grain that could be fermented to make ethanol. Any supply of sugar can be used to produce ethanol. Wheat or potatoes are used to make vodka. Corn can be used to make whiskey. The sugars produced by the agave cactus are fermented to make tequila. In this lab we will use blackstrap molasses as a source of sugar to make a crude version of rum.

Molasses is a waste by-product produced in the refining of sugar. Granulated sugar purchased at the grocery store is the product of precipitation of a saturated solution of sugar extracted from sugar beets or sugar cane. The mother liquor is then concentrated and the precipitated product is light brown sugar. The cycle is repeated again to make dark brown sugar. The mother liquor at the end of this process is cheaply sold as molasses.

As the world looks to develop renewable sources of energy, interest in ethanol as a fuel has grown. All gasoline in the United States is required to contain as much as 10% ethanol. Most ethanol in the U.S. is produced from corn, and there is significant controversy regarding the use of valuable food for the production of fuel. Utilizing a waste byproduct such as molasses to make ethanol could begin to address some of the drawbacks inherent to corn ethanol.



Source: Wang et al, *Environmental Research Letters*, Vol. 2, 024001, May 22, 2007

Once ethanol is produced, either for fuel or for consumption, it must be separated from water. Distillation is the most common way to accomplish that goal. Simple and fractional distillation are important methods for separating mixtures of two or more volatile components. Simple distillation is less effective and requires that one component be much less volatile than the other (i.e., their boiling points must be at least 100 °C apart). Fractional distillation allows the separation of mixtures having boiling point differences of only a few degrees. In this experiment, a mixture of ethanol (bp = 78 °C) and water (bp = 100 °C) will be separated by fractional distillation.

Analyses of the distillation fractions will be carried out by refractometry. In refractometry, the composition of a liquid mixture is determined by linear interpolation, comparing the refractive indices of the mixture with those of each pure component. For example, a mixture of ethanol (nD = 1.361) and water (nD = 1.333) which has an nD (mixture) = 1.354 is 75% ethanol and 25% water. This process is most conveniently carried out graphically.

TECHNIQUE: Distillation

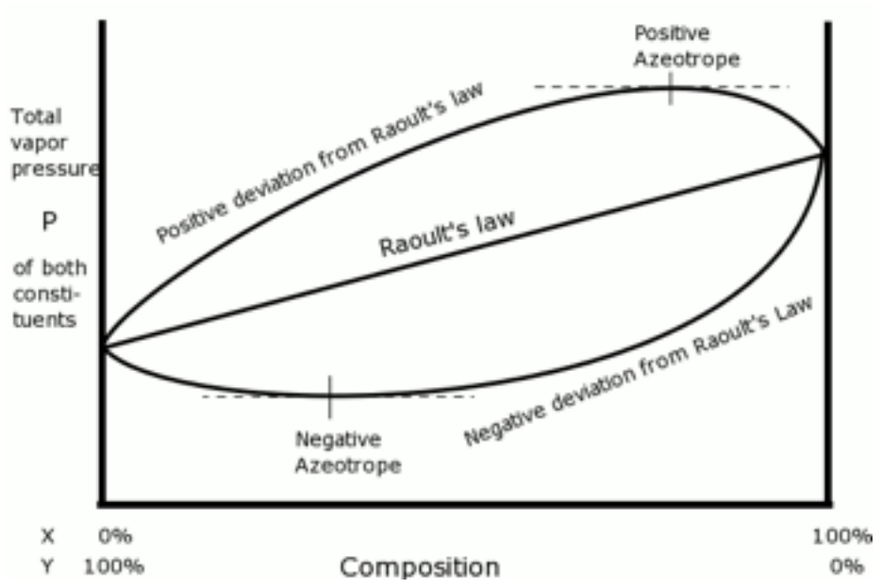
Distillation involves the vaporization of a liquid, condensation of the vapor, and collection of the condensate or distillate in another container. This process is often used to separate two compounds with different boiling points.

We will be using two types of distillation:

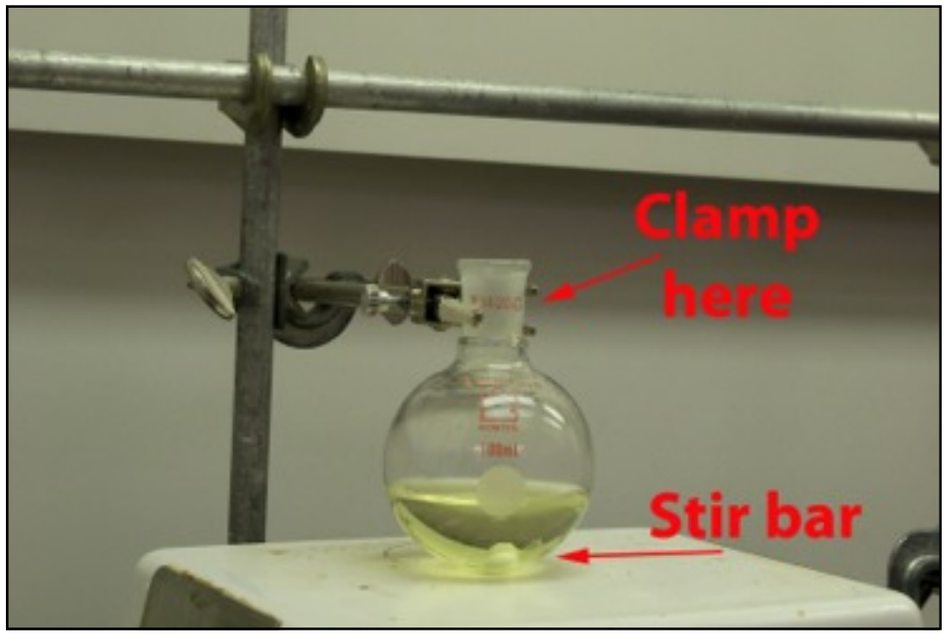
1. Simple Distillation

The process of performing a simple distillation is fairly straightforward. A mixture of liquids is boiled (refluxed) in a round bottom flask. Raoult's law states that the vapor from this boiling mixture will be enriched in the component that has a higher vapor pressure. Simple distillation works best with components with vastly different boiling points (>100 °C) and vapor pressures. As a result, the vapor will be highly enriched in the lower boiling solvent. A thermometer measures the temperature of the vapor before it encounters the attached condenser that cools the enriched vapor back to the liquid phase. A container at the end of the condenser is used to collect the liquid distillate, which now contains a higher fraction of the lower boiling liquid.

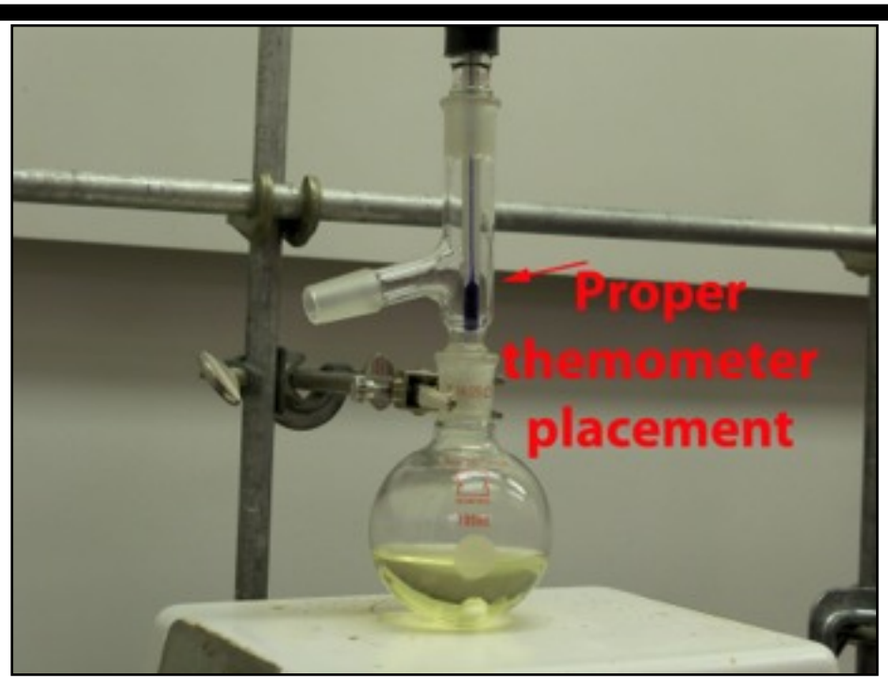
A simple distillation is set up as shown below. Place the liquid mixture in an appropriately sized round bottom flask (roughly 2 times the capacity of the volume of liquid that you will be distilling). Attach a distillation head to the top of the round bottom flask and place a thermometer in the top of the distillation head. Make sure that the top of the thermometer bulb is even with the entry to the condenser as shown. Attach a condenser and adapter to collect your distillate. Ensure that water is running through the jacket of the condenser with water going in the bottom and out of the top.



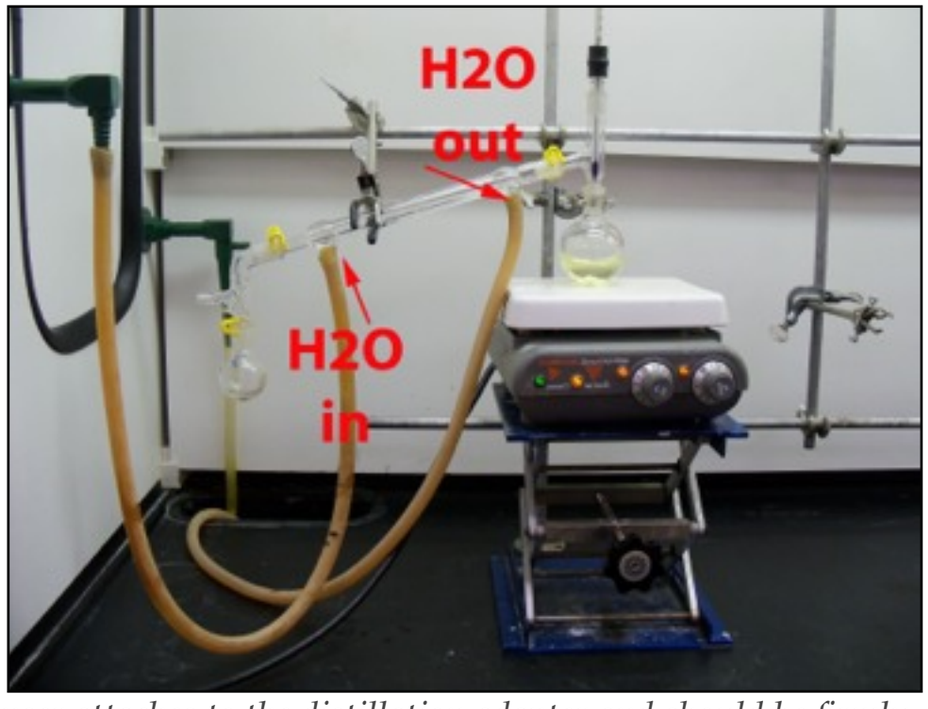
Positive and negative deviations from Raoult's law within a binary mixture of liquids. Azeotropes are denoted as maxima/minima in the curves. Images



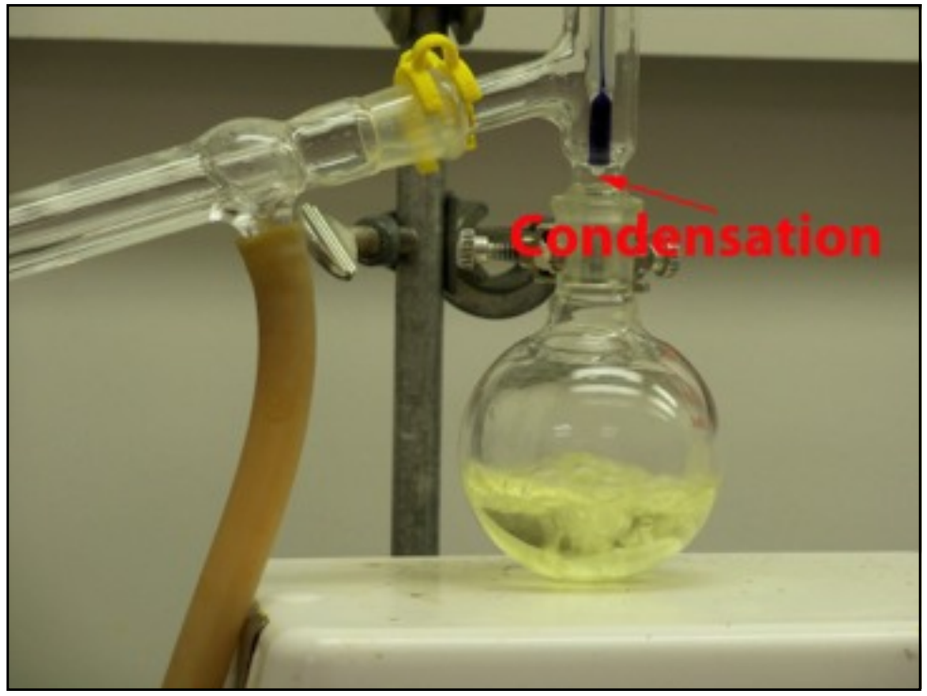
The liquid you are distilling should not exceed 1/2 of the volume of the round bottom flask. Secure the flask by clamping the neck of the RBF.



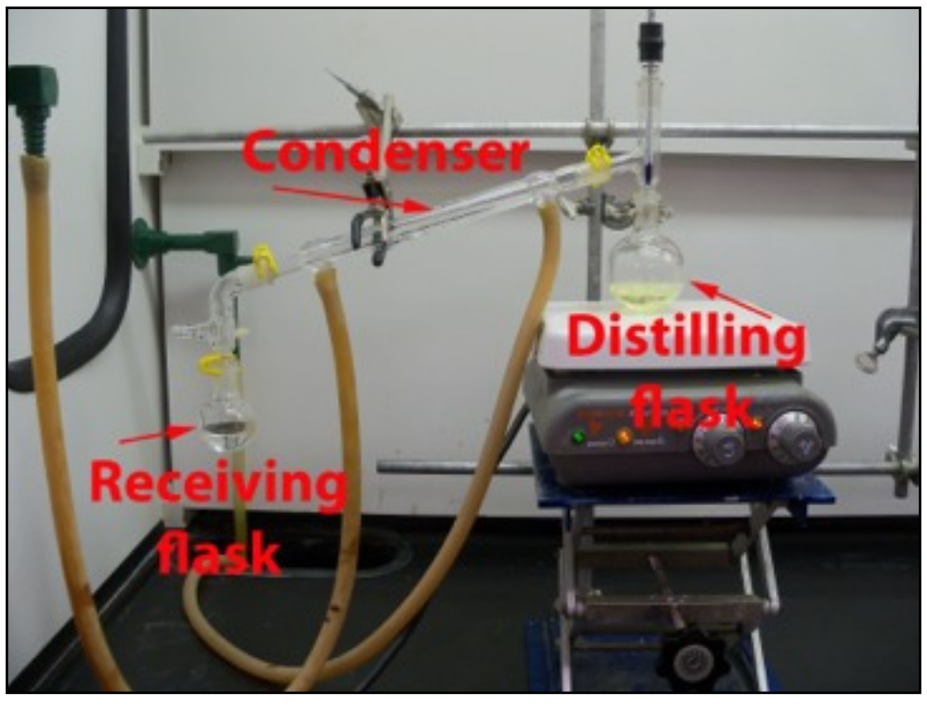
Attach the thermometer, the adapter, and the distillation head adapter. The thermometer bottom should be below the "T" of the distillation head to get an accurate temperature reading. Describe the proper thermometer placement in a distillation head adapter (be able to draw a diagram).



The condenser attaches to the distillation adapter and should be firmly clamped. The water inlet hose should be attached to the bottom of the condenser and the water out attached to the top. Where should the water inlet be attached to the condenser, top or bottom?



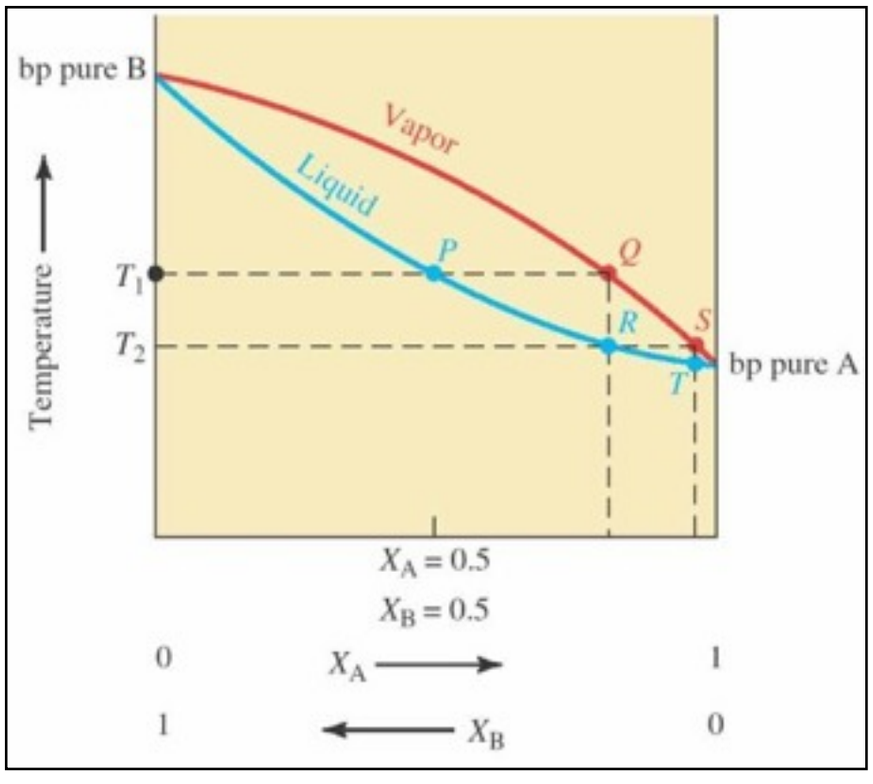
As distillation occurs you should see condensation occur on the thermometer. This will give the temp at which this compound distills.



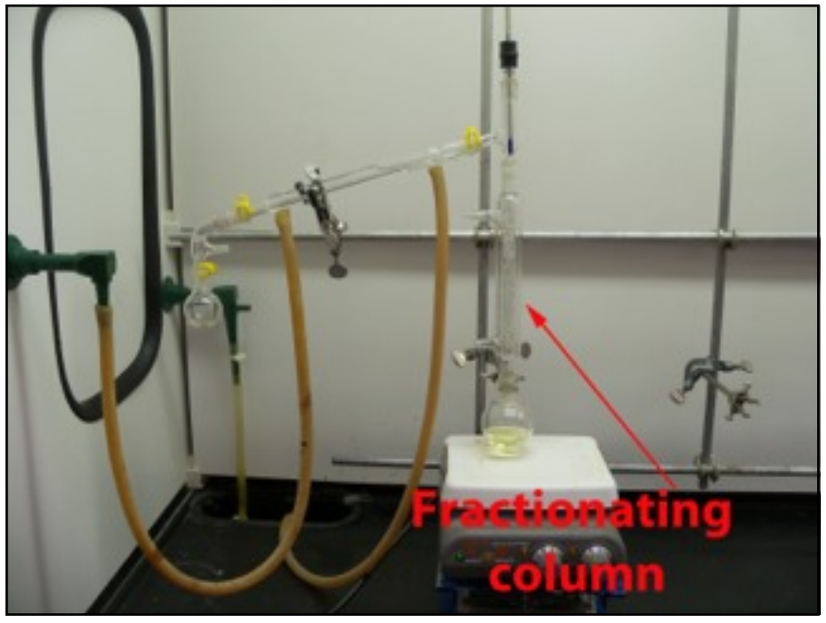
The vapor condenses in the water-cooled condenser and is collected in the receiving flask.

2. Fractional Distillation

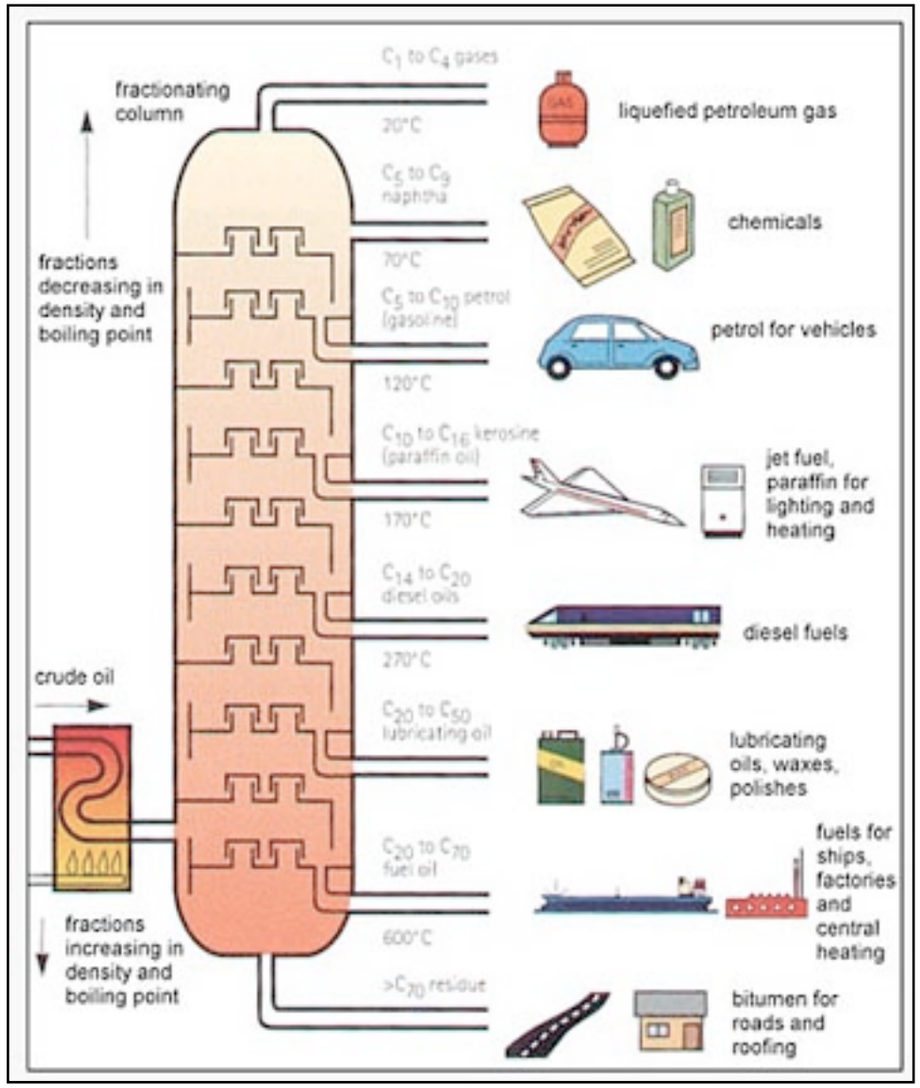
Fractional distillation is used to separate liquids with close boiling points. Fractional distillation is performed identically to simple distillation except that a fractionating column is placed between the round bottom flask and the condenser as shown. The fractionating column is packed with glass beads and works by creating hundreds of tiny surfaces where the liquid mixtures can vaporize and condense. According to the explanation of Raoult's law above, the vapor from the boiling mixture will be slightly enriched in ethanol since it has a lower boiling point than water and a higher vapor pressure. But what we want is pure ethanol, not 51% ethanol. So we need to perform dozens if not hundreds of cycles of vaporization and condensation to achieve purified ethanol. That is what happens on the fractionating column. The vapor from the boiling mixture encounters the glass beads and condenses. Then hot vapors from the round bottom flask heat the liquid and vaporize it again. Each time it re-vaporizes, the vapor will be more enriched in ethanol and less in water. Once the vapor reaches the top of the column, the mixture will be almost exclusively ethanol.



A fractional distillation set up is also shown below. Be able to draw a diagram of a fractional distillation and label the fractionating column. As before, place the liquid mixture in an appropriately sized round bottom flask. First attach a condenser filled with glass beads and then attach a distillation head to the top of the fractionating column. What is placed in the fractionating column? Place a thermometer in the top of the distillation head, and make sure that the top of the thermometer bulb is even with the entry to the condenser. Attach a condenser and adapter to collect your distillate. Ensure that water is running through the jacket of the condenser with water going in the bottom and out of the top. **Do not run water through the fractionating column.**



Because of hydrogen bonding interactions between ethanol and water, the mixture does not behave ideally and does not exactly obey Raoult's law (negative deviation). Ethanol and water form an azeotrope that boils at 78.2 °C containing 95.6 % ethanol and 4.4% water. An azeotrope is a mixture with an exact composition that cannot be altered by distillation. No matter how hard we try or how long our fractionating column is, we cannot obtain continue to separate ethanol and water by distillation past the azeotropic mixture.



Fractionating columns are utilized throughout industry. The above picture shows how petrochemical refining plants separate hydrocarbons with very similar boiling points by using the technique of fractional distillation. Image

EXPERIMENTAL PROCEDURE:

A. Performed in Week 1: Production of Ethanol from Molasses

- Mix 70 mL of molasses with 70 mL of water in a 250 mL side arm Erlenmeyer flask. Add 0.5 g of yeast to the flask and swirl until everything is completely mixed. Stopper the top of the flask with a rubber stopper. Attach one end of a length of rubber tubing to the side arm and immerse the other end of the tubing into a large test tube that is about two-thirds full of a solution of $Ca(OH)_2$ (limewater). The limewater serves two purposes. It is an airlock that allows carbon dioxide from the reaction to escape while preventing oxygen to enter the reaction. Be able to give at least one purpose for the limewater. Introducing oxygen to the reaction could cause the ethanol to be further oxidized to acetic acid (vinegar). The sterile limewater solution also prevents other microorganisms from entering the reaction and competing with the yeast for the nutrient rich reaction medium. Make sure everything will not spill and store this reaction in your drawer until next week.

B. Performed in Week 2: Simple and Fraction Distillation

- You will perform both a simple and a fractional distillation. Pour your reaction mixture into the largest size round bottom flask and attach the flask to a simple distillation apparatus (see Distillation Technique). Be able to draw a diagram for a simple distillation and label glassware. Simple distillations are used to separate compounds with large boiling point differences (>100 °C). Think about what compounds we are separating by performing this first simple distillation. What are we separating by simple distillation?

- The simple distillation can be done rapidly, so try to collect your distillate at a rate of 2-3 drops per second. Collect your distillate in a 100 mL (or 50 mL) graduated cylinder. As the receiving graduated cylinder is filling write down the temperature for every 10 mL that is collected. Collect at least 50 mL of distillate (you should therefore obtain 5 temperature measurements). Be careful not to let the molasses co-distill over into the graduated cylinder. After the simple distillation transfer **exactly** 10 mL of the distillate to a pre-weighed 10 mL graduated cylinder and record the weight. When done, place all of your distillate from the simple distillation in a round bottom flask (roughly twice the capacity of the distillate volume) and set up a fractional distillation apparatus (See Distillation Technique). You can use most of the set-up that is already assembled for the second distillation. Fractional distillation will now be used to separate the ethanol and water mixture obtained from the simple distillation. Begin distilling and collect your distillate in the same pre-weighed 10 mL graduated cylinder. Try to maintain at least 1 drop a second rate of distillation. During the fractional distillation record the temperature of distillation every 2 mL. Try to collect at least 10 mL of distillate (thus you will have 5 temperature data points). You may stop the distillation after 10 mL. Weigh-out **exactly** 10 mL of the distillate as before.

- Weigh-out 10 mL of sample remaining in the pot in a 10 mL graduated cylinder. Similarly, weigh-out 10 mL of pure water, and 10 mL of pure ethanol. You will determine the percent composition of ethanol within each fraction you collected using density analysis.

DATA PRESENTATION:

Include the following in your formal laboratory report discussion:
Distillation Data:

- Construct a table with a column for increasing volume of distillate (in 5 mL increments from 5-50) and a column listing the observed boiling points at each 5 mL increment during the distillation for the simple distillation. Add two more columns and include the same data for the fractional distillation (except that the data will be in 2 mL increments).

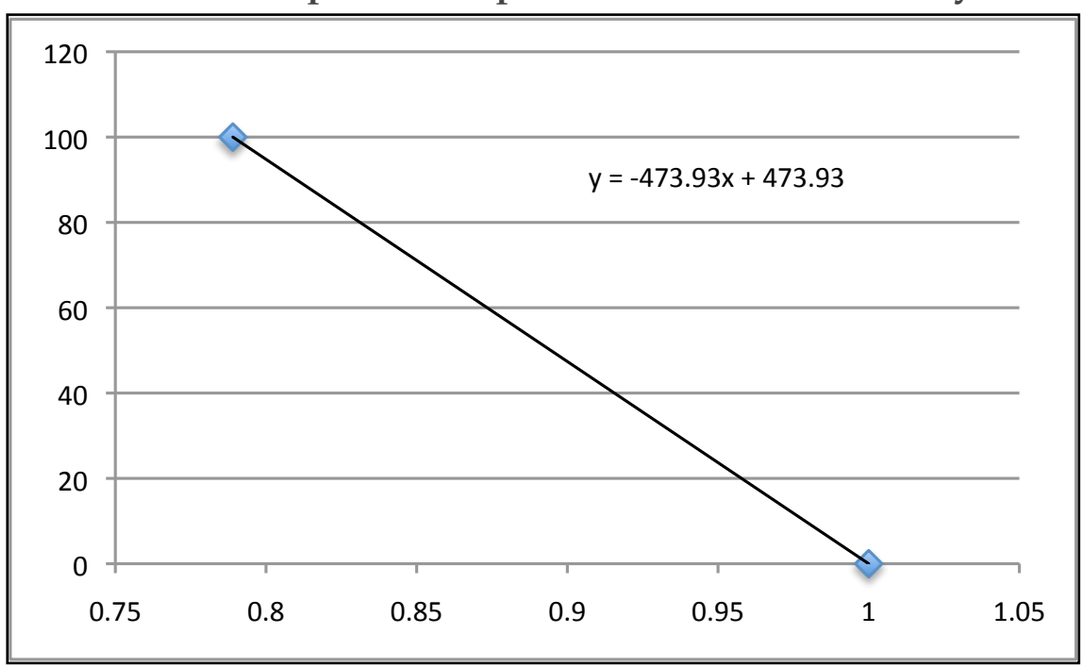
- Next, using the above data, plot 2 separate graphs: a) boiling point (y axis, with a scale of 60-120 °C) vs. volume of distillate (x axis, with a scale from 5-50 mL), and b) boiling point (y axis, with a scale of 60-120 °C) vs. volume of distillate (x axis, with a scale from 0-10 mL). Draw a smooth curve through each set of points (or use excel). Discuss the differences in the two curves in your formal lab report.

Density Analysis Data:

- The graph to the right shows the percent ethanol (y axis, scale 0-100%) vs. density (x axis, density of ethanol to density of water). This graph will allow you to determine the ethanol content and percent water of your three samples (simple, fractional and distillation pot). Using the slope-intercept equation determine the ethanol content for all three samples.

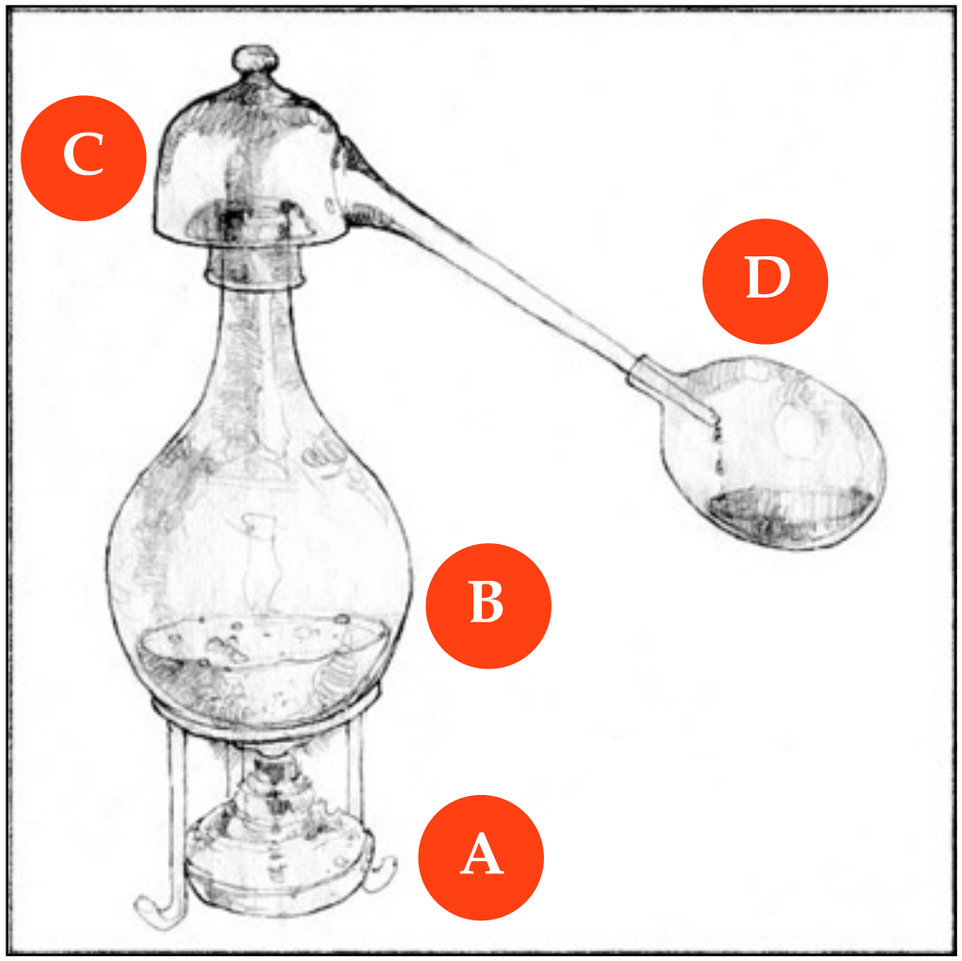
- Construct another table with three columns: sample identity (simple distillate, fractional distillate, distillation pot) , percent ethanol, and percent water for each sample.

Relationship between percent ethanol and density:



Additional Pre-Lab Questions:

- Will the fractional distillation separate ethanol and water, which boil close together, more effectively than the simple distillation?
- How does the fractionating column achieve a better separation?
- The following diagram represents a distillation apparatus used by early Arab chemists in the 7th and 8th century. Explain the purpose of components A-D. What are the primary differences between this apparatus and the apparatus you assembled in lab?

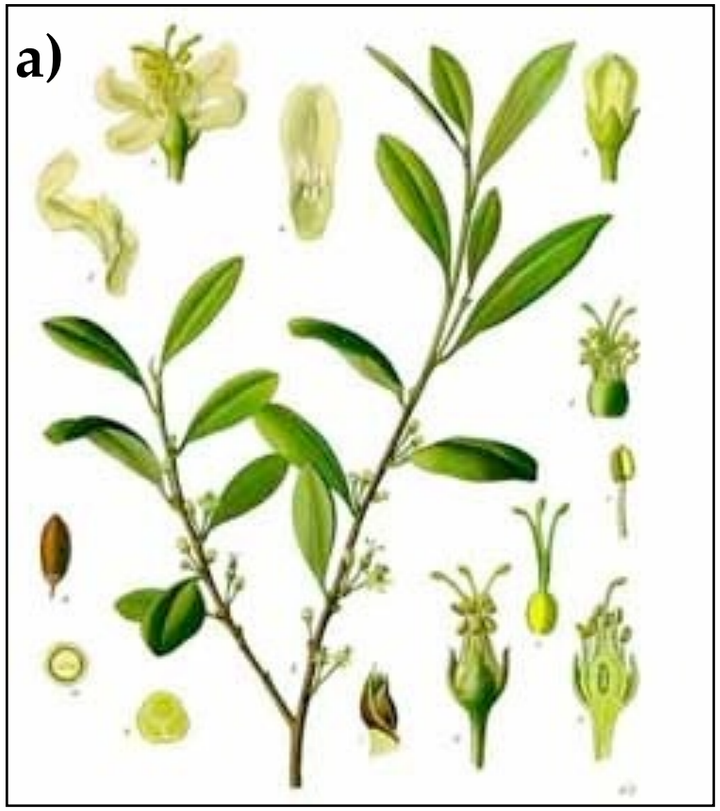


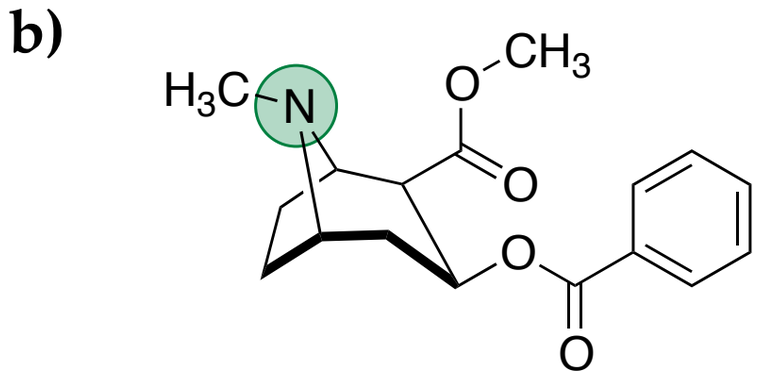
Image

Acid-Base Extraction

Laboratory Techniques:

1. Proper use of a separatory funnel for extractions.
2. The use of acids/bases to selectively remove organic molecules that possess acidic or basic functionality.
3. Vacuum filtration utilizing a Buchner funnel.
4. Use of drying agents to remove water from organic compounds.
5. Determination of purity by melting point ranges.
6. Identification of unknown compounds by melting point analysis.





a) Botanical diagram of the Peruvian Coca Leaf. b) Structure of cocaine with the basic tertiary amine highlighted in green. Image

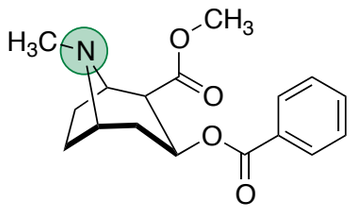
It might seem particularly daunting to try and selectively remove all of one molecule from a plant or animal while leaving the millions of other types of molecules behind. Nevertheless, extracting molecules from natural sources is a fairly common procedure and can be done on an industrial scale for a variety of biologically active molecules. Indeed, many important life-saving drugs on the market are originally isolated from natural sources. The question remains: how is this done?

Some organic molecules possess acidic or basic functional groups. These groups can be protonated or deprotonated in a solution given the right pH. When the organic molecule has undergone an acid-base reaction it becomes charged in the form of an ionic salt. In turn, this charge increases the solubility of the molecule in aqueous (or polar) solvents, and decreases the solubility of the molecule in nonpolar, organic/greasy solvents. This solubility difference allows the molecule to be selectively pulled out of the "soup" of other molecules.

Let us illustrate how this chemistry works through a real-world example: the isolation of cocaine from coca leaves.

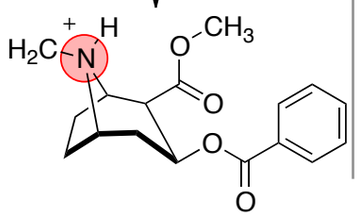
Step 1: Cocaine's journey begins in a jungle lab in South America. The harvested coca leaves are first soaked in gasoline (octanes, but equivalent to hexanes: a very non-polar, greasy organic solvent) inside metal drums. At this point many of the thousands of organic molecules in the coca leaf indiscriminately migrate into the gasoline solvent.

Step 2: The gasoline solvent that contains all the organic molecules is now drained and filtered from the metal drums into an **aqueous solution** of dilute acid. The acid protonates the basic nitrogen on cocaine which makes it **ionic and soluble in the aqueous layer** and not soluble in the gasoline. The aqueous and organic layers separate into two phases. The gasoline layer is thrown away at this point.



soluble in gasoline

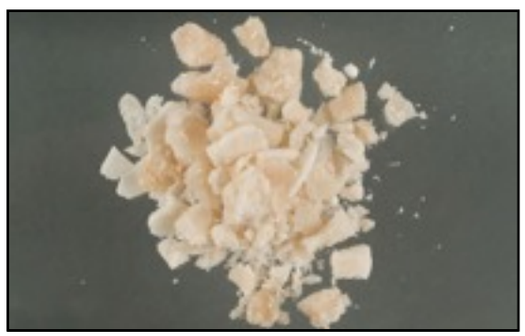
H_3O^+
dilute acid



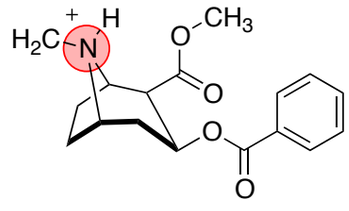
soluble in water

Step 3: Sodium bicarbonate or ammonia (both weak bases) are then added to the acidic, aqueous solution of protonated cocaine until the pH becomes basic. When this happens the cocaine becomes deprotonated again (free-base), and is once again soluble in organic solvents **and not water**. The result is the precipitation of cocaine from the water solution.

Step 4: The cocaine is then dried and recrystallized (purified) from an organic solvent such as ethyl acetate, acetone, or ether (we will cover recrystallization in next week's lab). For stability reasons, the purified cocaine is often re-acidified, stored, and sold as the cocaine hydrochloride salt. Cocaine with the basic nitrogen unprotonated is called "free-base cocaine" and is typically made by dissolving the HCl cocaine salt in a mixture of water and sodium bicarbonate (baking soda). The resulting product (after drying) is often termed crack cocaine.

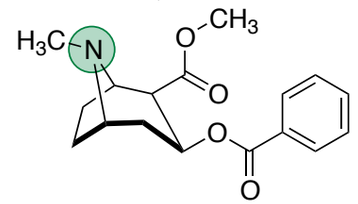


Images



soluble in water

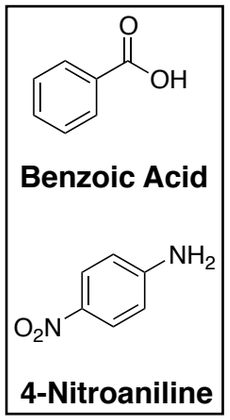
$NaHCO_3$
weak base



insoluble in water,
precipitates out of solution

TECHNIQUE: Liquid-Liquid Extraction

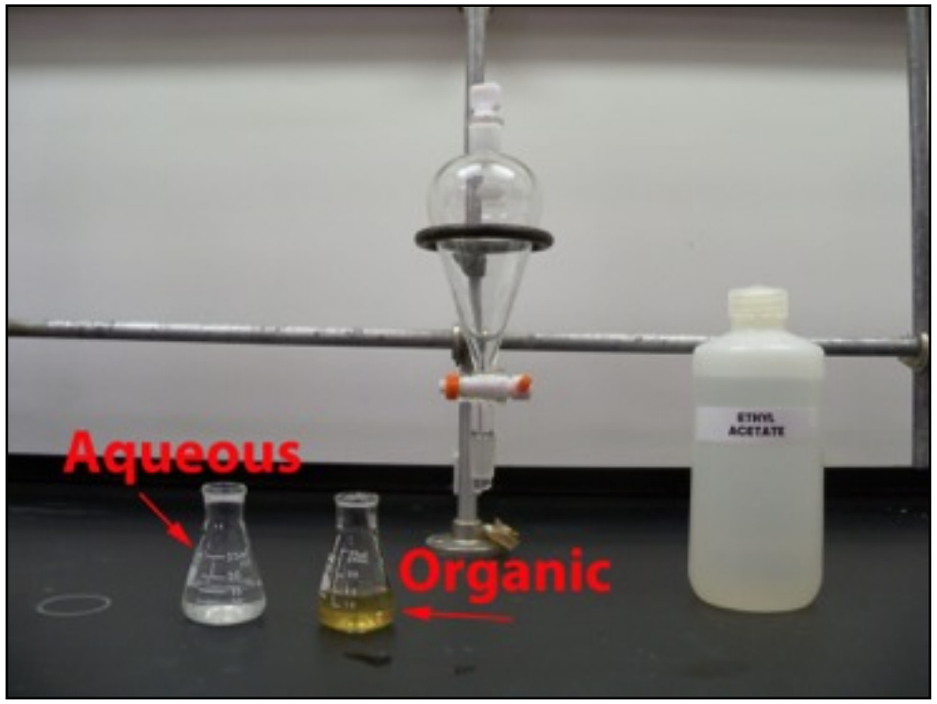
Liquid-liquid extraction is the process used to transfer something dissolved in one liquid to a different, immiscible liquid. In the organic laboratory this process is extremely useful in separating and purifying complex mixtures of compounds (akin to removing cocaine from all the other molecules in the coca leaf). As you already know from General Chemistry, "like dissolves like". That means that nonpolar organic compounds prefer to dissolve in nonpolar organic solvents such as hexanes or ethyl acetate. However, certain organic compounds readily undergo acid-base reactions to produce ionic salts, which are highly polar and thus water soluble. We will exploit these properties to separate three organic compounds: an **unknown neutral organic molecule**, benzoic acid, and p-nitroaniline. Which of these molecules is the acid? Which the base?



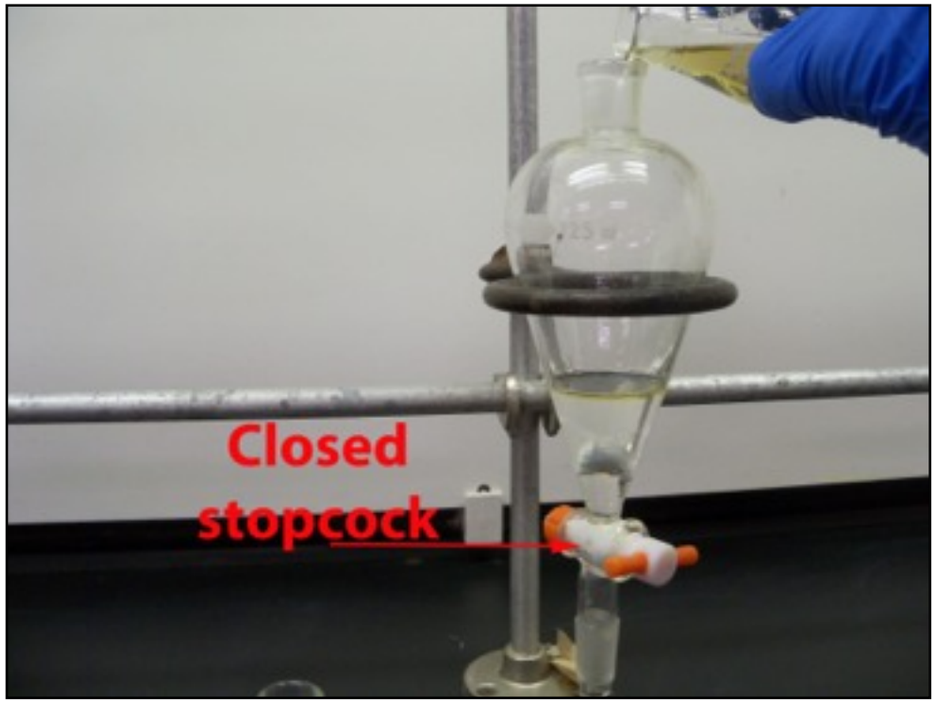
Laboratory scale extractions typically rely on a separatory funnel (and not a gasoline drum) to efficiently carry out a liquid-liquid extraction. These glassware are useful for separating two **immiscible** liquids. The less dense liquid is always the top layer and the more dense liquid is always the bottom layer, just like how oil (less dense) floats on water (more dense).

Vegetable Oil: Less dense than water

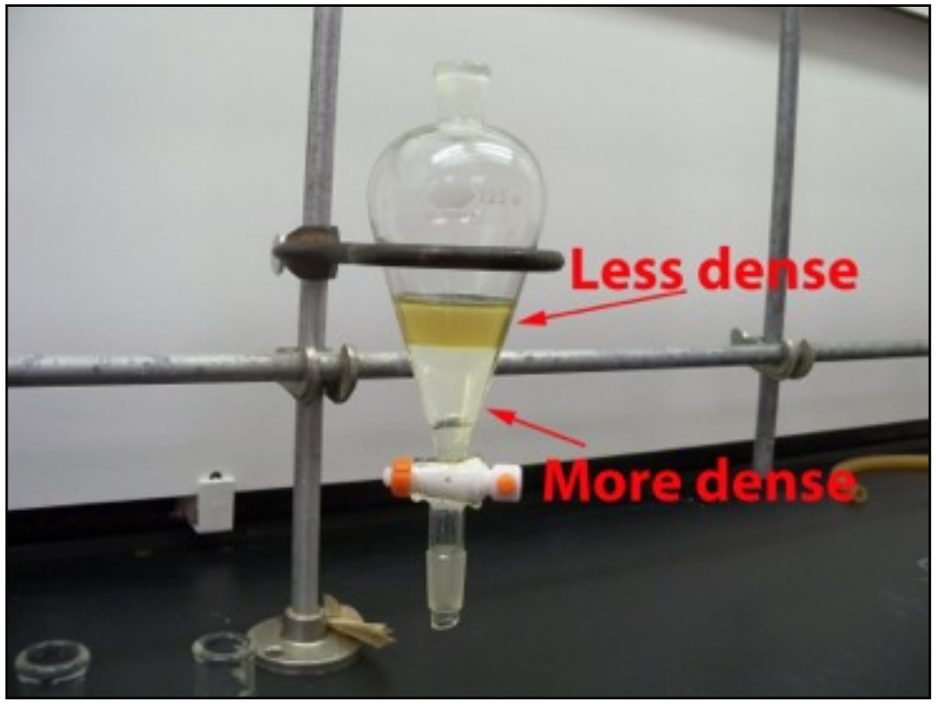
Water: More dense than vegetable oil



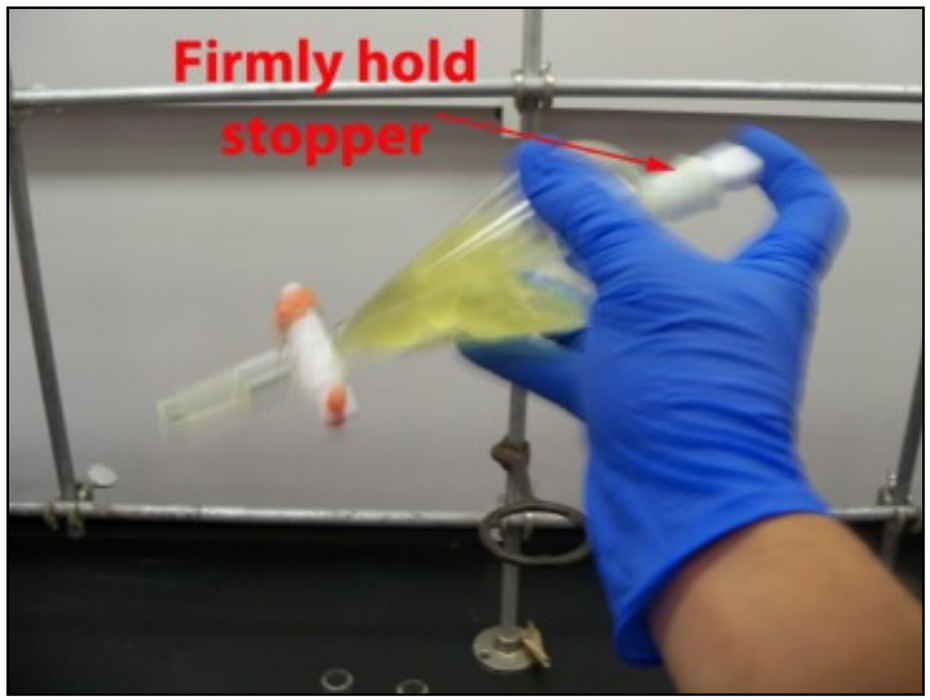
The sep funnel, ring attachment, the aqueous layer and organic layer.



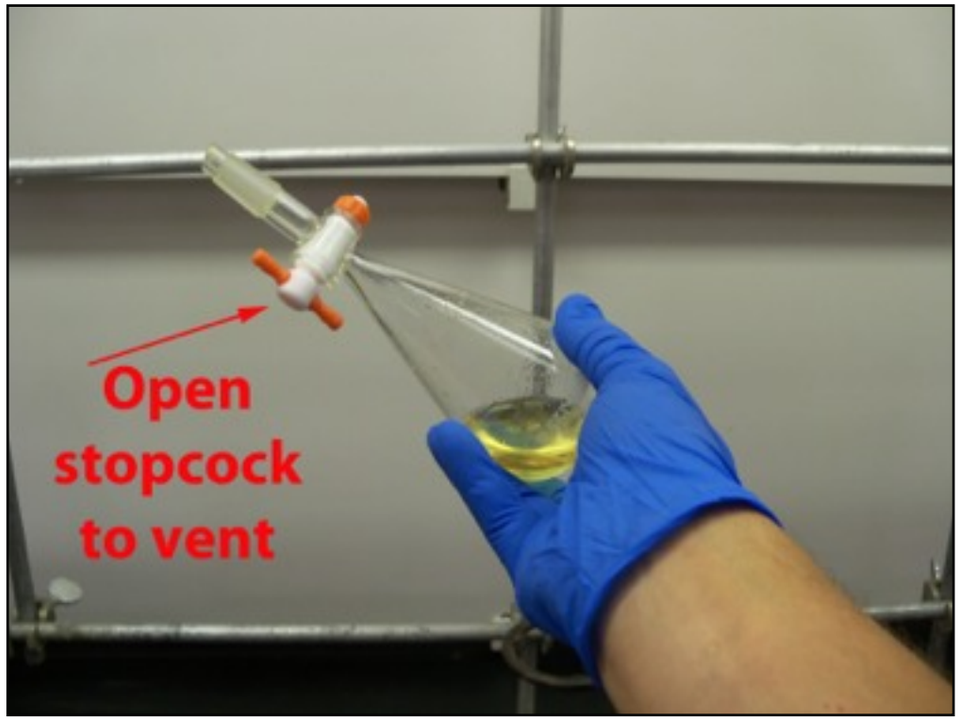
With the stopcock closed, add the two phases to the sep funnel.



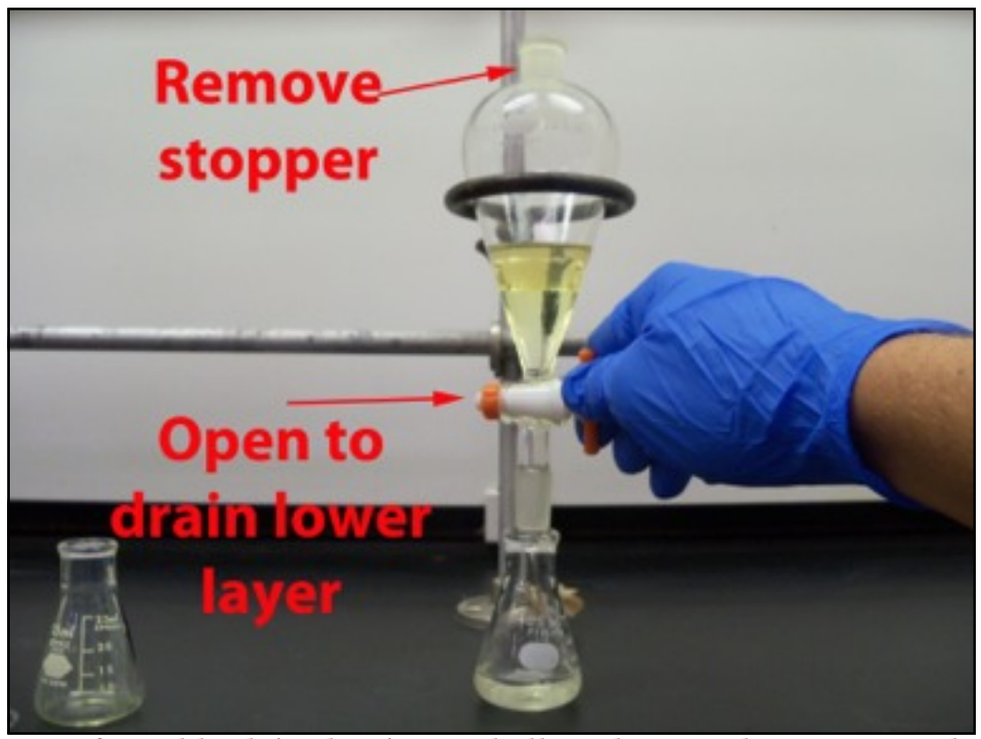
The less dense layer rises to the top above the more dense layer.



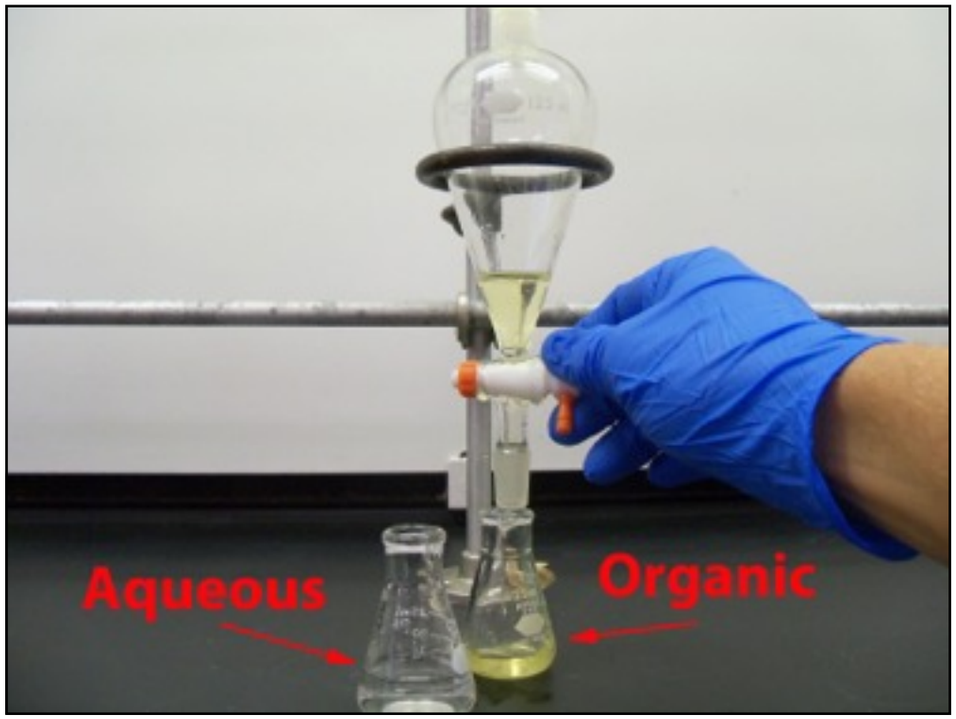
Firmly holding the stopper, vigorously shake (to mix) the two layers



Invert the sep funnel to vent the liquid. Typically you will shake the sep funnel and vent 3-4 times before you allow the phases to completely separate.

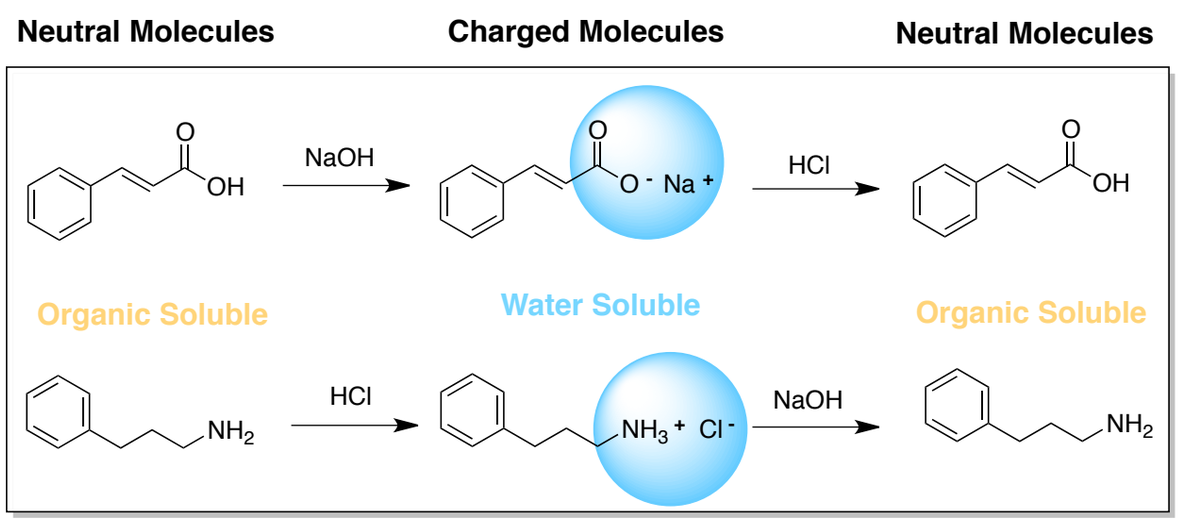


Put the sep funnel back in the ring and allow the two phases to completely separate. Open the stopcock to drain the lower layer into an Erlenmeyer.

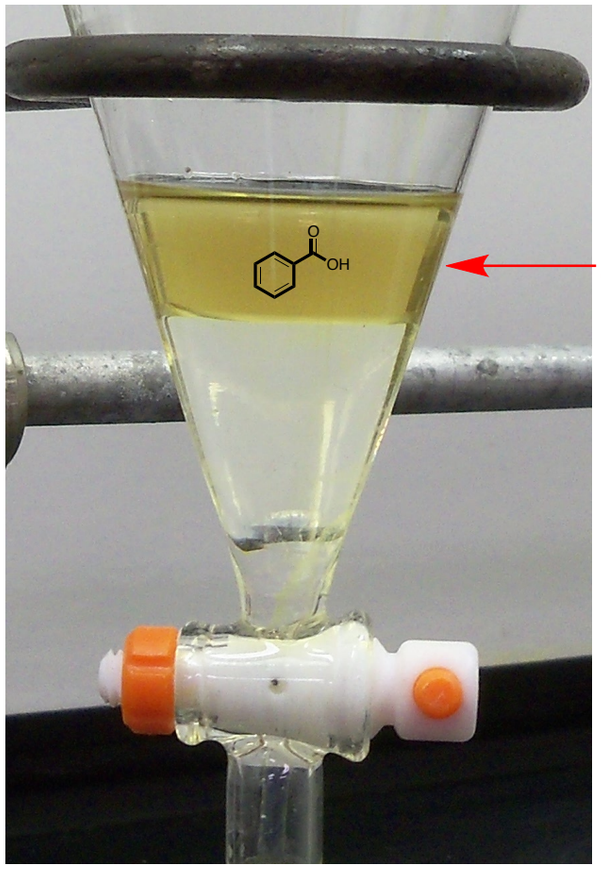


Drain the top phase into a different Erlenmeyer flask.

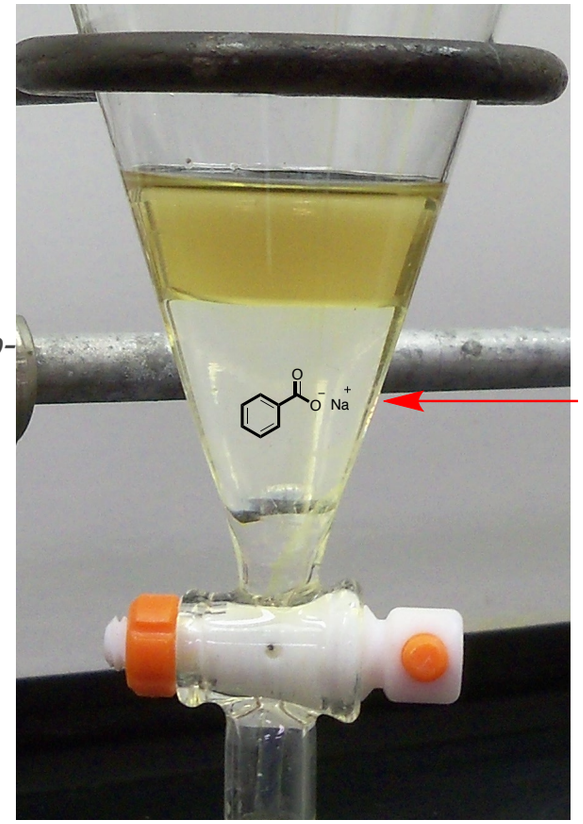
In this lab we will begin with all three organic compounds dissolved in an organic solvent, ethyl acetate, and successively extract (remove) one component by exploiting acid-base chemistry and the solubility properties discussed above. Treating benzoic acid with NaOH creates a water soluble salt, sodium benzoate, thus removing benzoic acid from the organic solvent. Likewise, treating the basic p-nitroaniline with HCl creates a water soluble salt (akin to cocaine). Why are protonated amines soluble in water? Only the unknown neutral compound then remains in the organic solvent, and we will have effectively separated all three compounds. The organic acid and base can be recovered by neutralizing the individual aqueous extracts (akin to free-basing) to render the organic compounds insoluble.



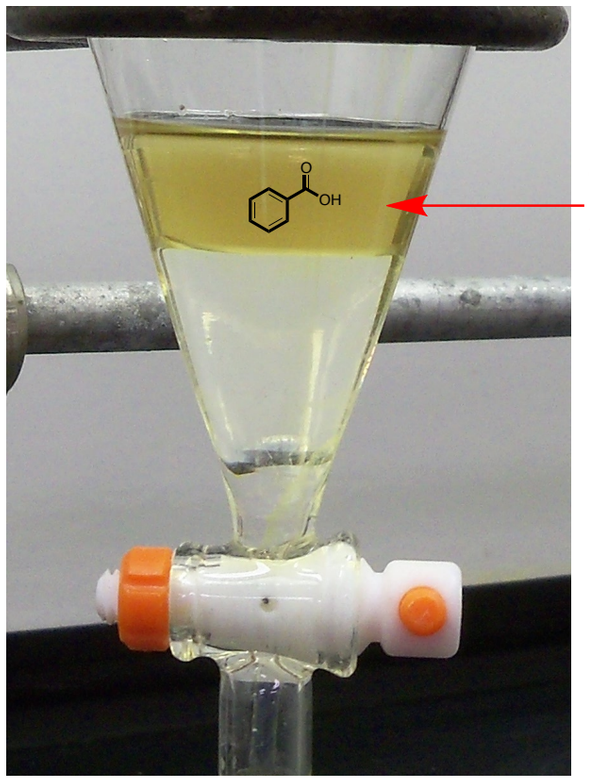
Uncharged, relatively non-polar, organic molecules will always be solvated by the organic phase.



Washing/mixing the organic phase with a weak base causes an acid-base reaction with the benzoic acid to form sodium benzoate. This molecule is charged. It therefore migrates to the aqueous phase.

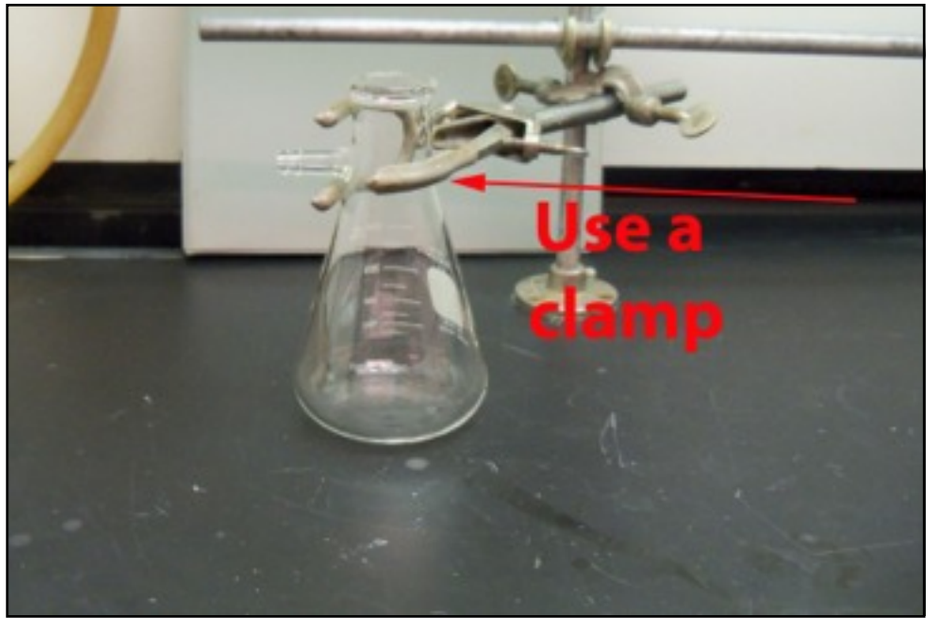


If the aqueous phase is washed with acid to neutralize the sodium benzoate, the resulting benzoic acid will migrate back to the organic phase. Why does neutralizing sodium benzoate cause it to migrate to the organic phase?

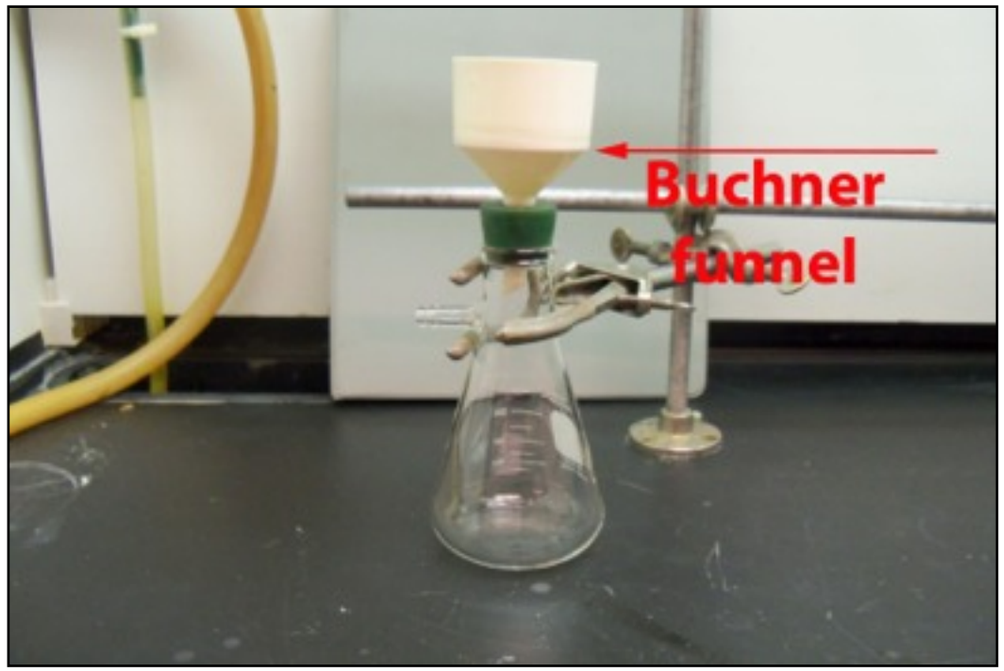


TECHNIQUE: Vacuum Filtration

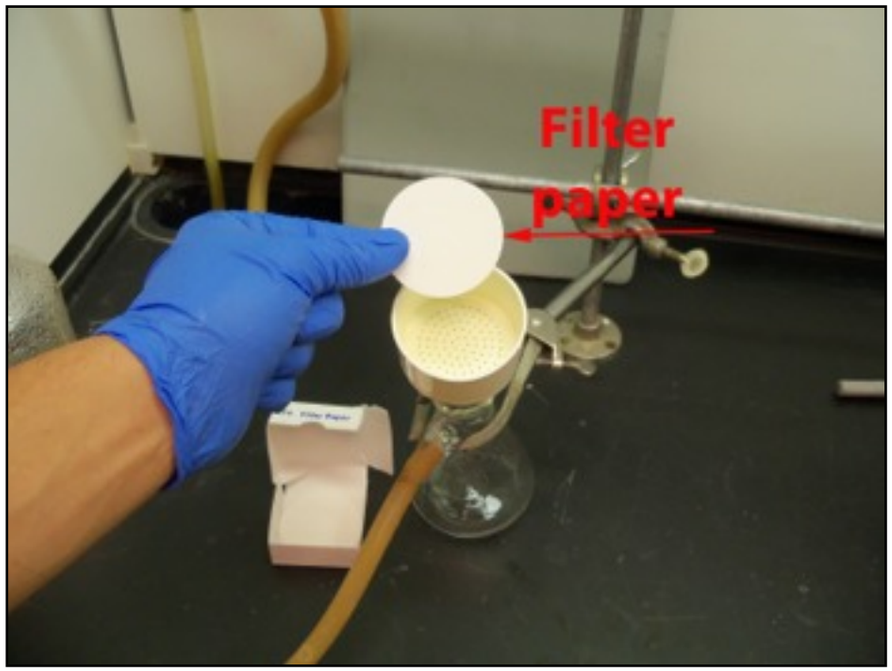
Vacuum or suction filtration is a faster filtration technique than gravity-induced filtration, and is most often used to collect solid products generated from precipitation or recrystallizations. In a vacuum filtration, an Erlenmeyer flask with a sidearm (a **filter flask**) is used. The sidearm is connected to a source of vacuum. In this case rubber tubing joins the filter flask to the water aspirator trap (vacuum = approximately 10-20 *mm* Hg). A **Buchner funnel** is fitted on top of the filter flask by a rubber stopper/adaptor. The flat bottom of the Buchner funnel is covered with an unfolded piece of circular filter paper. It may be necessary to cut the filter paper down to a size that completely covers the holes in the Buchner funnel (do not allow the filter paper to extend up the sides of the funnel). Finally, "wet" the surface of the filter paper with a small amount of the wash solution to allow the paper to adhere to the Buchner funnel.



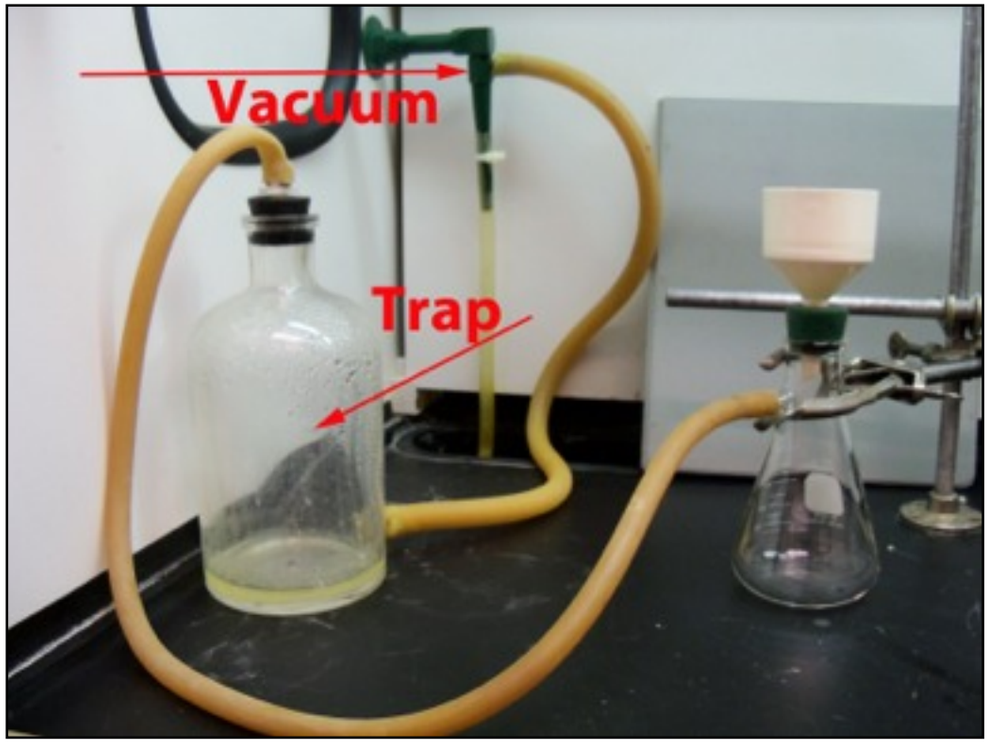
Always clamp the filter flask. They are prone to tipping over during filtration.



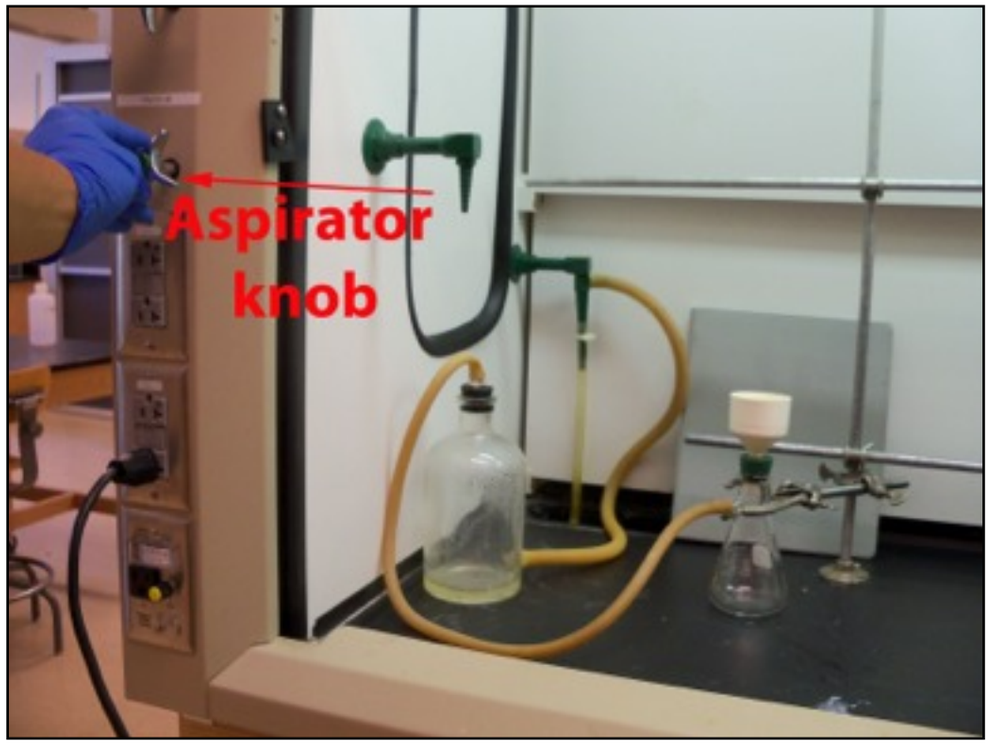
Attach the Buchner funnel through a sealed stopper.



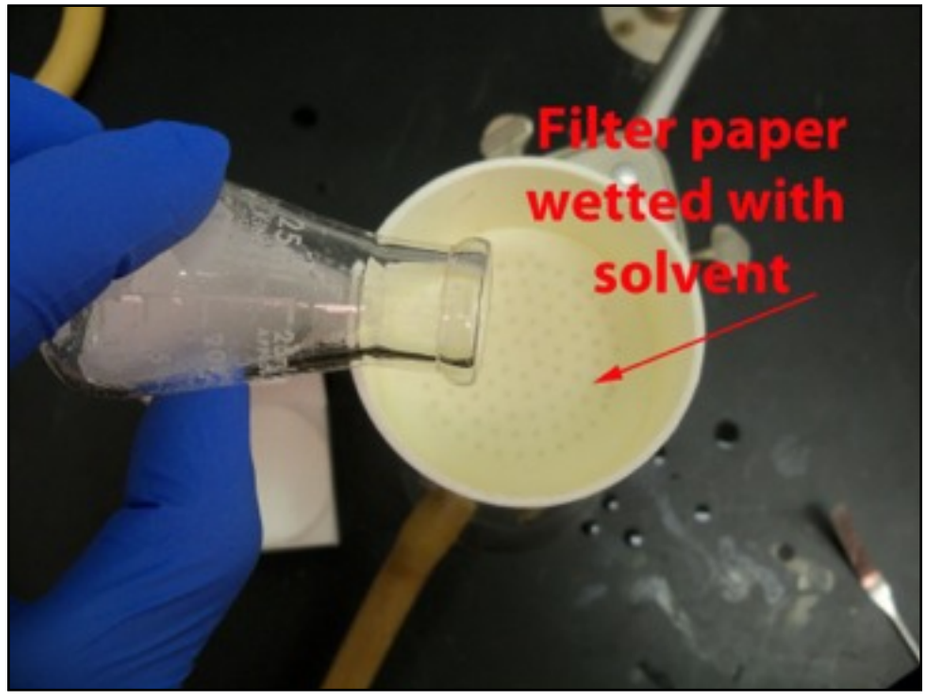
Place filter paper in the Buchner funnel. Depending upon the size of the funnel you may need to cut the paper.



The hose from the filter flask is attached first to the trap and then the trap is attached to the water aspirator.



Turn on the aspirator knob to start the vacuum.



First wet the paper with the solvent, then slowly pour your slurry through the funnel. Why do we wet the filter paper on Buchner funnels?

In some cases you may want to wash the solid with cold solvent to further the purification of the solid.

EXPERIMENTAL PROCEDURE:

A. Extraction of a Ternary Mixture

- Weigh out 0.5 grams of a solid mixture containing equal quantities of (1) benzoic acid, (2) p-nitroaniline, and (3) one of the unknown organic compounds (write the unknown number down in your notebook!). Dissolve the mixture in 10 mL of ethyl acetate in a small Erlenmeyer flask warming slightly on the hot plate if necessary. Upon dissolution, transfer the solution to a separatory funnel and rinse the Erlenmeyer flask with a small amount of ethyl acetate.

- Add 3 mL of 6 M NaOH, cap the separatory funnel, and shake it vigorously. Remember to vent your separatory funnel. Allow the two phases to separate completely. You should see two distinct layers (see Liquid-Liquid Extraction Technique).

- Transfer the lower layer to a small Erlenmeyer flask and label as AQUEOUS BASE EXTRACT. Keep the upper organic layer in your separatory funnel and extract again with 3 mL of 6 M NaOH. Combine the two aqueous base layers and save them.

B. Extraction of a Binary Mixture

- Add 3 mL of 6 M HCl to the organic layer in the separatory funnel, carrying out an extraction like you did with the aqueous base. Put the aqueous acid in another flask and repeat the procedure with a second 3 mL of acid. Combine the two aqueous acid layers and label as AQUEOUS ACID EXTRACT.

- In another Erlenmeyer flask remove any traces of water from the remaining ethyl acetate layer by adding a small amount of anhydrous sodium sulfate, swirling the mixture until the solution is no longer cloudy. Separate the liquid from the solid by gravity filtration through a cotton plug (place a ball of cotton in the bottom of a funnel and pour the solution through it to filter) and label the filtrate ORGANIC SOLUTION. You should now have three separate solutions: (1) AQUEOUS BASE EXTRACT containing the organic acid, (2) AQUEOUS ACID EXTRACT containing the organic base, and (3) ORGANIC SOLUTION containing the neutral organic compound.

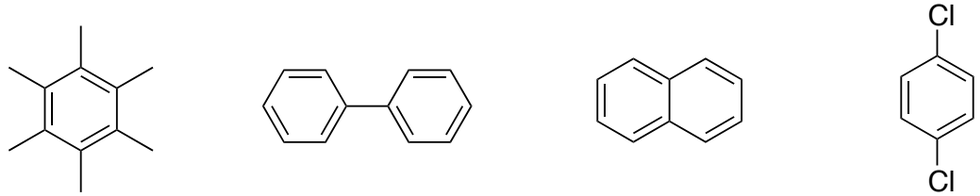
C. Isolation and Analysis of the Individual Components

- Cool the aqueous base extract in ice and then neutralize it by adding 6 M HCl gradually with stirring until it is acidic with pH paper. This neutralization will require ~ 4-6 mL of 6 M HCl. An insoluble solid should be observed at this point. If you do not see a solid, you may need more HCl or you may need to cool your sample further. Isolate the solid by vacuum filtration (see Vacuum Filtration Technique), and wash the solid with a small amount of cold water. Let the solid dry before determining its weight and melting point. You may need to heat this compound slightly on a hot plate to dry it fully.

- Repeat the above procedure on the aqueous acid extract using 6 M NaOH. After you isolate this solid, allow it to dry before obtaining its weight and melting point.

- Evaporate the ethyl acetate from the organic layer by boiling off the solvent on a hotplate in the hood. Note that ethyl acetate boils at a very low temperature, so your hot plate only needs to be warm (HEAT SETTING 1 or 2). When most of the liquid has evaporated, allow the sample to cool so that the neutral organic compound will crystallize. (Note that the unknown compound may melt and appear as a liquid on the hotplate.) Let the solid dry before determining its weight and melting point.

Possible Unknown Neutral Organic Molecules:



Hexamethyl-Benzene mp: 165 º	Biphenyl mp: 71 º	Naphthalene mp: 82 º	1,4-Dichloro-benzene mp: 56 º

DATA PRESENTATION:

Include the following in your formal laboratory report discussion:

- Using melting points determine the identity of the unknown organic solid. Comment on the purity of each recovered component (acid, base and neutral compound) as determined by melting point (compare the melting points to known literature values). **Remember that mixtures of compounds will typically display broadened and depressed melting points.** Thus, if your extractions of the other two components was not complete your mp of the unknown will be affected!

- Include a flow chart to describe the separation of the mixture and the isolation of each component.

- Calculate the percent recovery of each component in the mixture. Assume that each component was present in equal amounts in your sample.

Additional Pre-Lab Questions:

- If we used dichloromethane (density = 1.33g/mL) as the organic solvent for the extraction, explain which layer in the separatory funnel, top or bottom, would be the aqueous layer and the organic layer. Why?

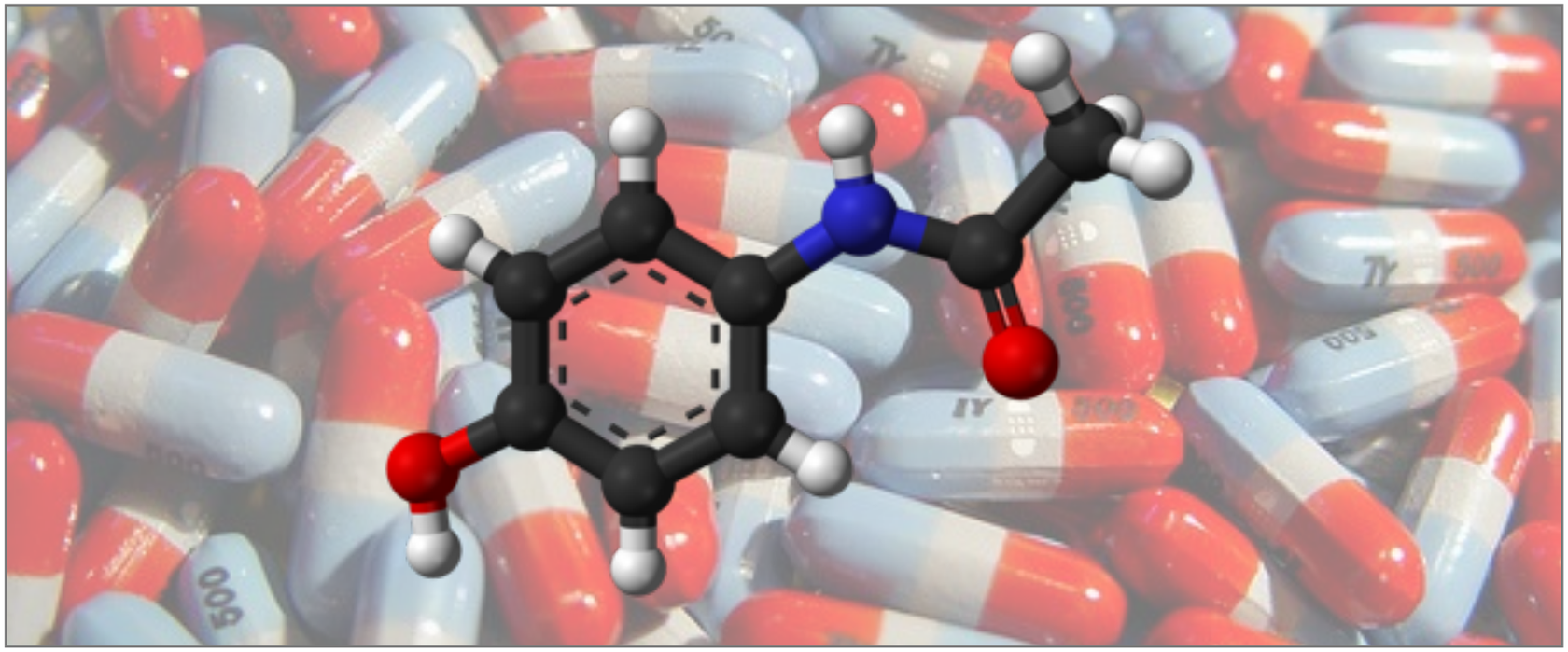
- Be able to show each acid-base reaction that took place, using the skeletal structures of the molecules. Use curved arrows to depict electron flow for each reaction. Label each organic compound as water soluble or organic soluble. **There should be a total of four acid-base reactions.**

- Should it make any difference if the mixture is extracted first with HCl or NaOH?

Synthesis of Acetaminophen (Tylenol): Recrystallization of a Solid

Laboratory Techniques:

1. Recrystallization as a purification method for solid organic compounds.
2. Vacuum filtration utilizing a Buchner funnel.
3. Analysis of purity by melting point analysis.
4. Determination of theoretical yield and percent yield of product from a chemical reaction.



Tylenol (acetaminophen) an analgesic and antipyretic drug commonly used to reduce pain, fever, and the symptoms of cold and flu.

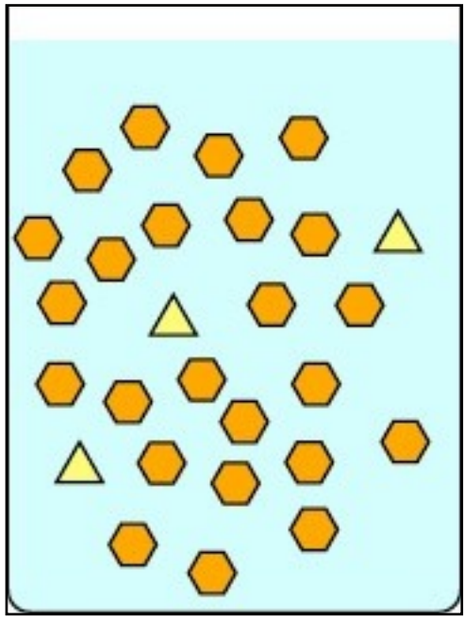
In this experiment, you will prepare an analgesic compound found in the over-the-counter drugs used to relieve pain and control fevers. Originally synthesized in 1877 by Harmon Morse, it was not until 1955 that acetaminophen was marketed as a pain-relief medication under the trademark Tylenol. Currently, hundreds of generic versions are available and are utilized daily by millions of people worldwide.

In your synthesis today it will be necessary to purify the product by recrystallization. Your laboratory notebook should be in the format of a synthetic preparation with a synthesis table.

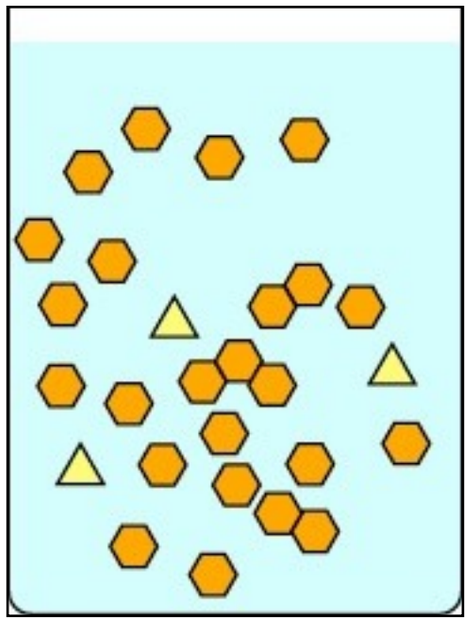
TECHNIQUE: Recrystallization

Crystallization is a technique chemists utilize to purify solid compounds. In effect, crystallization is based on the principles of solubility: organic compounds will generally be more soluble in hot solvents than they are in cold solvents. Are organic compounds more soluble in hot or cold solvents? If a saturated, hot solution is allowed to cool, the dissolved compounds will no longer be soluble in the solvent and preferentially crystallize as pure compounds. Impurities are excluded from the growing crystals and can be physically separated *via* filtration.

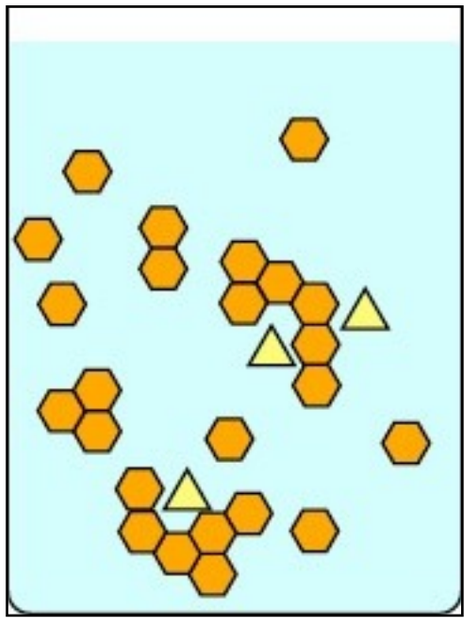
On a fundamental level, the following must take place for crystallization to successfully take place: the solid compound is dissolved in just enough hot solvent for complete dissolution. This flask now contains both the freely moving desired compound as well as impurities. The solution is then cooled allowing for some of the desired solute molecules to leave the solution. During the cooling process, as more molecules come out of solution they will preferentially co-crystallize with similar geometrically shaped molecules. If done correctly, the geometric differences between molecules (the desired solid, and impurities) will be great enough to create pure crystals of only one type of molecule.



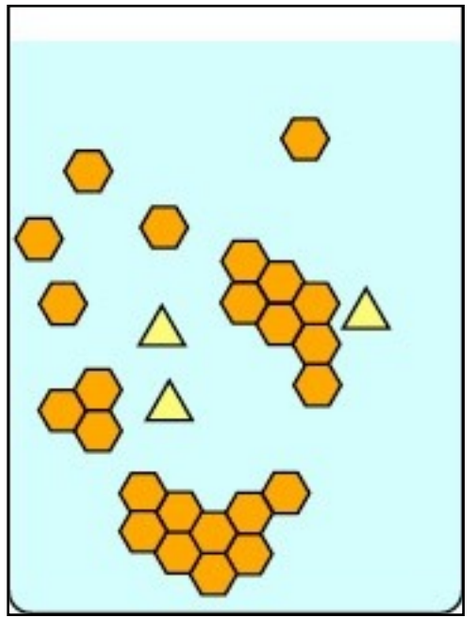
*Beginning of Crystallization: Both the desired compound (octagons) and the impurity (triangles) are fully solvated in the **hot** solution.*



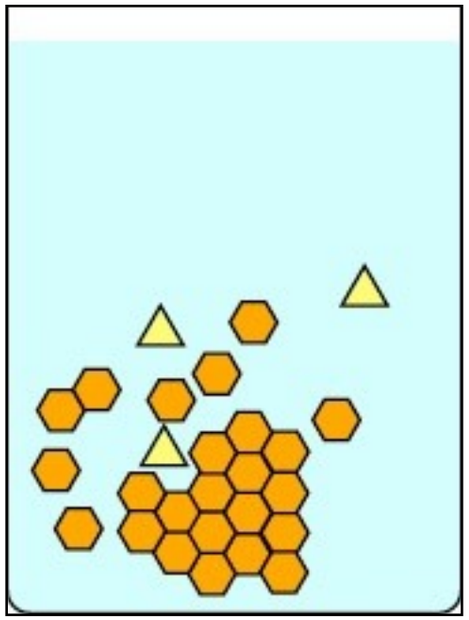
As cooling begins, so does agglomeration of the desired compound.



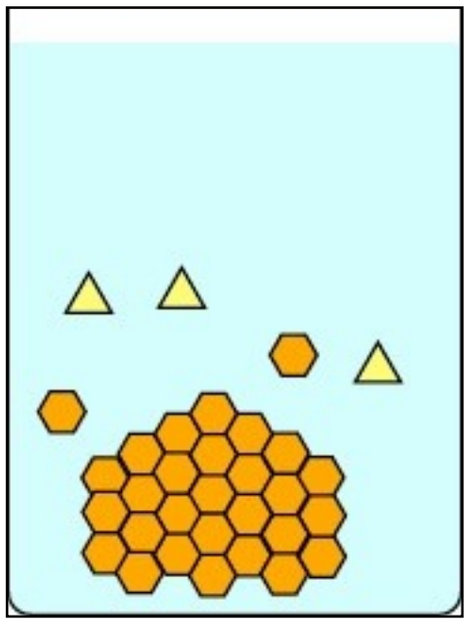
Larger crystals begin to form. The impurities also try to co-crystallize with the product but have difficulty due to incompatible geometries.



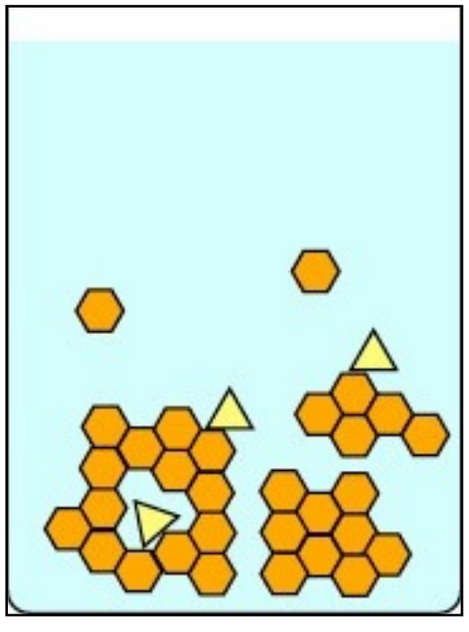
Crystallization continues as the solution reaches room temperature.



The solution is cooled by an external ice-bath, allowing for rapid crystal growth.



End: Finally, the crystals can be harvested from the flask. The impurities remain in solution and can be washed away from the product. A small amount of product loss is expected in the wash.



*This is an example of what happens when a solution is **cooled too fast** and impurities become trapped in the crystals. (Bad!)* Why is it bad to rapidly cool a recrystallization?

In practice, **there are four essential steps for a recrystallization**:

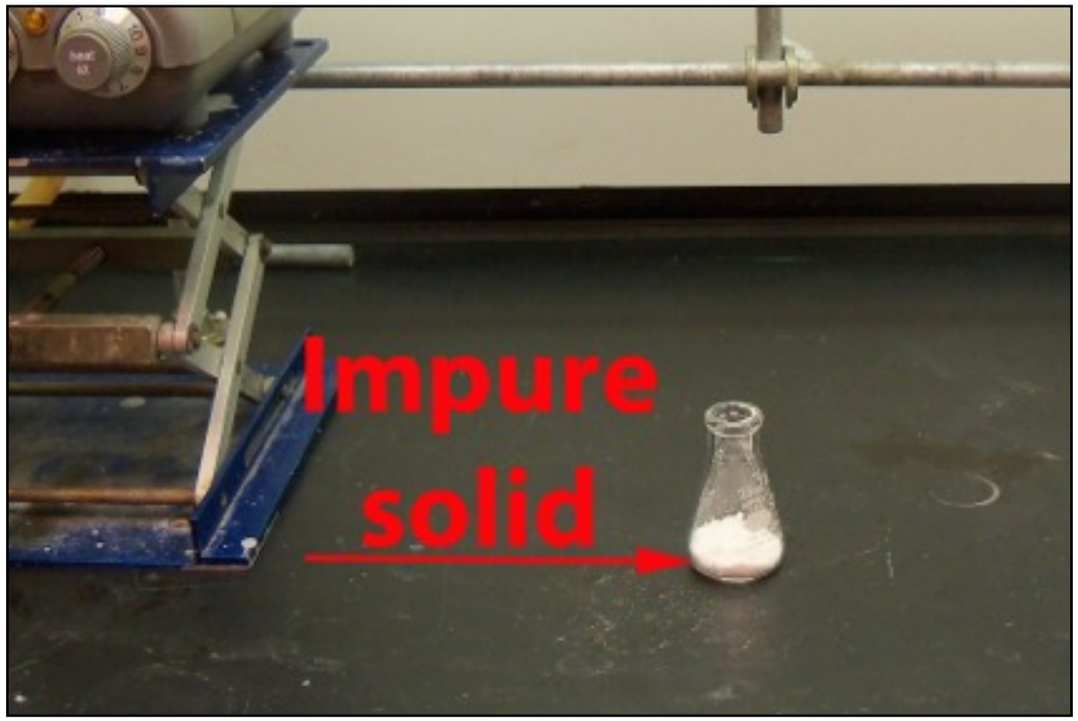
1. The impure solid is dissolved in a minimum amount of hot (usually boiling) solvent to create a saturated solution. Why is a minimum of hot solvent used for recrystallization? This process is always done in an Erlenmeyer flask rather than a beaker.

2. If there are insoluble particles (hair, etc.) the hot solution should be filtered, while keeping the saturated solution hot at all times, to remove the insoluble materials. This type of filtration is called gravity filtration and is performed over a hotplate with a folded filter paper in a plastic funnel.

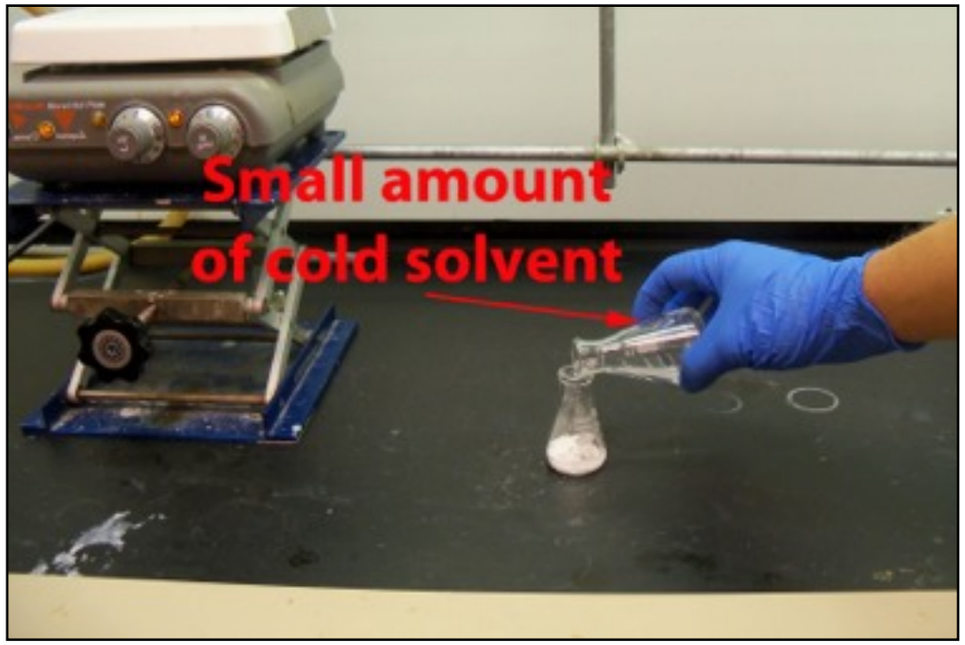
3. Crystallization is then induced by first scratching the glass inside the flask with a glass stirring rod to initiate crystallization, and then the hot solution is covered with a cork and allowed to cool very slowly to room temperature. Why is the saturated solution cooled during recrystallization? Then it is cooled further to 0 °C in an ice bath. If crystals are allowed to form very slowly in this manner they usually are much purer than if they "crash out" of solution rapidly (see "Stages of recrystallization" for an example of crystals that have "crashed-out").

4. The crystals are then collected from the cold solution by vacuum filtration, quickly washed with a minimum amount of ice-cold solvent, and then allowed to dry completely on a watch glass or petri dish before determining the melting range. Complete evaporation of the solvent usually requires at least several hours before an accurate melting point can be measured. In certain cases the drying process can be accelerated by placing the watch glass with your crystals on top of a hot plate set on a low setting.

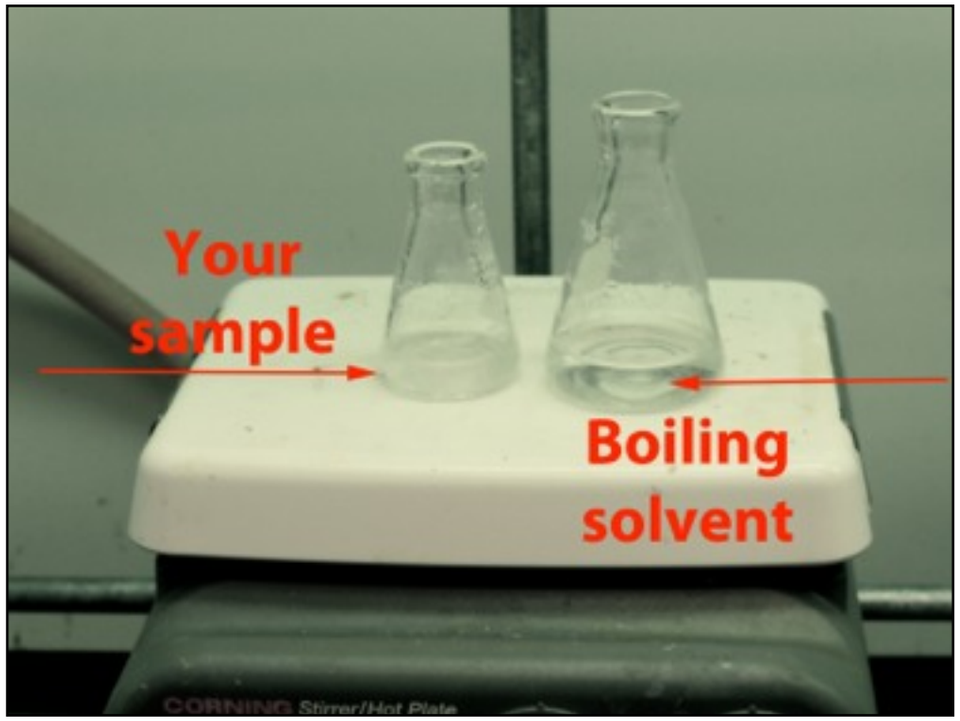
5. Occasionally it may be desirable to obtain a second crop of less pure crystals from the filtrate by evaporating the solvent down to half or one-third volume, until the compound is once again saturated at the boiling point of the solvent, and then repeating the process described in steps 3 and 4 above.



Place your impure solid in a small Erlenmeyer flask.

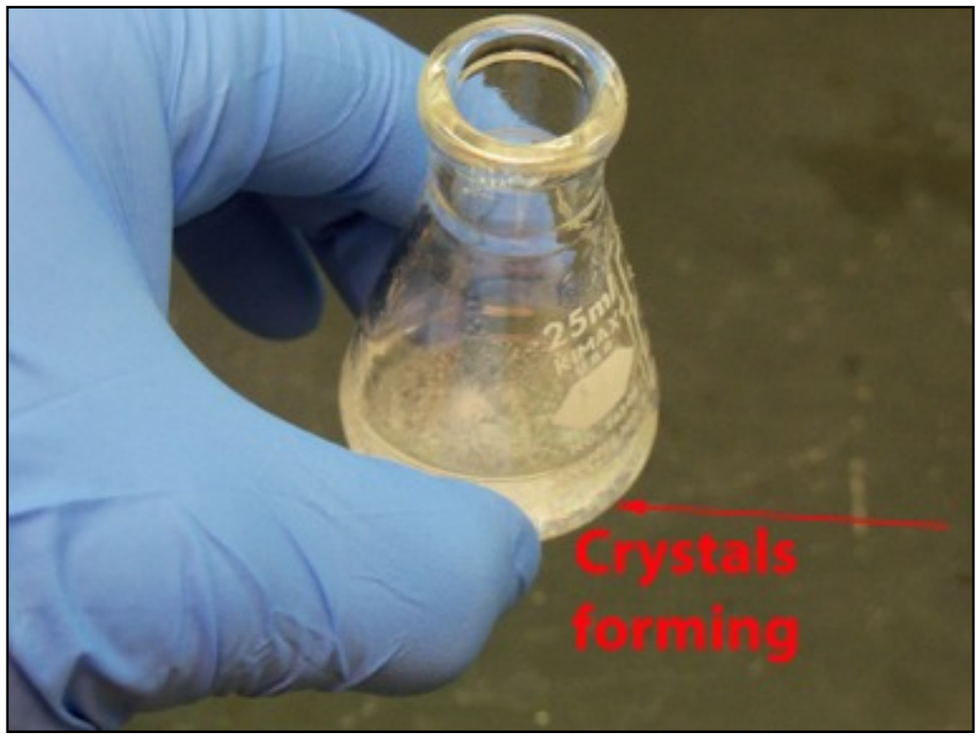


You can either begin by adding a small amount of the boiling solvent, or by adding a very small amount of the cold solvent and then heating the slurry on the hotplate.

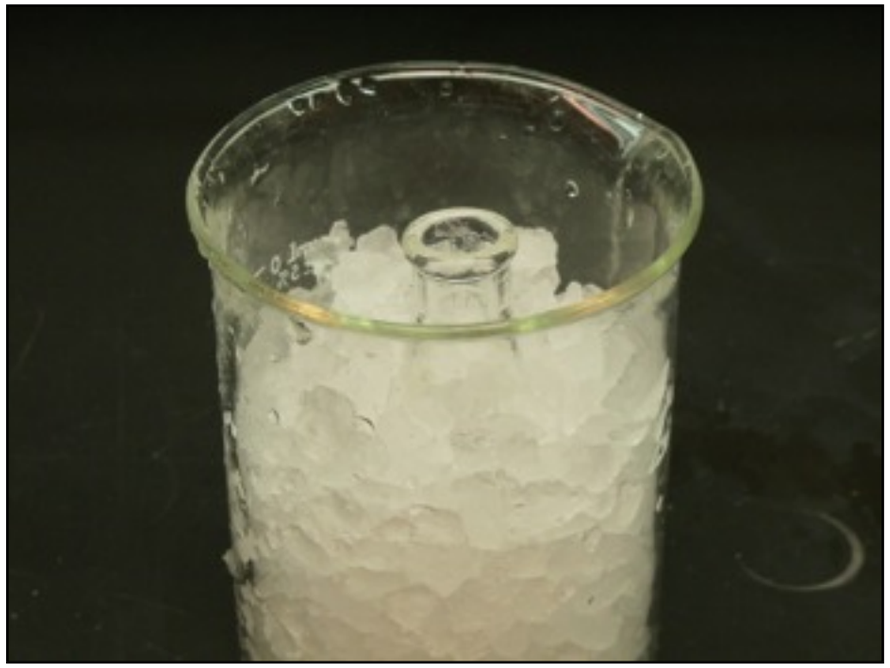


Heat the slurry until complete dissolution occurs. Add boiling solvent if needed.

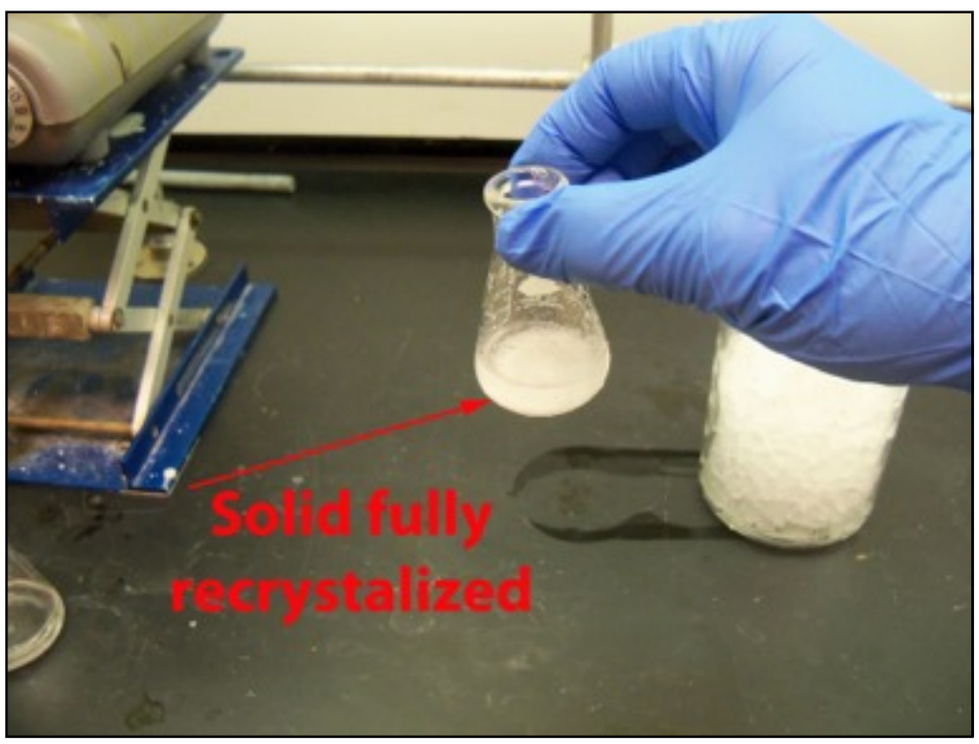
Remove the dissolved sample from the heat source and let it gradually return to room temperature.



Crystals should begin forming even at room temperature. If this does not happen, try scratching the bottom of the Erlenmeyer with a glass rod and waiting for a few minutes.

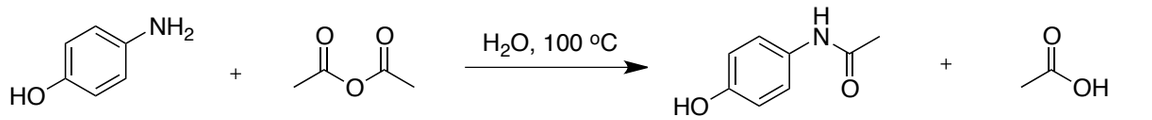


Cool the mixture further with an ice bath.



Remove the fully recrystallized solid from the ice bath, filter, then high-five your labmate.

EXPERIMENTAL PROCEDURE:



p-Aminophenol **Acetic anhydride** **Acetaminophen** **Acetic Acid**

A. Synthesis of Acetaminophen

- Weigh out 1.5 g of p-aminophenol and place this in a 50 mL Erlenmeyer flask. Using a graduated cylinder, add 4.5 mL of water and 1.7 mL of acetic anhydride. Place a magnetic stir bar in the flask.

- Heat the reaction mixture with stirring directly on a hot plate (using a thermometer to monitor the internal temperature). Try to heat to about 100 °C. After the solid has dissolved (it may dissolve, precipitate, and redissolve), heat the mixture for an additional 10 minutes at 100 °C to complete the reaction.

- Remove the flask from the hotplate and allow the solution to cool to room temperature. If crystallization has not occurred, scratch the bottom of the flask with a glass rod to initiate crystallization. Cool the mixture thoroughly in an ice bath for ~15 min and collect the crystals by vacuum filtration in a Buchner funnel (see Vacuum Filtrations). Rinse the flask with ~5 mL of ice water and transfer to the Buchner funnel. Wash the crystals in the funnel with 2 sequential additions of ~5 mL of ice water and then allow the crystals to dry on the funnel for ~5 min by allowing air to draw through the funnel with the vacuum on. During this time break up any large chunks with a spatula.

- Transfer the crude solid to a watch glass and obtain a mass. Set aside a small sample for a melting point determination later.

- Place the crude acetaminophen in a 50 mL Erlenmeyer flask. Recrystallize the material from a solvent mixture composed of 50 % water and 50 % methanol by volume (see Recrystallization). The solubility of acetaminophen in this hot (nearly boiling) solvent is roughly 1g/5 mL. After you have dissolved the solid in a *minimum* amount of the hot solvent combination, allow the solution to cool **slowly** to room temperature. Once the mixture has reached room temperature (~20-25 °C), place the flask in an ice bath (~ 0 °C) for at least 10 minutes. It may be necessary to induce crystallization by scratching the flask with a glass rod. Collect the crystals using a vacuum filtration apparatus fitted with a Buchner funnel. Dry the crystals for 5 to 10 minutes by allowing air to draw through the funnel while the vacuum is on. Why do we dry the crystals following filtration? Weigh the crystallized acetaminophen.

B. Analysis of the Purified Product

- Prepare three melting point capillaries as described below and place all four in the mp apparatus simultaneously.
    1. Your crude acetaminophen.
    2. Your final pure acetaminophen.
    3. An authentic sample of commercial acetaminophen from the prep hood.

WASTE DISPOSAL

Flammable waste for all organic liquids. Used capillary tubes can be disposed in the designated sharps container.

DATA PRESENTATION:

Include the following in your formal laboratory report discussion:

- Your report should be written in the format of a synthesis as previously described.

- Calculate the theoretical yield as well as the percent yield of the crude acetaminophen and the purified acetaminophen that you synthesized.

- Report the melting point ranges of all four samples when melted side by side at the same time. Comment on the purity of your two samples as determined by the melting point ranges.

Additional Pre-Lab Questions:

- During the crystallization of acetaminophen, why was the mixture cooled in an ice bath?

- In the reaction between *p*-aminophenol and acetic anhydride to form acetaminophen, 4.5 mL of water was added. What was the purpose of the water?

- Why should you use a minimum amount of water to rinse the flask while transferring the purified acetaminophen to the Buchner funnel?

- If 1.30 g of *p*-aminophenol is allowed to react with excess acetic anhydride, what is the theoretical yield of acetaminophen in moles? In grams?

- Give two reasons why the crude product in most reactions is not pure.

- Would you expect the acetaminophen before recrystallization to have higher, lower, or the same melting point as recrystallized acetaminophen?

Analysis of Analgesic Drugs: Thin-Layer Chromatography

Laboratory Techniques:

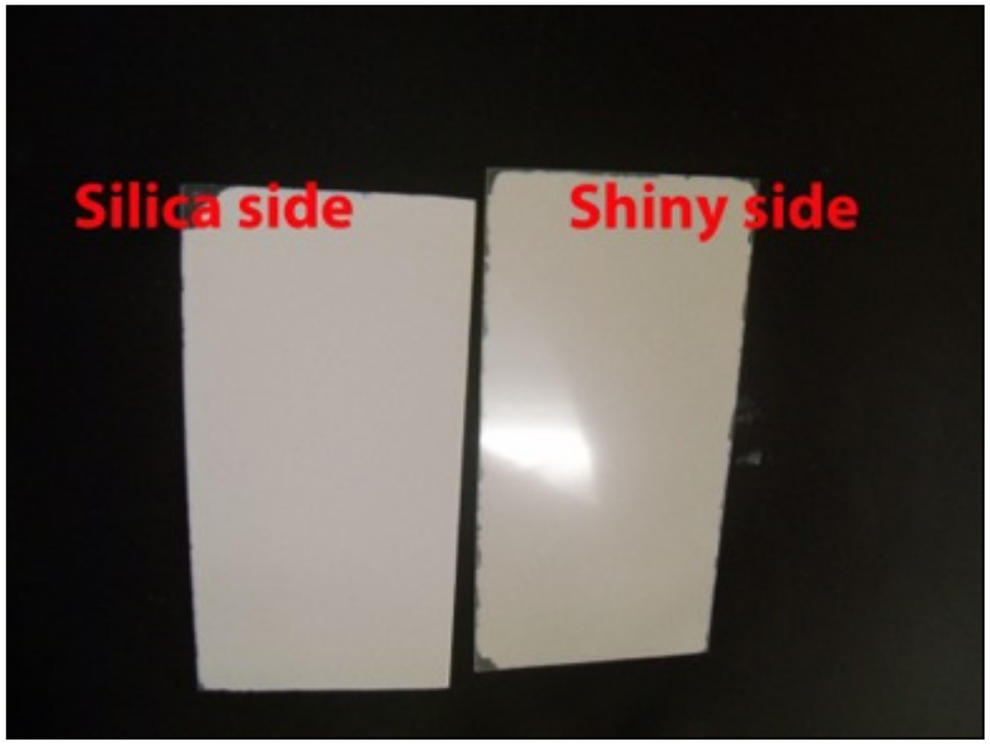
1. Spotting and developing a TLC plate.
2. Determining the proper solvent polarity combination to analyze multiple compounds at once.
3. Visualizing spots on TLC using an iodine chamber, stains, or UV light.
4. Calculating Rf values.

Organic chemists face the daily challenge of determining the identity of individual components within a complex mixture. This is due in part to the fact that chemical reactions often have side-products or unreacted starting material that was not anticipated at the onset of the reaction.

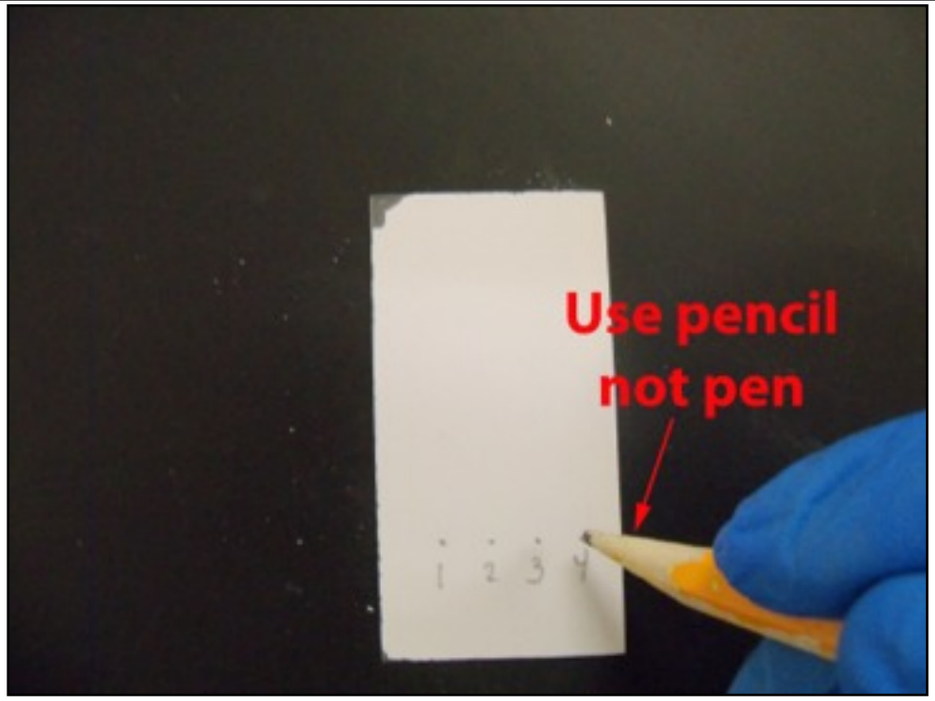
In this experiment you will learn a rapid and reliable method of analyzing compounds to determine the purity and identity of compounds. Thin layer chromatography (TLC) will be used to analyze the constituents of analgesic drugs (Asprin, Tylenol, BC Powder, Excedrin, Anacin). Known samples of caffeine, aspirin, salicylamide and acetaminophen will be provided to aid in the TLC identifications. You may also wish to analyze the acetaminophen you prepared in last week's lab to further confirm its identity and purity.

TECHNIQUE: Thin-Layer Chromatography

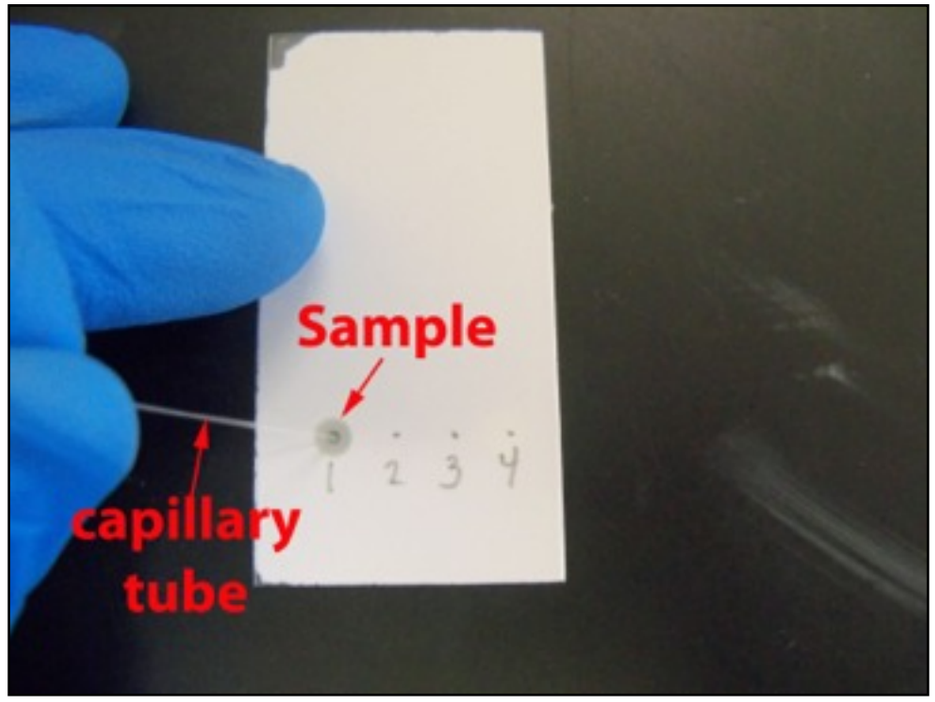
In thin layer chromatography, a mixture of compounds is "spotted" with a micropipet near the bottom (about ½ cm from the edge) of the chromatographic sheet. The sheet is placed into a jar containing a small amount of solvent; the solvent moves up the sheet, carrying with it the components of the mixture, each at a different rate. The rate of ascension depends on relative polarities of the compounds: **non-polar compounds ascend rapidly while polar compounds bind more strongly to the silica gel surface and ascend more slowly.** Do polar molecules or non-polar molecules ascend silica more quickly? More slowly?



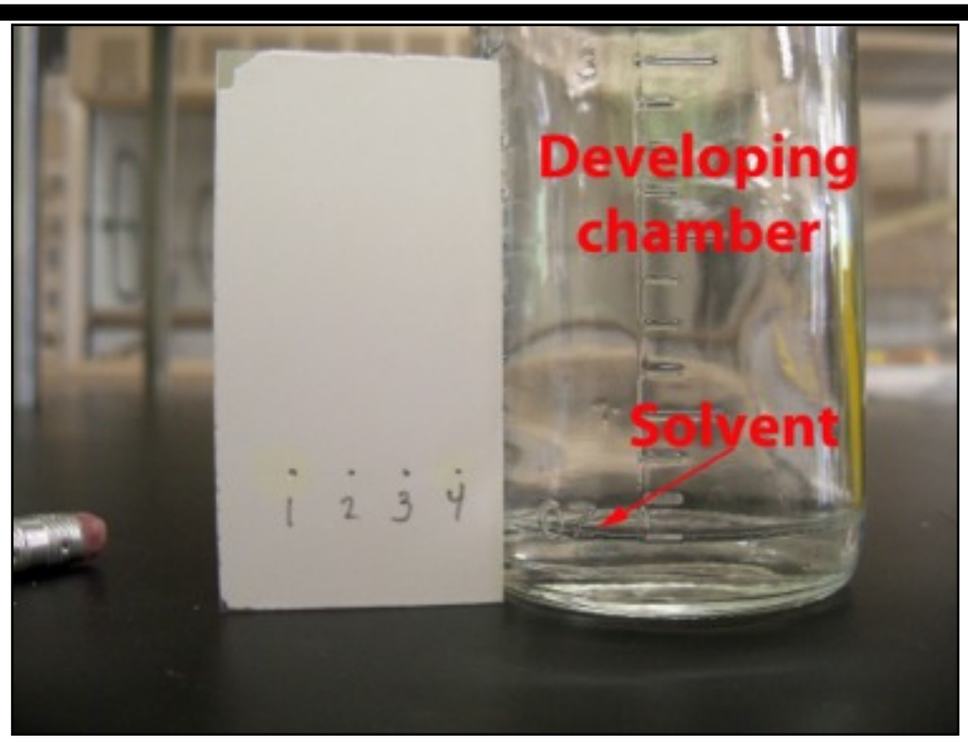
Make sure to use the silica gel side of the TLC and not the plastic shiny side!



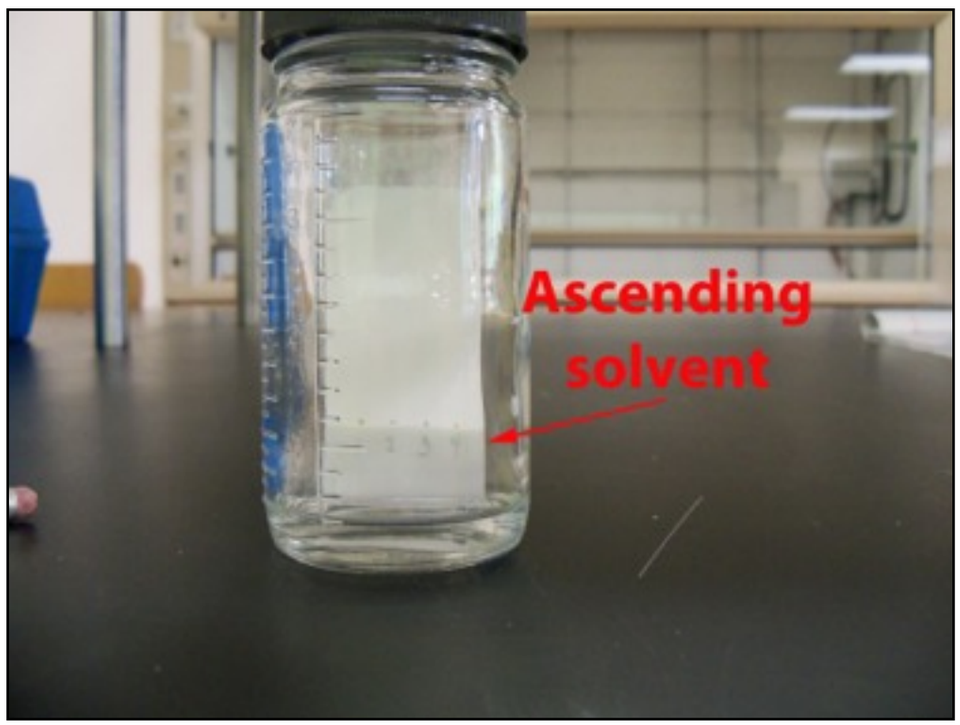
First, mark the locations of where you will spot the TLC plate. Make sure to use a pencil and to leave roughly 1/2 cm of space from the bottom of the plate. Press lightly with the pencil.



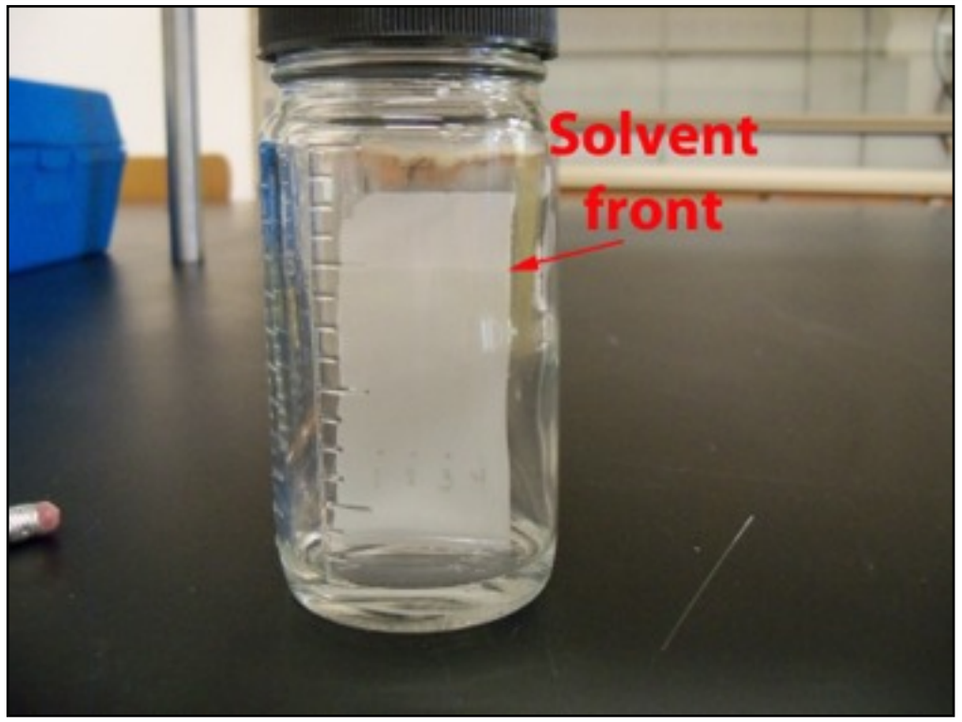
Draw a small amount of your compound dissolved in a solvent into your capillary tube. Quickly, and lightly spot your compound on the TLC plate. Don't make your spot too big.



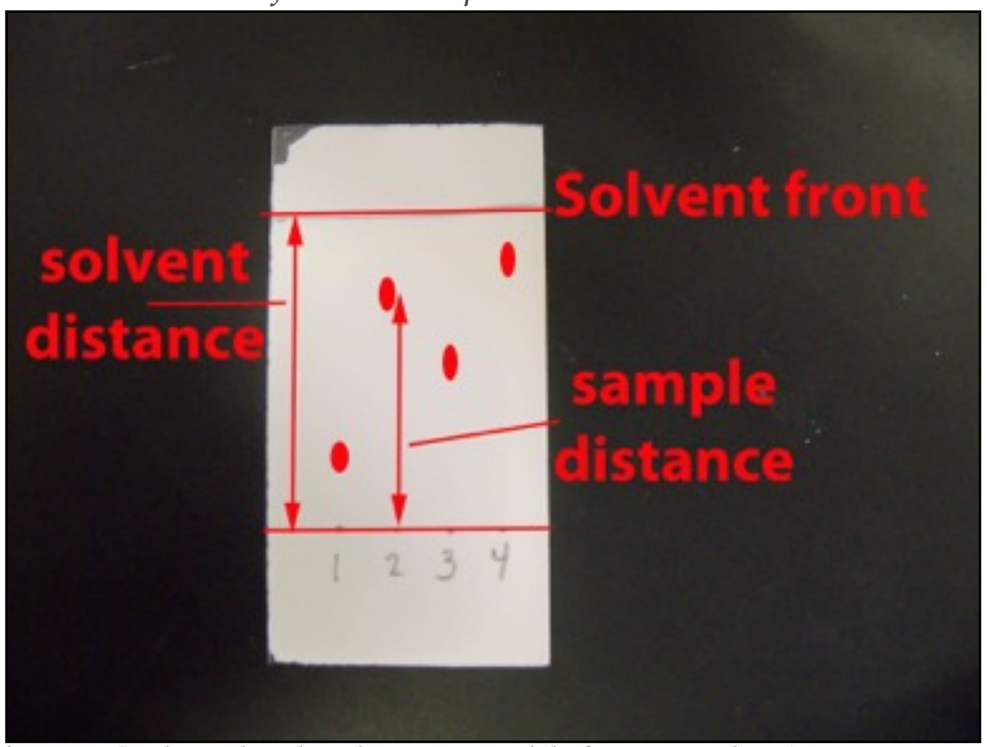
Importantly, the spots need to be above the solvent level in your developing chamber or the TLC will not work. If it is not, pour out some of the solvent in the chamber. What must the TLC spot be above?



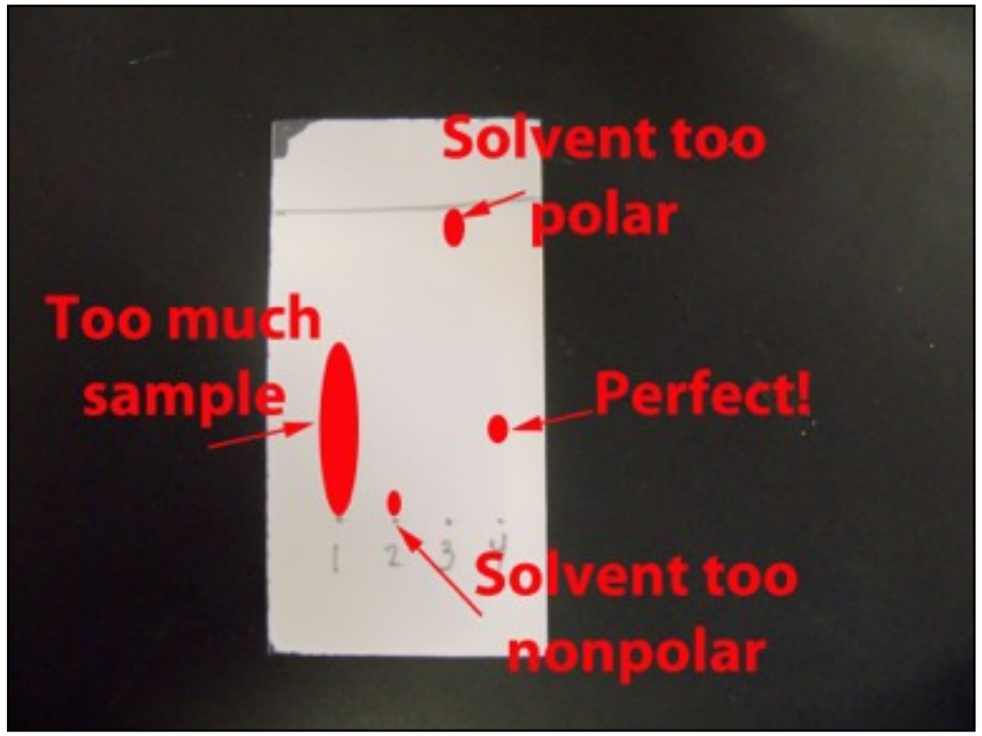
When the TLC plate is placed in the capped chamber you can watch the solvent ascend the silica gel.



The solvent front tells you when to stop running the plate. Ideally, you want to remove the TLC when the solvent gets to about 1/2 cm from the top. Mark the solvent front with a pencil.



Here is a TLC plate that has been run with four samples. You can see the solvent distance and the sample distance (sample distance/solvent distance gives Rf).



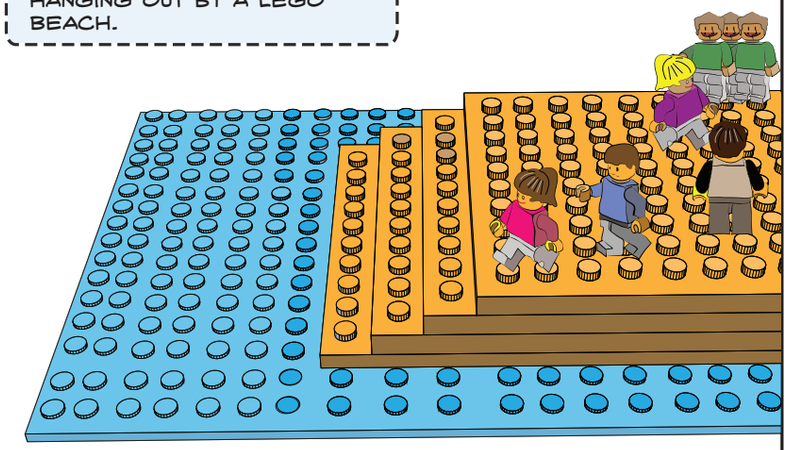
Here is a fictitious TLC plate with some of the common errors. Too much sample/spotting gives unreadable streaks. Spots at the top or bottom indicate too polar or not polar enough solvents. Be able to list three common errors with TLC plates.

The chromatographic sheet is removed from the jar when the solvent is about ½ cm from the top of the sheet. The level of the solvent front is marked with a pencil, and the solvent is allowed to evaporate. The positions of the various compounds are determined by "visualization" procedures, which may involve examination under a UV lamp, saturation with iodine vapor, or "staining" with various reagents to make the compounds become colored. What methods can be used to visualize your spots on a TLC? If complete separation has occurred, the number of "spots" on the chromatographic sheet corresponds to the number of compounds present in the original mixture. The position of each compound is described by an Rf value. Rf is determined by dividing the distance from the baseline to the spot by the distance from the baseline to the solvent front-line (Rf values are always less than 1, e.g., 0.2).

Selection of the best solvent to develop the TLC plate is critical to the success of the analysis. If a solvent is chosen that is not polar enough, none of the compounds will move very far up the TLC plate and it will not be possible to see clean separation of multiple components of an unknown mixture. On the other hand, if the solvent chosen to develop the plate is too polar, all of the compounds will move nearly all of the way to the top of the TLC plate. This situation also makes it difficult to see clean separation of multiple components or to distinguish one compound from another. The ideal solvent is usually a mixture of **miscible solvents**, one of which is more polar than the other, in the proportion that allows the components of the mixture to run between **Rf 0.2 and Rf 0.8** on the developed TLC plate. What is the ideal Rf value range for a TLC spot? The ideal proportions of the two solvents are determined by trial and error. Please refer to the following Solvent Polarity Guide when you are determining which solvent mixtures to use in your TLC analyses.

IMAGINE...

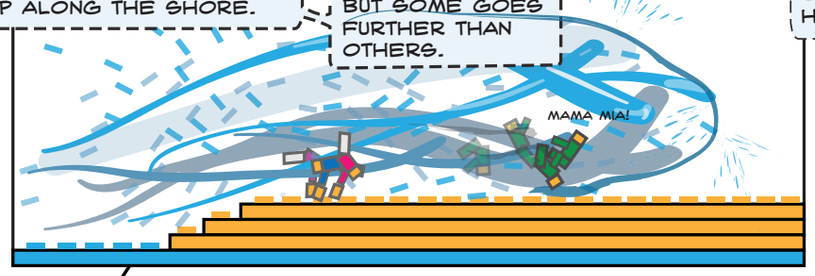
A BUNCH OF LEGO KIDS ARE HANGING OUT BY A LEGO BEACH.



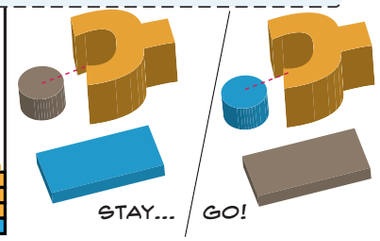
HALF ARE NORMAL LEGO... AND THE OTHER HALF ARE ***MUTANT*** LEGOS WITH BLOCKS FOR HANDS!

WHEN A LARGE WAVE COMES RUSHING IN... EVERYONE GETS WASHED UP ALONG THE SHORE.

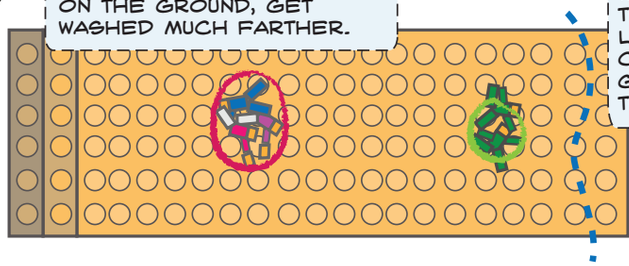
BUT SOME GOES FURTHER THAN OTHERS.



SINCE BETTER INTERACTIONS BETWEEN HOMO LEGOIENS WITH THE GROUND THAN THE WAVE HELP IN STAYING PUT...

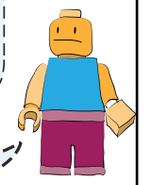


THE MUTANTS, WITH ***NO*** GRIP ON THE GROUND, GET WASHED MUCH FARTHER.



AFTER THE WATER DRIES, WHAT WE'RE LEFT WITH ARE THE MUTANTS AND NORMAL LEGO SEPARATED INTO 2 CLUMPS, NEITHER COULD GO FARTHER THAN WHERE THE WATER HAS GONE.

HOW MANY CLUMPS WILL WE HAVE, IF THERE'S ALSO THESE SEMI-MUTANTS AT THE BEACH? WHERE WOULD WE FIND HIM AT THE END?

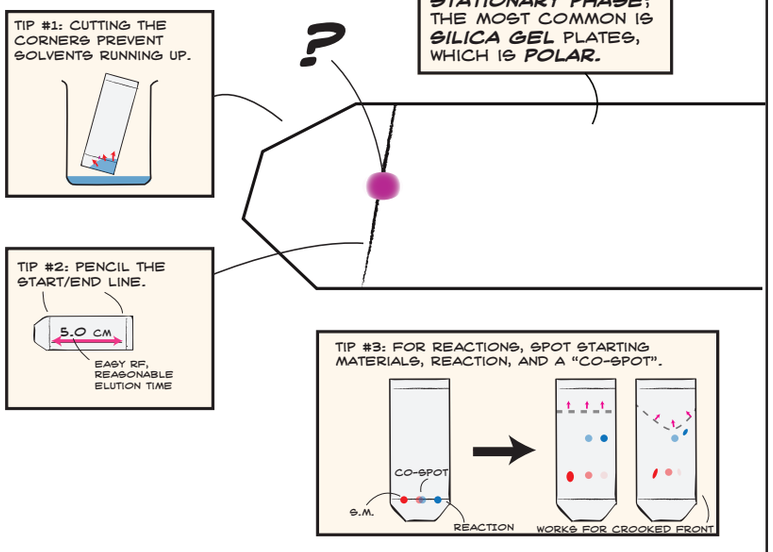


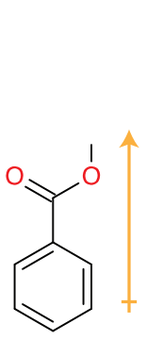
NOW CONSIDER...

A DROP OF AN ***UNKNOWN*** CHEMICAL WAS SPOTTED ON A TLC PLATE, AND THEN DIPPED IN AN ELUENT.

THERE ARE ACTUALLY TWO COMPOUNDS IN THE UNKNOWN - ONE OF THESE IS CHEMICALLY DIFFERENT - IT'S MUCH MORE ***POLAR***!

STATIONARY PHASE; THE MOST COMMON IS ***SILICA GEL*** PLATES, WHICH IS ***POLAR***.

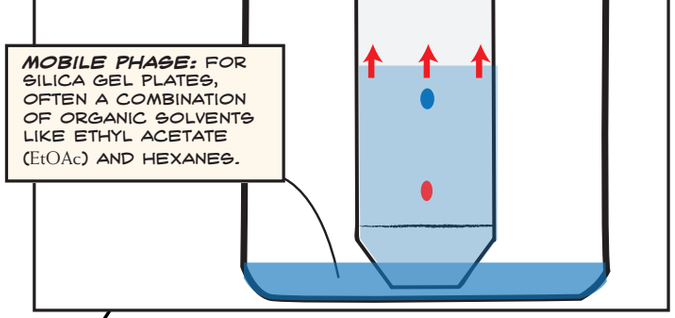




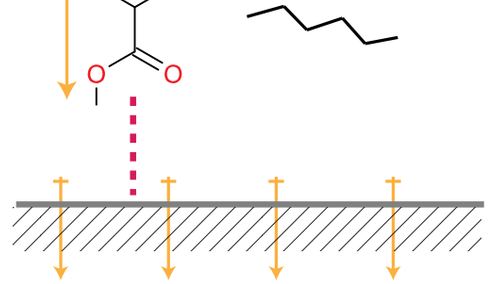
WHEN THE ***MOBILE PHASE*** SWEEPS UP THE PLATE, OUR MOLECULES GET WASHED ALONG.

BUT SOME GOES FURTHER THAN OTHERS.

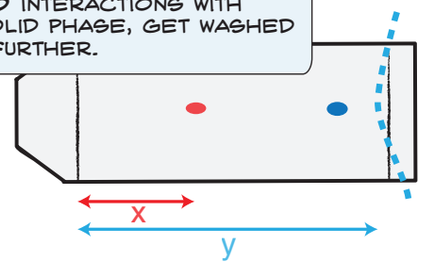
MOBILE PHASE: FOR SILICA GEL PLATES, OFTEN A COMBINATION OF ORGANIC SOLVENTS LIKE ETHYL ACETATE (EtOAc) AND HEXANES.



SINCE BETTER INTERACTIONS BETWEEN MOLECULE WITH THE STATIONARY PHASE THAN THE MOBILE PHASE HELP IN STAYING PUT...



THE NON-POLAR MOLECULES, WITH ***NO*** INTERACTIONS WITH THE SOLID PHASE, GET WASHED MUCH FURTHER.



AFTER THE SOLVENT DRIES, WHAT WE'RE LEFT WITH ARE THE COMPOUNDS SEPARATED INTO 2 CLUMPS, NEITHER COULD GO FURTHER THAN WHERE THE MOBILE PHASE HAS GONE.

Compound	R_f
A	0.16
B	0.75
C	0.16

0.16 = ...?

X/Y, THE RATIO BETWEEN THE DISTANCE A COMPOUND TRAVELED AND THE ***SOLVENT FRONT***, IS CALLED THE ***R_F***. IT IS A PROPERTY OF A MOLECULE, AND MEASURES THE ABILITY OF THE MOLECULE TO INTERACT WITH THE STATIONARY PHASE.

BUT BE CAREFUL: R_F IS CONDITION-DEPENDENT, SO YOU NEED TO SPECIFY BOTH THE (I) STATIONARY AND (II) MOBILE PHASES WHEN REPORTING.**

AND THEN, MANY DIFFERENT COMPOUNDS WITH SIMILAR POLARITY MAY SHARE SIMILAR R_F-, SO IT'S NECESSARY BUT NOT SUFFICIENT EVIDENCE FOR HAVING A PARTICULAR COMPOUND.

Thin Layer Chromatography / feat. Lego

Jon Chui / jkwchui@uvic.ca

** YOU SHOULD ALSO SPECIFY (III) THE METHOD YOU USED TO VISUALIZE THE SPOT, TO ENSURE OTHERS CAN SEE WHAT YOU SAW!

SOLVENT POLARITY GUIDE

SOLVENT	FORMULA	DIELECTRIC CONSTANT	MISCIBLE W / WATER
Water	H_2O	80	Yes
Dimethyl Sulfoxide	CH_3SOCH_3	45	Yes
Methanol	CH_3OH	35	Yes
Ethanol	CH_3CH_2OH	25	Yes
Acetone	CH_3COCH_3	21	Yes
Ethyl Acetate	$CH_3CO_2CH_2CH_3$	6	No
Chloroform	$CHCl_3$	5	No
Methylene Chloride	CH_2Cl_2	4	No
Diethyl Ether	$C_2H_5OC_2H_5$	4	No
Hexanes	C_6H_{14}	2	No
Petroleum Ether	C_7H_{16}	2	No

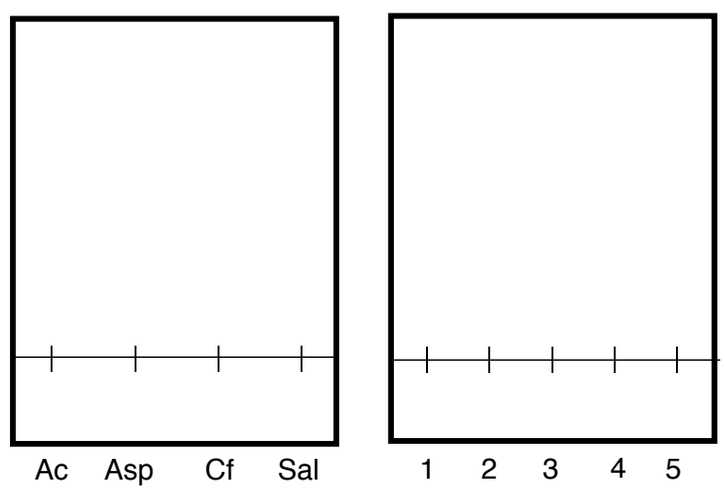
Note: The solvents in this table are arranged in decreasing polarity from the most polar (water), which has a very large dielectric constant (80), to the least polar (hexane) which has a dielectric constant of only 2. Mixtures of solvents can involve any combination except that water does not mix with any of the solvents less polar than acetone. Be able to list two solvents miscible in water, and two solvents miscible in hexanes.

EXPERIMENTAL PROCEDURE:

A. Development of the Reference TLC

- You will need many capillary micropipets to spot the plates (these will be provided by the instructor). Obtain a pre-cut TLC plate from your instructor. These plates have a flexible backing, but should not be bent excessively. Handle these plates carefully or the silica gel adsorbent may flake off (also try to avoid getting finger prints on the surface of the TLC plate). Using a lead pencil (not a pen) draw a line across the plates about 1 cm above the bottom (see TLC Technique).

- On the first plate, starting from left to right, spot acetominophen, then asprin, caffeine, and salicylamide (this is alphabetic and will avoid later confusion). Dilute solutions of these compounds can be found in the back hood. It is important that the spots be made as small as possible (1-2 mm diameter maximum). If the spot is made too large the spots will tail and streak up the plate during development (making Rf determination impossible). Also, when using the micropipets make sure to not cross-contaminate your spotters with the samples.

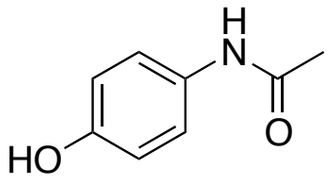


- After the reference plate has been completely spotted, obtain a 16-oz wide-mouth, screw cap jar for use as a development chamber. Fill the chamber with about 0.5-0.7 cm of a development solvent system. Recall that the solvent level must not exceed that of the spots on the plates or the samples will dissolve off the plate into the reservoir instead of developing. The objective of this part of the lab is, through trial and error, to find a suitable solvent system that will move all five standards off of the baseline to different Rf values. It is necessary that all of the spots are distinguishable from each other, otherwise it will not be possible to determine the composition of the analgesics accurately. You may use any available solvent combination, but you may find that mixtures of ethyl acetate and hexanes will work well.

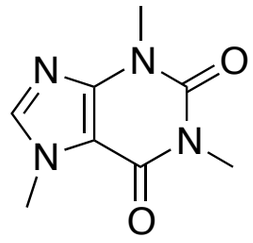
- Develop your reference plate. When the solvent has risen to about 0.5 cm from the top of the plate, remove the plate and quickly mark the solvent line with your lead pencil. After the plate is dry you can visualize the spots using a short-wavelength UV lamp (draw circles around the spots), or by placing your TLC in an iodine vapor chamber for about 30 seconds. Using a ruler calculate the Rf value for each compound. If some compounds have not moved off of the baseline you will need to increase the amount of polar solvent, and if too many compounds are traveling too far on the TLC plate you will need to increase the amount of the non-polar solvent. It may take several attempts (different solvent combinations) to successfully differentiate all of the reference spots. Make sure that the development chamber is dry before you add the next solvent system.

B. Analysis of Commercial Analgesics/Unknowns

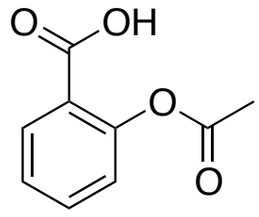
- Next, obtain a spatula tip of crushed analgesic tablet/powder and dissolve it in 3 mL of **dichloromethane** in a small test tube. On a new TLC plate, using a lead pencil, draw a line across the bottom of the plate. Mark TLC spot stations 1-5 for the five analgesic unknowns. As before, going from left to right, spot each unknown in a TLC lane. Then, using the solvent system that you previously developed to visualize all four of the reference compounds, develop this plate to about 0.5 cm from the top of the plate. Using a ruler calculate the Rf values for each compound. Note: in some cases you should see several spots in a lane.



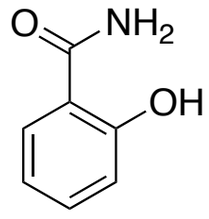
Acetaminophen



Caffeine



Asprin



Salicylamide

DATA PRESENTATION:

Include the following in your formal laboratory report discussion:

- Trace **each** TLC plate that you run in your notebook and label it completely. **Do not tape or place the TLC plate directly into your notebook!** Labeling includes identifying each compound or unknown that was spotted on each lane of the TLC plate, marking the height of the solvent front on the TLC plate, identifying the solvent mixture that was used to develop each TLC plate, describing the "visualization" methods used, and calculating the Rf value for each spot. Remember to write down your unknown numbers!

- Include the following in your lab report:
    1. What solvent system(s) worked best in your analyses? Should you expect to use a single solvent system for positive identification of each of these unknowns?
    2. What are the components of each of the unknowns you analyzed? **What are the unknowns**?

Additional Pre-Lab Questions:

- What must be done to improve the TLC analysis in each of the following situations:

a) The spots are too large and form a streak making it difficult to see separate compounds.

b) The spots have an Rf value above 0.8 and are not well resolved when the solvent is 4:1 (ethyl acetate : hexane).

c) The spots have an Rf value less than 0.2 and are not well resolved when the solvent is 4:1 (hexane : acetone).

- Why do you have to dilute both liquid and solid compounds in a solvent before spotting them on a TLC plate?

- What can you say about the relative polarities of two compounds when compound A has an Rf value of 0.75 and compound B has an Rf value of 0.15 on a silica gel TLC plate.

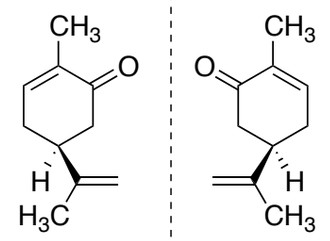
Spearmint and Caraway Oils: Introduction to Optical Rotation and IR Spectroscopy

Laboratory Techniques:

1. Be able to utilize the polarimeter to determine optical rotation and to distinguish between the two enantiomorphic forms of a molecule.
2. Be able to use FTIR to identifiy characteristic functional groups on organic molecules.

The chiral forms of the carvone molecule on top of the chiral forms of the human hand. The left enantiomer of carvone is found in dill and caraway seeds, while the right enantiomer is found in spearmint essential oil. Image

In this experiment you will learn how enantiomeric compounds differ in some ways and how they are identical in other ways. You will work in a group and compare the physical behavior of two enantiomeric compounds found in the essential oils of spearmint and caraway. The compounds, (S)-carvone and (R)-carvone, will be compared by TLC, index of refraction, optical rotation, and infrared spectroscopy (IR). How many stereocenters does (S)-carvone possess?



(S)-carvone (R)-carvone

TECHNIQUE: Refractometry

The refractive index (n) is a fundamental physical property of a substance and can be used to confirm the identity of a compound, confirm the purity of a composition, or measure the concentration of a compound. Fundamentally, as light passes through different materials the wavelength and velocity of the radiation is reduced (with respect to the light's values as it passes through a vacuum). Broadly defined, for a given vacuum wavelength of light (lo), the resulting wavelength in the medium is l=lo/n. Therefore, a vacuum has a refractive index of 1. For visible light most transparent compounds have a refractive index between 1 and 2. Why is a refractive index less than 1 impossible?

For your experiments you will be measuring your samples using yellow light (the sodium D-line with a wavelength maxima at 589 nm). It is important to note that the refractive index is strongly influenced by temperature. Most measurements are taken at room temperature and are reported as nD20, where "n" is the refractive index, "D" is the 589 nm wavelength, and the 20 is the temperature in Centigrade. As an example, the RI of water at 20 degrees taken at the Sodium D line is: 1.3330 D20

Visible light passing through air (RI = 1.0003 D0) and water (RI=1.3330 D20). Image

EXPERIMENTAL PROCEDURE:

You will work in groups of four on this project. With a partner, you will analyze either d- or l-carvone. The other pair in your group will analyze the other enantiomeric carvone. With your partner, perform the following analyses on your unknown compound:

A. Determination of Optical Rotation, TLC, Refractive Index

- Work in your group of two to obtain the polarimetry data for your enantiomer of carvone. Prepare your sample for a polarimeter reading by making 10 ml of a 10% solution (by weight). Specifically, weigh out 1.00 g (+/- 0.10 g) of your unknown into a 10 mL volumetric flask and add methanol to the 10 mL mark. What solvent are we using to dissolve the carvones in the polarimetry experiment? Transfer the solution to a 1.0 dm polarimeter tube and measure the rotation angle, alpha. **Save a portion of your polarimetry solution for later TLC analysis**. Promptly clean the volumetric flask and polarimeter cell by rinsing with methanol, and return all glassware to the polarimetry area. Exchange polarimetry data with the other pair of students in your group. **NOTE: The polarimeter cells are VERY expensive ($180 each). Please handle them with care.** Do you expect the optical rotations of each enantiomer to be the same or different?

- Find the refractive index of your pure sample. Do you expect the refractive indices of both enantiomers to be the same or different?

OBSERVATION

PUDDLES AND WORMS...

IT MUST HAVE RAINED.

INFERENCE

OBSERVATION

AN IR BAND OF THIS SIZE AND SHAPE...

PROBABLY *THAT* FUNCTIONAL GROUP.

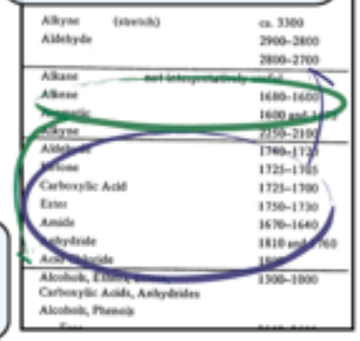
INFERENCE

ALL IR BANDS ARE EQUAL, BUT SOME ARE MORE EQUAL THAN OTHERS.

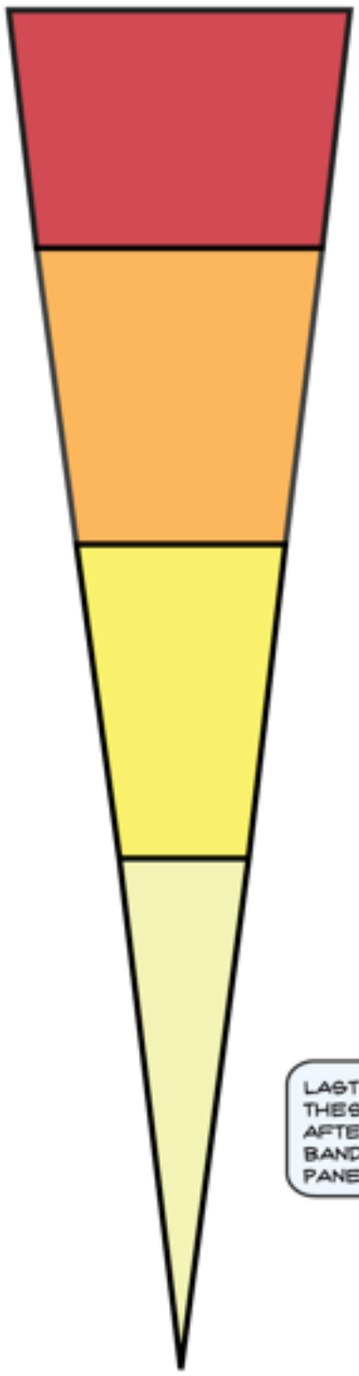
Alkyne (stretch)	ca. 3300	ca.
Aldehyde	2900–2800	3.41
	2800–2700	3.51
Alkane	not interpretationally useful	
Alkene	1680–1600	5.95
Aromatic	1600 and 1475	6.25
Alkyne	2250–2100	4.44
Aldehyde	1740–1720	5.75
Ketone	1725–1705	5.80
Carboxylic Acid	1725–1700	5.80
Ester	1750–1730	5.71
Amide	1670–1640	6.00
Anhydride	1810 and 1760	5.52
Acid Chloride	1800	5.56
Alcohols, Ethers, Esters, Carboxylic Acids, Anhydrides	1300–1000	7.69
Alcohols, Phenols		

MOVING DOWN THE CHART ONE AT A TIME, MATCHING BANDS AS YOU GO, IS NOT A USEFUL STRATEGY.

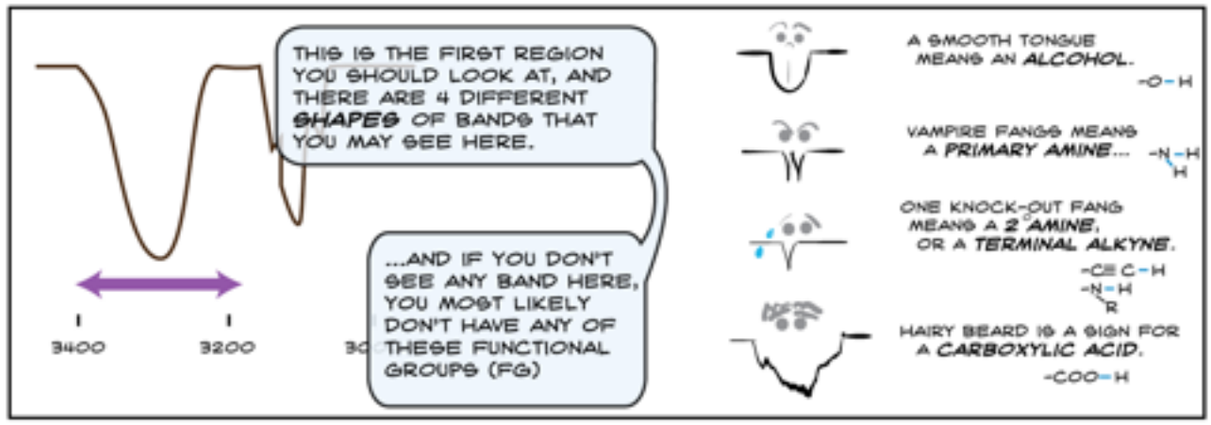
INSTEAD, LET'S ARRANGE THEM BY THEIR *INTERPRETIVE POWER*.



GREAT INTERPRETIVE POWER



WIMPY INTERPRETIVE POWER



THIS IS THE FIRST REGION YOU SHOULD LOOK AT, AND THERE ARE 4 DIFFERENT *SHAPES* OF BANDS THAT YOU MAY SEE HERE.

...AND IF YOU DON'T SEE ANY BAND HERE, YOU MOST LIKELY DON'T HAVE ANY OF THESE FUNCTIONAL GROUPS (FG)

A SMOOTH TONGUE MEANS AN *ALCOHOL*.

-O-H

VAMPIRE FANGS MEANS A *PRIMARY AMINE*...

-N-H
H

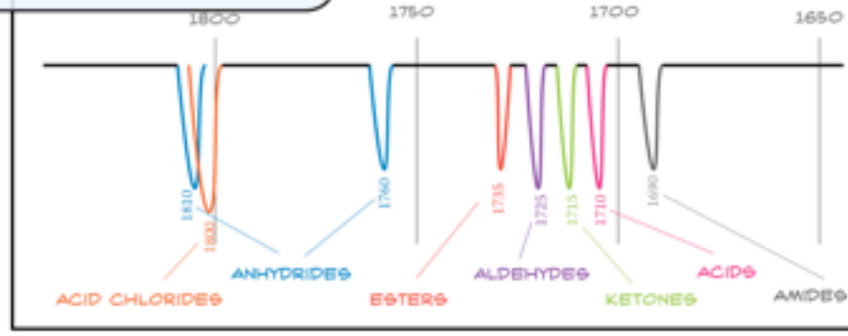
ONE KNOCK-OUT FANG MEANS A *2° AMINE*, OR A *TERMINAL ALKYNE*.

-C≡C-H
-N-H
R

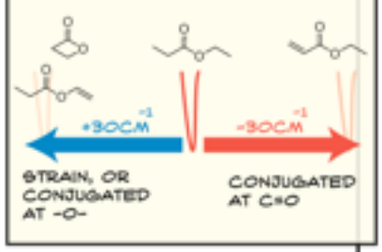
HAIRY BEARD IS A SIGN FOR A *CARBOXYLIC ACID*.

-COO-H

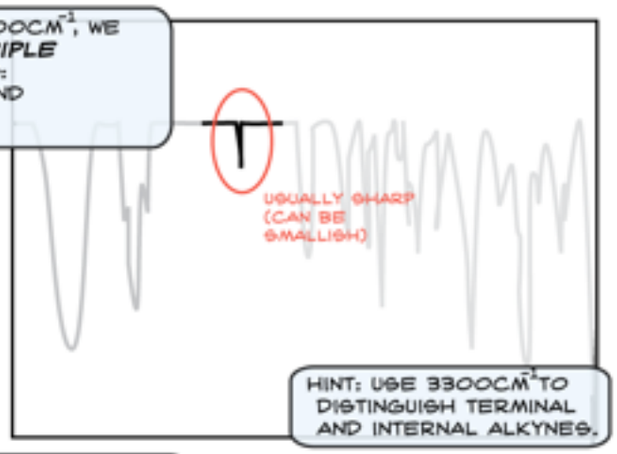
IN THE C=O REGION, IT'S NOT THE SHAPE, BUT THE EXACT *LOCATION* THAT REVEALS THE IDENTITY OF THE FG.



NOTE THAT THE EXACT POSITION DEPENDS ON THE SURROUNDING ENVIRONMENT:



AT ~2200CM^{-1}, WE FIND *TRIPLE BONDS*:
C≡C, AND
C≡N

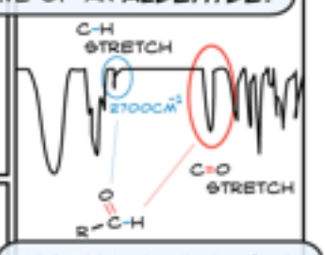


HINT: USE 3300CM^{-1} TO DISTINGUISH TERMINAL AND INTERNAL ALKYNES.

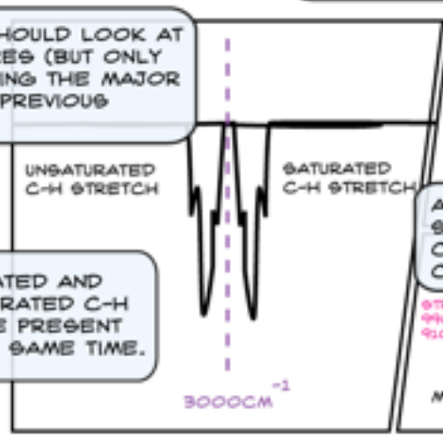
Interpreting IR spectra

JON - JKWCHUI@UVIC.CA

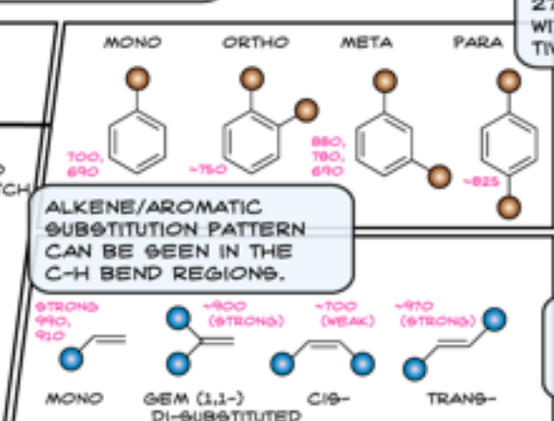
LASTLY, A PEAK AT 2700CM^{-1}, TOGETHER WITH A C=O, IS INDICATIVE OF AN *ALDEHYDE*.



LASTLY, YOU SHOULD LOOK AT THESE FEATURES (BUT ONLY AFTER ANALYSING THE MAJOR BANDS IN THE PREVIOUS PANES)



SATURATED AND UNSATURATED C-H CAN BE PRESENT AT THE SAME TIME.



ALKENE/AROMATIC SUBSTITUTION PATTERN CAN BE SEEN IN THE C-H BEND REGIONS.

KETONES HAVE NO C-H IN THEM AND CAN HAVE NO 2700 C-H STRETCH PEAKS.

WE LOOKED AT THESE LAST BECAUSE THEY CAN BE AMBIGUOUS TO INTERPRET, OR THEY HAVE ONLY A NARROW NICHE OF USEFULNESS.

NOTES

** IF YOU'RE NOT SURE WHAT THE DIFFERENCE BETWEEN AN ACID AND AN ALCOHOL IS, DO THE QUICK "FUNCTIONAL GROUP IDENTIFICATION" EXERCISE.

** ...IF YOU HAVE ONE FG. TWO 2° AMINE WOULD LOOK LIKE A 1 AMINE.

- Use your polarimetry sample for TLC analysis, spotting the 10% methanolic solution on the TLC plate (see Thin Layer Chromatography). Obtain a sample of the other enantiomer of carvone dissolved in methanol from the other pair of students in your group. Analyze both R- and S-carvone on the same TLC plate. Develop the TLC sheet with a mixture of hexane and ethyl acetate (try 4:1 hexane : ethyl acetate to start with). UV light should work well to visualize the two compounds on the TLC plate. Each student should run their own TLC plates using the two enantiomeric methanolic carvone solutions from the polarimetry experiment. Do you expect the Rf values for both enantiomers to be the same or different?

B. Analysis by Infrared Spectroscopy

- Each student should take an infrared spectrum of either the R- or the S-carvone enantiomer. Work with the other pair of students in your group so that each of you obtains IR spectra of both enantiomers. If you each print two copies of your IR spectrum, you can exchange spectra for your lab reports.

- To take an infrared spectrum of your carvone sample, place a very small amount (about 1/2 drop) of the pure compound on the sample window. Use the "Find Peaks" icon to show the exact frequency of each absorption peak in the spectrum. Be sure to use the pure R- and S-carvones for the IR analysis, not the polarimetry sample that contains methanol.

- Compare and share your data with the other pair in your group. You should have data for all four parts of this experiment for both the d- and the l-carvone: two refractive indices, two sets of optical rotation data, a TLC plate with two spots, and two IR spectra.

DATA PRESENTATION:

Include the following in your formal laboratory report discussion:

- Describe how you made each physical measurement, and report the results for both R- and S-carvones.

- Calculate the specific rotation and the optical purity of the two carvone enantiomers (for help with these calculations see your textbook: Section 5.4, pp. 205-210).

- In which measurements were the R- and S-carvones identical? Which were different? Why?

Additional Pre-Lab Questions:

- If the bp of (S)-carvone is 231 degrees, would you expect the bp of the enantiomer to be higher, lower, or the same?

- Why do the two enantiomers of carvone smell different?

- Draw the enantiomer of (S)-carvone shown on the board.

- If you diluted a 1g/dL sample of (+)-carvone, would you expect the observed optical rotation to increase or decrease?

- If you combined a 1g/1dL sample of (S)-carvone with a 1g/dL sample of (R)-carvone, predict what you would measure for the optical rotation.

Applications of Organic Chemistry

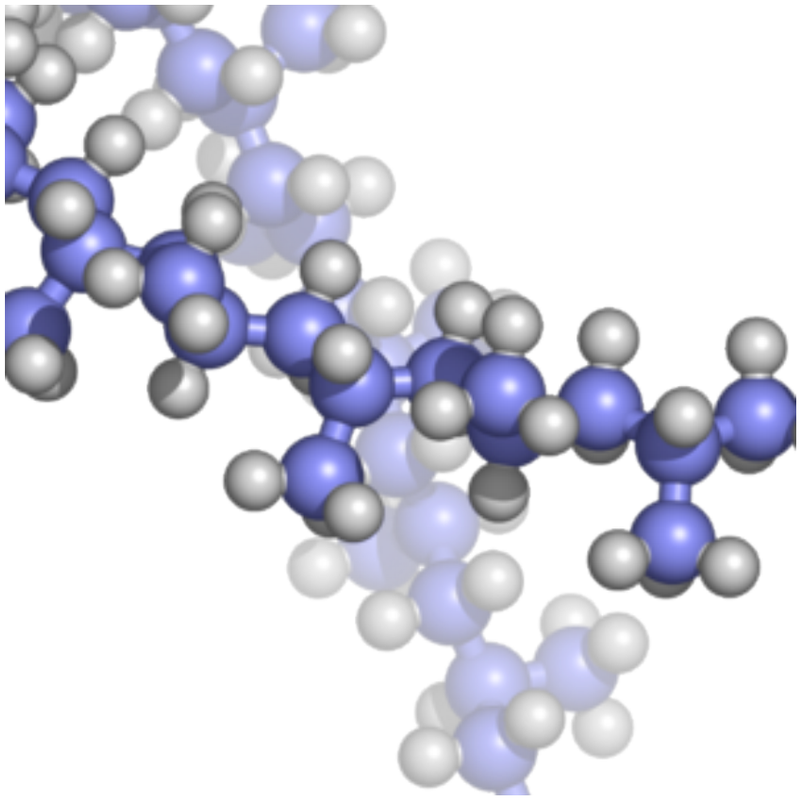
Very few fields have benefitted as much from synthetic materials as modern sports. Climbing, in particular, has evolved from an activity laden with heavy, ineffectual materials such as wool and hemp, to one where ultra-light weight protective gear, ropes, shoes and clothing is the norm. Reducing the overall weight that climbers must carry up rock faces has fundamentally altered what is possible in this sport. Indeed, much of what is now considered beginner's climbs (5.5 - 5.7) would have been at the limits of most climber's abilities 50 years ago.

Brody Greer and Dave Littman on *Tales of the Scorpion* (VI 5.10 A3+), Zion National Park, Utah Photo by Eric Draper, Image

Polymer Chemistry: Polyesters, Nylon, and Polystyrene

The team time trial in the Tour de France. On this particular section of the Tour teams can average over 60 km/h (38 mph). All attempts are made to reduce the overall weight of the riders. Clothing is produced from a synthetic fiber (polyurethane-polyurea copolymer); helmets are made from either polystyrene, polycarbonate, or carbon fiber; and the bikes are primarily produced from carbon fiber (made from a precursor polymer such as polyacrylonitrile with a composite resin binding agent). Image

Polymers are high molecular weight molecules (~1,000 to 10,000,000 MW) made up of many repeating units of a simple monomer unit. There are many examples of these materials, including dacron, polyethylene, teflon, nylon, and polyurethane. These materials are solid and since they can easily be molded, they are rapidly replacing metals in nearly all manufacturing applications.



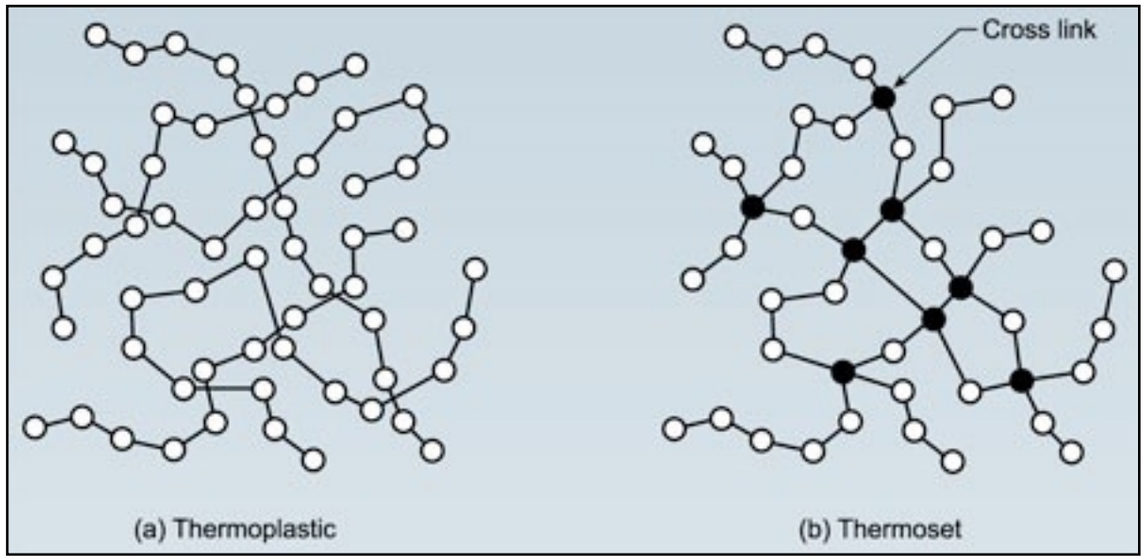
Synthetically, polymers are classified as condensation or addition polymers. Condensation polymers are formed when di- or poly-functional molecules react with each other with the elimination of a small molecule (like H_2O or HCl). Addition polymers are formed when monomer units add to each other in a step-wise fashion to ultimately produce high molecular weight molecules.

This iPad cover is composed of polyurethane, a condensation polymer.

Many new glasses (including most eyeware) are composed of polycarbonate, a condensation polymer, and not actually glass.

Polymers are classified as either thermoplastics or thermoset plastics. Thermoplastics can be melted and remolded over and over again. Thermoplastic molecules are usually linear with virtually no cross-linking between strands. Thus the molecules easily "slip" past one another at elevated temperatures. Thermoset plastics cannot be melted and remolded due to extensive crosslinking between strands. In cross-linked structures, the molecules cannot "slip" past one another, and a rigid structure results. Most recyclable plastics are thermoplastics. What is the major difference between thermoset and thermoplastics?

Legos are polyethylene and polypropylene; addition, thermoplastic polymers.



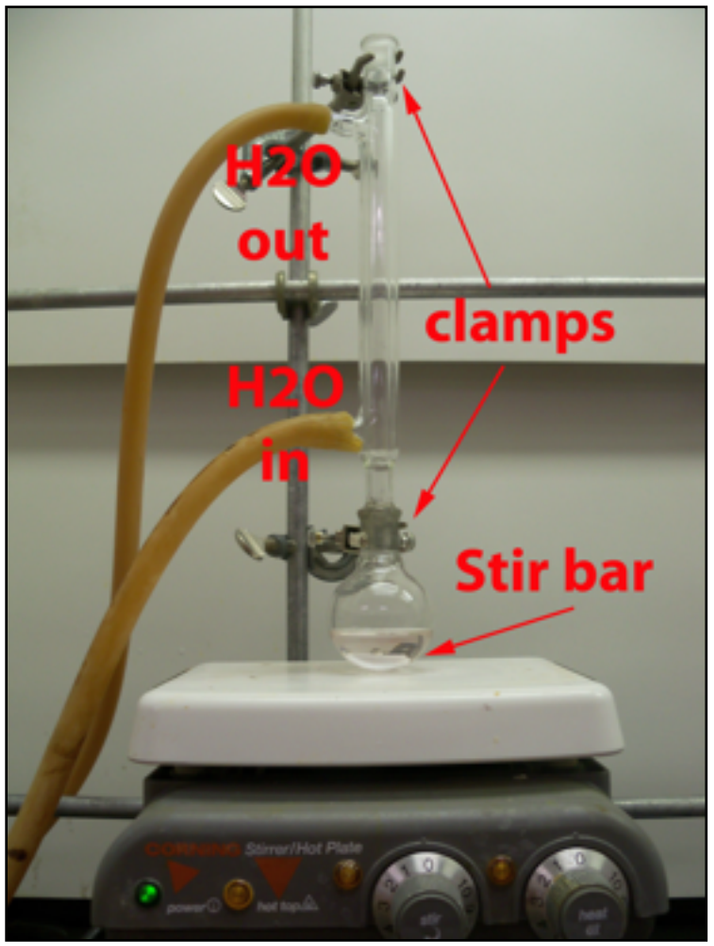
Cross linking prevents the polymer structure from disentangling itself when heat is applied. Image

Climbing rope is composed of woven Nylon (a polyamide, condensation polymer). The elasticity of the rope is intrinsically linked to the molecular structure of the polymer backbone.

TECHNIQUE: Refluxing a Reaction Mixture

One of the most common reaction conditions that you will encounter in organic synthesis is to "reflux" a reaction mixture. To reflux is nothing more than keeping the reaction mixture at its boiling point for prolonged periods of time. This temperature is the maximum temperature to which you can heat a reaction without applying external pressure. What is the temperature at which water refluxes in Durango?

Unfortunately, there is an intrinsic problem with doing this: boiling a liquid means converting it from a liquid phase to a vapor. As a result, if you wanted to reflux a reaction for 24 h, it is unlikely that much, if any of the liquid would remain in the flask after that time period (think reducing a stew on your stove by simmering the water for extended periods of time). Therefore, whenever chemists want to perform a reflux we attach a special piece of glassware to the top of our reaction flask: the water cooled reflux condenser. The condenser is jacketed with cold flowing water that re-condenses the vapor produced from the reflux. Gravity then forces the resultant liquid to drop back into the reaction flask. The result is a net zero loss of reaction volume despite heating to the boiling point of the liquid.

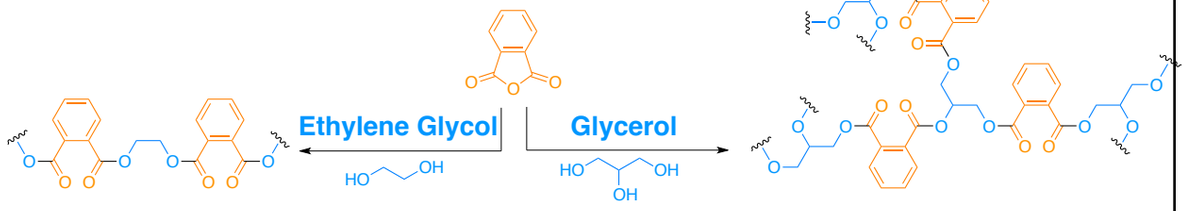


Be able to draw a diagram (with labels) of a reaction undergoing reflux

EXPERIMENTAL PROCEDURE:

Complete sections A, B, and C. If time permits you can do all four experiments for extra credit. You may perform the experiments in any order. Parts A and B require the most amount of time, so it is advisable for you to begin setting those up first.

A. Preparation of Linear and Cross-Linked Polyesters

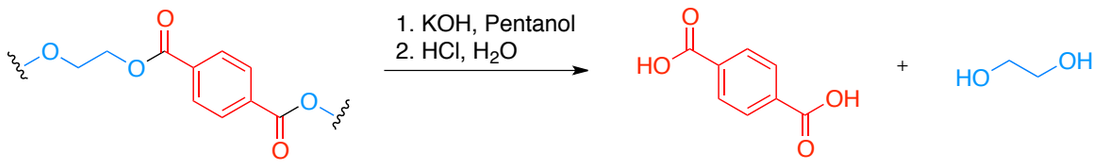


Linear Polymer A-B-A-B **Cross-Linked Polymer**

- Place 1 g of phthalic anhydride and 0.05 g of sodium acetate in each of two small test tubes. To one tube add about 1/2 mL of ethylene glycol (very viscous liquid!) and to the other add about 1/2 mL of glycerol. Clamp both tubes so that they can be heated simultaneously with a heating mantle. Heat the tubes gently until the solutions appear to boil, then continue heating for about 1 hour. Allow the tubes to cool to room temperature, and compare their properties. Which alcohol starting material makes a cross-linked polymer?

B. Degredation of Polyesters. One Way to Recycle PETE

- This reaction will consume most of the laboratory period. Use scissors to cut a clean PETE bottle into ¼ inch pieces or smaller. Though 2-liter soda bottles are satisfactory, others such as Heinz ketchup bottles are better because they are constructed of 3 shells each of which is thinner than the single shell of soda bottles. You will only need 1.0 g of cut PETE for this activity.



- To a 25 mL round bottom flask add 7 mL of pentanol, 1.0 g of PETE, and 1.0 g of KOH. Affix a condenser and use a heating mantle to heat the mixture to reflux while stirring with a magnetic stirrer. (The PETE does not dissolve in the solvent.) After a short time a thick white suspension results; if stirring becomes impossible, more solvent may be added; check with your instructor before doing so. Continue the reflux for a total of 1.5 hr.

- After the reaction mixture has cooled to room temperature, add 25 mL of water to the reaction flask and stir to dissolve the white terephthalate salt that is present. Transfer the mixture to a large test tube. Remove the upper organic layer with a pipet. Pour the lower aqueous layer containing the terephthalate salt into a 50 mL Erlenmeyer flask.

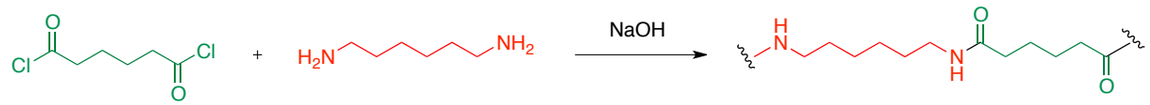
Hyundai QarmaQ's shell is composed of recycled polyethylene terphthalate (PETE) from plastic bottles. Image

- Place a magnetic stirbar in the flask. While stirring slowly add dilute HCl to acidify the aqueous extracts to pH 2. Note that if the HCl is added rapidly, the terephthalic acid may form such fine crystals that filtration is difficult. Cool the acidified mixture in an ice bath. Use suction filtration to collect the white terephthalic acid that has formed. Turn in your terephthalic acid sample in a properly labeled vial after it has dried completely on a watch glass.

C. FT-IR Analysis of an Unknown Polymer

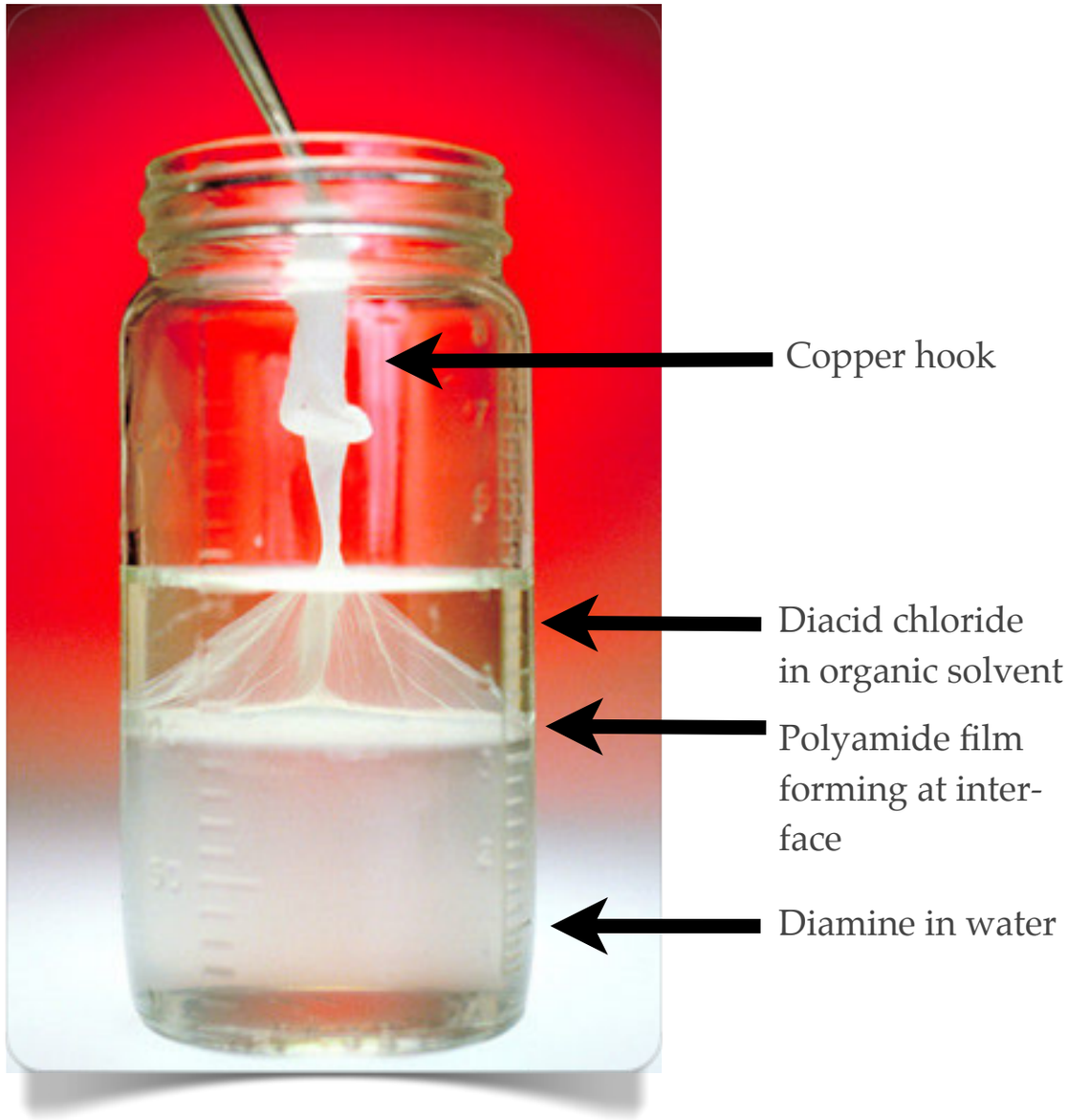
- Bring in a sample of a transparent plastic film or find a piece of transparent plastic from lab and take an IR spectrum of it on the ATR FT-IR. Identify the unknown polymer by comparing the IR spectrum to the spectra of known polymers using the IR database on the ATR FT-IR. Draw the molecular structure of the repeating polymer backbone on the IR and include it in your lab report.

D. Preparation of Nylon



- Pour 10 mL of a 5 % aqueous solution of hexamethylenediamine into a 50 mL beaker. Add 10 drops of sodium hydroxide solution. Carefully add 10 mL of a 5% solution of adipoyl chloride in cyclohexane to the solution by pouring it down the wall of the slightly tilted beaker. Two layers will form and there will be an immediate formation of a polymer at the liquid-liquid interface. Using a copper wire hook, the polyamide and draw out the nylon.

- If you are careful and slow you can pull out several feet of nylon thread. Rinse the rope several times with water and dry on a paper towel.



Interfacial (between surfaces/phases) synthesis of nylon. As the thread is slowly removed more of the two reagents are exposed to each other. This, in turn, generates additional nylon polymer. *Image*

- Be sure to wash your nylon well with water in the hood. Caution: HCl gas is generated in this reaction. To avoid noxious fumes, please keep the nylon in the hood!

WASTE DISPOSAL

Flammable waste for all organic liquids. Make sure to thoroughly mix the nylon layers together before disposing in a waste container. Also, do not discard the nylon down the sink; use a waste container.

DATA PRESENTATION:

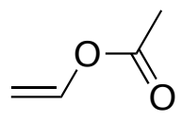
Include the following in your formal laboratory report discussion:

- Describe how you made each polymer. Also describe the physical characteristics of the plastic.
- Write a chemical equation for each reaction that you performed.
- Explain what type of polymer is prepared in each of your experiments: Did you make a condensation or an addition polymer? A termoset plastic or a thermoplastic?
- Include the IR of the polymer and its structure in your lab report
- Give 5 examples of objects that contain the polymer that you found in the IR in section C. Do not include the object that you used to take the IR. Make sure to cite your sources if necessary.

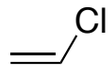
Additional Pre-Lab Questions:

Note: For help on some of these questions see the following sections in your textbook (Klein): Chapter 9.3 (p. 405), Chapter 27 (p. 1269)

- Draw the structure for the polymer produced from the monomer vinylidene chloride ($CH_2=CCl_2$).
- Draw the structure of the copolymer produced from vinyl acetate and vinyl chloride. This copolymer is employed in some paints, adhesives, and paper coatings.

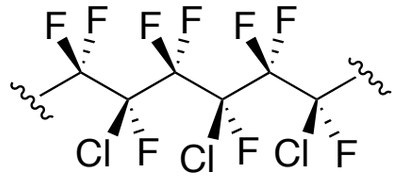


Vinyl Acetate

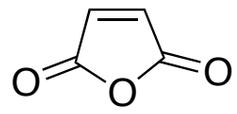


Vinyl Chloride

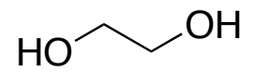
- Isobutylene ($CH_2=C(CH_3)_2$) is used to prepare cold-flow rubber. Draw a structure for the addition polymer formed from this alkene.
- Kel-F is an addition polymer with the following partial structure. What is the monomer used to prepare it?



- Maleic anhydride reacts with ethylene glycol to produce a resin. Draw the structure of the condensation polymer produced.

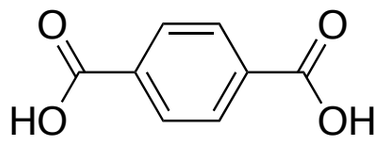


Maleic Anhydride

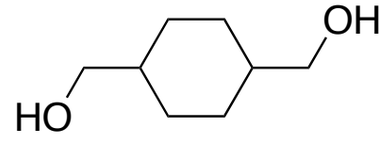


Ethylene Glycol

- Kodel is a condensation polymer made from terepthalic acid and 1,4-cyclohexanedimethanol. Write the structure of the resulting polymer.

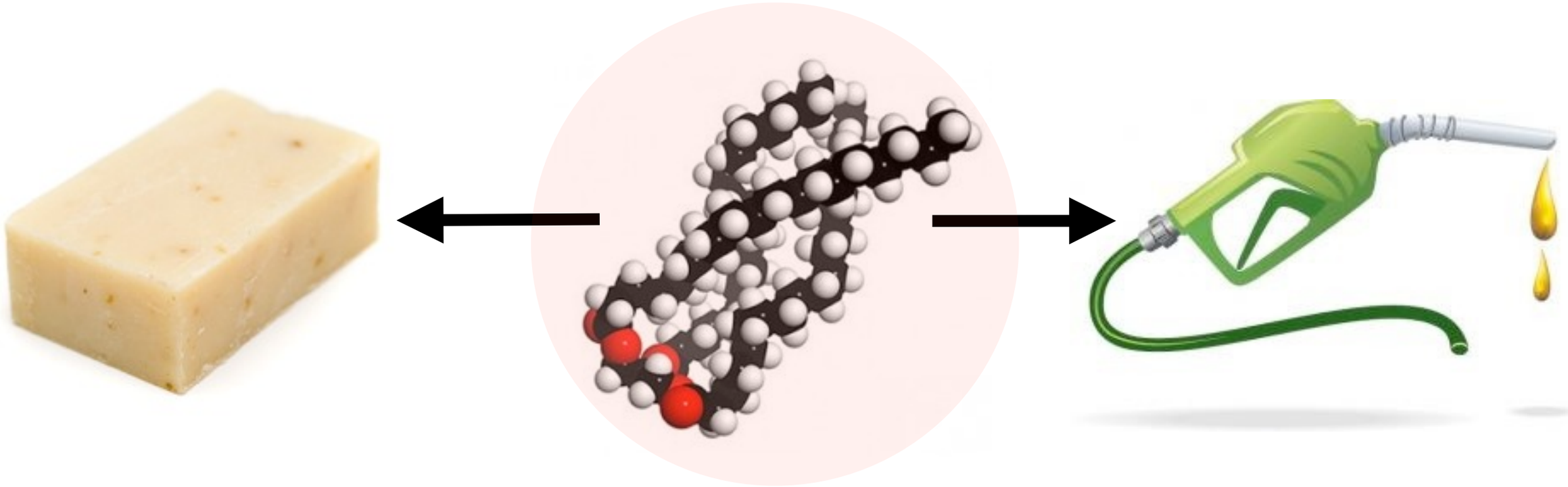


Terephthalic Acid



1,4-Cyclohexanedimethanol

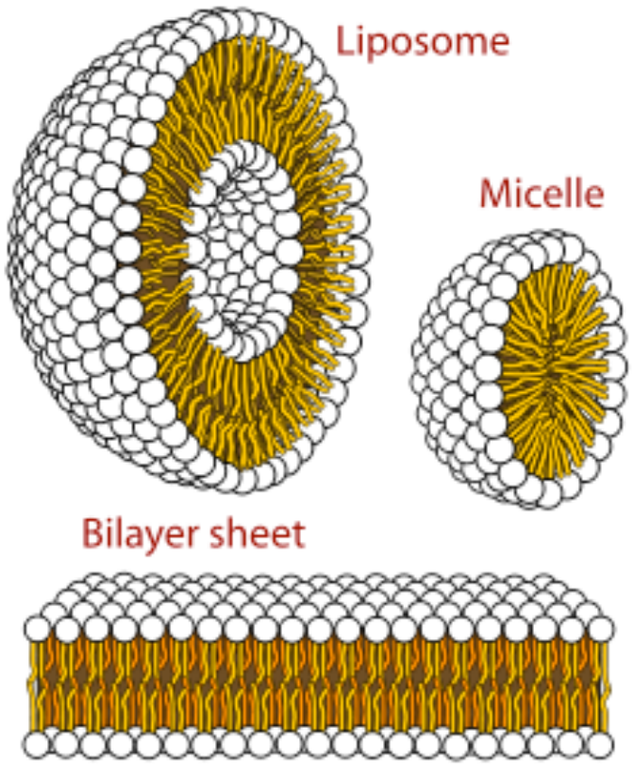
Synthesis of Soap or Biodiesel



Triglyceride molecules (center) can be readily converted to soap or biodiesel. Simply by changing the reaction conditions, either a surfactant (soap) or a long-chain ester (diesel fuel) is produced.

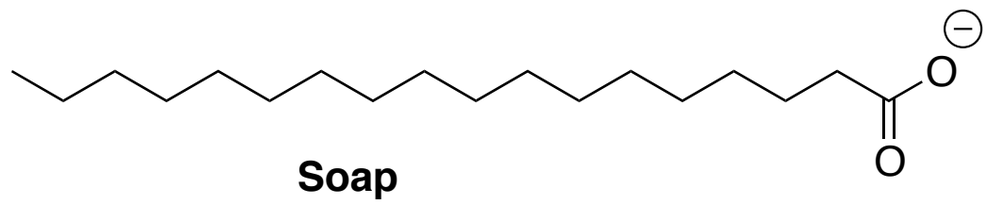
Soaps:

Soaps have been used for thousands of years. Many soaps are natural constituents of plants, known as saponins. The manufacture of soaps has a long history as well and depends upon a simple chemical reaction called saponification. In this process, an animal or plant oil or fat is heated with an alkali such as sodium hydroxide in water. This reaction changes ester linkages in the triglycerides of the fat or oil to the triol, glycerol ($C_3H_8O_3$), and the sodium salt of a long chain carboxylic acid (from 16 to 20 carbon atoms) called a carboxylate salt. This salt has the characteristics we associate with soaps: the ability to form bilayer membranes when shaken in air (creating bubbles), and creating micelles (microscopic, invisible water soluble droplets) in the presence of greasy non-polar materials.

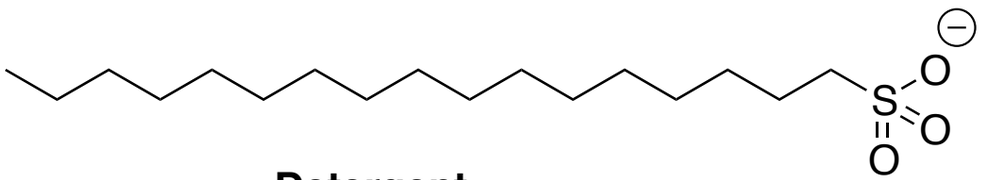


Examples of an aggregate of surfactant molecules dispersed in a liquid colloid. The hydrophillic and hydrophobic groups (carboxylate salt and hydrocarbon tail respectively) self-associate to form bilayer supramolecular structures. These structures, called micelles and liposomes, are readily formed when soaps are placed in an aqueous environment. Image

Detergents are another form of cleansing agent that features long chain sulfonate salts in place of the carboxylate salts of soaps. The solution chemistry of soaps and detergents differs because of the different solubilities of the metal salts, such as Fe^{+3} and Ca^{+2}, of long chain sulfonates and long chain carboxylates in water.



Soap



Detergent

Biodiesel:

The United States is the largest consumer of fossil fuels in the world, and each year we consume more than 125 billion gallons of gasoline and 60 billion gallons of diesel fuel. Shipping and agriculture account for most of the diesel fuel used in the U.S. by semi-trucks, boats, trains, and farm machinery. Diesel powered cars typically get better mileage compared to gasoline-powered cars, but both gasoline and diesel are petroleum products. The Earth's supply of fossil fuels is limited and efforts are underway to replace these non-renewable sources of power with renewable ones.

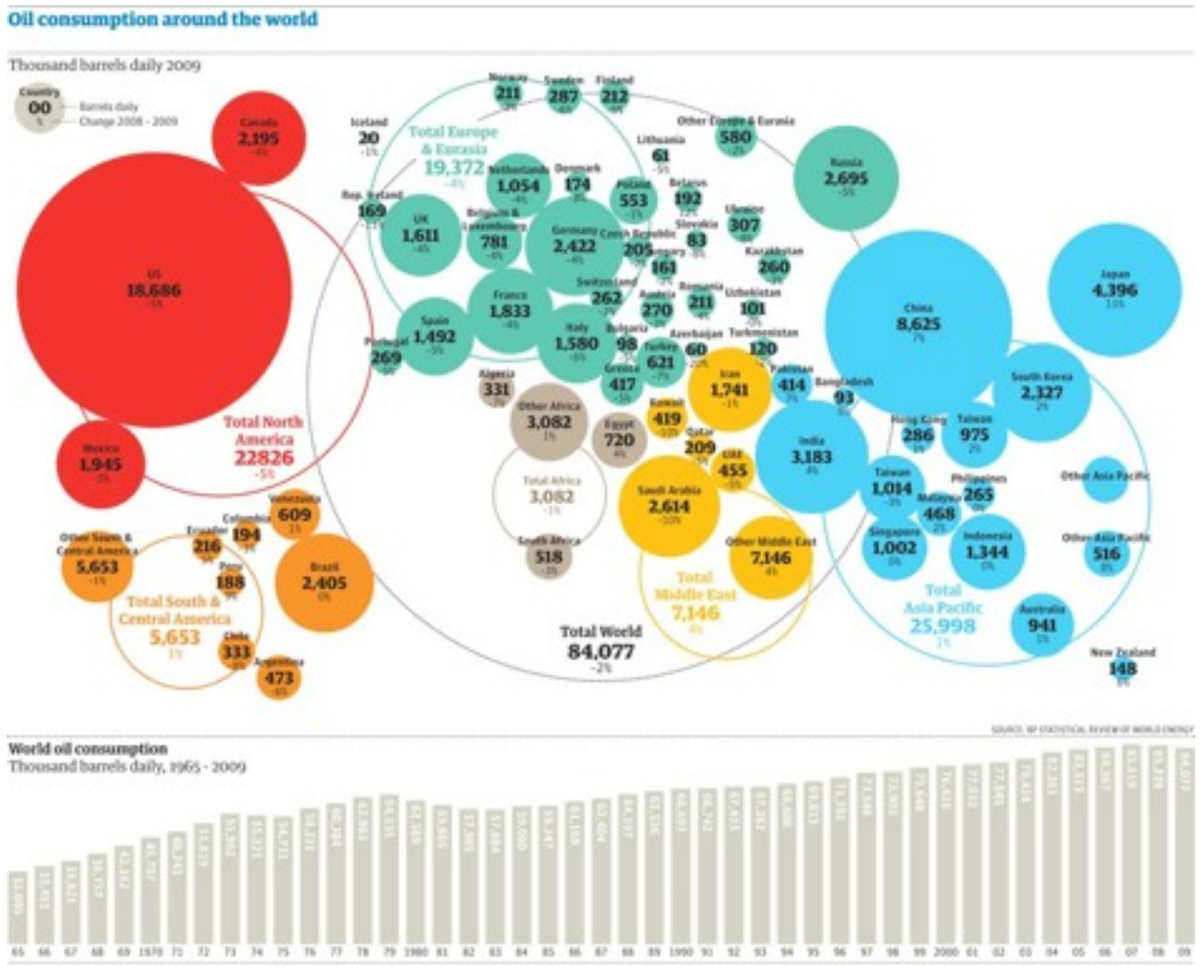
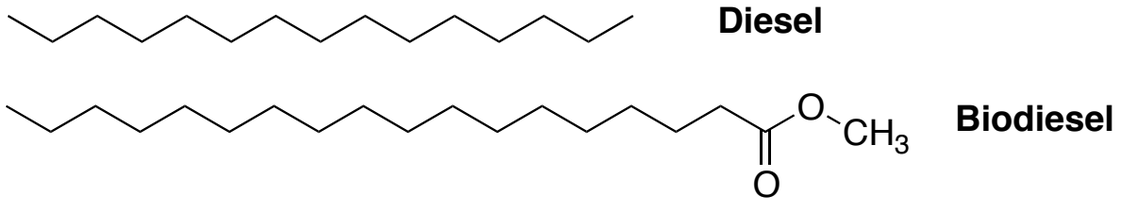


Image generated by: BP statistical review of world energy

Biodiesel has shown some promise as a readily available, renewable replacement for petroleum derived diesel fuel and can be synthesized by individuals in their garage or on an industrial scale. Most notably, biodiesel can be synthesized from waste cooking oil, and the U.S. restaurant industry produces 3 billion gallons of used cooking oil per year. Production of biodiesel from this waste oil would have a dramatic environmental impact, both by reducing the amount of oil that ends up in landfills and by utilizing a renewable resource to power cars and trucks.

The use of biodiesel in vehicles also reduces the amount of the greenhouse gas carbon dioxide released into the environment. How does using biodiesel reduce greenhouse emissions? This is because the carbon in the biodiesel was absorbed by the corn plants from the atmosphere and stored as corn oil. This carbon dioxide is released back into the atmosphere upon combustion of the fuel in an engine. According to the EPA's Renewable Fuel Standards Program Regulatory Impact Analysis released in February 2010, biodiesel from vegetable oil results, on average, in a 57% reduction in greenhouse gases compared to fossil diesel, and biodiesel produced from waste grease results in an 86% reduction.

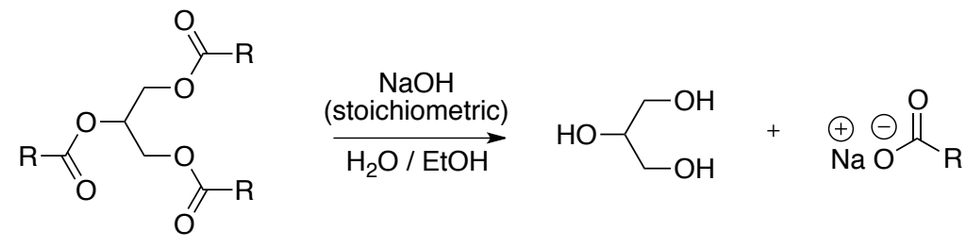
From a structural standpoint it should be noted that while biodiesel is called "diesel", the two fuels are intrinsically different on a molecular level. Diesel actually refers to a mixture of long chain, saturated hydrocarbons (typically C_{10} to C_{15} in length) mixed with aromatic hydrocarbons such as naphthalenes and alkylbenzenes. Biodiesel on the other hand is the fatty acid methyl ester from the transesterification reaction of triglycerides.



EXPERIMENTAL PROCEDURE:

During this lab you can choose to prepare either soap by a saponification reaction or biodiesel by a transesterification reaction. Is soap an ionic compound?

A. Preparation of Soap



Triglyceride **glycerol** **soap**

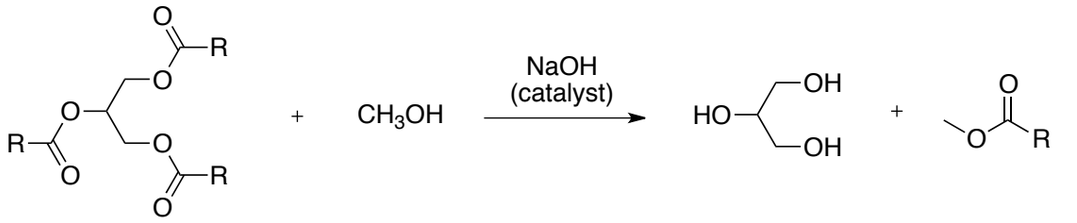
- Begin by preparing a fully dissolved solution of sodium hydroxide (2.5 g) in 10 mL water and 10 mL 95% ethanol. What base are we using to prepare soap from fat? Weigh out 5 g of either shortening, cooking oil, or lard (typically a commercial solid shortening works best) in a 250 mL beaker. Add the basic solution to the fat.

- Heat the mixture for at least 45 minutes in a boiling water bath. To make a boiling water bath, partially submerge the 250 mL beaker in a larger beaker filled with boiling water. Prepare 20 mL of 1:1 solution of ethanol:water and add it over the 45 min period. Stir the mixture occasionally with a glass stir rod.

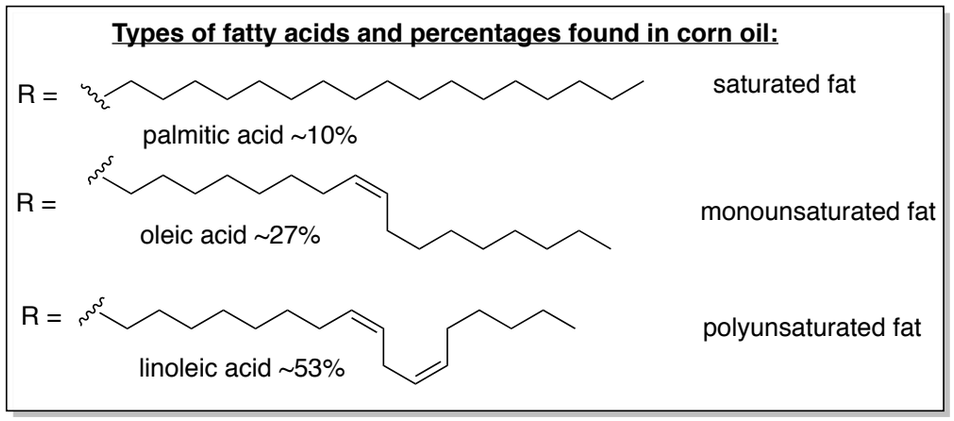
- Prepare a solution of brine (25 g of sodium chloride in 75 mL water) in a 400 mL beaker. You may need to heat the solution for complete dissolution. If this is the case you need to cool the brine solution in an ice bath. Pour the hot mixture into the cooled salt solution. Stir the mixture for several minutes and then let it cool to room temperature in an ice bath.

- Using a Buchner funnel equipped with filter paper, collect the precipitated soap. Rinse the soap in the funnel with portions of ice-cold water. Draw air through the soap to dry the product partially. Weigh the soap.

B. Synthesis of Biodiesel Is biodiesel an ionic compound?



Triglyceride **glycerol** **biodiesel**



- Add 0.35 g of finely ground NaOH to 20 mL of methanol in a 250 mL Erlenmeyer flask containing a magnetic stirbar. Stir vigorously until all of the NaOH has dissolved. The flask now contains a solution of sodium methoxide. Draw an acid base reaction with curved arrows depicting the reaction of NaOH with methanol. Sodium methoxide is a strong base and should be handled with care.

- Warm up 100 mL of vegetable oil to 40 °C in a 250 mL beaker. What is the triglyceride starting material for the synthesis of biodiesel? Warming the oil increases the reaction rate and allows for the completion of the reaction during the allotted time. Pour the oil into the sodium methoxide solution while stirring vigorously. Continue to vigorously stir for 15-30 minutes.

- Transfer the reaction to a 250 mL separatory funnel (see Liquid Liquid Extraction). The emulsion will slowly begin to separate into two layers. The denser glycerol will fall to the bottom, and the less dense biodiesel will remain on top. In the biodiesel lab, which product forms the bottom layer? Which forms the top layer? While complete separation will occur after an hour, use a pipette to obtain a few drops of the biodiesel layer and glycerol layer. Make sure you obtain a sample that is not cloudy. Obtain an IR spectrum of the biodiesel and obtain an IR spectrum of the glycerol.

- After the biodiesel and glycerol have sufficiently separated (or after an hour), collect the glycerol in a small, preweighed beaker. Make sure not to get any biodiesel in the glycerol. If there is a cloudy emulsion between the two layers, drain this into another beaker. Finally, drain the pure non-cloudy biodiesel layer into a second preweighed beaker.

WASTE DISPOSAL

Organic waste in the waste container provided.

DATA PRESENTATION:

Soap Lab
Include the following in your formal laboratory report discussion:

- Ivory soap is made from beef tallow (you can find the structure on wikipedia). Assuming that you used tallow in your soap experiment, draw the structure of the triglyceride found in your oil or fat and the soap reaction products: glycerol and the carboxylate salts.

Additional Pre-Lab Questions:

- Coconut oil is primarily composed of C12, saturated esters appended to the glycerol backbone. Why is soap derived from coconut oil so soluble in water?

- Sodium acetate and sodium propionate are poor soaps. Why?

Biodiesel Lab
Include the following in your formal laboratory report discussion:

- Fully interpret the IR of glycerol and biodiesel. Compare these to known IR spectra of vegetable oil, glycerol and biodiesel. Which peak in the IR spectrum of glycerol is not present in the IR spectra of vegetable oil or biodiesel? Which peak in the IR spectrum of biodiesel is not present in the IR spectrum of glycerol? Include the IR spectra in your lab report.

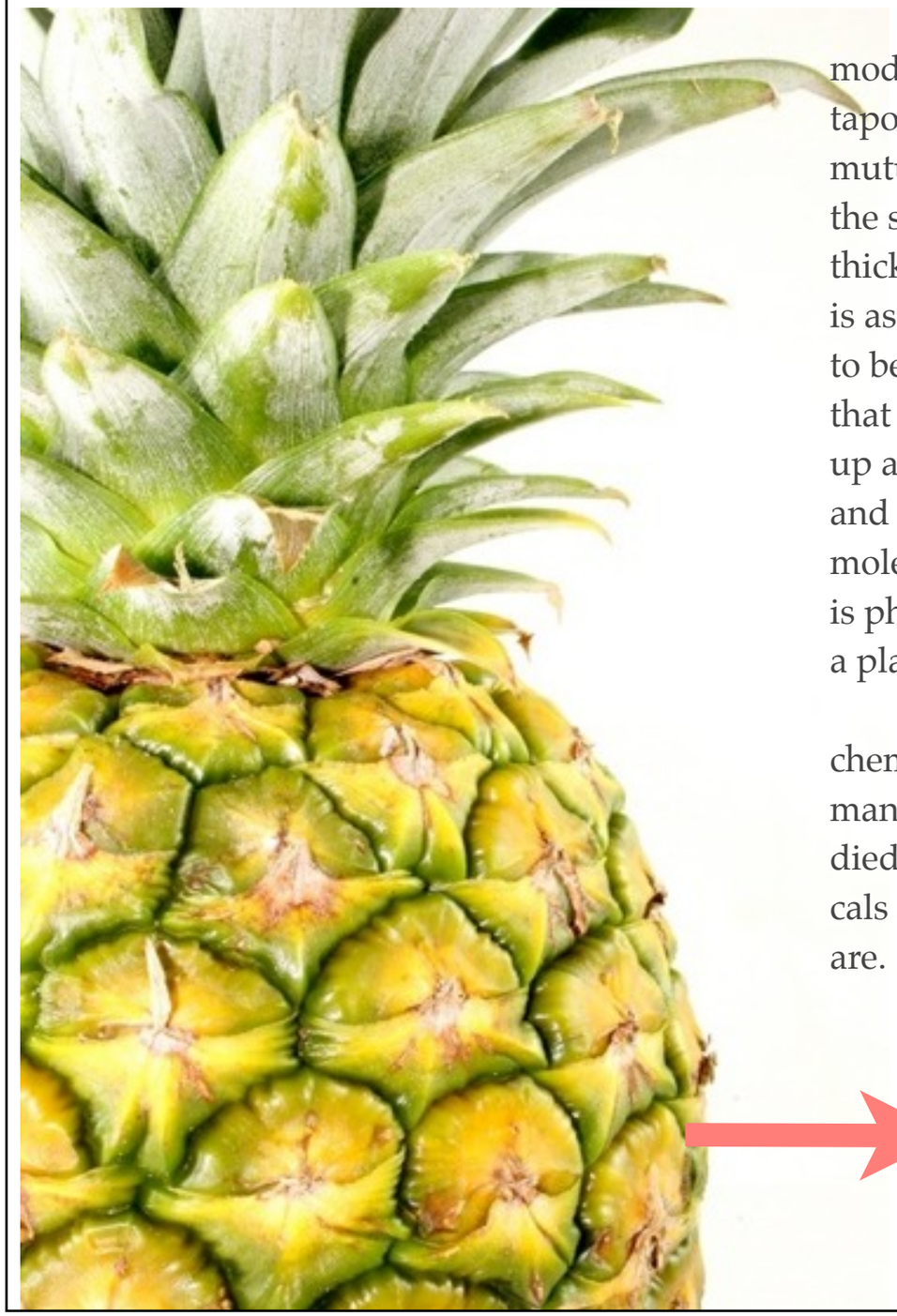
Additional Questions (to be answered at the end of the report):

- What is more polar, glycerol or biodiesel?

- When the reaction for making biodiesel occurs, two layers are formed: biodiesel and glycerol. In which layer will most of each of the following substances be found?

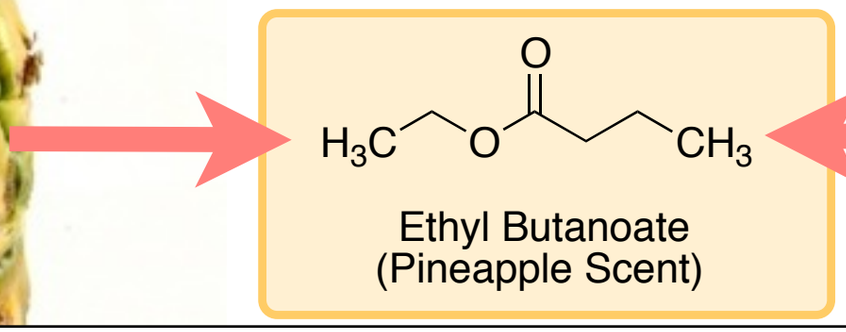
  CH_3O^- Na+ OH-

Natural Product Isolation



Plants have provided and continue to provide the inspiration and foundation for modern medicines. However, in the 21st century vernacular the word "chemical" stands juxtaposed to the term "natural", and increasingly in public opinion the two are considered mutually exclusive occurrences. It is common to assume that chemicals are the domain of the scientific laboratory, arising out of beakers and flasks at the hands of people wearing thick lensed glasses, lab coats and having poor communication skills. The word "chemical" is associated with toxicity and destructiveness. Conversely, anything "natural" is assumed to be harmless and beneficial. The connection that is not readily made is that chemicals make up all aspects of reality, from the very animate and biological to the inanimate mineral. The molecule synthesized by the chemist in the lab is physiologically identical to that produced by a plant.

While it is true that many manmade chemicals are toxic, the same can be said about many compounds produced by plants (Socrates died by drinking poison hemlock tea). Chemicals are not inherently good or bad, they just are.



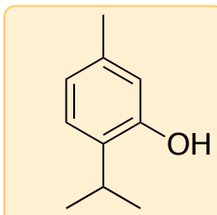
In order to demonstrate that the synthetic and the natural compound are the same, a bioactive molecule will be isolated from a plant and compared to synthetically manufactured equivalents using IR spectroscopy and TLC. You can choose to isolate either thymol from thyme (*Thymus vulgaris*), citral from lemongrass (*Cymbopogen*), or camphor from sagebrush (*Artemisia tridentata*).

Plant Background:

Thyme (*Thymus vulgaris*):

Thyme has a long history of use in Europe and the middle east. It was used by the Egyptians as part of their embalming process and the Sumerians wrote about its antiseptic and antifungal properties. The herb occupied a well loved position in popular cultures wherever it thrived, and was used most commonly as a food preservative and to combat respiratory issues. The Romans associated thyme with courage and, with this in mind, used it extensively in ritual where it was burnt as incense, placed in helmets before war and drank as an infusion.

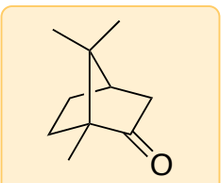
Today, thyme maintains its popularity and, as well as being a culinary mainstay, is now used and studied in pharmacology for the very properties that have been attributed to it over the ages. Thyme's antiseptic properties can be attributed to the thymol molecule. Thymol is the active ingredient in Listerine™ and has been studied extensively.



Thymol

Sagebrush (*Artmisia tridentata*): Sagebrush is the keystone species of the semi-arid temperate regions of North America, and it has a long history of traditional use in regions where it grows. Decoctions of sagebrush were used to treat the flu, menstrual disorders and indigestion. Its characteristic scent is due to a combination of highly volatile compounds, one of which is camphor.

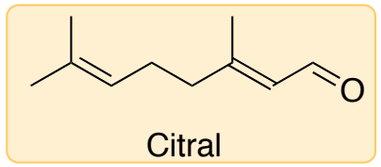
Camphor was originally isolated from the camphor laurel tree indigenous to southeast Asia, where it was known as "dragon's brain perfume" in reference to its invigorating odor. It was first brought from the far east to the west via Indian merchants as an exotic perfume in the 6th century. It continued to play a role in trade from that time. Camphor has been used medicinally in much the same way as it is now. Today it is manufactured on a commercial level and functions as a cough suppressant in products such as Vicks VapoRub™. It is also the active ingredient in some antipruritic creams.



Camphor

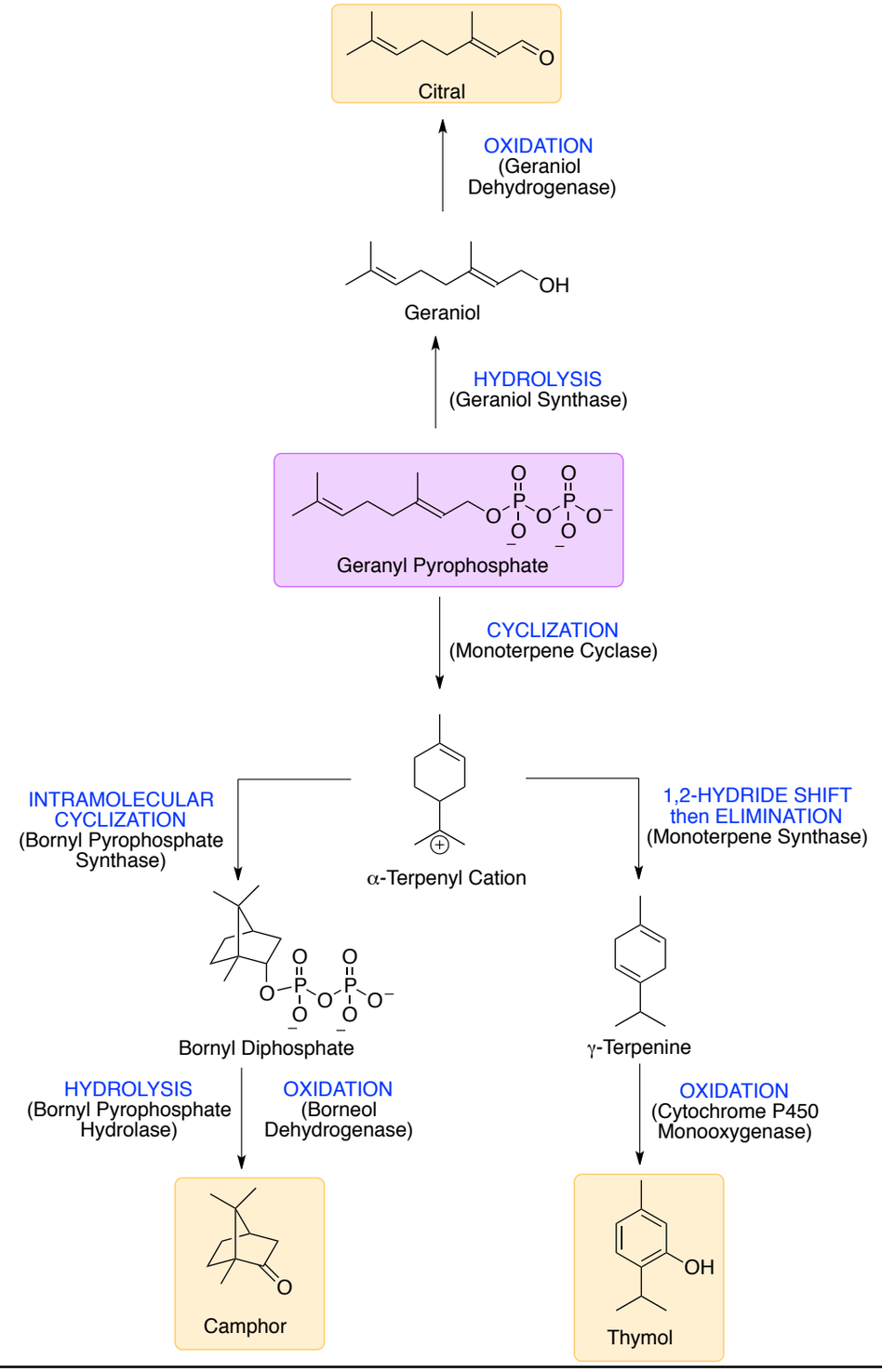
Lemongrass (*Cymbopogon citratus*): Citronella is mentioned in the Bible and in ancient Hindu texts. The name citronella and lemongrass are often used synonymously, but in fact there are sev-

eral species of *Cymbopogon* that yield citronella oil. Commercially two subspecies of *Cymbopogon nardus*, commonly called the Java and Ceylon types, are utilized as the main sources of citronella oil. It has consistently been one of a handful of aromatic essential oils contributing significantly to international trade and the economies of those exporting the oil. Citronella is still commonly used as an ingredient in fragrances and as an insect repellant. It is one ingredient in Burt's Bees Lip Balm™. One of the main compounds in the oil is citral which has demonstrated antimicrobial activity. Its use as an insectifuge is due to its interaction with insect pheromones.



Biosynthesis:

Biological systems use enzymes to facilitate chemical transformations. Nature uses enzymes to perform chemical transformations using the mechanisms and reactions described in the organic chemistry classroom. In plants two isoprene units attached to two phosphate groups forms the basic monoterpene building block, geranyl pyrophosphate. How many carbon atoms are in isoprene? Through substitution, elimination, cyclization and oxidation reactions geranyl pyrophosphate is modified into acyclic, monocyclic and bicyclic molecules. The molecules isolated in this lab represent just three of many possible outcomes in the biosynthetic modification of geranyl pyrophosphate. Though each compound possesses unique characteristics in terms of both structure, smell and physiological action, ultimately their origins share a unified biosynthetic precursor.



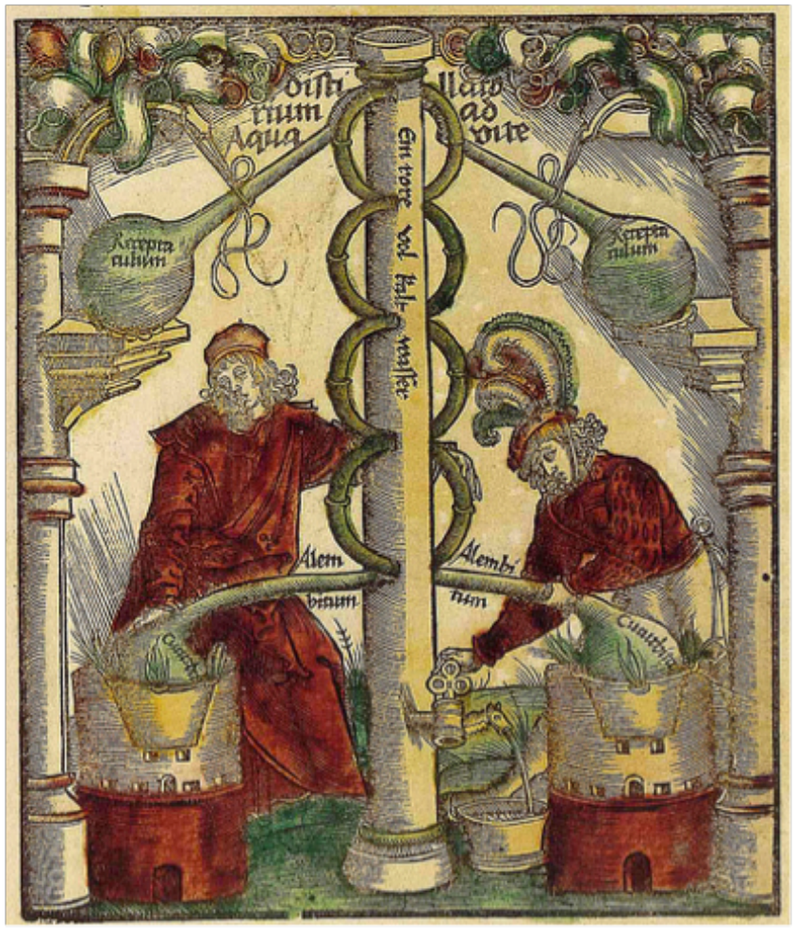
Thymol is a monocyclic monoterpene phenol biosynthesized from geranyl pyrophosphate. Initial cyclization is assisted by a monoterpene cyclase enzyme. This step leads to the α-terpenyl cation, a crossroads molecule in the biosynthetic pathway of many terpenoids. A 1,2 – hydride shift followed by an elimination (affected by a monoterpene synthase enzyme) results in γ-terpinene. From this point, cytochrome P450 monooxygenase facilitates a series of oxidative transformations, and thymol is produced. How many hydrogens must be removed to convert γ-terpinene to thymol?

Camphor is a bicyclic monoterpene biosynthesized from geranyl pyrophosphate. How many isoprene units are there in geranyl pyrophosphate? In both thyme and sagebrush geranyl pyrophosphate is modified by a monoterpene cyclase enzyme to produce the α-terpenyl cation. From this point the pathways diverge due to the action of different enzymes. In sage brush, the α-terpenyl cation undergoes a secondary intamolecular cyclization by the enzyme bornyl pyrophosphate synthase, with concomitant hydrolysis by bornyl pyrophosphate hydrolase. Finally, borneol dehydrogenase oxidizes the alcohol in borneol to a ketone to produce camphor.

Citral is a monoterpene that is synthesized from geranyl pyrophosphate. The enzyme geraniol synthase hydrolyzes the oxygen pyrophosphate bond to produce the terminal alcohol, geraniol. Oxidation of geraniol to the aldehyde by the enzyme geraniol dehydrogenase results in the citral molecule. How can you tell the difference between citral and geraniol on an IR?

TECHNIQUE: Steam Distillation

In principle, steam distillation works by separating volatile, water-insoluble compounds from non-volatile compounds through co-distillation (see Distillation Technique). Be able to draw a diagram of a distillation apparatus. Water and the non-volatile compounds present in the plant are immiscible and as such form a two phase system called a heterogeneous azeotrope. The combined vapor pressures of the two compounds results in a lowered boiling point for the entire system. As a result the water and volatile compounds co-distill, which preserves the volatiles that would potentially decompose when exposed to higher temperatures. Steam distillation has been used for hundreds of years to isolate essential oils from plants.



A simple distillation apparatus uses a set amount of water. The plant material and the water are placed in a round bottom flask, which is attached to a condenser. A receiving vessel collects the distillate, which consists of water and volatiles. The organic component is then isolated

EXPERIMENTAL PROCEDURE:

Choose **one of the following three isolations** to perform during the lab period:

A. Isolation of thymol from thyme

- Weigh out 10 g of dried thyme and place it in a high speed blender with 200 mL of distilled water. Blend until a fine slurry results. Transfer the slurry to a 500 mL round bottom flask, and place directly on the hot plate. Rinse the blender with an additional 50 mL of distilled water and add this to the distillation flask. Attach a distillation apparatus to the round bottom flask. Use a 200 mL beaker as the receiving vessel.

- Turn the heat on high and allow the distillation to proceed until approximately 100 mL of distillate has been collected.

- Transfer half of the collected distillate to a 125 mL separatory funnel. Add 30 mL of diethyl ether to the funnel and shake the contents. Drain the aqueous phase into a beaker. Add the remaining distillate to the organic phase in the sep. funnel. Shake the contents and remove the aqueous layer again. Collect the organic layer. Add magnesium sulfate to the organic layer. Using a filter and funnel, gravity filter the organic layer to remove the magnesium sulfate.

- Place the filtrate directly on the heating mantle at medium heat. Remove the flask when bubbling ceases.

- Prepare the TLC standard by dissolving 0.1 g of synthetic thymol in 5 mL of diethyl ether.

- Compare the product to the standard using TLC. Develop the TLC plate in 4:1 hexanes/ethyl acetate. Describe how you would determine the Rf value for a TLC of one of your molecules.

- Obtain IR spectra of both the isolated molecule as well as the synthetic standard.

B. Isolation of camphor from sagebrush

- Weigh out 10 g of dried sagebrush and place it in a high speed blender with 200 mL of distilled water. Blend until a fine slurry results. Transfer the slurry to a 500 mL round bottom flask, and place directly on the hot plate. Rinse the blender with an additional 50 mL of distilled water and add this to the distillation flask. Attach a distillation apparatus to the round bottom flask. Use a 200 mL beaker as the receiving vessel.

- Turn the heat on high and allow the distillation to proceed until approximately 100 mL of distillate has been collected.

- Transfer half of the collected distillate to a 125 mL separatory funnel. Add 30 mL of pentane to the funnel and shake the contents. Drain the aqueous phase into a beaker. Add the remaining distillate to the organic phase in the sep. funnel. Shake the contents and remove the aqueous layer again. Collect the organic layer. Add magnesium sulfate to the organic layer. Why do we add magnesium sulfate to our organic layer? Using a filter and funnel, gravity filter the organic layer to remove the magnesium sulfate.

- Place the filtrate directly on the heating mantle at medium heat. Evaporate the solvent until approximately 2 mL remain in the flask. Remove the flask from heat, and allow the remaining solvent to evaporate at room temperature. (**Note:** Camphor possesses the unusual property of subliming at room temperature. Be careful not to evaporate off all of the solvent, since doing so will result in sublimation of the product.)

- After the solvent has evaporated, add 1 mL of diethyl ether to the flask and swirl. Use this to spot a TLC plate and to obtain an IR spectrum. (**Note:** it may appear that nothing remains in the flask, but take a whiff)

- Prepare the standard by dissolving 0.1 g of synthetic camphor in 5 mL of diethyl ether. Compare the product to the standard using TLC. Develop the TLC plate in 4:1 hexanes/ethyl acetate. Which solvent is the polar phase and which is the nonpolar phase?

- Obtain IR spectra of both the isolated molecule as well as the synthetic standard.

A. Isolation of citral from lemongrass

- Weigh out 10 g of dried lemongrass and place it in a high speed blender with 200 mL of distilled water. Blend until a fine slurry results. Transfer the slurry to a 500 mL round bottom flask, and place directly on the hot plate. Rinse the blender with an additional 50 mL of distilled water and add this to the distillation flask. Attach a distillation apparatus to the round bottom flask. Use a 200 mL beaker as the receiving vessel.

- Turn the heat on high and allow the distillation to proceed until approximately 100 mL of distillate has been collected.

- Transfer half of the collected distillate to a 125 mL separatory funnel. Add 30 mL of diethyl ether to the funnel and shake the contents. Drain the aqueous phase into a beaker. Add the remaining distillate to the organic phase in the sep. funnel. Shake the contents and remove the aqueous layer again. Collect the organic layer. Add magnesium sulfate to the organic layer. Using a filter and funnel, gravity filter the organic layer to remove the magnesium sulfate.

- Place the filtrate directly on the heating mantle at medium heat. Remove the flask when bubbling ceases.

- Compare the product to the standard using TLC. Develop the TLC plate in 4:1 hexanes/ethyl acetate.

- Obtain IR spectra of both the isolated molecule as well as the synthetic standard.

WASTE DISPOSAL

Flammable waste for all organic liquids. The remaining plant material can be disposed of in a trash receptacle.

DATA PRESENTATION:

Include the following in your formal laboratory report discussion:

- Fully interpret the IR of your isolated molecule. Compare these to known IR spectra of the synthetic standard. Identify all of the functional groups that are present in your molecule and their corresponding peak locations in the IR. Include the IR spectra in your lab report.

- Given an IR spectrum of one of the three isolated molecules, describe how you would use IR to determine which molecule the spectra corresponds to (be specific).

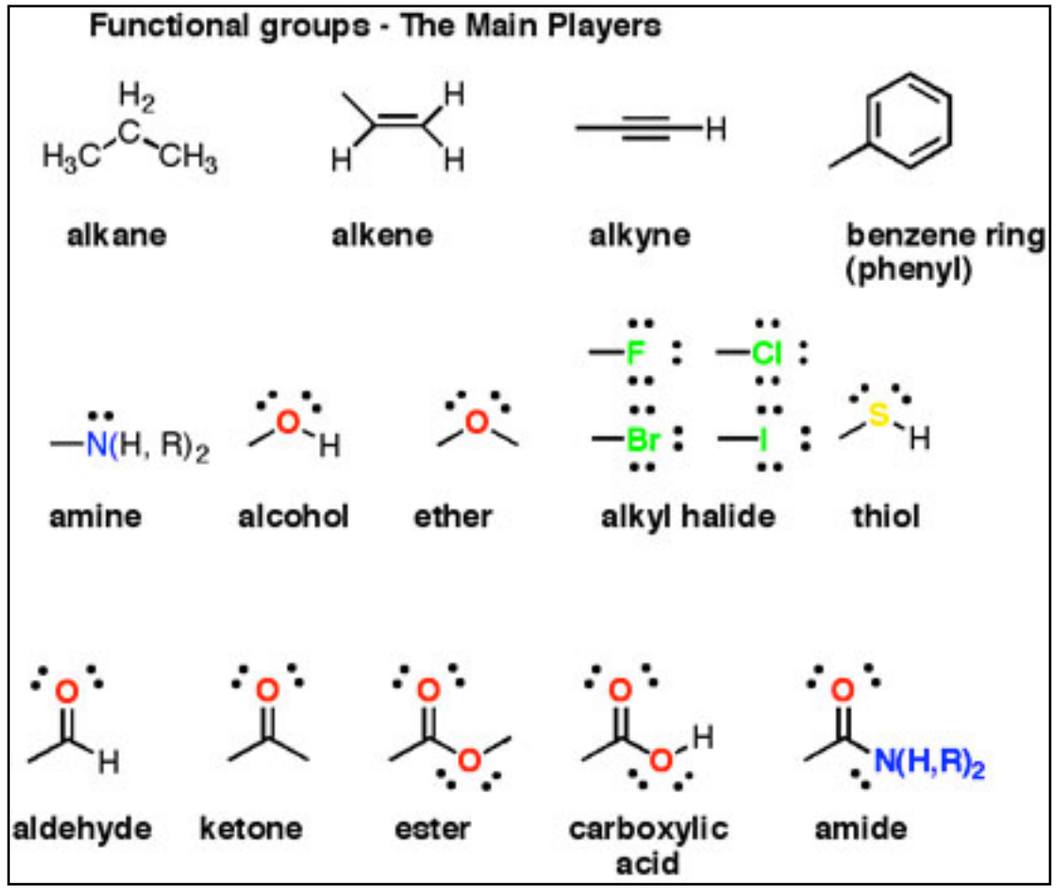
- Trace the TLC plate that you ran in your notebook and label it completely. **Do not tape or place the TLC plate directly into your notebook!** Labeling includes identifying each compound or unknown that was spotted on each lane of the TLC plate, marking the height of the solvent front on the TLC plate, identifying the solvent mixture that was used to develop each TLC plate, describing the "visualization" methods used, and calculating the Rf value for each spot.

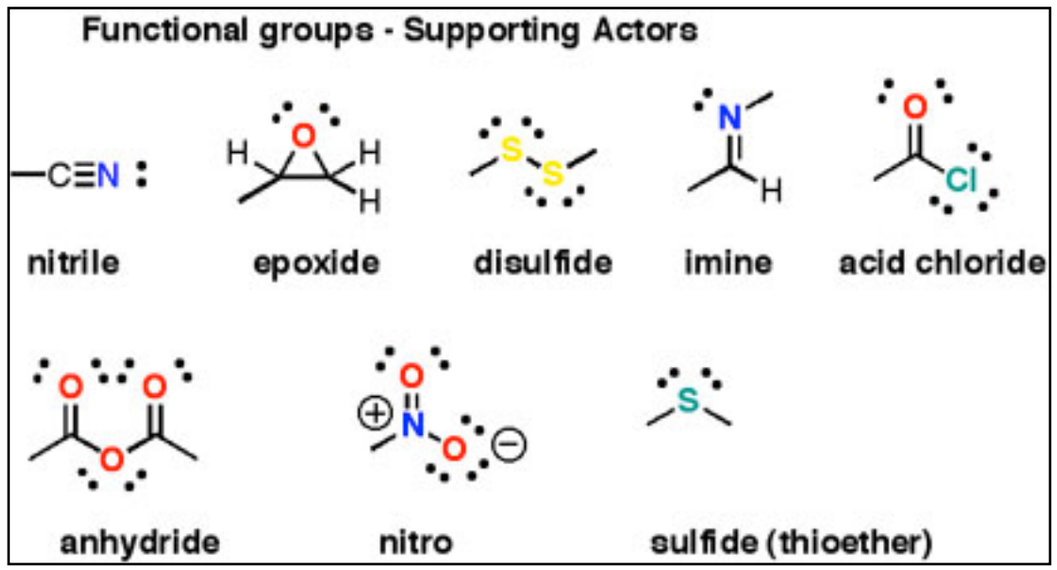
- Draw the biosynthetic pathway for your isolated molecule starting from geranyl pyrophosphate. Identify all functional groups (except alkane) for all molecules on the pathway.

Additional Pre-Lab Questions:

- Given a functional group, determine whether it is capable of hydrogen bonding.

- Given two functional groups, determine which is more polar.





Introduction to the Synthetic Preparation of Molecules

Synthetically prepared molecules are all around us. From the food we eat, to the clothes we wear, to the cars that we drive; we are very much reliant on molecules made by chemists. In this section we will combine the techniques introduced in earlier sections with reactions that we have recently learned in lecture to successfully prepare and analyze new molecules. At the end of this section we will execute a multi-step synthesis wherein the product outcome is not immediately apparent. Ultimately, you will need to utilize your knowledge of reaction mechanisms to help determine what you isolate from your flask.

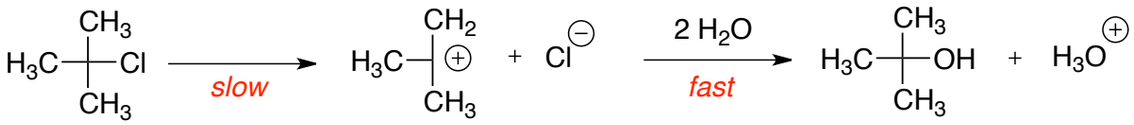
Nucleophilic Substitution (Sn1): Factors Affecting Rate

Hydrangeas are a natural pH indicator. At neutral to high pH (6.5 to basic) Hydrangeas will have a pink hue. At low pH (5.5 and below) they will turn purple. If the soil pH is low enough (below 4.5) they will become blue. Image

The rate at which a reaction takes place is of particular importance in chemistry because it provides information about the detailed path over which reactants travel on their way to becoming products, i.e., the reaction mechanism. The correct interpretation of rate data depends on knowledge of those factors that influence the rate of reaction, and these include:

- **The structure of the compound entering into the reaction**
- **The temperature**
- **The solvent medium in which the reaction is carried out**
- **The concentrations of the reacting species (for most reactions)**

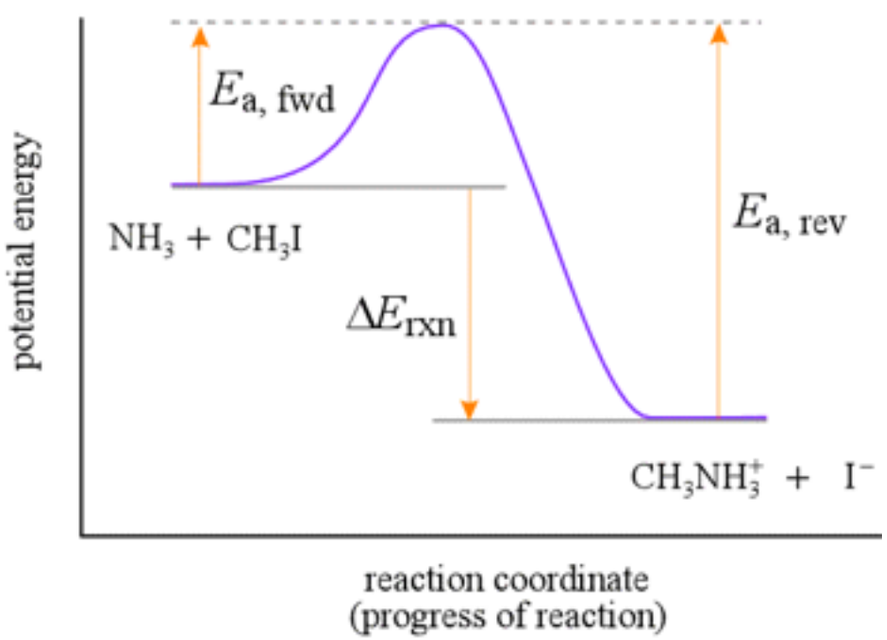
You will investigate some of these effects on a simple but important process in organic chemistry, unimolecular solvolysis, also called the SN1 reaction. Such a reaction involves three steps. These steps are illustrated below with the reaction to be studied in this experiment: the hydrolysis of *tert*-butyl chloride:



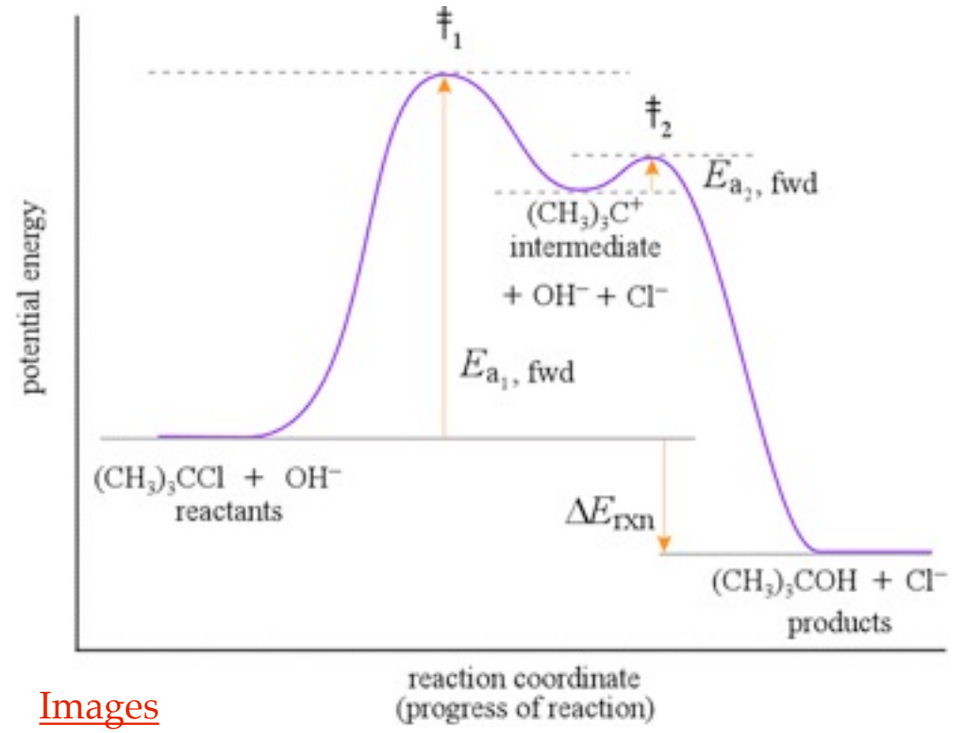
In the first step, the carbon-halogen bond of *tert*-butyl chloride breaks to form a reactive intermediate carbocation and a chloride ion. Draw the slow, rate-determining step for the solvolysis of tBuCl in water. The carbocation, in the second step, reacts rapidly with water to form *tert*-butyl alcohol and a hydronium ion. Draw the carbocation intermediate formed in the solvolysis of tBuCl. **Note that the reaction mixture becomes more acidic as the reaction progresses**.

In a multistep mechanism, the rate of the slowest step determines the overall rate of the reaction. For this reaction, the first step is the rate-determining step, and hence the rate law is: rate = k[t-BuCl]. In this reaction, the rate-determining step involves only one molecule; therefore, it is considered to be a **unimolecular reaction**. Many reactions require that two molecules collide with one another with sufficient energy before a reaction takes place. These are called **bimolecular reactions**. An SN2 reaction is an example of a bimolecular reaction.

Reaction coordinate diagram for the Sn2 Reaction:



Reaction coordinate diagram for the Sn1 Reaction:



Images

EXPERIMENTAL PROCEDURE:

Note: All glassware must be dry at all times as the halides react with water. Use a little acetone to remove the water each time before using the glassware again.

Obtain and place in labeled test tubes the following solutions: 15 mL of 0.1 M NaOH in water and 25 mL of 0.1 M t-butyl chloride solution in acetone. These two solutions will be used in Parts A, B and C of this experiment. Later in the lab period, you should obtain the other three solutions: 6 mL of 0.1 M t-butyl bromide in acetone, 3 mL of 0.1 M s-butyl bromide in acetone, and 3 mL of 0.1 M triphenylmethyl chloride in acetone for use in Part D of this experiment.

Practice your pipetting technique before starting. Be sure you know how to deliver the correct amount of solution with each pipet (check with your lab instructor if you are unsure). Also make sure that you can repeatedly deliver the required amounts with good accuracy. Being consistent from run to run is crucial to obtain meaningful data. Use acetone sparingly to clean and dry glassware between each run. After each run, collect the "waste" reaction mixture in a 250 mL Erlenmeyer flask, and at the end of the lab period dispose all of the accumulated wastes in the waste container provided in the hood.

A. Determination of Time for 10% Reaction. Solvent Mixture is 70% water - 30% acetone

Repeat the following procedure two times. Perform a third trial if your results differ in time by more than 10%. Describe your procedures in detail in your lab report.

Record the time for 10% reaction, when the reaction solution turns from blue to green, and the reaction temperature. Determine the average time in seconds. Remember to do a third trial if the time differs by more than 10%.

- Pipet 3 mL (use the 10.0 ml pipet) of the 0.1 M t-butyl chloride solution into a dry 25 mL Erlenmeyer flask and place the flask on white paper.

- Pipet 0.3 mL (use the 1.0 mL pipet) of 0.1 M sodium hydroxide solution into a second dry 25-mL flask and then add 6.7 mL (use a different 10.0 mL pipet) of distilled water. Add several drops of bromphenol blue indicator solution to the flask with water and sodium hydroxide.

- Measure the temperature of the water solution and then pour the acetone solution of 0.1 M t-butyl chloride into the basic water solution. Swirl for a second and then immediately pour the solution back into the other flask to ensure complete mixing of the two solutions. Note the time and then wait for the indicator to turn from blue to green. Note the temperature of the reaction mixture and the time when the color change occurs. This is the time required for 10% reaction.

- Before beginning a new experiment, rinse the two flasks with water followed by a little acetone and allow them to drain. Why do we rinse flasks between experiments?

B. Temperature Effects on Reaction Rates

- **Part 1: (lower temperature).** Follow the **same procedure** as you used in Part A, but before you mix the two solutions allow the temperature of the Erlenmeyer flasks to equilibrate in a water bath that is maintained at about 10 °C below room temperature for 5 minutes. ***Keep the reaction mixture in the cold water bath throughout the reaction.*** Record the temperature of the water bath. Perform the reaction twice and determine the average time, in seconds, for the indicator to change colors from blue to green. What effect will cooling the Sn1 reaction have on its rate? (faster, slower, no change)

- **Part 2: (higher temperature).** Follow the **same procedure** as you used in Part A, but before you mix the two solutions allow the temperature of the Erlenmeyer flasks to equilibrate in a water bath that is maintained at about 10 °C above room temperature for 5 minutes. ***Keep the reaction mixture in the warm water bath throughout the reaction***. Record the temperature of the water bath. Perform the reaction twice and determine the average time, in seconds, for the indicator to change colors from blue to green. Perform a third trial if the first two differ in time by more than 10%. What effect will warming the Sn1 reaction have on its rate?

C. Solvent Effects on Reaction Rates. Solvent mixture is 80% water - 20% acetone

- Using two Erlenmeyer flasks, pipet 2 mL of the 0.1 M t-butyl chloride solution into one of the flasks and 0.2 mL of the 0.1 M sodium hydroxide solution plus 7.8 mL of water and several drops of bromophenol blue indicator into the other.
- This solvent mixture is 80% water-20% acetone. Carry out the reaction twice and determine the average time in seconds for the indicator to change color. Is this reaction solution more or less polar than the solution used in Part A?

D. Structural Effects on Reaction Rates

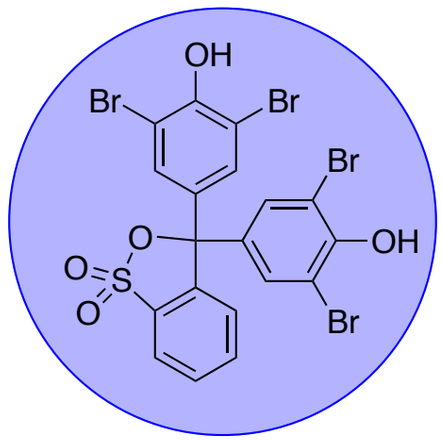
- **Part 1: Leaving Group Effect:** Perform the procedure of Part A, but use 0.1 M t-butyl bromide instead of 0.1 M t-butyl chloride. Perform the reaction twice and record the average time, in seconds, for the indicator to change color from blue to green.

- **Part 2: Structural Effect:** Perform the procedure of Part A but use 0.1M s-butyl bromide in place of 0.1 M t-butyl chloride. Do not wait more than 5 minutes for a reaction to occur!

- **Part 3: Structural and Resonance Effect:** Perform the procedure of Part A but use 0.1 M triphenylmethyl chloride solution instead of 0.1 M t-butyl chloride. Perform the reaction twice, recording the average time, in seconds, for the indicator to change color from blue to green.

WASTE DISPOSAL

Place all organics in the flammable waste.



Bromophenol Blue

DATA MANIPULATION

1. Rate Constant Calculations

The percent completion of the reaction is given by:

$$\% \text{ completion} = \frac{A_0 - A_t}{A_0}$$

Upon rearrangement, one obtains:

$$1 - \% \text{ completion} = \frac{A_t}{A_0}$$

The integrated rate expression for the disappearance of an alkyl halide by a unimolecular (1st order) reaction is:

$$-2.303 \log\left(\frac{A_t}{A_0}\right) = kt$$

Substitution of $\frac{A_t}{A_0}$ yields:

(note that the sign has changed)

$$2.303 \log\left(\frac{1}{1 - \% \text{ completion}}\right) = kt$$

or:

$$k = \frac{2.303}{t} \log\left(\frac{1}{1 - \% \text{ completion}}\right)$$

Therefore, the relationship between the rate constant k, and 10% reaction is given by:

$$k = \frac{2.303}{t} \log\left(\frac{1}{1 - 0.10}\right) = \frac{2.303}{t} \log(1.111)$$

or:
(where t is in seconds)

$$k = \frac{0.105}{t}$$

Using the above relationship, calculate the rate constants for the reactions performed in all parts of this experiment.

2. Activation Energy Calculation

Molecules must have a certain minimum energy before a reaction can take place. The energy of activation is related to the rate constant by the Arrhenius Equation (below), in which k is the rate constant, A is a pre-exponential constant, Ea is the activation energy (in cal/mol), R is the gas constant (1.99 cal/K mol), and T is the absolute temperature (K).

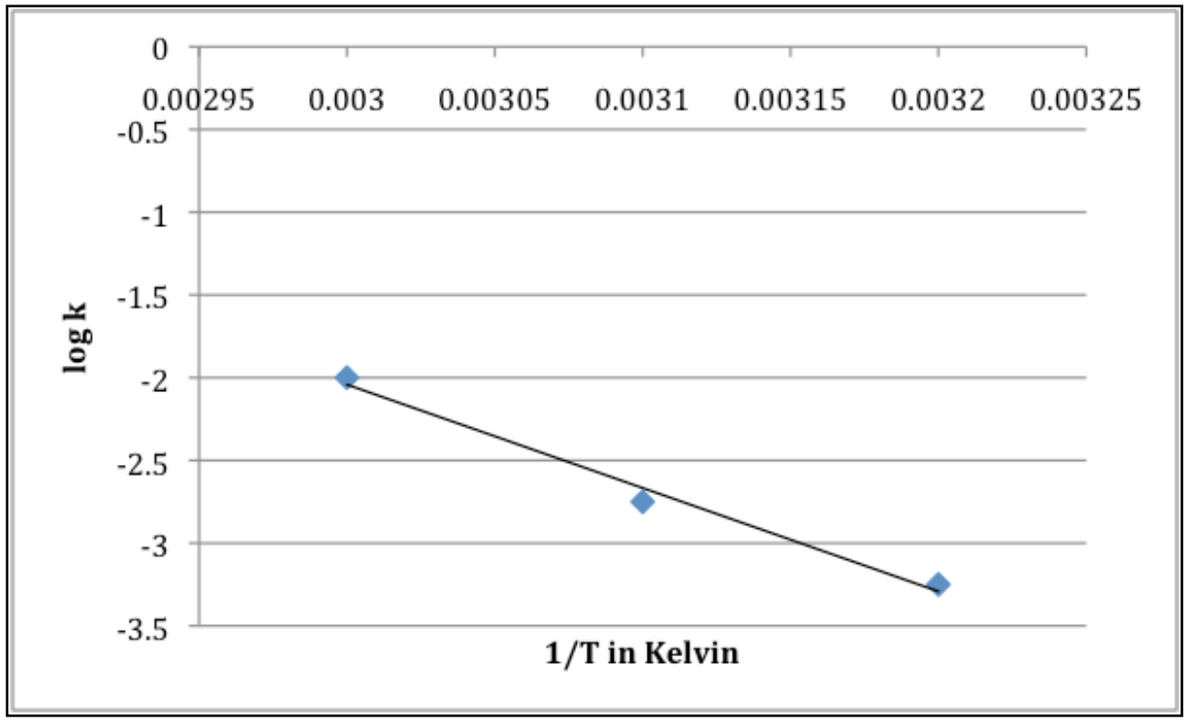
Image

k = Ae-Ea/RT

Taking the logarithm of both sides of the equation gives the expression below. Because this is a linear equation, a plot of **log k** (dependent variable, y axis) versus **1/T** (independent variable, x axis) will yield a straight line with **slope equal to -Ea/4.58**:

$$\log k = \frac{-E_a}{4.58\,T} + A$$

A typical Arrhenius plot is illustrated below.



DATA PRESENTATION

Include the following in your formal laboratory report discussion:

- Describe in detail your experimental procedures and all measurements (amounts, temperatures).

- Use your data for the three temperatures from Experiment A and Experiment B to construct a table having the following columns: Temp (^{o}C), Temp (K), 1/Temp (K), k (sec^{-1}), and log k.

- Determine the activation energy for your Sn1 reaction. Plot log k values on the dependent (Y) axis vs. 1/Temp (K) values on the independent (X) axis. Determine the slope of the line and calculate the Ea: **[Ea (cal/mol) = -4.58(slope)]**. Change Ea from cal/mol to Kcal/mol. Remember that the slope is equal to the change in the log k divided by the change in the inverse temperature (1/K). If your data is scattered (the three points could be on different lines because one is inaccurate) then plot two slopes and take the average.

- Summarize how the structures of the alkyl group and the leaving group influence the reaction rate and therefore the rate constant for unimolecular solvolysis.

- Thermal energy of molecular collisions at room temperature (20 ^{o}C) supplies about 15 kcal/mol of energy to the average molecular collision, more in some cases and less in others, seemingly randomly. Does your value for the activation energy for hydrolysis of t-BuCl at room temperature seem reasonable? Because it is slow it should be a few kcals higher than 15 kcal/mole. What value for Ea would you estimate for the hydrolysis of t-BuBr, a compound that reacted faster? For sec-butyl chloride? For triphenylmethyl chloride?

Additional Pre-Lab Questions:

- If you pipet 3 mL of a 0.1 M t-BuCl solution, how many millimoles of t-BuCl does it contain?

- If you pipet 0.3 mL of a 0.1 M NaOH solution, how many mMols of NaOH does it contain?

- Note that the rate-determining step of this reaction involves the production of a positively charged ionic intermediate. What effect on the solvolysis rate would you expect a more polar solvent medium to have?

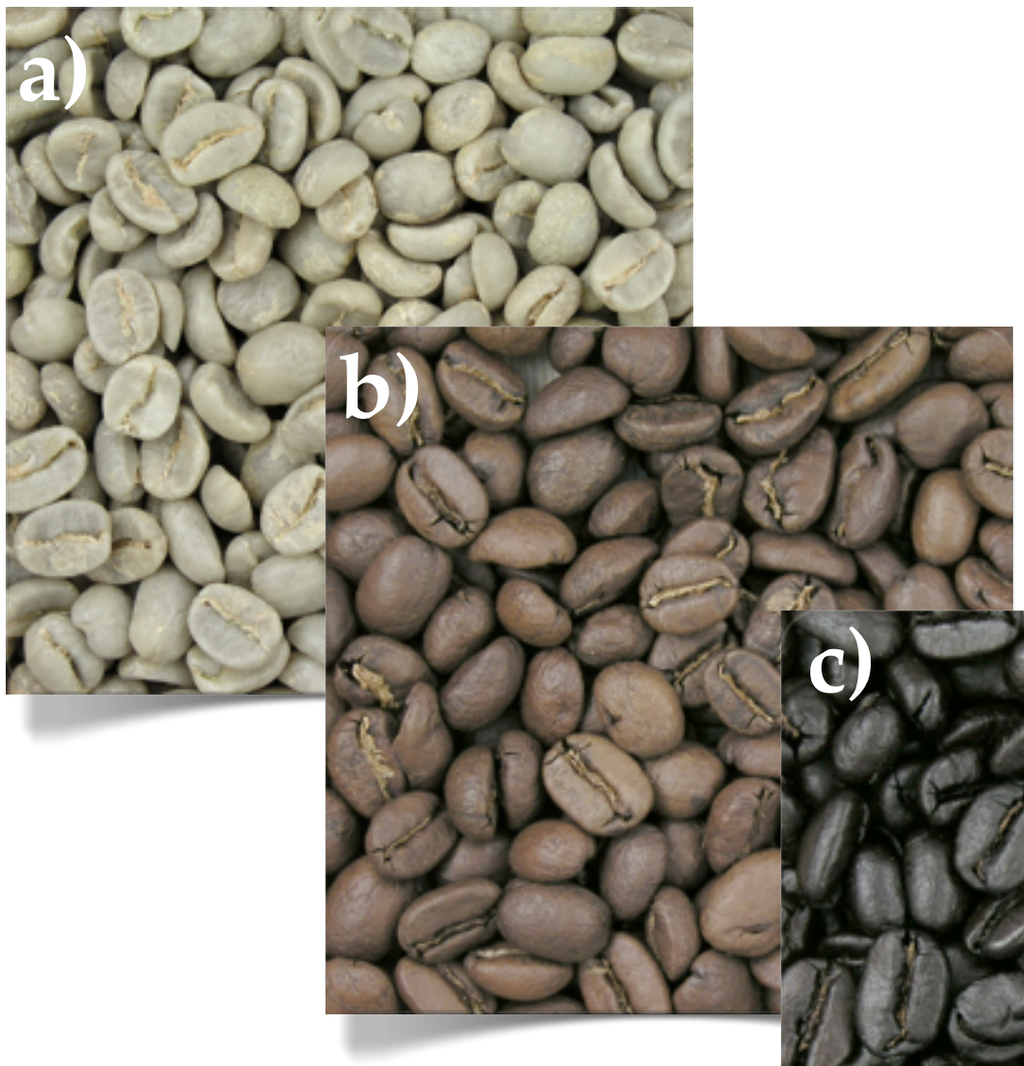
- In each experiment we are measuring the number of _____ before a color change occurs.

- How many times is each experiment repeated?

- How many steps are involved in an Sn2 reaction?

- If you pipet 0.3 mL of a 0.1 M NaOH solution, how many mMols of NaOH does it contain?

Acid-Catalyzed Elimination (E2 / E1): Dehydration of an Alcohol



a) Coffee beans taken direct from farms, b) American roast (210 °C): the traditional roast for eastern U.S., c) Italian roast (245 °C): heavy burnt tones, common roast for espresso blends. Images

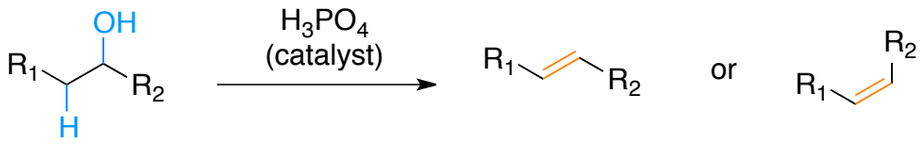
Elimination reactions are found throughout our daily life. The dehydration of alcohols is a particularly common reaction, as sugar molecules, known as carbohydrates, undergo non-enzymatic E1 and E2 elimination reactions readily to form a variety of small molecules. Examples of these reactions include: the caramelization of white sugar (glucose), toasting bread, frying onions, malting barley (to make malt whiskey or beer), and cooking many meats (these processes are also simultaneously undergoing an interesting amine condensation reaction-which we will learn second semester-called the Malliard reaction).

Another example is the preparation of coffee. For coffee to obtain its characteristic taste and smell, it needs to be first roasted (heated for extended periods of time). This heating induces a variety of chemical transformation, including the dehydrative elimination of the alcohol groups on the carbohydrate molecules within the coffee bean. These elimination reactions produce alkene molecules which provide the complex aroma and flavor we associate with coffee.

In this experiment, you will carry out an acid-catalyzed dehydration of an unknown alcohol to give an unknown alkene. You will be able to determine the identity of both the alcohol and the alkene by measuring the physical properties of the purified alkene. Note that you should use the synthesis format for your laboratory report.

EXPERIMENTAL PROCEDURE:

A. Preparation of the Alkene



- Place 5.0 g of your unknown alcohol (**be sure to record the unknown number!**) along with 2 mL of 85% phosphoric acid in a 25 mL or 50 mL round bottom distilling flask. Save any unused alcohol for later analysis. Set up a simple distillation apparatus with a magnetic stirrer and a screw-cap test tube immersed in ice water for the receiver (see Distillation Technique). Draw a diagram of a labeled distillation apparatus. Your product will be very volatile in some cases, so collecting the distillate in an ice bath will decrease evaporation and maximize your yield. Begin heating the well-stirred solution in the reaction flask. When the solution reaches a gentle boil maintain the temperature such that a slow rate of distillation occurs continuously. Overheating will result in the starting material, a higher boiling alcohol, distilling along with the lower boiling alkene reaction product. You may stop the distillation when the residue in the reaction flask starts to smoke, indicating that only phosphoric acid remains. Set your distillate aside for a minute, and immediately clean your distillation glassware and rinse all wet surfaces with a small amount of acetone to promote drying.

- Add a small amount (1 mL) of 10% Na_2CO_3 solution and a spatula-full of NaCl to the distillate, cap the tube, and shake to mix. This will remove traces of phosphoric acid and will decrease the solubility of the upper alkene layer in the lower aqueous layer. How does adding sodium carbonate purify your product? Transfer the upper alkene layer with a Pasteur pipet to another screw-cap test tube.

- Add a spatula-full of anhydrous Na_2SO_4, cap the test tube, and shake. Add more Na_2SO_4 until the crystals are no longer clumping up. Sodium sulfate is a drying agent that removes water from organic liquids by becoming bound to the water, like cement. How does adding sodium sulfonate purify your product?

- Transfer the dry alkene into a clean 25 mL round bottom flask with a magnetic stirrer and attach it to your clean, dry distillation apparatus again using a test tube as the receiver in an ice water bath. Distill the alkene again and record the boiling point. The distillate should be clear, not hazy, indicating the absence of water. If it is cloudy, add a little Na_2SO_4. Tare a clean vial and immediately pipet your alkene into the vial to obtain its mass. Determine the refractive index of your alkene.

- From the physical properties, bp and RI, of the purified alkene, the identity of the unknown alcohol can be deduced. What techniques can you use to determine the identity of the unknown alcohol? The unknown alcohols, and their corresponding alkenes, are listed below, along with **physical data for the alkenes**.

B. Testing for and Analysis of Alkenes

- Test both the starting alcohol and the alkene product for unsaturation using two different alkene addition reactions: 1) bromine in carbon tetrachloride and 2) potassium permanganate solution.

- You should also use IR to characterize both your alcohol and alkene.

ALCOHOL	ALKENE	BP (^{O}C, 760$_{MM}$)	N_D^{20}
cyclopentanol	cyclopentene	44	1.4225
cyclohexanol	cyclohexene	83	1.4465
cycloheptanol	cycloheptene	115	1.4552
cyclooctanol	cyclooctene	138	1.4698
2-heptanol	2-heptene	98	1.4040
3-methyl cyclohexanol	3-methyl cyclohexene	103	1.4414
3-pentanol	2-pentene	36	1.3793
2-octanol	*trans*-2-octene	123	1.4130
t-amyl alcohol	3-methyl-2-butene	35	1.4050
2-methyl cyclohexanol	1-methyl cyclohexene	110	1.4503

WASTE DISPOSAL

Place all organic waste in the flammable waste container

DATA PRESENTATION:

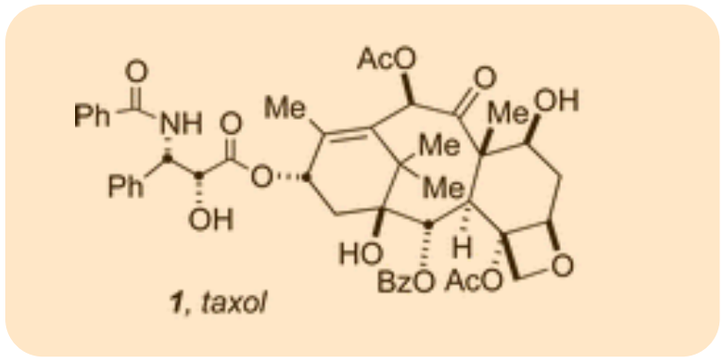
Include the following in your formal laboratory report discussion:

- Write your lab report in the form of a synthesis report.
- Calculate the theoretical yield and the percent yield of the alkene. Identify your alkene by comparing its boiling point and refractive index to the literature values given.
- What differences did you see in the IR spectra of the alcohol and the alkene?
- Provide a stepwise reaction mechanism for the acid catalyzed elimination of water from the alcohol that you were given as an unknown.

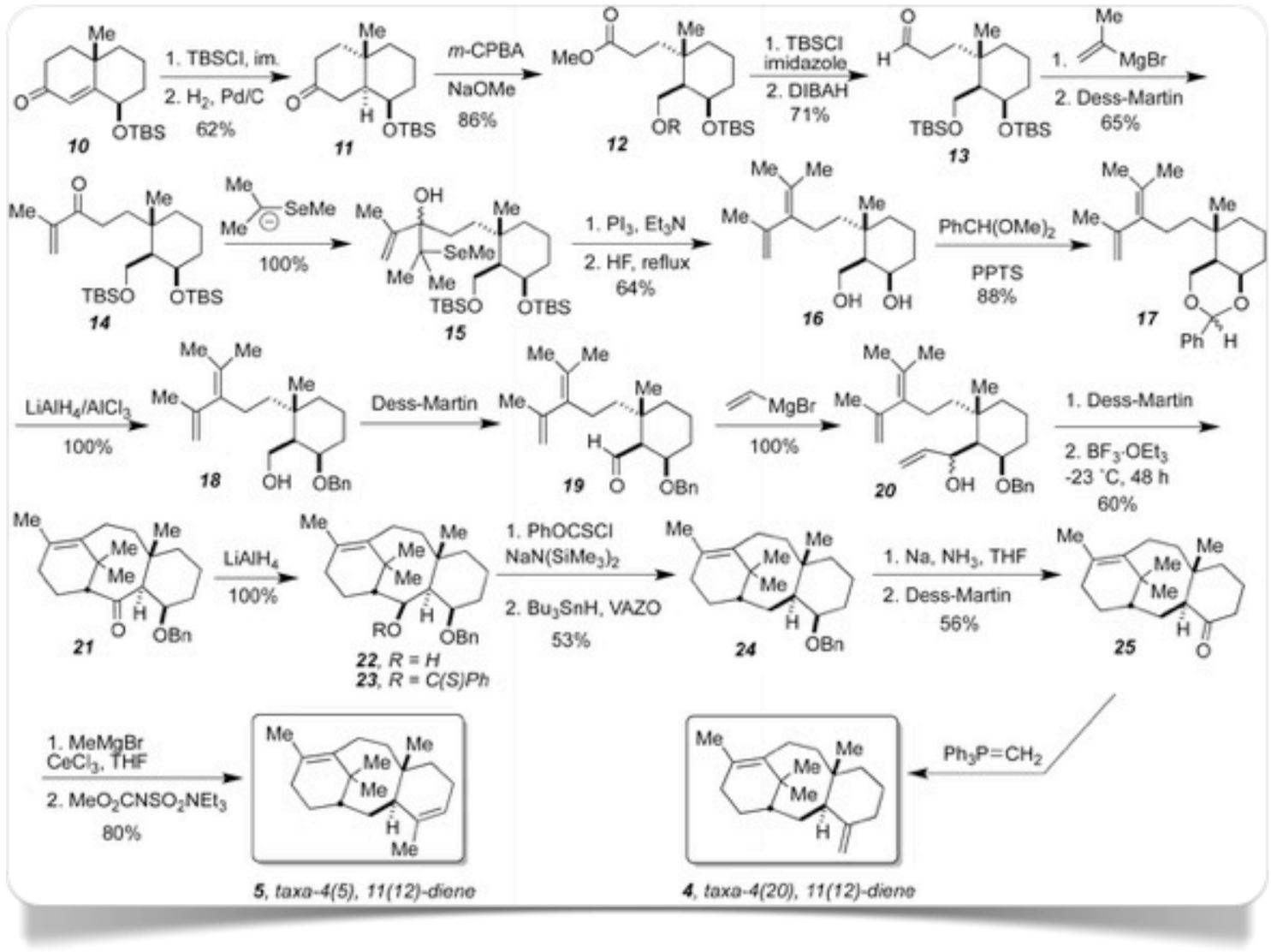
Additional Pre-Lab Questions:

- Outline a mechanism for the dehydration of 4-methylcyclohexanol catalyzed by phosphoric acid.
- What major alkene product is produced by the dehydration of the following alcohols?
  a. Cyclohexanol
  b. 1-Methylcyclohexanol
  c. 2-Methylcyclohexanol
  d. 2,2-Dimethylcyclohexanol

Two-Step Organic Synthesis



*Above: taxol, a potent mitotic inhibitor, particularly effective against certain strains of lung, ovarian, and breast cancer. Right: one of the multi-step syntheses of the core of taxol. Taken from: Guerra, J.; Croteau, R.; Williams, R. Nat. Prod. Rep., 2012, **29**, 683-696.*



In many cases, complex molecules cannot be synthesized in a single synthetic operation. Instead, organic chemists must use their knowledge of known synthetic transformations to assemble the molecule piecewise, one step at a time. As molecular targets have become increasingly more challenging, chemists must rely upon their ingenuity to try and develop the fastest (least steps) chemical route to the final product. In reality, the difference between an efficient, high-yielding synthesis and an inefficient, low-yielding synthesis of a particular molecule (especially a pharmaceutical) determines the marketability of the molecule.

This experiment will challenge your technique. You will carry out a two-step organic synthesis using 0.5 gram of starting compound for the first step and only 0.5 gram of the product from the first step as the starting material for the second step. The product from the second step will be recrystallized to purify it for melting point identification. **The recrystallization can be tricky so be prepared for it.**

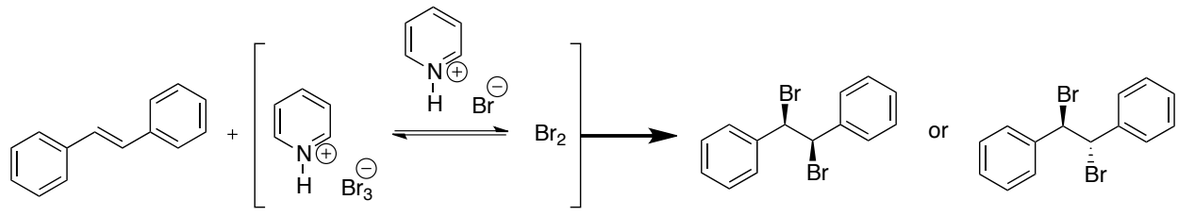
In the first step, addition of bromine to trans-stilbene (E-1,2-diphenylethene) will be conveniently done by using a bromine "carrier" called pyridinium hydrobromide perbromide (a stable solid complex which liberates Br_2 in the presence of an alkene). The products could be either stilbene dibromide or meso-stilbene dibromide, or a mixture of the two. **Consideration of the stereochemistry of the addition of bromine to an alkene will help you predict which product you will obtain.** Based on what we have learned in class, which bromination product would you expect to form?

In the second step, either a substitution or an elimination reaction could occur under the high temperature and strongly basic reaction conditions. If a substitution reaction occurs, the products could be the stilbene diols. If an elimination reaction occurs, loss of one equivalent of HBr would yield the Z-stilbene bromide while loss of two equivalents of HBr would result in the formation of the alkyne, diphenylacetylene. You will be able to determine the course of this reaction by measuring the melting point range of the purified (recrystallized) reaction product, a beautiful flaky white solid.

EXPERIMENTAL PROCEDURE:

A. Step 1: Bromination of the Alkene What is the stereochemical relationship between the two bromination products?

- Prepare a heating bath by bringing a beaker of water to a gentle boil. Select a beaker that will accommodate a 50 mL Erlenmeyer flask.



trans-stilbene (mp 125 °C) | stilbene dibromide (mp 114 °C) | *meso* dibromide (mp 238 °C)

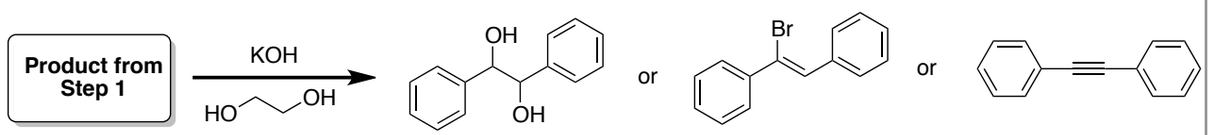
- In a 50 mL Erlenmeyer flask with a magnetic stirrer, add 0.5 g of trans-stilbene in 10 mL glacial acetic acid. Dissolve the reactants by heating the flask for a short time. **Use caution in manipulating the reaction flask in the hot water bath.**

- Once the trans-stilbene is dissolved, add 1 g of pyridinium hydrobromide perbromide to the reaction flask and continue heating and stirring the reaction flask for 5-10 minutes. The dibromide should separate immediately as white microcrystalline plates. Cool the reaction flask in cold, ~10 °C water, not ice water, because the acetic acid will crystallize below 5 °C. What happens if you cool step 1 in an ice bath instead of a cold water bath?

- Prepare a filter paper on a Buchner funnel by sucking water through the filter into a clean sidearm suction flask to secure the filter to the Buchner funnel (see Vacuum Filtration Technique) then pour the reaction mixture through the filter paper and rinse the crystals with a **minimum** amount of ice cold methanol (1-2 mL maximum!). If you use too much methanol, the crystals will dissolve and you will get a lower yield. What happens if you wash the first product with too much methanol? The crystals should be white. Leave the crystals on the Buchner funnel under vacuum for a few minutes to dry.

- Determine the mass of your product by gently scraping it from the filter paper onto a tared watchglass. Now weigh out 0.5 g of your dibromide crystals to prepare for the next reaction step. If you do not have 0.5 g of product, consult your instructor or TA. Save the remaining dibromide sample for melting point analysis after it is thoroughly dry, and then place it in a correctly labeled vial for grading.

B. Step 2: Reaction of the Stilbene Dibromide with KOH



stilbene diol (mp 120 ºC)
meso-diol (mp 137 ºC)

2-bromostilbene
(mp 179 ºC)

diphenylacetylene
(mp 61 ºC)

- In a 25 mL round bottom flask with a magnetic stirbar, place 0.5 g of the dibromide from Step 1, three or four KOH pellets, and 3 mL of ethylene glycol. Attach a condensor with a moderate flow of water and begin heating the mixture on your stirrer/hotplate. Allow the solution to reflux (see Reflux Technique) for 25-30 minutes. Look very closely at the condenser to see if the liquid is refluxing.

- After 30 min of refluxing, cool the reaction flask in an ice bath for 5 min, and then add 10 mL of cold water. Collect the granular solid reaction product by vacuum filtration into a clean sidearm flask. Recrystallize the solid reaction product from a minimum quantity of warm (50 °C) 95% ethanol (see Recrystallization Technique). Why do we recrystallize the product from step 2?

- If a pile of beautiful crystals do not form after cooling, warm the solution up again and add a few drops water to the warm ethanol solution to decrease the solubility, and then cool the solution again slowly to form crystals. Collect the crystals by vacuum filtration and allow them to dry for at least an hour in an open container. Weigh the crystals, determine their melting range when they are thoroughly dry, and place the sample in a correctly labeled vial for grading. Why do we dry the crystals before weighing them? **This compound needs to be saved, as it will be used in a multi-step synthesis next semester in Organic II!**

C. Analysis and Data Presentation

- Obtain melting ranges for the products of both reaction steps. Compare your measured melting ranges to the melting points listed above to determine the identity of your products.

WASTE DISPOSAL

Place all organic material in Flammable waste container

DATA PRESENTATION

Include the following in your formal laboratory report discussion:

- Write up both reactions procedures in the synthesis format beginning with tables of reactants and products.
- What reaction products did you make in each step of the reaction?
- Calculate the percent yields for both products. Show your calculations.
- Did the bromination reaction produce a single diastereomer of the dibromide in Step 1? If yes, why do you think so?

Additional Pre-Lab Questions:

- Provide a step-by-step reaction mechanism that illustrates the stereochemical course of the bromination reaction (you may use Br_2 instead of the pyridinium reagent).
- How will you identify which product is formed in the first step?
- How will you identify which product is formed in the second step?